~~Confidential~~

Helsinki, 02 November 2023

Addressees
Registrant(s) of [redacted] as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
22/12/2017

Registered substance subject to this decision ("the Substance")
Substance name: bis[1-carbamimidoyl-kN'-urea-kO)]copper(2+) dinitrate
EC/List number: 800-038-5

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***7 August 2026***.

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

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

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

2. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111)

3. Adsorption/ desorption screening (Annex VIII, Section 9.3.1.; test method: EU C.18/OECD TG 106)

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

4. Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2; test method: EU B.58/OECD TG 488) in transgenic mice or rats, oral route on the following tissues: male germ cells tissues collected from the seminiferous tubules.

5. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

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

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

8. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25./OECD TG 309) at a temperature of 12°C.

9. Identification of degradation products (Annex IX, 9.2.3.; test method: EU C.25/OECD TG 309).

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

Information required depends on your tonnage band

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

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

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

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

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

Appendix 1: Reasons for the decision

Contents

0. Reasons common to several requests

0.1. *Assessment of your adaptations for the long-term aquatic toxicity testing*

1 Similar considerations are relevant for the adaptation of the information requirements on long-term toxicity testing on aquatic invertebrates (Annex IX, Sections 9.1.5) and on fish (Annex IX, Sections 9.1.6.) which are therefore addressed here, before addressing endpoint-specific issues under Requests 6 and 7.

0.1.1. Information provided

2 For both of information requirements on aquatic toxicity you have provided the following justification:

3 "*According to REACH Annex Section 3 and ECHA R.5 guidance, to avoid unnecessary animal testing, testing in accordance Annex IX may be omitted if exposure is absent or not significant throughout the whole life cycle of the substance, based on the exposure scenario(s) developed in the Chemical Safety Report. As described in the CSR, no environmental exposure has been demonstrated during the different steps of lifecycle of* [redacted] *Therefore, no release to environment is expected. When included in article* [redacted] *Concerning classification and labelling needs,* [redacted] *is already classified as hazardous to aquatic environment: aquatic acute (category 1, with a M factor of 10) and aquatic chronic (category 1). Additional testing will not provide useful data for this purpose (except for chronic M factor). For PBT/VPvB assessment, persistence and bioaccumulation criteria are not met,* [redacted] *is not considered as PBT/VPvB. Furthermore, T criteria is already an evidence in regard to acute toxicity testing on invertebrates, mutagenicity results and repeated exposure toxicity by oral route. Additional testing will then not provide useful data for PBT/VPvB assessment.*"

0.1.2. Assessment of the information provided

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

5 We understand that you claimed adaptation under Annex XI, Section 3.2 (a) and/or (c) (Substance-tailored exposure-driven testing) and therefore, evaluated your adaptation against requirements of this section of REACH.

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

(a) It can be demonstrated that all the following conditions are met:
   i. the absence or no significant exposure in all scenarios of the manufacture

and all identified uses referred to in Annex VI, Section 3.5., and

ii. a PNEC can be derived from available data, which:
- must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes and therefore must be based on reliable information on the hazardous properties of the substance on at least three trophic levels;
- must take into account the increased uncertainty resulting from the omission of the information requirement, in this case by selecting an appropriate assessment factor (AF) as described in Guidance on IRs and CSA, Section R.10.3.
- the ratio between the results of the exposure assessment (PECs) and the PNEC are always well below 1

(c) For substances incorporated in articles with no intended releases, the following conditions are met:

i. the substance is not released during its life cycle and,

ii. the likelihood that workers and the general public are exposed to the substance under normal or reasonable foreseeable conditions is negligible, and

iii. the substance is handled according to the conditions as set out in Article 18(4)(a) to (f) during all manufacturing and production stages including the waste management of the substance during these stages.

0.1.2.1. *Exposure assessment for all life-cycle stages are not provided (Section 3(2)a)*

7 According to Annex XI, Section 3.1(a)(i) of REACH, the exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses.

8 In the CSR you provide two exposure scenarios (ES): ES1 Use at industrial sites - Production of gas generators and ES2 Use at industrial sites - Development of gas generators (prototype). Your CSR does not provide an exposure scenarios for further life-cycle stages before produced gas generators are disposed as waste, e.g. covering [redacted] etc.

9 In the absence of this information, the adaptation is not based on rigorous exposure assessment in accordance with Annex XI, section 3.2.

