EUROPEAN CHEMICALS AGENCY

Helsinki, 12 December 2017

Addressee: [redacted]

Decision number: CCH-D-2114382075-49-01/F
Substance name: ZINC BIS(DIBENZYLDITHIOCARBAMATE)
EC number: 238-778-0
CAS number: 14726-36-4
Registration number: [redacted]
Submission number: [redacted]
Submission date: 12/11/2010
Registered tonnage band: Over 1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Composition of the substance (Annex VI, Section 2.3.);**

2. **Description of the analytical methods (Annex VI, Section 2.3.7.);**

3. **Water solubility (Annex VII, Section 7.7.; test method: EU A.6./OECD TG 105) with the registered substance;**

4. **Partition coefficient n-octanol/water (Annex VII, Section 7.8.; using an appropriate test method) with the registered substance;**

5. **Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111) with the registered substance;**

6. ***In vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method: OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method: OECD TG 487) with the registered substance;**

7. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats with the registered substance;**

8. **Transgenic rodent somatic and germ cell gene mutation assays (Annex IX/X, Section 8.4., column 2; test method: EU B.58/OECD TG 488) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach, with the registered substance; germ cells and duodenum shall be harvested and stored for up to 5 years. Duodenum shall be analysed only if the results of the glandular stomach and of the liver are negative.**

   OR

In vivo **mammalian alkaline comet assay (Annex IX/X, Section 8.4., column 2; test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum with the registered substance;**

9. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance;**

10. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2., column 2; test method: EU B.31./OECD TG 414) in a second species ([rat/rabbit/rat or rabbit]), oral route with the registered substance;**

11. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56./OECD TG 443) in rats, oral route with the registered substance specified as follows:**

    - **Ten weeks premating exposure duration for the parental (P0) generation;**
    - **Dose level setting shall aim to induce some toxicity at the highest dose level;**
    - **Cohort 1A (Reproductive toxicity);**
    - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;**
    - **Cohorts 2A and 2B (Developmental neurotoxicity);**

12. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the registered substance;**

13. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**

14. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

15. **Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25./OECD TG 309) at a temperature of 12 °C with the registered substance;**

16. **Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24./OECD TG 308) at a temperature of 12 °C with the registered substance;**

17. **Identification of degradation products (Annex IX, 9.2.3.) using an**

appropriate test method with the registered substance;

18. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305) with the registered substance; aqueous route is the preferred route and shall be used whenever possible;**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **21 June 2021** except for the information requested under point 7 for a sub-chronic toxicity study (90-day) which shall be submitted in an updated registration dossier by **19 December 2018** from the date of the decision. You may only commence the extended one-generation reproductive toxicity study as requested under point 11 after **19 March 2019**, unless an indication to the contrary is communicated to you by ECHA before that date. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

[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

0. Grouping of substances and read-across approach

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests. Such other means include the use of information from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met".

In the registration, you have adapted the standard information requirements for

- Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.)
- *In vivo* genotoxicity (Annex IX, Section 8.4.)
- Sub-chronic toxicity (90-day) (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity, first species (Annex IX, Section 8.7.2)
- Extended one-generation toxicity (Annex X, Section 8.7.3)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

by applying a read-across adaptation following REACH Annex XI, Section 1.5.

Annex XI, Section 1.5. requires a structural similarity among the substances within a group or category such that relevant properties of a substance within the group can be predicted from the data on reference substance(s) within the group by interpolation. The following analysis presents your justification for the proposed grouping approach and read-across hypothesis, together with ECHA's analysis concerning the justification in both a generic and a endpoint-specific context.

0.1. Information provided on the grouping and read-across approach

You have provided read-across justifications as Appendices 1, 4, 5 and 6 in the CSR in the registration dossier. You have also provided data matrices of physico-chemical, environmental fate and (eco)toxicological properties of registered and source substances.

You propose to use grouping and read-across approach to adapt the following standard information requirements for the registered substance zinc dibenzyldithiocarbamate (ZBEC, CAS no 14726-36-4, EC no 238-778-0, the target substance) by using the following source substances:

- zinc bis(dibutyldithiocarbamate) (ZDBC, CAS no 136-23-2, EC no 205-232-8) for a sub-chronic (90-day) study,
- zinc bis(dimethyldithiocarbamate) (ZDMC, CAS no 137-30-4, EC no 205-288-3) for *in vivo* genotoxicity, two-generation reproductive toxicity and hydrolysis as a function of pH studies, and
- zinc bis(diethyldithiocarbamate) (ZDEC, CAS no 14324-55-1, EC no 238-270-9) for a pre-natal developmental toxicity study, for growth inhibition study aquatic plants and long-term toxicity testing on aquatic invertebrates.

You have provided the following hypothesis for repeated dose toxicity:

"*This report addresses the analogue approach for the read-across of acute and repeated dose toxicity of zinc bis(dibenzyldithiocarbamate) (ZBEC) with its structural analogue zinc bis(dibutyldithiocarbamate) (ZDBC). Both substances are zinc salts of two dialkylcarbamodithioic acids, differing only in the substituents at nitrogen atom of dithiocarbamate moieties (benzyl vs. butyl). They are metabolized by a hydrolysis of a parent compound into the respective acid, which undergoes either a transformation to CS_2 further oxidized into CO_2, or a conjugation with glucuronic acid or GSH (see for example the review report 6508/VI/99-Final of European Commission, Health & Consumer Protection Directorate – General on a structurally related substance zinc bis(dimethyldithiocarbamate)). Human toxicological properties of both substances are therefore expected to be governed by human toxicological properties of the respective cation and the organic moiety. As the substances have identical cations and structurally similar organic moities with the same functionality, it is considered acceptable to derive the lacking data on human toxicological properties of ZBEC by read-across from ZDBC*",

the following hypothesis for pre-natal developmental toxicity:

"*This report addresses the analogue approach for the read-across of developmental toxicity of zinc bis(dibenzyldithiocarbamate) (ZBEC) with its structural analogue zinc bis(diethyldithiocarbamate) (ZDEC). Both substances are zinc salts of two dialkylcarbamodithioic acids, differing only in the substituents at nitrogen atom of dithiocarbamate moieties (benzyl vs. ethyl). They are metabolized by a hydrolysis of a parent compound into the respective acid, which undergoes either a transformation to CS2 further oxidized into CO2, or a conjugation with glucuronic acid or GSH (see for example the review report 6508/VI/99-Final of European Commission, Health & Consumer Protection Directorate – General on a structurally a structurally related substance zinc bis(dimethyldithiocarbamate)). Human toxicological properties of both substances are expected to be governed by human toxicological properties of the respective cation and the organic moiety. As the substances have identical cations and structurally similar organic moities with the same functionality, it is considered acceptable to derive the lacking data on human toxicological properties of ZBEC by read-across from ZDEC*",

and the following hypothesis for *in vivo* genetic and reproductive toxicity:

"*This report addresses the analogue approach for the read-across of in vivo genetic and reproductive toxicity of zinc bis(dibenzyldithiocarbamate) (ZBEC) with its structural analogue zinc bis(dimethyldithiocarbamate) (ZDMC). Both substances are zinc salts of two dialkylcarbamodithioic acids, differing only in the substituents at nitrogen atom of dithiocarbamate moieties (benzyl vs. methyl). They are metabolized by a hydrolysis of a parent compound into the respective acid, which undergoes either a transformation to CS2 further oxidized into CO2, or a conjugation with glucuronic acid or GSH (see for example the review report 6508/VI/99-Final of European Commission, Health & Consumer Protection Directorate – General on zinc bis(dimethyldithiocarbamate)). Human toxicological properties of both substances are expected to be governed by human toxicological properties of the respective cation and the organic moiety.*

As the substances have identical cations and structurally similar organic moities with the same functionality, it is considered acceptable to derive the lacking data on human toxicological properties of ZBEC by read-across from ZDMC".

You have provided the following hypothesis for the endpoints of hydrolysis as a function of pH, growth inhibition study aquatic plants and long-term toxicity testing on aquatic invertebrates:

"This report addresses the analogue approach for the read-across of environmental endpoints of zinc bis(dibenzyldithiocarbamate) (ZBEC) with its structural analogues zinc bis(dibutyldithiocarbamate) (ZDBC), zinc bis(diethyldithiocarbamate) (ZDEC) and zinc bis(dimethyldithiocarbamate) (ZDMC). All four substances are zinc salts of dialkylcarbamodithioic acids, differing only in the substituents at the nitrogen atom of dithiocarbamate moieties (benzyl or different alkyl chain lengths). Comparison of available aquatic toxicity data among the four substances seems to indicate a decrease in toxicity with increasing size of the organic moieties present." (section 1 of Annex A1 in the CSR).

0.2. ECHA analysis of the grouping and read-across approach in light of the requirements of Annex XI, 1.5.

ECHA understands that your read-across hypothesis is based on:

- structural similarity of the substances: *"substances are zinc salts of dialkylcarbamodithioic acids, differing in the substituents at nitrogen atom of dithiocarbamate moieties (benzyl vs. butyl, ethyl or methyl).",* and

- similar physico-chemical properties: *"Physico-chemical properties of the four substances follow a logical similar trend. The substances are all solids with negligible vapour pressure and are poorly soluble in water."*

In addition, for human health endpoints:

- similar toxicokinetics: *"They are metabolized by a hydrolysis of a parent compound into the respective acid, which undergoes either a transformation to CS_2 further oxidized into CO_2, or a conjugation with glucuronic acid or GSH.*

- similar toxicological properties because the dialkylamine in the nitrogen atom is considered to have low/no impact on toxicity and thus the toxicity is driven by the amine function: *"No significant difference in toxicological behavior is expected to be seen between dibenzyl- and dibutylamine/ diethylamine/ dimethylamine formed in the process of hydrolysis of dithiocarbamates, as their properties are primarily governed by the amine function and the substituents at the nitrogen atom are expected to have only a minor influence."*

Specifically for the endpoint Hydrolysis as a function of pH:

- similar hydrolysis properties: "*Dithiocarbamates all posse the same hydrolysable functional group*" and "*Hydrolysis data is available for ZDMC only; for the structural analogues with Na+ as the cation the hydrolysis half-life seems to increase with decreasing size of the organic moieties present. Therefore, the hydrolysis half-life of ZDMC is taken into account as a worst-case assumption*"

Specifically for aquatic toxicity endpoints:

- regular pattern of aquatic toxicity with toxicity decreasing with increasing molecular weight (prediction is worst-case): "*Comparing all available experimental results on aquatic toxicity of ZBEC, ZDBC, ZDEC and ZDMC (see Table 1), it is likely that the toxicity of ZBEC is lower than the toxicity of ZDBC, ZDEC and ZDMC. A trend is observed that with increasing molecular weight, and larger substituents at the nitrogen atom of dithiocarbamate moieties (benzyl or different alkyl chain lengths,) the toxicity decreases.*" You further indicate that "*The data from ZDBC will be used in the assessment as it is expected that the toxicity of ZDBC is closer to ZDBC than ZDEC and ZDMC. When no data is available for ZDBC, ZDEC will be used as the source chemical. A safety factor is not applied as the use of ZDBC and ZDEC as a source chemical for ZBEC is already a worst-case assumption.*"

  ECHA understands that for the aquatic toxicity endpoints of Growth inhibition study aquatic plants and Long-term toxicity testing on aquatic invertebrates you propose a one-to-one read-across prediction from ZDEC to the registered substance (ZBEC), supported by a category of four substances: ZDMC, ZDEC, ZDBC and ZBEC (listed here in order of increasing molecular weight).

