~~Confidential~~

Helsinki, 04 June 2024

Addressee
Registrant of THPC-urea-amine-JS as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
17 November 2022

Registered substance subject to this decision ("the Substance")
Substance name: Reaction products of tetrakis(hydroxymethyl)phosphonium chloride, urea and tetradecan-1-amine
EC/List number: 436-230-7

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 ***11 December 2028***.

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

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

1. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202).

2. Growth inhibition study on aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3/OECD TG 201).

3. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. A/B/C/D/E/F/OECD TG 301A/B/C/D/E/F or EU C.29./OECD TG 310) on relevant constituent(s)/fraction(s) of the Substance, as described under the corresponding appendix on reasons for the request.

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

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

5. *In vivo* genetic toxicity study also requested below (triggered by Annex VIII, Section 8.4., Column 2).

6. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: EU C.1./OECD TG 203).

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

7. *In vivo* genetic toxicity study (triggered by Annex IX, Section 8.4.4,) to be selected according to the following specifications:

a) If the results of the *in vitro* micronucleus study requested under request 4 are **negative:**

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

OR

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

b) If the results of the *in vitro* micronucleus study requested under request 4 are **positive:**

In vivo mammalian alkaline comet assay (test method: OECD TG 489) combined with *in vivo* mammalian erythrocyte micronucleus test (test method: OECD TG 474) in rats, or if justified, in mice, oral route. For the comet assay the following tissues shall be analysed: liver, glandular stomach and duodenum. For the micronucleus test:

- centromere staining must be performed if the substance induces an increase in the frequency of micronuclei in the OECD TG 474, unless the aneugenic potential has been conclusively investigated in the in vitro micronucleus study requested under Section 6.
- target tissue exposure must be demonstrated if the result of the OECD TG 474 is negative.

8. In case of a positive result in any of the somatic tissues in the Transgenic rodent somatic and germ cell gene mutation assays (OECD TG 488) (requested as one of the options under request 7):
    - Analysis of male germ cells collected, in line with request 7, from the seminiferous tubules (Annex IX, Section 8.4.5; test method: OECD TG 488).

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

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

The reasons for the requests are explained in Appendix 1.

Information required depends on your tonnage band

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

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, in Appendix I, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met, and the specification of the study design are provided. Only one study is to be conducted.

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

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

Appendix 1: Reasons for the request(s)

Reasons common to several requests

0.1. Read-across adaptation rejected

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

- *In vitro* micronucleus study (Annex VIII, Section 8.4.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study on aquatic plants (Annex VII, Section 9.1.2)
- Ready biodegradability (Annex VII, Section 9.2.1.1)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6)

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

3 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

4 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

0.1.1. Scope of the grouping of substances

5 You provide a read-across justification document under each relevant IUCLID section.

6 You predict the properties of the Substance from information obtained from the following source substances:

- ITC 826, UVCB condensation product of: tetrakis-hydroxymethylphosphonium chloride, urea and distilled hydrogenated C16-18 tallow alkylamine, EC 422-720-8.
- THPS, Tetrakis(hydroxymethyl)phosphonium sulphate (2:1), EC 259-709-0

7 In your comments to the draft decision you provided an updated read-across justification document which includes another source substance:

- Perform CC, Tetrakis [hydroxyl methyl] phosphonium chloride and urea, EC 500-057-6.

8 You provide the following reasoning for the prediction of (eco)toxicological/environmental fate properties:

9 Regarding ITC 826:

- "*both molecules are very similar regarding the chemical structure of their main components*."

- "*N-hexadecyl aminomethyl trishydroxymethyl phosphonium chloride is mainly present in ITC 826 whilst N-tetradecyl aminomethyl trishydroxymethyl phosphonium chloride is present in* [the Substance]";
- "*They have similar physico-chemical properties*".

10 Regarding THPS:

- *"This read-across is based on the hypothesis that the source and target substances have similar physico-chemical and toxicological properties because of their structural similarity (tetrakis hydroxymethyl phosphonium (THP+) salts, also called THPX compounds). This is explained by the fact that they have a similar route of synthesis, based on the mixture of tetrakis(hydroxymethyl)phosphonium salt with urea."*
- *"The only difference is that two tetrakis(hydroxymethyl)phosphonium salts are used: a sulfate for the source substance and a chloride for the target substance."*

11 In your read-across justification provided with the comments you provide the following reasoning regarding the Substance, the source ITC826 and the source Perform CC:

- *"In the case of the target substance Perform STi, the source ITC826 and the analogue Perform CC, they have all common functional groups, and common main constituents throughout.*

12 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substances.