10 In your comments to the draft decision you acknowledge the need to review and update the dossier. You propose to refine the lifecycles of the Substance to address the exposure scenarios for further lifecycle stages before produced gas generators are disposed as waste, e.g. covering [redacted] etc.

0.1.2.2. *RCRs for marine/freshwater are not well below 1 (Section 3(2)a)*

11 Under Annex XI, Section 3.2(a), a study may be omitted only if it can be demonstrated that exposure of the environment is always well below the derived PNECs, taking full account of the increased uncertainty resulting from the omission of the information requirement.

12 In your chemical safety report you do not report results of exposure estimation and risk characterisation for the local scale and for the regional scale you report results of the risk characterisation with RCRs for marine and freshwater of [redacted] and [redacted] respectively.

13 Thus, you have not demonstrated that the ratio between the PECs and PNECs are always well below 1 for marine and fresh waters neither at local nor at regional scales and the requirements of Annex XI, section 3.2(a)(ii) are not met.

14 In your comments to the draft decision you propose to review and demonstrate in the context of CSR that the ratios between PECs and PNECs are always well below 1 for marine and fresh environment at local and regional scales.

0.1.2.3. *The Substance is not handled under strictly controlled conditions (Section 3(2)c)*

15 According to Article 18 (4) to demonstrate strictly controlled conditions:

(a) the substance is rigorously contained by technical means during its whole lifecycle including manufacture, purification, cleaning and maintenance of equipment, sampling, analysis, loading and unloading of equipment or vessels, waste disposal or purification and storage;
(d) in the case of cleaning and maintenance works, special procedures such as purging and washing are applied before the system is opened and entered.

16 Guidance on Intermediates, Section 2.1. explains that "*Release of the substance should be prevented through containment systems, such as combinations of suitable mechanical barriers (e.g. enclosures) and air dynamic barriers (e.g. Local Exhaust Ventilation (LEV) as integrated part of the containment and differential pressure). […]* In containment level 2, LEV is applied, but the LEV is not further integrated into a system of mechanical barriers. Since the substance is still manipulated directly and thus PPE may be required, in general, level 2 does not constitute rigorous containment. […] *It should be emphasized that strictly controlled conditions must be achieved without taking into account the use of personal protective equipment (PPE) except for the exceptional situations hereunder (accidents, incidents, maintenance and cleaning).*"

17 In your CSR you indicate that:

1. "[redacted]". (ES1)
2. "[redacted]." (ES1)
3. "[redacted]." (ES2)
4. "[redacted] […] [redacted]". (ES1) No information provided about special procedures before the cleaning/maintenance operations for the ES2.

18 The use of LEV without use of partial/full mechanical enclosure and use of PPE does not justify rigorous containment by technical means. Furthermore, there is no special procedures such [redacted] for both ESs reported in the CSR.

19 Therefore, you have not demonstrated that the Substance is rigorously contained by technical means throughout the life cycle and the requirement of Annex XI, section 3.2 (c) (iii) is not met.

20 In your comments to the draft decision you mention: *"we will also work on the determination of the Substance handled under strictly controlled conditions"*. We understand that you indicate the intention to demonstrate that the Substance is handled under strictly controlled conditions[2].

0.1.2.4. *The Substance is released during its life cycle (Section 3(2)c)*

21 The substance must not be released during its life cycle.

22 In the CSR for each reported ES you note that release factor to air after on site risk management measures applied is [redacted].

23 Thus, this condition is not met.

24 We further note that your considerations on the classification and labelling and on the PBT/vPvB assessment do not relate to any valid adaptation rule under Annex IX, Section 9.1 and Annex XI, Section 3.2.

25 Therefore, your proposed adaptation under Annex XI, Section 3.2 (a) and (c) is rejected.

26 Based on the information provided in your comments and in the dossier there is currently no information available to assess whether your adaptation fulfils the requirements of Section 3 of Annex XI to the REACH Regulation, as you have not provided a thorough and rigorous exposure assessment. You remain responsible for complying with this decision by the set deadline.

0.2. *Assessment of your adaptation for the degradation testing*

27 Similar considerations are relevant for the application of the Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2), which are therefore addressed here, before addressing endpoint-specific issues under Request 8.