Structural similarity

In order to meet the provisions in Annex XI 1.5 to predict physicochemical and toxicological properties from data for a reference substance within the group by interpolation to other substances in the group, ECHA considers that structural similarity alone is not sufficient. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible.

You state that the target and source substances are zinc salts of two dialkylcarbamodithioic acids, differing only in the substituents at nitrogen atom of dithiocarbamate moieties (benzyl in the target substance vs. butyl/ethyl/methyl in the source substances). You further claim that these structural differences (dithiocarbamate moieties) are not expected to impact the toxicokinetic and toxicodynamic behavior of the substances since the properties of the target and source substances are governed by the (eco)toxicological profiles of the Zn^{2+} cation and the respective dithiocarbamate anions. Furthermore you claim that the toxicity of the organic anion is "*primarily governed by the amine function*" and that "*the substituents at the nitrogen atom are expected to have only minor influence*".

ECHA observes that while both the target and source substances share similar core structures, the target substance has four benzyl side chains while the source substances have linear methyl/ethyl/butyl side chains. ECHA notes that you have not provided adequate information to support the argument how these structural differences affect the

predicted environmental and human health hazard properties. More specifically, you have not explained how these structural differences such as different chain lengths and linear vs. benzyl moiety attached to nitrogen atom relate to their toxicokinetic, especially metabolism, hydrolysis (including half-lives and identity of hydrolysis products) and (eco)toxicological properties. Consequently, there is not a robust basis for predicting the properties of the registered substance from the data of the source substances.

Toxicokinetics

Annex XI 1.5 provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances.* One prerequisite for a prediction based on read-across therefore is that the substance involved are structural similar and are likely to have similar properties. One important aspect in this regard is the comparison of absorption, distribution, metabolism and elimination of source and target substances to allow assessing the qualitative and quantitative internal systemic exposure of the test organism when exposed to source and target, respectively.

Based on the toxicokinetic data provided the source substance ZDMC is hydrolysed to CS_2, COS and CO_2 (exhaled air), and the following metabolites (found in urine): 2-dimethylamine-thiazolidine carboxylic acid, the S-glucuronide of dimethyldithiocarbamic acid and an unknown metabolite of apparent mass 326.

You claim that "*based on structural similarity, dimethyl- and dibenzyldithiocarbamate anions shall be metabolized via similar pathways, as it is not expected that the difference in the substituents at the amine function of dithiocarbamate moieties shall have a profound difference on the substances reactivity".*

ECHA notes that the hydrolysis of ZDMC contains several steps and due to differences in the dithiocarbamate moieties in the target and other source substances, the intermediate and final hydrolysis products will be different. Since the hydrolysis rate of the target and the source substances may be different the parent substances and the intermediate hydrolysis products may have a different impact on the toxicity profile of these substances.

ECHA notes that the claim that the substituents in the nitrogen atom have only a minor influence is not supported by data. In addition, no data has been provided to demonstrate that similar hydrolysis with similar rate resulting in similar hydrolysis products occurs also with the registered substance and the other source substances (ZDBC and ZDEC). More specifically you have not provided experimental evidence to support similarity between the registered substance, ZDBC, ZDEC and ZDMC regarding (i) the hydrolysis/metabolism pathway, (ii) identification of similar breakdown products CS_2, COS and CO_2 and dissimilar breakdown products (benzyl-, butyl- and ethyl-dialkylamines), and (iii) the rate of the hydrolysis/metabolism, and how these (dis)similarities may influence the toxicological profile of the substances

ECHA therefore concludes that you have not addressed the structural differences between the target and source substances and did not explain why those differences would not lead to differences regarding hydrolysis/metabolism and the toxicological properties of the substances. The explanation provided is not considered valid to establish the link between structural similarity and the prediction. ECHA therefore considers that there is no adequate basis for predicting the properties of the registered substance from the source substances.

Support of a similar or regular pattern as a result of structural similarity

Annex XI, 1.5 provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances. One prerequisite for a prediction based on read-across therefore is that the substances involved are structurally similar and are likely to have similar properties or follow a regular pattern. One important aspect in this regard is the data matrix comparing properties of source and target substances.

ECHA notes that for each human health endpoint a different source substance has been used to predict the properties of the registered substance. ECHA observes that data for some endpoints is available also from the other source substances. Therefore, in addition to analysing the read-across approach for each endpoint and proposed source substance, ECHA has analysed the available additional data of the other source substances.

- Genotoxicity

In the technical dossier you have provided a Mammalian Spermatogonial Chromosome Aberration test (OECD TG 483, GLP) and Mammalian Bone Marrow Chromosome Aberration Test (OECD TG 475, GLP) conducted with the source substance ZDMC. In the read-across justification document you state that ZDMC has been assessed by the European Commission, Health and Consumer Protection – Directorate General and concluded that "*there is no sufficient evidence to consider ZDMC genotoxic in vivo*", and "*considering that genotoxicity basically reflects the ability of the substance to interact with DNA, from the lack of in vivo genotoxic potential for ZDMC it is concluded that its structural analogue ZBEC is also not genotoxic in vivo*", and "*dibenzylamine can be essentially regarded as a derivative of toluene (methylbenzene), the human toxicological properties of which have been extensively assessed in the European Union Risk Assessment Report (2003, rapporteur [redacted]). Based on the available evidence, it was concluded that toluene is not genotoxic. Respectively, it is concluded that the difference in the substituents at the nitrogen atom of the dithiocarbamate moieties between two substances will not lead to substantial differences in terms of their genotoxicity*".

You further explain that ZDMC is more potent than the registered substance regarding systemic toxicity and state that "*This phenomenon can be partially related to a lower molecular weight and smaller molecule size of ZDMC, enhancing its absorption and metabolism rate by the body. Taking this into account and considering that genotoxicity basically reflects the ability of the substance to interact with DNA, from the lack of in vivo genotoxic potential for ZDMC it is concluded that its structural analogue ZBEC is also not genotoxic in vivo*".
ECHA notes that your claim regarding non-genotoxic potential of the registered substance is not supported by any data or mechanistic explanation. ECHA notes that as explained above in sections Structural similarity and Toxicokinetics, you have not provided information regarding the impact of structural differences between the registered substance and ZDMC to the toxicokinetics (especially metabolism) and systemic toxicity of the target and source substances. Furthermore, you have not provided any information - except for the generic statement that "*dibenzylamine can be essentially regarded as a derivative of toluene (methylbenzene)*" - to explain how the genotoxic potential of the registered substance can be predicted from toluene. As stated above, ECHA considers that structural similarity alone

is not sufficient. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. Finally, ECHA notes that based on the available data ZDMC appears to be more potent than the other source substances. However, you have not explained how enhanced absorption and metabolism rate and more potent systemic toxicity is related to genotoxicity. ECHA notes that similar/more potent repeated dose toxicity cannot be used to justify similar genotoxicity potential; read-across is always endpoint-specific and requires endpoint-specific justification.

ECHA further notes that the following results were obtained in the *in vitro* genotoxicity tests; Ames test: negative with the registered substance and ZDBC, positive/negative with ZDEC and positive with ZDMC; Gene mutation in mammalian cells (OECD 476): positive with the registered substance and negative with source substances, *In vitro* cytogenicity study (OECD 473): ambiguous with ZDBC, positive with ZDEC and negative with ZDMC. ECHA considers that these results suggest different *in vitro* genotoxicity profiles of the substances. *In vivo* studies such as OECD 475, OECD 474 and OECD 483 with the source substances were negative. However, no *in vivo* studies are available for the registered substance.

ECHA concludes that the presented evidence does not support a similar genotoxicity profile of the target and source substances and thus there is no adequate basis for predicting properties of the registered substance from the source substance(s).

- Repeated dose toxicity

You have provided an oral 17-week non-GLP, non-guideline study in rats conducted with the source substance ZDBC. ECHA notes that the study cannot be accepted as reliable source of information on repeated dose toxicity (see section 7 of this appendix). No repeated dose toxicity studies are available for the target substance.

ECHA observes that in the read-across justification document you have provided a LOAEL value of 2.5 mg/kg bw/d based on severe toxic effects obtained from the repeated dose toxicity study for the source substance ZDMC. ECHA observes that ZDMC has a STOT RE2 classification whereas the target substance and source substances ZDBC and ZDEC are not classified for repeated dose toxicity. ECHA notes that based on this data the source substances ZDBC, ZDEC and ZDMC have a different toxicological profile and/or different potency.

ECHA notes that in the read-across justification you state that "*The overall human toxicological profile of ZDMC suggests that this substance is more potent than ZBEC in terms of systemic toxicity. The latter is evident from the lower LD50 values in acute toxicity studies and significantly lower NOAELs for systemic toxicity in available repeated dose toxicity studies. This phenomenon can be partially related to a lower molecular weight and smaller molecule size of ZDMC, enhancing its metabolism rate by the body*".
ECHA observes that instead of the more potent source substance ZDMC, you have chosen a less toxic source substance (ZDBC) to predict the properties of the target substance.

Further, no screening/repeated dose toxicity data is available for the registered substance and thus no comparison on the repeated dose toxicity profile of the registered substance with the source substances can be made. ECHA considers that the presented evidence does

not support a similar or regular pattern of toxicity after repeated administration of source substances ZDBC and ZDMC as a result of structural similarity and thus there is no adequate basis for predicting properties of the registered substance from the source substance(s).

- Pre-natal developmental toxicity

You have provided an oral non-guideline non-GLP prenatal toxicity study in rats conducted with the source substance ZDEC. No screening/developmental toxicity studies have been provided for the target substance.

ECHA notes that two pre-natal developmental toxicity studies are available also for the source substance ZDMC. The maternal NOAELs are 125 mg/kg bw/day ("*based on severe signs of maternal toxicity, including mortality*") for ZDEC, and 3-4 mg/kg bw/day (based on increased water and/or decreased food consumption and/or reduction in body weight gain) for ZDMC. The corresponding NOAELs for developmental toxicity are 250 mg/kg bw/day ("*no adverse effects at the highest dose tested*") and 3-4 mg/kg bw/day (based on e.g. reduced litter and mean foetal weight, increased post-implantation loss and crown/rump length) for ZDEC and ZDMC, respectively.

ECHA notes that the maternal and developmental NOAEL values differ significantly between the source substances ZDEC and ZDMC. Further, no screening/repeated dose toxicity data is available for the registered substance and thus no comparison on pre-natal toxicity profile of the substances can be made. ECHA considers that the presented evidence does not support a similar or regular pattern of developmental toxicity after administration of source substances ZDEC and ZDMC as a result of structural similarity. Thus there is no adequate basis for predicting properties of the registered substance from the source substance(s).

- Extended one-generation reproduction toxicity

You have provided an oral two-generation reproduction toxicity study (equivalent or similar to OECD 416, GLP) in rats conducted with the source substance ZDMC. No screening/reproduction/developmental toxicity studies or other relevant reproductive toxicity information have been provided for the registered substance and source substances ZDBC and ZDEC and thus no comparison on the reproductive toxicity profile of the substances can be made. Accordingly, there is no adequate basis for predicting properties of the registered substance from the source substance(s).