28 We understand that you have adapted this information requirement by using Annex XI, Section 3.2. and therefore evaluated your adaptation against requirements of this general adaptation rule in REACH. To support the adaptation, you have provided following information:

29 *"The study does not need to be conducted because direct and indirect exposure of sediment is unlikely. As described in the CSR, the lack of environmental exposure has been demonstrated during the different steps of lifecycle of [redacted]. The [redacted]*

[2] Please consult Guidane on intermediates and Practical Guide 16: How to assess whether a substance is used as an intermediate under strictly controlled conditions and how to report the information for the intermediate registration in IUCLID.

Therefore, no release to environment is expected. [redacted]*. Sediment simulation testing is then not necessary."*

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

31 You refer to sediment simulation testing and to a ground for adaptation related to that simulation testing, not to the legal basis relevant for water simulation testing.

32 Therefore, your adaptation is rejected.

Reasons related to the information under Annex VIII of REACH

1. Screening for reproductive/developmental toxicity

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

1.1. *Information provided*

34 You have provided:

i. a Reproduction/Developmental Toxicity Screening Test (2013) with the Substance

1.2. *Assessment of the information provided*

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

1.2.1. The provided study does not meet the information requirement

36 To fulfil the information requirement, a study must comply with EU B.63/OECD TG 421 or EU B.64/OECD TG 422 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the highest dose level aims to induce toxicity or aims to reach the limit dose;

37 The study (i) is described as a a Reproduction/Developmental Toxicity Screening Test.

38 The study does not cover the key parameters of EU B.63/OECD TG 421

a) the highest dose levels tested was 300 mg/kg bw/d (i.e., below the limit dose of the OECD TG 421) and no adverse effect were observed.

39 Based on the above, the information you provided do not fulfil the information requirement.

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

41 In your comments on the draft decision, you submitted an explantion for the dose selection. ECHA has assessed the information against the requirement in OECD TG 421. The information you have provided in your comments addresses the incompliances identified in this decision for this information requirement. You also indicate that you will update the registration dossier to include the OECD TG 407 study results and include a complete justification for the maximum tolerated dose used in OECD TG 421. However, as the this data is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

1.3. *Specification of the study design*

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

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

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

2. Hydrolysis as a function of pH

45 Hydrolysis as a function of pH is an information requirement under Annex VIII to REACH (Section 9.2.2.1.).

2.1. *Information provided*

46 In your dossier, you have provided the following information:

47 *"According to preliminary water solubility tests and analytic report, [redacted] is dissociated in water at pH 4, 7 and 9, and lead to the formation of copper (ion) and N-guanylurea. These two products are stable and therefore, they are used to follow up the concentration of [redacted] in the different media. [redacted] is a substance which is stable according to analytical report at pH under 4 and remaining as a complex to form a visible suspension."*

2.2. *Assessment of the information provided*

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

2.2.1. No legal basis

49 Information on hydrolysis as a function of pH or an adaptation under Column 2 of Annex VIII must be provided.

50 You did not provide any legal basis for the information provided. The provided information describe only the dissociation process of the Substance. You have not investigated the hydrolysis behaviour of the Substance at three pHs: 4, 7 and 9 according to the OECD 111 specifications described above. Your dossier does not contain any measured half-life or DT50 value that would inform on hydrolytical stability or instability of the Substance at pH 4, 7 and 9. In addition, there is no information about the formation and identity of possible hydrolysis products.

2.2.2. No demonstration of ready biodegradability

51 In your comments on the draft decision, you have submitted an adaptation arguing that the Substance is ready biodegradable.

52 Under Annex VIII, Section 9.2.2.1., Column 2, first indent, the study may be omitted if the substance is readily biodegradable. According to OECD 301 TG, the pass level for ready biodegradability measured as DOC is the *decline* of DOC (i.e. the concentration of DOC *removed*) within the 28-day period.

53 In your comments to the draft decision you refer to an OECD 301C TG study included in your dossier: *"The testing results reached 96% DOC in the 28-days period. (…) the BOD calculation demonstrated that degradation has been reached above 70% after 14th day to 76% until the 28th day."* You further compare these values with pass levels for ready biodegradability according to OECD 301 TG (70% removal of DOC and 60% of ThOD or $ThCO_2$ production for respirometric methods) and conclude that the Substance is readily biodegradable, therefore, adaptation based on column II, Annex VIII, section 9.2.2.1 should apply.