- Hydrolysis as a function of pH

You have provided a hydrolysis as a function of pH study (EPA Guideline Subdivision N 161-1 (Hydrolysis), non GLP) conducted with the source substance ZDMC. No hydrolysis studies have been provided for the registered substance and source substances ZDBC and ZDEC.

ECHA considers that the presented evidence in the data matrix does not support the analogue approach for hydrolysis and the information provided is conflicting. On the one hand, you report that hydrolysis data are only available for the source substance ZDMC and that this source substance has the same hydrolysable functional group as the registered substance. On the other hand, you indicate that "*for the structural analogues with Na+ as the cation the hydrolysis half-life seems to increase with decreasing size of the organic moieties present.*"

ECHA notes that based on information given in the data matrix hydrolysis rates are available for only two Na+ carbamates with linear substituents (SDEC and SDMC).

ECHA considers that based on the data provided, consisting of only two data points, it cannot be concluded that the hydrolysis rate increases with increasing size of the organic moieties. Furthermore, you have not discussed how and why the hydrolysis results on Na+ carbamates with linear substituents could be used to conclude on the hydrolysis potential of the source and target substances, which are Zn+ dithiocarbamates with different chemical structures and lower water solubilities than the Na+ carbamates. Hence, ECHA concludes that you have not provided any data to support your claim that the source substance provides the worst case estimation of the hydrolysis potential of the registered substance.

In conclusion, ECHA considers that the presented evidence in the data matrix does not support a similar or regular pattern of hydrolysis as a result of structural similarity.

- Growth inhibition study aquatic plants and Long-term toxicity testing on aquatic invertebrates

In the technical dossier you have provided Endpoint Study Records (ESRs) for an Alga, Growth Inhibition Test study (OECD TG 201, non GLP) and a Long-term toxicity testing on aquatic invertebrates study (no guideline followed, non GLP), conducted with the source substance ZDEC. As indicated earlier, ECHA understands that for these two aquatic toxicity endpoints you propose a one-to-one read-across prediction from ZDEC to the registered substance (ZBEC). You consider that the one-to-one read-across is supported by a category of four substances, ZDMC, ZDEC, ZDBC and ZBEC, with a trend of decreasing toxicity with increasing molecular weight.
Concerning the read-across proposed ECHA notes the following. First, a mechanistic explanation, including a (presumed) mode of toxic action, should be provided to support the prediction of a regular pattern in aquatic toxicity. However, your hypothesis does not contain a mechanistic explanation to explain the proposed trend in toxicity of these four substances.

Second, ECHA notes that in the data matrix only limited physicochemical and environmental fate data is provided and you have not discussed how these properties influence the prediction of aquatic toxicity. Therefore, ECHA considers that the proposed trend is not supported by physicochemical and environmental fate data.

Furthermore, for a trend to be confirmed, valid aquatic data on more than two substances need to be available. In this case as both the target and source substances have indicated low water solubility, chronic aquatic data should be used for establishing a trend. For the two endpoints in question in the data matrix data is available for only two substances (ZDEC and ZDMC). However, the algae study on ZDEC cannot be considered valid, as fully discussed under section 12 below, and as no ESR has been submitted for the study on ZDMC it is not possible for ECHA to assess its validity. As a consequence these data can neither be used to conclude on the ecotoxicity of these two substances nor to support the proposed trend. For the endpoint of long-term toxicity to fish, data are reported in the data matrix for all four substances. However, this data can also not be used to conclude on the ecotoxicity of these substances because they are either not valid (data on registered substance ZBEC addressed under request 14 below) or it is not possible to assess their validity since no ESRs are included in the technical dossier. Therefore, due to the

deficiencies given above there is currently no data to allow comparison of the ecotoxicities of the target and the source substances and to support the proposed trend in aquatic toxicity.

ECHA considers that the presented evidence in the data matrix does not support a similar or regular pattern of aquatic toxicity as a result of structural similarity.

ECHA concludes that for the reasons explained above the available data provided in the technical dossier and read-across justification document does not support a similar or regular pattern of toxicity regarding the endpoints in consideration. Therefore ECHA considers that there is no adequate basis for predicting properties of the registered substance from the source substances.

ECHA notes that in your comments on the draft decision you agree to carry out the environment related studies requested in the decision on the registered substance. Your comments relating to the specific endpoints are addressed in the endpoint specific sections below.

In your comments to the draft decision you suggest a phased approach and the timing to be accepted by ECHA for the submission of the requested information. You outline a possible testing strategy for the category of zinc dithiocarbamates which includes combination of *in vivo* with *in vitro* studies to further improve the read-across justification for human toxicity.

With regard to your comments concerning the improvement of the read-across justification, ECHA refers you to the above assessment of the information submitted for read-across. In the absence of adequate and reliable documentation for predicting properties of the registered substance from the source substances, and therefore the rejection of the adaptations, ECHA requests by the decision the standard information as established in the annexes to the REACH Regulation. This decision however still allows you adaptations, provided that they are in accordance with the rules set by the REACH Regulation.
ECHA notes that the present decision includes a paragraph explaining adaptation possibilities that is also (partly) applicable to the approach you propose in your comments: "You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation."
ECHA, however, emphasises that any testing strategy or adaptation is your responsibility and that ECHA will examine any information submitted in consequence of a decision in line with Article 42 of the REACH Regulation only after the deadlines set by this decision.

ECHA points out that it is not its task to develop, justify or improve adaptations. It is your task to explain the premise for a read-across adaptation by creating an implicit or explicit hypothesis, and then show that the evidence supports that premise within the legal requirements of the REACH Regulation.

The deadline in the decision allows sequential testing and therefore enables you to follow the phased approach as you propose in your comments. The time limits set by ECHA are standard for all registrants in order to ensure equal treatment. Therefore, any case specific

extension of a standard time limit is not possible since this would imply preferential treatment by ECHA.

0.3. Conclusion of the read-across approach

In the light of the deficiencies as described above ECHA considers that the read-across approach does not comply with the general rules of adaptation as set out in Annex XI, 1.5. of the REACH Regulation. Therefore, this adaptation is not acceptable and there is a data gap for the endpoints covered by this read-across approach.

1. Composition of the substance (Annex VI, Section 2.3.)

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

According to chapter 4.2 of the "Guidance for identification and naming of substances under REACH and CLP" (version 2.1, May 2017) hereafter referred to as the "SID Guidance", the following applies for well-defined substances:

- Each main constituent (i.e. the constituent present at ≥80% for mono-constituent substance or each constituent present at ≥10% and 80% for multi-constituent substance) shall be identified and reported individually; and
- Each impurity present at ≥1% or relevant for the classification and/or PBT assessment of the registered substance shall be identified and reported individually.
- For each constituent, the typical, minimum and maximum concentration levels shall be specified regardless of the substance type.

The composition given in IUCLID section 1.2 of the registration dossier does not specify the concentration range of the reported main constituent [redacted] nor any impurity.

You need to include the appropriate concentration range for the main constituent and impurity (if present ≥1% or relevant for the classification and/or PBT assessment) in the reported composition of your substance.

The information shall be included in section 1.2 of the registration dossier.

If necessary, section 1.2 of the registration dossier should also be amended to address the information requested in the context of incompliances discussed under section 2 below.

In your comments on the draft decision you agree to fulfil this request.

2. Description of the analytical methods (Annex VI, Section 2.3.7.)

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

According to Annex VI, section 2.3.7 of the REACH Regulation, the registration needs to contain a "Description of the analytical methods or the appropriate bibliographical references for the identification of the substance and, where appropriate, for the identification of impurities and additives. This information shall be sufficient to allow the methods to be reproduced". This includes a description of the analytical methods, and the corresponding results, used in the identification and quantification of the main constituents and impurities required to be reported in the composition of the substance.

You provided only spectral data (including IR, UV, H-NMR spectra) in IUCLID section 1.4, whereas you did not provide any quantification of the composition of the substance including the results of the quantification of the counter-ion Zinc.

The spectral data alone is not sufficient to verify the composition of the registered substance.

You are requested to provide a detailed description of the analytical method(s) used for the quantification of the registered substance including the main constituent and any impurities required to be reported in the composition of the registered substance. The description shall be sufficient for the methods to be reproduced and shall therefore include details of the experimental protocol followed, any calculation made and the results obtained.

If the quantification is based on chromatography, the information shall include a legible print-out of the chromatogram as well as the report from the chromatographic analysis including the table of peak assignments that report the peak areas and corresponding amounts of each relevant constituent/impurity.

In addition, you shall ensure that the composition reported in IUCLID section 1.2 is in line with the information provided in section 1.4, which shall be sufficient to identify and quantify the substance.

The information shall be included in section 1.4 of the registration dossier.

In your comments on the draft decision you agree to fulfil this request.

3. Water solubility (Annex VII, Section 7.7.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation.

"Water solubility" is a standard information requirement as laid down in Annex VII, Section 7.7 of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a water solubility study (EU A.6./OECD TG 105) with the analogue substance zinc bis(diethyldithiocarbamate) (EC No 238-270-9, CAS No 14324-55-1) as a key study. Furthermore, you have provided further argumentation on why the study is scientifically unjustified "*In accordance with Section 1 of REACH Annex XI, the conductance of the study on water solubility of zinc*

bis(dibenzyldithiocarbamate) is scientifically unjustified. (...) As zinc bis(dibenzyldithiocarbamate) has a significantly higher molecular weight and a bulkier organic substituents in dithiocarbamate moieties (benzyl vs. ethyl), it is very likely that its water solubility shall be even lower and will be below the limit of 1 mg/L."
However, your adaptation of the information requirement cannot be accepted, as explained below.

ECHA *Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance* (version 6.0, July 2017) indicates that "*For the determination of the water solubility read-across is usually not possible. However, interpolation may still be possible within homologous series.*"

Therefore, as read-across should not be used for water solubility ECHA considers the approach taken by you to be unacceptable. Furthermore, you have not provided a homologous series which may have allowed prediction of this physico-chemical property. You have provided a single data point for the proposed source substance zinc bis(diethyldithiocarbamate) (EC No 238-270-9) and assumptions based on the target and source substances structure. However, the assumptions lack experimental evidence.

Additionally, ECHA considers that it would be technically feasible to perform the test. The methods proposed for water solubility determination in the EU A.6./OECD TG 105 guidelines allow the determination of water solubility at values below the 1mg/l limit.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

In your comments on the draft decision (DD) you agree to fulfil this request. You further indicate that you have acquired access to a water solubility study conducted according to OECD 105, with a result of 2.3 µg/L.

ECHA notes however that you have not provided the robust study summary (RSS) of the new water solubility study in the comments on the DD. It is therefore not possible for ECHA to assess the validity of the study and, hence, to consider it for the final decision. You are moreover reminded of the fact that ECHA does not take into account dossier updates submitted after the notification of the draft decision under Article 50(1) of the REACH Regulation for the purpose of this decision. ECHA will examine the information submitted in later updates of the registration dossier at the stage of the follow-up to the dossier evaluation in accordance with Article 42 of the REACH Regulation.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Water solubility (test method: EU A.6./OECD TG 105).

4. Partition coefficient n-octanol/water (Annex VII, Section 7.8.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation.