54 Based on your dossier, the DOC = 96% is not the pass level, but the average percentage detection of DOC, i.e. the DOC that *remained* after 28 days in the test solution. This

demonstrates that the Substance was not fully mineralised, and on that basis it cannot be concluded as readily biodegradable. This conclusion is supported by the key result reported in your dossier, namely BOD = 0% (-5%). In addition, the value of BOD > 70% after 14th day and 76% until 28th day mentioned in your comment is the result for the reference compound (aniline).

55 On that basis your adaptation is rejected.

56 Therefore, the information requirement is not fulfilled.

3. Adsorption/ desorption screening

57 Adsorption/desorption screening is an information requirement under Annex VIII to REACH (Section 9.3.1).

3.1. *Information provided*

58 You have adapted this information requirement by using Column 2 of Annex VIII, Section 9.3.1, first indent. To support the adaptation, you have provided following information:

59 *"(…) In accordance with column 2 of REACH Annex VIII, the test was not performed because n-octanol/water partition coefficient of n-guanyl urea is low (log Kow < 0.3) suggesting a low affinity for suspended matter."*

60 You also stated another ground for adaptation as follows: "*In addition, the environmental exposition is not expected because the production is performed in closed system without any environmental release (cf. CSR part 9)*."

3.2. *Assessment of the information provided*

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

3.2.1. Assessment of adaptation based on low n-octanol-water partition coefficient

62 Guidance on IRs and CSA, Section R.7.1.15.4 explains that a *measured* adsorption coefficient is usually needed for ionising substances, since it is important to have information on pH-dependence (cationic substances in particular generally adsorb strongly). In such a case, log Kow may not represent the substance's potential for adsorption.

63 In your registration dossier you mention that the Substance is *"dissociated in water at pH 4, 7 and 9"* which leads *"to the formation of copper (ion) and N-guanylurea"*. You also refer to the biodegradation study which provides the following information: "*Under the test conditions of this study, the test item: Copper Guanylurea nitrate, a salt formed from copper-N-guanylurea complex ion (cationic component) and nitric acid ion (anionic component) is rapidly hydrolyzed in water (transformation products: N-guanylurea, nitric acid ion and copper).*" The above information indicate the ionisable properties of the Substance.

64 You have not addressed this indication of ionisable properties and its impact on the potential for adsorption of the Substance.

3.2.2. Assessment of adaptation based on exposure considerations

65 Annex VIII, Section 9.3.1., Column 2 does not allow omitting the need to submit information on adsorption/desorption on the basis of exposure considerations. Furthermore, according

to the Annex XI, Section 3.1 substance-tailored exposure-driven testing adaptation options listed in Annex XI, section 3 are not applicable to the information requirement under Annex VIII, Section 9.3.1.

66 Therefore, your adaptation is rejected and information requirement is not fulfilled.

67 In your comments to the draft decision you propose to update your dossier with the adsorption/desorption studies for N-guanylurea, copper and nitric acid - the substances formed in result of enclosed chemical reactions that the Substance is subject to. You also mention that additional tests are ongoing to characterise the mechanism of these reactions. In case this mechanism cannot be characterised, you propose to conduct the new adsorption/desorption study.

68 However, at present no adsorption/desorption studies are available in the dossier, therefore, no conclusion on the compliance can currently be made. On that basis the above request remains in this decision.

3.3. *Study design and test specifications*

69 To fulfil the information requirement for the ionic Substance at the 100 tonnes per year band, the batch equilibrium method (test method OECD TG 106) would be the most appropriate (Guidance on IRs and CSA, Section R.7.1.15.4).

Reasons related to the information under Annex IX of REACH

4. Transgenic rodent somatic and germ cell gene mutation assays

70 Under Annex IX, Section 8.4, column 2 of REACH, a germ cell genotoxicity investigation must be considered if two conditions are fulfilled: 1) an *in vivo* genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity on the basis of all available data.

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

72 In relation to the condition 1) above, your dossier contains positive results for an in vivo mammalian alkaline comet assay on liver cells (TG 489, 2016). Moreover, the in vitro gene mutation study in mammalian cells (TG476, 2014) showed positive results, which raise the concerns for gene mutations.

73 In relation to the condition 2) above, ECHA notes that you have self-classified the Substance as Muta 2 according to CLP, supporting the need to investigate further (see ECHA Guidance R.7a, section R.7.7.6.3, p.573). Moreover, you have not provided toxicokinetic data nor your considerations for germ cell mutagenicity. Furthermore, your dossier does not contain any data allowing to conclude on germ cell mutagenicity.