"Partition coefficient n-octanol/water" is a standard information requirement as laid down in Annex VII, Section 7.8 of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Section 2 of REACH Annex XI, with the following justification *"the study cannot be conducted, as the substance is virtually insoluble in water".*
ECHA considers that you did not provide enough information that demonstrates that it "is technically not possible to conduct the study as a consequence of the properties of the substance", as stated in Section 2 of REACH Annex XI. You did not provide any data or justification to prove that you could not use any of the methods given in ECHA *Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance* (version 6.0, July 2017) to measure "Partition coefficient n-octanol/water". Specifically, you have not demonstrated that it would be impossible to determine the substance concentration in either n-octanol or water.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA notes that in appendix A of the CSR document you have provided a calculated value for Log Kow of 5.41. You have however not provided any information on how that value was calculated. Therefore, it is not possible for ECHA to evaluate if the calculation provided would be sufficient to cover the information requirement.

In your comments on the draft decision (DD), you agree that new information on the n-octanol/water partition coefficient is needed for the registered substance. However, you intend to adapt the current standard information requirement according to Annex XI, Section 1.5. of the REACH Regulation and provide a read-across justification document in Appendix 1 of the comments on the DD. You propose to use results from a Partition Coefficient (1-Octanol/Water): Slow-Stirring Method study (OECD TG 123) carried out in 2013 with the analogue substance copper bis(dibutyldithiocarbamate) (CDBC) (CAS No 13729-71-4) to fulfill the current standard information requirement. ECHA notes that your proposed adaptation of the information requirement cannot be accepted, as explained below.

First, ECHA notes that the substance identifier (CAS 13729-71-4) provided by you for the source substance CDBC is not correct. ECHA understands that as a source substance you refer to the substance bis(dibutyldithiocarbamato-S,S')copper (CAS 13927-71-4, EC 237-695-7). ECHA notes that no Robust Study Summary (RSS) has been provided for the Log Kow study on the proposed source substance you intend to read-across to. Hence, it is not possible for ECHA to assess the quality of the data provided.

Second, ECHA notes that, according to ECHA's *Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance* (version 6.0, July 2017), "*For the determination of the partition coefficient n-octanol/water read-across is usually not possible. However, interpolation may still be possible within homologous series.*" Therefore, as read-across should not be used for partition coefficient n-octanol/water, ECHA considers the approach taken by you to be unacceptable. Consequently the justification for the read-across is considered not acceptable.

Furthermore, you have not provided a homologous series which may have allowed prediction of this physico-chemical property. Instead, you have provided a single data point for the proposed source substance CDBC (CAS No 13729-71-4) and have made assumptions based on the structures of the target and the source substances. However, these assumptions lack experimental evidence. Finally, ECHA notes that basic physicochemical data such as reliable information on Log K_{OW} is needed to properly conduct and assess environmental fate and effect studies. Furthermore, information on Log Kow is also pivotal to be able to evaluate any future proposed read-across adaptations.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Partition coefficient n-octanol/water. Guidance for determining appropriate test methods for the partition coefficient n octanol/water is available in the ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.1.8.3 (version 6.0, July 2017).

5. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation.

"Hydrolysis as a function of pH" is a standard information requirement as laid down in Annex VIII, Section 9.2.2.1 of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a hydrolysis as a function of pH study (EPA Guideline Subdivision N 161-1 (Hydrolysis)) with the analogue substance zinc bis(dimethyldithiocarbamate) (ZDMC; EC No 205-288-3, CAS No 137-30-4) as a key study. However, your adaptation of the information requirement cannot be accepted, as explained below.

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement cannot be accepted.

Furthermore, the read-across study submitted does not provide the information required by Annex VIII, Section 9.2.2.1., because it is not valid for the reasons set out below.

ECHA notes that the read-across study submitted is a non GLP study conducted according to EPA Guideline Subdivision N 161-1 (Hydrolysis) and not to the OECD TG 111, which is the

standard guideline recommended by ECHA Guidance. According to the OECD TG 111 hydrolysis needs to be measured at 4 different pH values: at pH 1.2 (if physiologically important), and at pH 4.0, 7.0 and 9.0. In the study submitted only results for pH 5, 7 and 9 are submitted. Therefore, the study submitted study does not fulfil the conditions of Annex XI, 1.1.2 for being considered equivalent to the test methods referred to in Article 13(3) of the REACH Regulation.
ECHA concludes that the key study is not valid. It thus cannot be used to fulfil the standard information requirement for the present endpoint nor does it meet the requirements of Annex XI, Section 1.5 of REACH (be adequate for the purpose of classification and labelling and/or risk assessment).

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In your comments on the draft decision (DD), you consider that based on the results of a new water solubility study conducted on the registered substance, the substance is not readily soluble (water solubility of 2.3 µg/L). Hence, ECHA understands that you intend to adapt the current standard information requirement according to Annex VIII, Section 9.2.2.1., column 2. However, ECHA notes also as you have not provided the RSS of the new water solubility study in the comments on the DD it is not possible for ECHA to assess the validity of the study. Consequently it is not possible for ECHA to assess whether an adaptation according to column 2 of Annex VIII, Section 9.2.2.1. would be acceptable in this case.

You are in this context reminded that ECHA does not take into account dossier updates submitted after the notification of the draft decision under Article 50(1) of the REACH Regulation for the purpose of this decision. However, ECHA will examine the information submitted in later updates of the registration dossier at the stage of the follow-up to the dossier evaluation in accordance with Article 42 of the REACH Regulation.

ECHA notes that guidance on when the standard information requirement on hydrolysis can be adapted is given in section R.7.9.2.2 of ECHA's Guidance on Information Requirements and Chemical Safety assessment, Chapter R.7b (version 4.0, June 2017). ECHA notes further that if you decide to adapt the testing requested according to the specific rules outlined in Annex VIII, Section 9.2.2.1. and/or according to the general rules contained in Annex XI of the REACH Regulation any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, together with adequate and reliable documentation.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Hydrolysis as a function of pH (test method: EU C.7/OECD TG 111).

6. *In vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study (Annex VIII, Section 8.4.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

You have not provided any study record of an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study in the dossier with the registered substance that would meet the information requirement of Annex VIII, Section 8.4.2.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for an *in vivo* somatic cell study (chromosomal aberrations) (OECD TG 475) and an *in vivo* mammalian germ cell study (OECD TG 483) with the analogue substance zinc bis(dimethyldithiocarbamate) (ZDMC, CAS no 137-30-4, EC no 205-288-3).

You have provided the following justification: "*In accordance with Column 2 of REACH Annex VIII, the study does not need to be performed, as reliable in vivo data are available for the structural analogue of zinc bis(dibenzyldithiocarbamate) (ZBEC), zinc bis(dimethyldithiocarbamate) (ZDMC), from which information on genotoxicity of ZBEC will be derived by read-across*".

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA considers that the *in vitro* mammalian chromosome aberration test (test method OECD TG 473) and the *in vitro* mammalian cell micronucleus test (OECD TG 487) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

In your comments to the draft decision you

1. agree on the need to gather new information on the potency of the substance to induce chromosome aberrations;
2. ask ECHA to allow you to perform a comet assay (OECD 489) combined to a chromosome aberrations test in vivo (OECD 475), instead of a chromosome aberrations test in vitro (OECD 473). You mention that such combined test would require a limited number of additional animals but, as a whole, it would be more efficient in terms of use of animals as well as costs.

In relation to point 2. above:

- ECHA considers that it is your responsibility to fulfil the information requirement using the data you choose. You have always the possibility to adapt the information requirement for in vitro cytogenicity data (OECD 473 or 487) with existing in vivo cytogenicity data (OECD 474 or 475), if you wish.

- Concerning the combination of the assays, ECHA notes that 1) the test guidelines for the micronucleus test (TG 474: para 1, 36, 37) and for the comet assay (TG 489: paras 7, 33) do foresee the possibility to combine both tests; 2) several articles mentioned in the TG 489 have described combined studies; and 3) on the other hand, TG 475 for the chromosomal aberration test states that "The micronucleus test (Test Guideline 474) should be viewed as the in vivo test of choice for chromosomal aberrations when integration with other studies is desired (para.32)".

- If you decide to perform a combined test:
  - there should be evidence that the substance or its metabolites will reach the target tissue (bone marrow).
  - careful consideration should be given to the logistics involved in tissue sampling for comet analysis alongside the requirements of tissue sampling for other types of toxicological assessments.

- In your comments you mentioned only the chromosome aberrations test in vitro (OECD 473) while the request in ECHA draft decision was either the micronucleus test in vitro (OECD 487) or the chromosome aberration test in vitro (OECD 473). You may thus consider combining the comet assay with either micronucleus test in vivo (OECD 474) or chromosome aberration test in vivo (OECD 475). Moreover, the combination of the comet with the micronucleus seems to be favoured in the OECD TGs (474, 475 and 489).
- Regarding the number of animals, it not clear to ECHA why additional animals would be needed to perform the combined study.

To summarize, you may, under your responsibility, perform a comet assay (TG489) (see request 8 of this decision) combined (preferably) with a micronucleus test (TG474) in order to adapt the information requirement for an in vitro cytogenicity study in mammalian cells (OECD TG 473) or in vitro micronucleus study (OECD TG 487).

However, ECHA did not modify the draft decision. The adequacy of the data provided will be evaluated by ECHA at the follow up stage.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian chromosome aberration test (test method: OECD TG 473) or *in vitro* mammalian cell micronucleus study (test method: OECD TG 487).

7. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "sub-chronic toxicity study (90 day)" is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a 17-week oral (in feed) study in rats, (non-guideline, non-GLP) with an analogue substance zinc bis(dibutyldithiocarbamate), (ZDBC, CAS no 136-23-2, EC no 205-232-8, publication, year 1978).

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

ECHA further notes that in the 17-week study ophthalmological examinations, test of the functional observation battery have not been performed and no results from histopathological investigations are reported. Furthermore, only a limited number of the clinical biochemistry parameters have been examined and clinical signs have not been specified. ECHA considers these limitations as major deviations from the OECD TG 408 requirements. In addition, the reporting of the study results does not allow an independent assessment of the findings, since tabular results and statistical analyses are not included. ECHA concludes that the study is not considered adequate.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement.

Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the substance is reported to occur as a dust with a significant proportion (>[redacted]% on weight basis) of particles of inhalable size (MMAD < 50 µm), there is no concern for effects in the respiratory tract as the substance not irritating/corrosive to skin/eyes). In addition, no oral repeated dose toxicity study is available to evaluate systemic toxicity following oral administration. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

According to the test method EU B.26./OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

In your comments on the draft decision you agree to fulfil this request.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats.

8. Transgenic rodent somatic and germ cell gene mutation assays (Annex X, Section 8.4., column 2) or In vivo mammalian alkaline comet assay (Annex X, Section 8.4., column 2)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Mutagenicity" is an information requirement as laid down in Annex VIII, Section 8.4. of the REACH Regulation. Column 2 of Annex IX, Section 8.4. provides that "If there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and there are no results available from an *in vivo* study already, an appropriate *in vivo* somatic cell genotoxicity study shall be proposed by the Registrant."

The technical dossier contains an *in vitro* gene mutation study in mammalian cells performed according to OECD TG 476 with the registered substance that show positive result. The results show that both in the presence and absence of metabolic activation (S9) a significant dose related increase in the mean mutant frequency compared to the negative control in the mouse lymphoma L5178Y cells is observed.

The positive result indicate that the substance is inducing gene mutations under the conditions of the test.

The technical dossier contains an *in vivo* Mammalian Bone Marrow Chromosome Aberration Test performed according to OECD TG 475 and an *in vivo* Mammalian Spermatogonial Chromosome Aberration Test performed according to OECD TG 483 conducted with the analogue substance zinc dimethyldithiocarbamate (ZDMC, CAS no 137-30-4, EC no 205-288-3) that show negative results.

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

Furthermore, ECHA notes that the provided *in vivo* studies (OECD TG 475 and TG 483) measure structural chromosome aberrations and are therefore not appropriate to follow up a positive *in vitro* result for mammalian gene mutation. Hence, ECHA concludes that the tests provided are not appropriate to follow-up a concern for gene mutations.

An appropriate *in vivo* genotoxicity study to follow up the concern on gene mutations is not available for the registered substance. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.7.6.3, the transgenic rodent somatic and germ cell gene mutation assays ("TGR assay", OECD TG 488) and the *in vivo*

mammalian alkaline comet assay ("comet assay", OECD TG 489) are suitable to follow up a positive *in vitro* result on gene mutation.

Hence, ECHA considers that the TGR and the comet assay are suitable tests to follow up the concern on gene mutation for the substance subject to the decision.

In case you decide to perform the TGR assay according to the test method EU B.58/OECD TG 488, the test shall be performed in transgenic mice or rats and the substance is usually administered orally.

According to the test method EU B.58/OECD TG 488, the test shall be performed by analysing tissues from liver as slowly proliferating tissue and primary site of xenobiotic metabolism, glandular stomach and duodenum as rapidly proliferating tissue and site of direct contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the substance, and probable different local absorption rates of the substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to sample both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract. However, duodenum shall be analysed if the results of the glandular stomach and of the liver are negative.

Male germ cells shall be collected at the same time as the other tissues (liver, glandular stomach and duodenum), and stored up to 5 years (at or below −70 °C). This duration is sufficient to allow the Registrant or ECHA, in accordance to Annex X, Section 8.4., column 2, to decide on the need for assessment of mutation frequency in the collected germ cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

In case you decide to perform the comet assay according to the test method OECD TG 489, the test shall be performed in rats. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

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

In your comments to the draft decision you

1. agree to perform a comet assay or a TGR assay, and noted the request for analysis of liver, glandular stomach and duodenum for the Comet assay, as well as the remarks on sampling of gonads;
2. ask ECHA to allow some level of flexibility to 'adapt the design as needed', also

based on data obtained from the 90-day study.

In relation to point 2. above:

- ECHA is not sure about the exact meaning of 'adapt the design as needed', whether it refers to the combination of assays, or to the choice of tissues to be sampled;
- ECHA considers that you may decide to 'adapt the design' by performing investigations that are additional to the information that is required under this section (section 8).

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision:

Transgenic rodent somatic and germ cell gene mutation assays (test method: EU B.58/OECD TG 488) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach; germ cells and duodenum shall be harvested and stored for up to 5 years; duodenum shall be analysed if the results of the glandular stomach and of the liver are negative.

or

In vivo mammalian alkaline comet assay (test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum.

Notes for your consideration

You are reminded that according to Annex X, Section 8.4., column 2 of the REACH Regulation, if positive results from an *in vivo* somatic cell study are available, "the potential for germ cell mutagenicity should be considered on the basis of all available data, including toxicokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered".

In case you decide to perform the comet assay, you may consider examining gonadal cells in addition to the other aforementioned tissues, as it would optimise the use of animals. ECHA notes that a positive result in whole gonads is not necessarily reflective of germ cell damage since gonads contain a mixture of somatic and germ cells. However, such positive result would indicate that the substance and/or its metabolite(s) have reached the gonads and caused genotoxic effects. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

9. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of

the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a pre-natal and post-natal toxicity study in rats, oral route (non-guideline, non-GLP) with the analogue substance zinc bis(diethyldithiocarbamate) (ZDEC, CAS no 14324-55-1, EC no 238-270-9), publication 1984.

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid/dust, ECHA concludes that testing should be performed by the oral route.

In your comments on the draft decision you agree to fulfil this request.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rat or rabbit) by the oral route.

10. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pre-natal developmental toxicity studies (test method EU B.31./OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The technical dossier contains information on a pre-natal developmental toxicity study in rats by the oral route using the analogue substance zinc bis(diethyldithiocarbamate) (ZDEC, CAS no 14324-55-1, EC no 238-270-9) as test material. However, as explained above in

Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

However, there is no information provided for a pre-natal developmental toxicity study in a second species.

The technical dossier does not contain an adaptation in accordance with column 2 of Annex X, Section 8.7.2. or with the general rules of Annex XI for this standard information requirement.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with rabbits or rats as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid/dust, ECHA concludes that testing should be performed by the oral route.

ECHA notes that in the comments to the draft decision you indicate that a PNDT study in second species it is not required by REACH at this juncture and imposing it would be disproportional and premature. You further note that:

- you will submit a testing proposal for the study only in case the read-across adaptation (supported by the results of 90 day toxicity study and PNDT study in 1st species with the registered substance) will not be considered appropriate.

ECHA understands that you do not agree that a pre-natal developmental toxicity study on a second species is a standard information requirement for a substance registered for 1000 tonnes or more per year. In this respect, ECHA emphasises that the pre-natal developmental toxicity study is an actual standard information requirement pursuant to Section 8.7.2., Annex X. This view was confirmed by the ECHA Board of Appeal in decision A-004-2012 of 10 October 2013 in which the Board of Appeal concluded that the provisions of the REACH Regulation, when read as a whole, mean that registrants manufacturing or importing substances at 1000 or more tonnes per year are required to perform a developmental toxicity study also on a second species, unless, as a result of the adaptations set out in the legislation, such a study is not necessary (see http://echa.europa.eu/about-us/who-we-are/board-of-appeal/decisions).

ECHA notes that according to column 2 of Annex X, Section 8.7. studies do not need to be conducted if the substance is a known genotoxic carcinogen; or if the substance is known to have adverse effects on fertility or to cause developmental toxicity (i.e. meeting the criteria for classification as Repro. 1A or 1B). ECHA concludes based on available information that the registered substance is not genotoxic and it does not meet the criteria for classification

as Repro. 1A or 1B; therefore a pre-natal developmental study in a second species is required.

Further, ECHA points out that any improved adaptation based on Annex XI, section 1.5, of the REACH Regulation needs to meet the provisions of this section and has to address the shortcomings of the grouping and read-across proposal addressed in this decision.

You further explain that if the read-across approach would not be appropriate you would submit a testing proposal for pre-natal developmental toxicity (test method: EU B.31./OECD TG 414) in a second species. ECHA notes that a possible future testing proposal is considered to be inadmissible because the information requirement is already subject to this compliance check process.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a second species rabbit or rat by the oral route.

Notes for your consideration

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must consider the specific adaptation possibilities of Annex X, Section 8.7., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species with other available information enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

11. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

The basic test design of an extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Further detailed guidance on study design and triggers is provided in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) The information provided

You have not provided any study record of an extended one-generation reproductive toxicity study with the registered substance in the dossier that would meet the information requirement of Annex X, Section 8.7.3. Instead, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a two-generation reproductive toxicity study (equivalent or similar to OECD TG 416) with the analogue substance zinc dimethyldithiocarbamate (ZDMC, CAS no 137-30-4, EC no 205-288-3).

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

Hence, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint. Thus, an extended one-generation reproductive toxicity study according Annex X, Section 8.7.3. is required. The following refers to the specifications of this required study.

b) The specifications for the study design

Information from studies to be conducted before the extended one-generation reproductive toxicity study

The sub-chronic toxicity study shall be conducted before the extended one-generation reproductive toxicity study and the results from that study shall be used, among other relevant information, to decide on the study design of the extended one-generation reproductive toxicity study following ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).The sub-chronic toxicity study may provide information on effects that is relevant for triggers (e.g. weight changes and histopathological observations of organs as indication(s) of one or more modes of action related to endocrine disruption which may meet the toxicity-trigger for extension of Cohort 1B or as evidence of specific mechanism/modes of action and/or neurotoxicity and/or immunotoxicity which may meet the particular concern criteria for developmental neurotoxicity and/or developmental immunotoxicity cohorts).

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 6.0, July 2017). Ten weeks exposure duration is supported also by the expected lipophilicity (partition coefficient is not provided in the dossier, but open source information indicate that the estimated log Pow is equal to 5.4) of the substance to ensure that the steady state in parental animals has been reached before mating.

The highest dose level shall aim to induce some toxicity to allow comparison of effect levels and effects of reproductive toxicity with those of systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

If there is no existing relevant data to be used for dose level setting, it is recommended that results from a conducted range-finding study (or range finding studies) are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Cohorts 2A and 2B

The developmental neurotoxicity Cohorts 2A and 2B need to be conducted in case of a particular concern on (developmental) neurotoxicity as described in column 2 of 8.7.3., Annex X. When there are triggers for developmental neurotoxicity, both the Cohorts 2A and 2B are to be conducted as they provide complementary information.

ECHA notes that results obtained with the analogue substance zinc bis dimethyldithio-carbamate (ZDMC) show developmental neurotoxicity in the offspring, such as increased motor activity and decreased mean peak startle response in a dietary two-generation reproduction and developmental neurotoxicity study (Nemec, 1996; in USEPA review Ziram/09/25/2001 available at: http://www3.epa.gov/pesticides/chem_search/cleared_reviews/csr_PC-034805_25-Sep-01_a.pdf). This information is not reported in the dossier. In this reference document also neurotoxic effects in adult animals (various species) are described for this substance. ECHA considers this substance (ZDMC) as a structural analogue of the registered substance which causes a particular concern for (developmental) neurotoxicity within the meaning of column 2 of Section 8.7.3., Annex X (existing information on effects caused by structurally analogous substances to the substance being studied). The common core of the registered substance and ZDMC (dithiocarbamate moiety) is considered relevant to trigger the conduct of the developmental neurotoxicity cohort (it should be noted that the read-across adaptation to ZDMC was rejected due to structural differences in the substituents at the nitrogen atom and was not related to the common core of the substances in question). Consequently this information is used to determine the design of the EOGRT study.

ECHA concludes that the developmental neurotoxicity Cohorts 2A and 2B need to be conducted because there is a particular concern on (developmental) neurotoxicity based on the results from the above-identified *in vivo* information on the structurally analogous substance zinc bis dimethyldithiocarbamate.

The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

Species and route selection

According to the test method EU B.56/ OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid (powder), ECHA concludes that testing should be performed by the oral route.

ECHA notes that in the comments on the draft decision you indicated that a testing proposal for the requested test will be submitted only in case read-across adaptation (supported by newly derived data as the results of 90 day toxicity study) will not be considered appropriate.

ECHA considers that a possible future testing proposal is considered to be inadmissible because the information requirement is already subject to this compliance check process. ECHA notes that you may only commence the extended one-generation reproductive toxicity study as requested after **19 March 2019**, unless an indication to the contrary is communicated to you by ECHA before that date.