74 Therefore, as the conditions 1) and 2) explained above are met, ECHA concludes that an appropriate in vivo germ cell mutagenicity study is necessary to address the concern identified in somatic cells in vivo.

4.1. *Information provided*

75 You have not submitted any information for this requirement.

4.2. *Assessment of the information provided*

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

77 You have not provided any information for this information requirement.

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

4.3. *Test selection*

79 According to the Guidance on IRs & CSA, Section R.7.7.6.3 the Transgenic rodent somatic and germ cell gene mutation assay ("TGR assay", OECD TG 488) in germ cells is suitable to follow up a positive *in vivo* result in somatic cells on a substance showing gene mutation concern.

80 In the comments to the draft decision, you agree that there is a data gap for Annex IX, Section 8.4., column 2. However, you state that, to your knowledge, no CRO is able to perform the requested test on tubule germ cells.

81 Therefore, you propose an alternative strategy and intend to investigate gene mutations in the liver with the TGR assay and to investigate germ cell genotoxicity with the Mammalian spermatogonial chromosomal aberration test (OECD TG 483).

82 Regarding the statement on the difficulty to find suitable CROs, in your comments to the draft decision, ECHA would like to mention, that we are aware of two European-based CROs [redacted]

[redacted] that perform the TGR assay in germ cells.

83 Regarding your proposal to investigate the liver in the TGR assay, please note that it is at your discretion to analyse somatic tissues in addition to male tubule germ cells as requested in this decision.

84 Moreover, ECHA notes that your proposal to perform an OECD TG 483 study on male germ cells is not appropriate because that test investigates chromosomal abberations, whereas the Substance raised a gene-mutation concern.

85 In addition, performing both the TGR assay on the liver and the Mammalian chromosomal aberration test on spermatogonia, as suggested in your comments, would imply testing more animals than only performing the TGR assay on male germ cells, with or without additional sampling of liver cells from the same animals.

86 It is also not clear from your proposed strategy how you intend to demonstrate that the germ cells are exposed to the Substance.

4.4. *Specification of the study design*

87 According to the test method OECD TG 488, the test must be performed in transgenic mice or rats.

88 Also, according to the test method OECD TG 488, the test substance is usually administered orally.

89 Based on the recent update of the OECD TG 488 (2022), you are requested to follow the new 28+28d regimen, as it permits the testing of mutations in somatic tissues and as well as in tubule germ cells from the same animals.

90 According to the test method OECD TG 488, the test must be performed by analysing male germ cells collected from the seminiferous tubules.

5. Pre-natal developmental toxicity study in one species

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

5.1. *Information provided*

92 You have adapted the following standard information requirement(s) without stating the legal basis, although you make reference to the possibility to adapt under Annex XI 3.2.(a)-(c):

- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

93 You have provided a justification for your adaptation in Section 7.8.1 and 7.8.2 of your dossier, and you conclude that the substance is incorporated into an article and is not released during the whole life cycle and that the likelihood of exposure of man or the environment is negligible.

94 To support the adaptation, you have provided the following information

(i) a data waiver: *"The product is* [redacted] *manufactured* [redacted] *. It includes air and human monitoring. According to*

guidance Chapter R 5. : "REACH provides for the option that information requirements may be adapted based on the justification: - that exposure is absent or not significant (Annex XI, section 3.2(a) (i); Annex VIII column 2 section 8.6.1 and 8.7.1) or unlikely (Annex IX column 2 section 9.4) or, - that strictly controlled conditions (Annex XI section 3.2 (b)) apply for the whole life cycle of the substance (including the waste stage), - and for substances incorporated into an article that the substance is not released during the whole life cycle and that the likelihood of exposure of man or the environment is negligible (Annex XI section 3.2 (c) (i) and 3.2 (c) (ii))." All manufacturing occurs in a closed environment and remotely because [redacted].

5.2. *Assessment of the information provided*

95 ECHA understands that you intend to apply a substance-tailored exposure-driven testing according to Annex XI, Section 3.2. (a), (b) and (c) for the endpoints listed above.

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

5.2.1. Substance-tailored exposure-driven testing adaptation rejected

97 As stated in Annex XI, Section 3, testing in accordance with Sections 8.6 and 8.7 of Annex VIII and in accordance with Annexes IX and X may be omitted based on the exposure scenario(s) developed in the CSR, by providing an adequate and scientifically-supported justification based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I and by communicating the specific conditions of use through the supply chain. Any one of the following criteria 3.2. (a), (b) or (c) shall be met. In particular:

98 (a) the manufacturer or importer demonstrates and documents that all of the following conditions are fulfilled:

i. the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5.;

ii. a DNEL or a PNEC can be derived from results of available test data for the substance concerned taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL or PNEC is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes. For this purpose and without prejudice to column 2 of Sections 8.6 and 8.7 of Annexes IX and X, a DNEL derived from a 28-day repeated dose toxicity study shall not be considered appropriate to omit a 90-day repeated dose toxicity study, and a DNEL derived from a screening test for reproductive/developmental toxicity shall not be considered appropriate

to omit a prenatal developmental toxicity study or an extended one-generation reproductive toxicity study.

iii. the comparison of the derived DNEL or PNEC with the results of the exposure assessment shows that exposures are always well below the derived DNEL or PNEC.

99 (b) where the substance is not incorporated in an article the manufacturer, or the importer demonstrates and documents for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Art 18(4)(a) to (f) apply;

100 (c) where the substance is incorporated in an article in which it is permanently embedded in a matrix or otherwise rigorously contained by technical means, it is demonstrated and documented that all of the following conditions are fulfilled:

i. the substance is not released during its life cycle; and

ii. the likelihood that workers or the general public or the environment are exposed to the substance under normal or reasonably foreseeable conditions of use is negligible; and

iii. the substance is handled according to the conditions set out in Article 18(4)(a) to (f) during all manufacturing and production stages including the waste management of the substance during these stages.

101 REACH Annex XI 3.2 specifies that in all cases, adequate justification and documentation shall be provided. According to ECHA Guidance Chapter R.5: Adaptation of information requirements (version 2.1 December 2011) in order to justify for a certain endpoint, the omission of the standard information requirement, a high level of confidence is needed to demonstrate no or no significant exposure or no release.

102 In accordance with REACH Annex XI Section 3.2(b) the demonstration and documentation of the strictly controlled conditions (SCC) for all relevant scenarios should be set out according to Article 18 (4) (a) to (f). In order to demonstrate that strictly controlled conditions are met, the registrants are required to provide a detailed description of all activities for each processing step throughout the whole life cycle of the substance according to ECHA Guidance on Intermediates (Version 2 December 2010) and to the corresponding practical guide (Practical Guide 16, June 2014).

5.2.1.1. *Exposure assessment (Section 3(2)(a))*

103 The adaptation must demonstrate absence or no significant exposure in all scenarios.

104 In your dossier, you have provided the following information:

105 In the CSR you provide two exposure scenarios (ES): ES1 Use at industrial sites - Production of gas generators and ES2 Use at industrial sites - Development of gas generators (prototype). Your CSR does not provide an exposure scenarios for further life-cycle stages before produced gas generators are disposed as waste, e.g. [redacted] etc.

106 In the comments to the draft decision, you propose to conduct a full and comprehensive exposure assessment and risk characterisation to demonstrate lack of risk to human health and environment without supporting information. You indicate your intention to provide an update of your registration dossier by the end of the year (2022), but no update has been submitted.

107 You have not demonstrated "absence of or no significant exposure in all scenarios of the manufacture and all identified uses".

108 In exposure scenario 1, contributing scenario 3, for example, you have used ECETOC TRA, version 3 to estimate [redacted] for dermal exposure. For the same exposure scenario, you calculate an RCR of [redacted] for combined routes, systemic, long-term exposure.

109 In the absence of information for part of the life-cycle, the adaptation is not based on rigorous exposure assessment in accordance with Annex XI, section 3.2.

110 Your exposure assessment is not thorough as you have only used ECETOC TRA which is a first tier exposure modelling tool. Demonstration that no significant exposure via inhalation or skin can occur cannot be done by using Tier 1 exposure modelling tool(s) as this is generally conservative, but also very uncertain. To demonstrate absence of or no significant exposure measured data or higher tier exposure modelling should be used.

111 REACH Annex XI, section 3.2(a)(ii) explicitly states "… a DNEL derived from a screening test for reproductive/developmental toxicity shall not be considered appropriate to omit a prenatal developmental toxicity study."

112 You have used a screening test for reproductive/developmental toxicity to derive the worker long-term systemic DNEL for inhalation effects and worker long-term, systemic DNEL for dermal effects.