ECHA points out that any improved justification for the use of an adaptation for the conduct of the extended one-generation reproductive toxicity study has to be submitted together with the results of the 90-day repeated dose toxicity study. Furthermore, any improved adaptation based on Annex XI, section 1.5, of the REACH Regulation needs to meet the provisions of this section and has to address the shortcomings of the grouping and read-across proposal addressed in this decision.

c) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce some toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;
- Cohorts 2A and 2B (Developmental neurotoxicity)

Currently, the extension of Cohort 1B and Cohort 3 (developmental immunotoxicity) are not requested. However, the sub-chronic toxicity study (90-day) requested in this decision and/or any other relevant information may trigger changes in the study design. Therefore, the sub-chronic toxicity study (90-day) is to be conducted first and the study results submitted to ECHA in a dossier update by the 12-month deadline indicated in this decision. If, on the basis of this update and/or other relevant information, a need for changes to the study design is identified, ECHA will inform you within three months after expiry of the 12-month deadline to provide the sub-chronic toxicity study (90-day), as indicated in this decision, of its intention to initiate a new decision making procedure under Articles 41, 50 and 51 of the REACH Regulation to address the design of the extended one-generation

reproductive toxicity study. If you do not receive a communication from ECHA by the expiry of the three months following the 12-month deadline for providing the results of the sub-chronic toxicity study (90-day), the request of the present decision for the extended one-generation reproductive toxicity study remains effective and you may commence the conduct of the study and the results will need to be submitted by the deadline given in this decision.

Notes for your consideration

When submitting the study results of the sub-chronic toxicity study (90-day) you are invited to also include in the registration update your considerations whether changes in the study design are needed (see also *ECHA Guidance on information requirements and chemical safety assessment Chapter R.7a, Section R.7.6 (version 6.0, July 2017)*.

Furthermore, after having commenced the extended one-generation reproduction toxicity study in accordance with the ECHA decision, you may also expand this study to address a concern identified during the conduct of it and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the changes in the study design must be documented. The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/ triggers must be documented.

12. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of growth inhibition on aquatic plants in the dossier that would meet the information requirement of Annex VII, Section 9.1.2.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing (a) study record for an Alga, Growth Inhibition Test (key study, reliability 2, 1985, non GLP, test method: OECD TG 201) with the analogue substance zinc bis(diethyldithiocarbamate) (ZDEC; EC No 238-270-9, CAS No 14324-55-1). However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement cannot be accepted.

Furthermore, the OECD TG 201 read-across study submitted does not provide the information required by Annex VII, Section 9.1.2., because it is not reliable for the reasons set out below.

Firstly, the robust study summary (RSS) lacks information on test conditions such as the concentrations tested and the pH. According to the OECD TG 201 par. 61 the test report

should include information on "*test concentrations and replicates*", and "*pH values at the beginning and at the end of the test at all treatments*".

Secondly, the test organisms used (*Chlorella pyrenoidosa*) is not one of the recommended test species given in Annex 2 of the OECD TG 201. As given in par. 18 of the OECD 201, when other species are used, it should be confirmed that exponential growth of the test alga can be maintained throughout the test period under the test conditions.

Thirdly, according to the OECD TG 201 (par. 11) a study can be considered valid when "*the biomass in the control cultures should have increased exponentially by a factor of at least 16 within the 72-hour test period*" and when "*the mean coefficient of variation for section-by-section specific growth rates...in the control cultures...must not exceed 35%*". No information on controls is provided in the RSS. ECHA notes that you have also not indicated in the relevant IUCLID field whether the validity criteria have been fulfilled. In the absence of information on exponential growth in controls, it is not possible for ECHA to determine whether the criteria of par. 11 have been fulfilled in the study submitted. Finally, ECHA notes that the only result provided is the EC50 of 1.1 mg/L (nominal, growth rate).

Since the RSS does not report details on the study results or observations made during the test, it is not possible for ECHA to verify the validity of the study. The study submitted thus cannot be used to fulfil the present standard information requirement nor does it meet the requirements of Annex XI, Section 1.5 of REACH (be adequate for the purpose of classification and labelling and/or risk assessment).

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

In your comments on the draft decision, you agree to perform the study requested. You further indicate that a test has already been executed and that the test report, which is currently not available, will be provided in an update of the technical dossier.

ECHA notes that any new information should be submitted in a form of a dossier update. While for the purpose of this decision making, ECHA does not take into account any dossier updates after the notification of this draft decision under Article 50(1) of the REACH Regulation, ECHA notes that dossier updates and any new information/adaptations therein will be evaluated by ECHA at the follow up stage.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Algae growth inhibition test, EU C.3./OECD TG 201).

Notes for your consideration

Due to the indicated low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

13. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a Long-term toxicity testing on aquatic invertebrates (key study, reliability 2, 1985, non GLP, test method: no guideline followed) with the analogue substance zinc bis(diethyldithiocarbamate) (ZDEC; EC No 238-270-9, CAS No 14324-55-1). However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement cannot be accepted.

Furthermore, the read-across study submitted does not provide the information required by Annex IX, Section 9.1.5., because it is not reliable for the reasons set out below.

In the endpoint study record (ESR) submitted under IUCLID section 6.1.4. "Long-term toxicity to aquatic invertebrates" you have indicated that the study conducted was a non-guideline study. However, as you state that it was "*near guideline study*" and "*a pre-guideline 21-day reproduction study*" ECHA has compared the validity criteria given in the OECD TG 211 (2012) with the information provided in the Robust Study Summary (RSS) for this study.

According to the validity criteria described in OECD TG 211 (2012), paragraph 8, a test is valid when:

1. the mortality of the parent animals (female *Daphnia*) does not exceed 20% at the end of the test;
2. the mean number of living offspring produced per parent animal surviving at the end of the test is > 60.

In the RSS only the effect values NOEC of 3.2 µg/L and a LOEC of 10 µg/L (nominal, reproduction of *Daphnia magna*) have been provided and there is no information on control mortality or the number of living offspring produced. ECHA notes that you have also not indicated in the relevant IUCLID field whether the validity criteria have been fulfilled. In absence of information on mortality of parent animals and mean number of living offspring in the controls, it is not possible to verify whether the validity criteria set in the OECD TG 211 (par. 8) for a reproduction study on *Daphnia*, have been fulfilled in the study submitted.

Furthermore, ECHA notes that there is inconsistency between the units of the effect concentrations (NOEC of 3.2 µg/L and LOEC of 10 µg/L, nominal) and those of the nominal test concentrations, reported to be "*At least: 0, 3.2, 5.6, 10 and 18 mg/l*". The given nominal concentrations are above the water solubility value of 1.06 mg/L (given in the data matrix in the read-across document). Furthermore, as the test concentrations have not been analytically measured, it has not been demonstrated that the test substance, which is poorly water soluble, has been kept in solution. It is therefore not possible to know to which concentrations the test organisms were exposed to.

Therefore ECHA concludes that the key study is not reliable. It thus cannot be used to fulfil the standard information requirement for the present endpoint nor does it meet the requirements of Annex XI, Section 1.5 of REACH (be adequate for the purpose of classification and labelling and/or risk assessment).

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

Furthermore, ECHA notes that Column 2 of Annex VII, Section 9.1.1 specifies that long-term aquatic toxicity study on *Daphnia* (Annex IX, section 9.1.5) shall be considered if the substance is poorly water soluble. ECHA notes that while information on water solubility is requested in this decision, based on the information provided in the technical dossier there are indications that the registered substance has low water solubility. Therefore, ECHA considers that long-term testing is justified for the registered substance.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

In the comments on the draft decision, you agree to proceed with the study requested. You further indicate that a test has already been executed and that the test report, which is currently not available, will be provided in the update of the technical dossier.

ECHA notes that any new information should be submitted in a form of a dossier update. While for the purpose of this decision making, ECHA does not take into account any dossier updates after the notification of this draft decision under Article 50(1) of the REACH Regulation, ECHA notes that dossier updates and any new information/adaptations therein will be evaluated by ECHA at the follow up stage.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *Daphnia magna* reproduction test (test method: EU C.20./OECD TG 211).

Once results of the proposed test on long-term toxicity to aquatic invertebrates are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

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14. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for a Fish, Early-Life Stage Toxicity Test (key study, reliability 2, 1991, non GLP, test method: OECD TG 210). However, this study does not provide the information required by Annex IX, Section 9.1.6.1 / 9.1.6.2 / 9.1.6.3., because it is not valid.

You indicate that this study was performed according to the OECD TG 210 guideline or a guideline equivalent to it. ECHA has therefore compared the validity criteria and study design given in the OECD TG 210 (1992) with the information provided in the Robust Study Summary (RSS) for the study submitted under IUCLID section 6.1.2. Long-term toxicity to fish.

ECHA observes the following differences between the study submitted and the study design described in the OECD TG 210:

- The total test duration was only 11 days, instead of the 30 days post-hatch for the species tested *Danio rerio* given in Annex II of OECD TG 210
- According to paragraph 3 of the OECD TG 210, the test is initiated by placing fertilised eggs in test chambers and is continued until the control fish reaches the species-specific juvenile life-stage. However, in the study submitted "*only eggs were exposed to the test medium*".
- According to the validity criteria outlined in par. 7 of the OECD TG 210 analytical monitoring is compulsory for a test to be valid. In the study submitted, semi-static conditions were used and no analytical monitoring of test concentrations took place. Since "*The medium was renewed after two or three days*", in absence of analytical monitoring it has not been demonstrated that the substance, which is indicated to be poorly water soluble, has been kept in solution. It is therefore not clear to which concentrations the test organisms were exposed to.
- You indicate that "*Test containers were polystyrene multi-dishes with 6 holes each containing 5 ml of test mediu. Five to 7 eggs were transferred to each hole*", whereas at least 80 eggs per concentration should be used, as given in paragraph 19 of OECD TG 210.

Furthermore, the RSS does not report details on the study results or observations made during the test in the controls and in the test solutions, as required according to par. 34 of the OECD TG 210. Only the effect values, such as the NOEC of 0.1 mg/L (nominal, number hatched), have been provided. ECHA notes that you have not indicated in the relevant

IUCLID field whether the validity criteria have been fulfilled. Since the RSS does not report detailed results, such as overall survival of fertilised eggs and post-hatch success in the controls, it is not possible to verify whether the validity criteria of OECD TG 211, par. 8, have been fulfilled for the study submitted.

In conclusion, ECHA considers that due to the deficiencies given above the study cannot be considered valid and cannot be used to fulfil the information requirement of Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.).

Therefore, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

Furthermore, ECHA notes that Column 2 of Annex VIII, Section 9.1.3 specifies that Long-term toxicity testing on fish (Annex IX, Section 9.1.6.) shall be considered if the substance is poorly water soluble. ECHA notes that while information on water solubility is requested in this decision, based on the information provided in the technical dossier there are indications that the registered substance has low water solubility. Therefore, ECHA considers that long-term testing is justified for the registered substance.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish early-life stage (FELS) toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), *Chapter R7b, Figure R.7.8-4).*

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA *Guidance Chapter R7b,* version 4.0, June 2017).

In your comments on the draft decision, you agree to perform the study requested. ECHA acknowledges that you indicate that you may perform the study at maximal solubility levels, will determine concentrations as far as technically feasible and consider radiolabelling. As due to its physicochemical properties the substance may be difficult to test ECHA refers you to the guidance for testing poorly water soluble substance given in the notes for your consideration section below.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Note for your consideration for requests 13-14

Due to the indicated low water solubility of the substance the Integrated testing strategy (ITS) outlined in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4), is not applicable in this case and the long-term studies on both invertebrates and fish are requested to be conducted.

Due to the indicated low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

15. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Simulation testing on ultimate degradation in water" is a standard information requirement as laid down in Annex IX, section 9.2.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex IX, Section 9.2., column 2. You provided the following justification for the adaptation "*In accordance with Column 2 of REACH Annex IX, degradation simulation testing in water and/or sediment does not need to be conducted as based on the available data risks are controlled and a refinement of the PECs with additional information on the degradation of the substance and its degradation products in water and sediment is therefore not required.*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Column 2 of Annex IX, Sections 9.2 and 9.2.1.2. for the reasons set out below.