113 Furthermore, as explained above (request 1) the screening test for reproductive/developmental toxicity is rejected.

114 Therefore, the DNEL is considered inappropriate and the information available in your comments to the draft decision is not capable of changing this conclusion.

5.2.1.2. *Strictly controlled conditions (3(2)(b))*

115 The substance must be handled under strictly controlled conditions.

116 You have not provided evidence of strictly controlled conditions throughout the life cycle as set out in Article 18(4)(a) to (f).

117 You have estimated exposures that are not indicative of strictly controlled conditions, for example in exposure scenario 1, contributing scenario 3 you estimate dermal exposure of [redacted].

118 Therefore, the use of the Substance under strictly controlled conditions is not demonstrated.

5.2.1.3. *Substance incorporated into an article (3(2)(c))*

119 To benefit from this adaptation, the substance must not be released during its life cycle.

120 You have not provided evidence to demonstrate that the substance is not released from the article during its lifecycle. As described above, you have demonstrated that workers are exposed to the substance and the substance is not handled under strictly controlled conditions.

121 Therefore criterion 3.2.(c) is not fulfilled

122 Based on the above, your adaptation according to Annex XI, Section 3 is rejected.

123 Based on the information provided in the comments, there is currently no information to assess whether your adaptation fulfils the requirements of Section 3 of Annex XI to the REACH Regulation, as you have not provided a thorough and rigorous exposure assessment. You remain responsible for complying with this decision by the set deadline.

5.2.2. Classification criteria are not met

124 In the comments to the draft decision, you indicate *"based on the result of the OCDE 488 (alternatively 483), and if relevant, a testing proposal will be submitted. This proposal also considers the compliance to articles 13 and 25 and annex XI section 1.2 of REACH Regulation 1907/2006/EC to avoid unnecessary animal testing."*

125 Regarding potential classification for germ cell mutagenicity we have assessed the information and identified the following issue:

126 Under Annex IX, Section 8.7., Column 2, the study does not need to be conducted if the substance is known to be a germ cell mutagen, meeting the criteria for classification in the hazard class germ cell mutagenicity (category 1A or 1B) and appropriate risk management measures are implemented.

127 The assessment must be made based on the information available.

128 The study under request 4.) is not yet available. Consequently, it can not be judged if the classification criteria for Muta. 1A/1B are met

129 Based on the above, your adaptation is rejected.

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

5.3. *Specification of the study design*

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

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

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

6. Long-term toxicity testing on aquatic invertebrates

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

6.1. *Information provided*

135 You have provided an adaptation under Annex XI, Section 3.2 (Substance-tailored exposure-driven testing).

6.2. *Assessment of the information provided*

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

137 As explained under section 0.1. of Appendix 1. (Reasons common to several requests) your adaption is rejected.

138 In your comments to the draft decision you propose to review and update the CSR which was already addressed under section 0.1 of Appendix 1 (Reasons common to several requests).

139 You also mention: *"(…) we will address a testing proposal if needed to investigate further the potency of the substance to aquatic organisms and depending on the CSR updated conclusions. We assume this proposal strategy also take into consideration the application*

of articles 13 and 25 of REACH (…) to avoid unnecessary animals testing that we will conduct if the CSR update failed to demonstrate the absence of risks to the aquatic organisms."

140 We acknowledge your intention to provide the testing proposal. There is a data gap and the assessment must be based on the information available at this stage, not based on hypothetical considerations. The minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI or Annex IX, Section 9.1.5., column 2

141 On that basis the above request remains in this decision.

7. Long-term toxicity testing on fish

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

7.1. *Information provided*

143 You have provided an adaptation under Annex XI, Section 3.2 (Substance-tailored exposure-driven testing).

7.2. *Assessment of the information provided*

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

145 As explained under section 0.1. of Appendix 1. (Reasons common to several requests) your adaption is rejected.

146 In your comments to the draft decision you propose to review and update the CSR which was already addressed under section 0.1 of Appendix 1 (Reasons common to several requests).

147 You also mention: *"(…) we will address a testing proposal if needed to investigate further the potency of the substance to aquatic organisms and depending on the CSR updated conclusions. We assume this proposal strategy also take into consideration the application of articles 13 and 25 of REACH (…) to avoid unnecessary animals testing that we will conduct if the CSR update failed to demonstrate the absence of risks to the aquatic organisms."*

148 We acknowledge your intention to provide the testing proposal. There is a data gap and the assessment must be based on the information available at this stage, not based on hypothetical considerations. The minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI or Annex IX, Section 9.1.6., column 2.

149 On that basis the above request remains in this decision.

7.3. *Study design and test specifications*

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

8. Simulation testing on ultimate degradation in surface water

151 Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

8.1. *Information provided*

152 In your registration dossier, you provided an adaptation without legal basis.

8.2. *Assessment of the information provided*

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

8.2.1. No legal basis

154 As explained under section 0.1. of Appendix 1. (Reasons common to several requests) your adaption is rejected.

8.2.2. No demonstration of readily biodegradable

155 In your comments to the draft decision, you submitted a Column 2 adaptation arguing that the Substance is readily biodegradable.

156 Under Annex IX, Section 9.2.1.2., Column 2, second indent, the study may be omitted if the substance is readily biodegradable.

157 In your comments to the initial draft decision you refer to the results of OECD 301C TG study included in your registration dossier and conclude that the Substance is readily biodegradable. On that basis you propose to waive the simulation according to column II, Annex VIII, section 9.2.2.1.

158 However, as explained under Request 2. (Hydrolysis as a function of pH), the Substance is not readily biodegradable under the test conditions.

159 Therefore, the adaptation based on column II, Annex VIII, section 9.2.2.1 does not apply.

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

8.3. *Study design and test specifications*

161 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

162 You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (Guidance on IRs and CSA, Section R.11.4.1.1.3.).

163 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

164 As specified in Guidance on IRs and CSA, Section R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test material concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Paragraph 52 of the OECD TG 309 provides that the "*total recovery (mass balance) at the end of the experiment should be between 90%*

and 110% for radiolabelled substances, whereas the initial recovery at the beginning of the experiment should be between 70% and 110% for non-labelled substances". NERs contribute towards the total recovery. Therefore, the quantity of the (total) NERs must be accounted for the total recovery (mass balance), when relevant, to achieve the objectives of the OECD TG 309 to derive degradation rate and half-life. The reporting of results must include a scientific justification of the used extraction procedures and solvents.

165 For the persistence assessment by default, total NERs is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NERs may be differentiated and quantified as irreversibly bound or as degraded to biogenic NERs, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website (NER - summary 2019 (europa.eu)).

166 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 309; Guidance on IRs and CSA, Section R.11.4.1.).

9. Identification of degradation products

167 Identification of degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

9.1. *Information provided*

168 You did not provide any information for this information requirement which, therefore, is not fulfilled.

9.1.1. No demonstration of readily biodegradable

169 Under Annex IX, Section 9.2.3., Column 2, the study may be omitted if the substance is readily biodegradable.

170 In your comments to the initial draft decision you refer to the results of OECD 301C TG study included in your registration dossier and conclude that the Substance is readily biodegradable. On that basis you propose to waive the simulation according to column II, Annex VIII, section 9.2.2.1.

171 However, as explained under Request 2. (Hydrolysis as a function of pH), the Substance is not readily biodegradable under the test conditions.

172 Therefore, the adaptation based on column II, Annex VIII, section 9.2.2.1 does not apply.

173 Therefore, this information requirement is not met.

9.2. *Study design and test specifications*

a) Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

174 Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported. In addition, identified transformation/degradation products must be considered in the CSA including PBT assessment.

175 To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (Request 8) must be conducted at 12°C and at a test concentration < 100 µg/L. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, e.g. 20°C) and at higher application rate (i.e. > 100 µg/L).

References

The following documents may have been cited in the decision.

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

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

Guidance on Intermediates; ECHA (2010).

Guidance on data-sharing; ECHA (2017).

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

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

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

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

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

Appendix 2: Procedure

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

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

The compliance check was initiated on 16 November 2021.

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

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

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

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Following the Board of Appeal's decision in case A-001-2022 ECHA revised the study design specifications for meeting the information requirement for simulation testing on ultimate degradation in surface water (Annex VIII, column 2, section 9.2 and/or Annex IX, first column, section 9.2.1.2).

Appendix 3: Addressees of this decision and their corresponding information requirements

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

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

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

Appendix 4: Conducting and reporting new tests for REACH purposes

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

1.1. Test methods, GLP requirements and reporting

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

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

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

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

1.2. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

(2) Information on the Test Material needed in the updated dossier
- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

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

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[4].

[4] https://echa.europa.eu/manuals