According to Annex IX, Section 9.2.1.2, column 2 of the REACH Regulation, simulation testing on ultimate degradation in surface water does not need to be conducted if the substance is highly insoluble in water or is readily biodegradable. ECHA notes that based on the information in the technical dossier, the registered substance is not readily biodegradable in a OECD TG 301 F (Ready Biodegradability: Manometric Respirometry Test) study (8% degradation after 28 days) and has low water solubility (below 1 mg/L based on non-valid read-across prediction, as fully described in request 3. above).

ECHA notes further that you base your adaptation on risk alone, while column 2 of Annex IX, Section 9.2. requires that the simulation study shall be conducted if a need is indicated by the chemical safety assessment (CSA) according to Annex I, including PBT assessment.

In your PBT assessment you state that "*In a GLP-compliant OECD 301F study (Modified Sturm Test) 7% degradation is observed ([redacted]., 2010a). Zinc bis(dibenzyldithiocarbamate) is therefore identified as potentially persistent. However, significant and substantial abiotic degradation occurs via hydrolysis. The half-live obtained in an hydrolysis test with the structurally similar substance zinc bis(dimethyldithio-carbamate) is 17.7 h at pH 7 and 25 °C (and does not fulfil the P(vP) criterion of t½ >40(60) days). (..)It is concluded that the major transformation products, dibenzylamine and carbon disulfide, are not PBT nor vPvB substances, no further testing of degradation is required for the PBT/vPvB assessment.*" However, ECHA notes that the hydrolysis data provided in the technical dossier based on a read-across prediction to the substance ZDMC (zinc bis(dimethyldithiocarbamate) are not valid, as fully described in section 0 and request 5. above. In particular, you have not demonstrated that the registered substance would hydrolyse to the same extent as the proposed analogue substance ZDMC and that the two would have the same hydrolysis products. Furthermore, ECHA notes that hydrolysis alone cannot be used to conclude that a substance is not persistent. Test results showing fast hydrolysis rates always need to be evaluated carefully in the context with other information on the substance, such as its partitioning and ionising properties, as described in *ECHA Guidance on information requirements and chemical safety assessment*, Chapter R.11, Section R.11.4.1.1 (version 3.0, June 2017) on PBT assessment. Such considerations would need to be taken into account if you would attempt to conclude on P based on hydrolysis once data become available.
ECHA notes that the registered substance is not readily biodegradable and based on the provided screening level information in the dossier there is insufficient evidence that the substance would not be P or vP. In the technical dossier there is also no information on the biodegradation products and their fate. In addition, information on relating PBT endpoints of bioaccumulation and aquatic toxicity is missing and has been requested in this decision. ECHA hence considers that due to the data gaps addressed in this decision the information in the chemical safety assessment (CSA) including the PBT/vPvB assessment is not complete. ECHA notes further that you have not provided adequate justification in your CSA or in the technical dossier why there is no need to investigate further the degradation of the substance and its degradation products. On this basis, the CSA cannot be used to justify that there is no need to investigate further the degradation of the substance and its degradation products.

In conclusion, ECHA considers that as explained above the information is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment.

In your comments on the draft decision (DD), you agree to provide additional information on the degradation of the registered substance, however you intend to perform only the sediment simulation testing according to OECD TG 308 (request 16 below). You consider that based on the results of a new water solubility study conducted on the registered substance (water solubility of 2.3 µg/L), a test on ultimate degradation in surface water (OECD TG 309) is not technically feasible and would not allow the identification of the degradation products. Furthermore, you consider that, based on the Log Koc value above 4, sediment is the relevant environmental compartment for the registered substance and only the sediment simulation test (OECD TG 308) should be performed.

ECHA notes that the OECD TG 309 is typically performed at concentrations between 1 and 100 µg/L and preferably in the range of <1-10 µg/L to ensure that biodegradation follows

first order kinetics, as indicated in paragraph 5 of this TG. Hence, although the validity of the water solubility value of 2.3 µg/L cannot currently be assessed (as explained in the reply to your comments under request 3), ECHA considers that for substances with water solubility typically above 1 µg/L the OECD TG 309 is applicable.

Furthermore, concerning the feasibility of the simulation study in surface water (OECD TG 309) for poorly water soluble substances, ECHA acknowledges that according to paragraph 15 of the OECD TG 309, "*The chemical analyses of many organic substances and their transformation products frequently require that the test substance is applied at a relatively high concentration, i.e. >100 µg/L*", as you indicated in your comments on the DD. However, ECHA considers that this general statement alone cannot be used to adapt standard information requirements relating to testing the surface water compartment. ECHA notes that "technically not feasible" means that it has been impossible, with allocation of reasonable efforts, to develop suitable analytical methods and other test procedures to accomplish testing in surface water to generate reliable results. Since your justification does not report any specifications on the availability of analytical methods and other test procedures, ECHA concludes that you have not adequately considered and justified that simulation testing in water is not technically feasible.

Concerning the choice of the relevant compartment for simulation testing, ECHA notes that in your justification you have considered fate properties only: you consider sediment as the relevant environmental compartment due to the high adsorption potential of the registered substance (LogKoc above 4). However, ECHA considers that fate properties alone cannot be used to adapt standard information requirements relating to testing the surface water compartment. According to the integrated testing strategy for persistency assessment described in Section R.11.4.1.1. of ECHA Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), ECHA considers that also the influence of the relevant environmental compartment(s) in terms of the identified uses and release patterns should be taken into consideration when choosing the most relevant environmental compartment to be tested first.

ECHA considers also that since by default the surface water compartment receives a significant amount of emission, a testing strategy on simulation testing should always start with the OECD TG 309 simulation study, as long as it is technically feasible to conduct the simulation surface water study. Also, the potential for formation of non-extractable residues (NERs) is minimised in a water simulation study, while especially for an adsorptive substance, NER formation in soil and sediment studies may be difficult to interpret.

Nevertheless, ECHA notes that if, based on the fate and release(s) of the substance, it is considered that water compartment is not a relevant environmental compartment at all, this should also be taken into account in the testing strategy (ECHA guidance Chapter R. 11. version 3.0, June 2017). In such a case you shall provide a full scientific justification as to why based on the registered substance properties, fate and use and release patterns and any other relevant information water testing is not technically feasible and/or not relevant for the registered substance.

While you indicate that you intend to conduct a sediment simulation study, you do not indicate if and when you consider that simulation studies in other compartments may be needed. ECHA notes that once it is possible to conclude that the P and/or vP criteria are fulfilled in one environmental compartment, including assessing P/vP for all constituents and

any potential transformation and/or degradation products, no further testing is needed for the other compartments. On the contrary, if based on a simulation study that is conducted it is not possible to conclude the P/vP assessment for all compartments, further simulation testing may be needed.

In conclusion, ECHA considers that the justifications provided in your comments on the DD cannot be used to adapt standard information requirements relating to testing the surface water compartments.

ECHA notes that if you should encounter technical difficulties to perform the requested test, for example related to sensitivity of the analytical method, such difficulties and attempted solutions should be clearly documented. Furthermore, ECHA notes that if you intend to adapt the current information requirement a scientifically valid justification will need to be provided as to why the CSA does not indicate the need to study the degradation of the substance further.

Therefore, your adaptation of the information requirement cannot be accepted.
As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Aerobic mineralisation in surface water – simulation biodegradation (test method EU C.25. / OECD TG 309) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.2.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of the REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 4.0, June 2017) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-8 (version 3.0 February 2016) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 309. Therefore, the test should be performed at the temperature of 12°C.

In the OECD TG 309 Guideline two test options, the "pelagic test" and the "suspended sediment test", are described. ECHA considers that the pelagic test option should be followed as that is the recommended option for P assessment. The amount of suspended solids in the pelagic test should be representative of the level of suspended solids in EU surface water. The concentration of suspended solids in the surface water sample used should therefore be approximately 15 mg dw/L. Testing natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable. Furthermore, when reporting

the non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Aerobic mineralisation in surface water – simulation biodegradation test (test method: EU C.25./OECD TG 309).

16. Sediment simulation testing (Annex IX, Section 9.2.1.4.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Sediment simulation testing" is a standard information requirement as laid down in Annex IX, section 9.2.1.4. of the REACH Regulation for substances with a high potential for adsorption to sediment. While information on water solubility and partitioning is requested in this decision, there are indications that the registered substance has low water solubility, high partition coefficient (log Kow 5.41, QSAR prediction, value given in the read-across data matrix) and high adsorption coefficient (log Koc 9.42, QSAR prediction), indicating high adsorptive properties. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex IX, Section 9.2., column 2. You provided the following justification for the adaptation "*In accordance with Column 2 of REACH Annex IX, degradation simulation testing in water and/or sediment does not need to be conducted as based on the available data risks are controlled and a refinement of the PECs with additional information on the degradation of the substance and its degradation products in water and sediment is therefore not required.*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Column 2 of Annex IX, Sections 9.2 and 9.2.1.3. due to the following. ECHA notes that you have not provided adequate justification in your chemical safety assessment (CSA), including the PBT assessment, nor in the technical dossier for why there is no need to investigate further the degradation of the substance and its degradation products, as fully discussed in request 15 (see above).

Furthermore, according to Annex IX, Section 9.2.1.4, column 2 of the REACH Regulation, simulation testing on sediment does not need to be conducted if the substance is readily biodegradable or if direct or indirect exposure of sediment is unlikely. ECHA notes that based on the information in the technical dossier, the registered substance is not readily biodegradable in a OECD TG 301 F (Ready Biodegradability: Manometric Respirometry Test) study (8% degradation after 28 days).

Regarding exposure of sediment, ECHA notes the substance has high adsorptive properties, as explained above. Furthermore, based on the uses reported in the technical dossier, ECHA considers that the exposure estimations that you provided in the Chemical Safety Report (CSR) indicate that there is potential exposure to sediment. For example in exposure scenario 2, Predicted Environmental Concentrations (PECs) for sediment are provided and

the risk characterisation leads to high RCRs of [redacted] for both freshwater and marine sediment. ECHA therefore considers that you have not demonstrated that sediment exposure is unlikely.

In conclusion, as indicated above and in request 15. of this decision, further information on degradation is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.
According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Aerobic and anaerobic transformation in aquatic sediment systems (test method EU C.24. / OECD TG 308) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.4.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 4.0, June 2017) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-8 (version 3.0 February 2016) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 308. Therefore, the test should be performed at the temperature of 12°C.

Simulation tests performed in sediment or in soil possibly imply the formation of non-extractable residues (NER). These residues (of the parent substance and/or transformation products) are bound to the soil or to the sediment particles. NERs may potentially be re-mobilised as parent substance or transformation product unless they are irreversibly bound by covalent bonds or incorporated into the biomass. When reporting the non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

In your comments on the draft decision (DD), you agree to provide additional information on the degradation of the registered substance and agree to perform the study requested. ECHA has addressed your choice of compartment for simulation testing under section 15. above.

However, in your comments on the DD, you do not agree to perform the sediment simulation study at 12°C as requested, due to the low water solubility and the expected low degradation of the registered substance. Instead, you request to perform the sediment

simulation study at 20°C. You indicate that a similar decision has been taken by ECHA for a "*related substance*" CDBC (Copper bis(dibutyldithiocarbamate), CAS 14726-36-4). ECHA notes that the CAS number provided by you for CDBC is the CAS number of the registered substance. Nevertheless, ECHA understands that as a "related substance" you refer to the substance bis(dibutyldithiocarbamato-S,S')copper with the following identifiers: CAS 13927-71-4 , EC 237-695-7. However, ECHA notes that you provide no explanation nor a scientific justification on why you consider a decision on the "related substance" to apply in this specific case as well.

Regarding your request to carry out the study at 12°C ECHA notes the following. As indicated above, new kinetic simulation studies should be conducted at environmentally relevant temperatures, by default at 12°C, when the principle aim of the study requested is to determine the half-life of the parent molecule for the purpose of the PBT/vPvB assessment (ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Section R.7.9.4. (version 4.0, June 2017)). The simulation study may be conducted at a different temperature if there are specific reasons of why it is not technically feasible to perform a new simulation test at 12°C. ECHA notes that you justify your request by low water solubility and expected low degradation only, and not by specifications on the analytical methods. ECHA hence considers that you do not explain why testing at 12°C is not technically feasible.

According to ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4. (version 4.0, June 2017) a higher test temperature of 20°C is appropriate if the purpose of the simulation test is principally the identification of metabolites. However, ECHA notes that as explained above the information from the study requested here is needed to also determine the half life of the parent molecule for the purpose of the PBT assessment, and not for the identification of the degradation products alone. In such a case the simulation test should be performed at 12°C (ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4. (version 4.0, June 2017). Nevertheless, ECHA notes that if you choose to adapt the request and conduct the study requested at a different temperature, a scientific and fully documented justification needs to be provided for any deviation from the study design.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Aerobic and anaerobic transformation in aquatic sediment systems (test method: EU C.24./OECD TG 308).

Notes for your consideration for requests 15-16

Before conducting the requested simulation tests (requests 15. and 16. of this decision) you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4 and R.7.9.6 (version 4.0, June 2017) and Chapter R.11, Section R.11.4.1.1 (version 3.0, June 2017) on PBT assessment to determine the sequence in which the simulation tests are to be conducted and the necessity to conduct all of them. The order in which the simulation biodegradation tests are performed needs to take into account the intrinsic properties of the registered substance and the identified use and release patterns which could significantly influence the environmental fate of the registered substance.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when results of the tests detailed above are available. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

17. Identification of degradation products (Annex IX, 9.2.3.)

In accordance with Articles 10(a) and 12(1) of the REACHs Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

The identification of the degradation products is a standard information requirement according to column 1, Section 9.2.3. of Annex IX of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

The biodegradation section in the technical dossier does not contain any information in relation to the identification of degradation products.

However, ECHA considers that you have sought to adapt this information requirement according to Annex IX, Section 9.2., column 2. You provided the following justification for the adaptation in section 5.2.2 "Biodegradation in water and sediment: simulation tests" of the IUCLID technical dossier: "*In accordance with Column 2 of REACH Annex IX, degradation simulation testing in water and/or sediment does not need to be conducted as based on the available data risks are controlled and a refinement of the PECs with additional information on the degradation of the substance and its degradation products in water and sediment is therefore not required.*"

ECHA notes that in your adaptation you propose that it is not necessary to obtain information on the degradation products based on risk alone.

However, according to Annex IX, Section 9.2.3., column 2 of the REACH Regulation, identification of degradation products is not needed if the substance is readily biodegradable. ECHA notes that based on the information in the technical dossier, the registered substance is not readily biodegradable as also discussed in requests 15. and 16. (see above).

ECHA notes further that for the endpoint of Hydrolysis you have submitted a read-across study on ZDMC (zinc bis(dimethyldithiocarbamate). In the Robust Study Summary (in IUCLID section 5.1.2.) you have provided information on the degradation products of ZDMC. However, as fully discussed in section 0 and request 5 of this decision the read-across is not acceptable nor can the hydrolysis study submitted be considered valid. ECHA notes that the information submitted in IUCLID section 5.1.2. can hence not be considered as applicable to the registered substance. There is accordingly no information on the degradation products of the registered substance.

Furthermore, ECHA notes that you have not provided any justification in your chemical safety assessment (CSA) or in the technical dossier why there is no need to provide information on the degradation products, as fully discussed in requests 15. and 16. (see above). ECHA considers that this information is needed in relation to the PBT/vPvB assessment and risk assessment.
As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

Regarding appropriate and suitable test method, the methods will have to be substance-specific. When analytically possible, identification, stability, behaviour, molar quantity of metabolites relative to the parent compound should be evaluated. In addition, degradation half-life, log Kow and potential toxicity of the metabolite may be investigated. You may obtain this information from the degradation studies (simulation and hydrolysis) also requested in this decision, or by some other measure. You will need to provide a scientifically valid justification for the chosen method.

In your comments on the draft decision (DD), you agree to fulfil this request and indicate that you will identify the degradation products in the sediment simulation test (OECD TG 308). While ECHA agrees that you may obtain information on the degradation products from relevant simulation studies requested in this draft decision, ECHA has addressed the choice of compartment for simulation testing fully under section 15 (see Above).

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision:

Identification of the degradation products (Annex IX, Section 9.2.3.) by using an appropriate and suitable test method, as explained above in this section.

Notes for your consideration

Before providing the above information you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R.7b., Sections R.7.9.2.3 and R.7.9.4. These guidance documents explain that the data on degradation products is only required if information on the degradation products following primary degradation is required in order to complete the chemical safety assessment. Section R.7.9.4. further states that when substance is not fully degraded or mineralised, degradation products may be determined by chemical analysis.

18. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2.of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to

meet this information requirement.

You have sought to adapt this information requirement and provided the following justification for the adaptation "*In accordance with section 1 of REACH Annex XI, the study does not need to be conducted as in water, significant and substantial abiotic degradation of zinc bis(dibenzyldithiocarbamate) occurs via hydrolysis and data is available for the degradation products that are potentially available for direct uptake in aquatic organisms.*" ECHA understands that you propose to adapt the standard information requirement of Annex IX, Section 9.3.2. by stating that the registered substance is not expected to bioaccumulate based on information on the bioaccumulation potential of its degradation products. ECHA assumes that the degradation products you are referring to are the hydrolysis products identified in the hydrolysis study with the proposed analogue substance ZDMC (zinc bis(dimethyldithiocarbamate).

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.3.2., column 2, nor the general rule for adaptation of Annex XI, Section 1 because, as fully discussed in section 0 and request 5 of this decision, no valid hydrolysis study on the registered substance is present in the technical dossier. In absence of valid hydrolysis data on the registered substance, you have not demonstrated that the rate of hydrolysis is greater than that for uptake by the exposed organisms and hence that the likelihood of bioaccumulation of the registered substance is greatly reduced, as described in *ECHA Guidance on information requirements and chemical safety assessment*, Chapter R.7c, Section R.7.10.3.4 (version 3.0, June 2017). In addition, since information on the identity of the hydrolysis products of the registered substance is lacking, it is not possible to conclude on their possibly low bioaccumulation potential. Hence, ECHA concludes that, since no reliable hydrolysis data is available for the registered substance, the adaptation of the standard information requirement of Annex IX, Section 9.3.2. based on hydrolysis cannot be accepted.

The registered substance has a high potential to bioaccumulate (estimated partition coefficient log Kow of 5.41, as given in the read-across data matrix, and estimated adsorption coefficient log Koc of 9.42). Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In addition, information on relating PBT endpoints of degradation (including identification of degradation products) and aquatic toxicity is missing and has been requested in this decision. ECHA hence considers that due to the data gaps addressed in this decision at this stage the information in the chemical safety assessment (CSA) including the PBT/vPvB assessment is not complete. ECHA notes further that you have not provided adequate justification in your CSA or in the technical dossier for why there is no need to investigate further the bioaccumulation of the substance or its degradation products. On this basis, the CSA cannot be used to justify that there is no need to investigate further the bioaccumulation of the substance or its degradation products.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7c* (version 3.0, June 2017) bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2. ECHA Guidance defines further that results obtained from a test with aqueous exposure can be used directly for comparison with the B and vB criteria of Annex XIII of REACH Regulation and can be used for hazard classification and risk assessment. Comparing the results of a dietary study with the REACH Annex XIII B and vB criteria is more complex and has higher uncertainty. Therefore, the aqueous route of exposure is the preferred route and shall be used whenever technically feasible. If due to substance properties you decide to conduct the study using the dietary exposure route, you shall provide scientifically valid justification for your decision. You shall also attempt to estimate the corresponding BCF value from the dietary test data by using the approaches given in Annex 8 of the OECD 305 TG. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG.

In your comments on the draft decision, you indicate that you intend to undertake a phased testing approach for the environmental fate related information requirements requested in this decision by first performing the degradation studies and identifying the degradation products (see above requests 15-17). You indicate that you will decide on the need to conduct the bioaccumulation study after reliable information becomes available on the bioaccumulation potential of the degradation products.

ECHA notes that guidance on how degradation products should be considered for various standard information requirements is given in different sections of ECHA's Guidance on Information Requirements and Chemical Safety assessment (e.g. Chapter R.7b, Version 4.0, June 2017; Chapter R.11, Version 3.0, June 2017).

ECHA notes further that if you intend to adapt the current information requirement, a scientifically valid justification will need to be provided as to why the CSA does not indicate the need to study the bioaccumulation of the substance.

Furthermore, in the comments on the DD you indicate that, if after performing the simulation studies, the newly derived information indicates that further bioaccumulation testing is required, you intend to submit a testing proposal for a fish bioaccumulation study. You propose a dietary exposure route for the bioaccumulation study due to the low water solubility of the registered substance (2.3 µg /L).

ECHA notes that a possible future testing proposal is considered to be inadmissible because the information requirement is already subject to this compliance check process.

Regarding the exposure route for the bioaccumulation study, ECHA notes that, for the reasons indicated in the draft decision, the aqueous route of exposure is the preferred route and shall be used whenever technically feasible. If due to substance properties you decide to conduct the study using the dietary exposure route, you shall provide scientifically valid justification for your decision. You shall also attempt to estimate the corresponding BCF value from the dietary test data by using the approaches given in Annex 8 of the OECD 305 TG. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision. Bioaccumulation in fish: aqueous or dietary exposure bioconcentration fish test (test method: OECD TG 305); aqueous exposure is the preferred route and shall be used whenever possible. The bioaccumulation or bioconcentration of each relevant constituent present in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study. For the PBT/vPvB assessment, the bioaccumulation or bioconcentration potential of degradation products shall also be investigated.

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), Chapter R.11.4. and Figure R.11-4 on the PBT assessment for further information on the integrated testing strategy for the bioaccumulation assessment of the registered substance. In particular, you are advised to first conclude whether the registered substance may fulfil the REACH Annex XIII criteria of being persistent or very persistent, and then to consult the PBT assessment for Weight-of-Evidence determination and integrated testing strategy for bioaccumulation assessment. You should revise the PBT assessment when information on bioaccumulation is available.

In addition, you are advised to consult the ECHA Guidance on the information requirements and chemical safety assessment, Chapters R.4, 5, 6, R.7b and R.7c. If you decide to adapt the testing requested according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation, ECHA refers you to the advice provided in practical Guides 4, 5 and 6.

Since there are indications that the substance may be difficult to test, you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6, in order to maintain the parent substance in the solution.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 15 March 2017.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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).

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.

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

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

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

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-57 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.