0.1.1.1. Incomplete characterisation of the group members (UVCB)

13 Under Annex XI Section 1.5., Structural similarity for UVCB substances (Unknown or Variable composition, Complex reaction products or of Biological materials) must be established on the basis of similarities in the structures of the constituents, together with the concentration of these constituents and variability in the concentration of these constituents. Qualitative compositional as well as quantitative characterisation of the individual constituents of these substances must be provided, to the extent that this is measurable (Guidance on IRs and CSA, Section R.6.2.5.5.).

14 In your read-across justification, you provide information on the composition of Tetrakis[hydroxyl methyl] phosphonium chloride and urea (Perform CC) with EC/List 500-057-6. You state that the analogue substance ITC 826 contains hexadecyl aminomethyl trishydroxymethyl phosphonium chloride as the main constituent. However, you fail to provide information on the identity of the other constituents of that substance as well as quantitative information.

15 In addition, you indicate in the justification document a significant difference in the impurities of the target and source substances. You mention that "Formaldehyde is present as a minor constituent at < 0.1% in source substance. However, Formaldehyde is present at > 0.1% in target substance."

16 Without qualitative and quantitative information on the compositions of the Substance and of the source substances, it is not possible to assess whether the attempted predictions are compromised by the composition of the source substances.

17 In your comments to the draft decision, you have attached a read-across justification document which addresses the deficiencies identified above. However, as this information is currently not available in your registration dossier, the data gap remains. You must therefore submit this information in an updated registration dossier by the deadline set in the decision.

0.1.2. Predictions for (eco)toxicological properties

0.1.2.1. Missing supporting information to compare the properties of the substances

18 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substances (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

19 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar source substances cause the same type of effect. In this context, relevant, reliable and adequate information allowing to compare the properties of the source substances is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration with the Substance and the source substances.

20 For the source substances, you provide the study used in the prediction in the registration dossier. Apart from that study, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that both substances cause the same type of effects.

21 In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties. Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

0.1.2.2. Inadequate or unreliable source studies

22 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

(1) be adequate for the purpose of classification and labelling and/or risk assessment;
(2) have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement;
(3) cover an exposure duration comparable to or longer than the corresponding study that shall normally be performed for a particular information requirement if exposure duration is a relevant parameter.

23 Specific reasons why the studies on the source substances do not meet these criteria are explained further below under the applicable information requirement section 1, 2, 3, 4, 6, 7 and 8. Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Conclusion

24 Based on the above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH

1. Short-term toxicity testing on aquatic invertebrates

25 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

1.1. Information provided

26 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on the following experimental data from the source substances:

(i) Short-term toxicity testing on aquatic invertebrates based on OECD TG 202 (1995) with the source substance ITC 826, EC 422-720-8.

1.2. Assessment of the information provided

1.2.1. Read-across adaptation rejected

27 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA identified endpoint specific issue addressed below.

1.2.1.1. The provided study on the analogue substance does not meet the specifications of the test guideline

28 To fulfil the information requirement, a study must comply with OECD TG 202 (Article 13(3) of REACH). Therefore, the following specification(s) must be met:

Reporting of the methodology and results

a) the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation;
b) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

29 In study (i):

Reporting of the methodology and results

a) tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported;
b) on the analytical method adequate information, i.e. performance parameters of the method are not reported.

30 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, due to the lack of tabulated data on the number of immobilised daphnids, it is not possible to confirm the fulfilment of the validity criteria of the test and to assess the interpretation of the results. Furthermore, in the absence of adequate information on the analytical method, it is not possible to assess the reliability of the derived endpoints.

31 On this basis, the specification(s) of OECD TG 202 are not met.

32 Therefore, the information requirement is not fulfilled.

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

2. Growth inhibition study aquatic plants

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

2.1. Information provided

35 You have provided:

(i) Growth inhibition study on algae based on OECD TG 201 (2001) with the Substance.

36 In addition, you have also adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on the following experimental data from the source substances:

(ii) Growth inhibition study on algae similar to OECD TG 201 (1995) with the source substance ITC 826, EC 422-720-8.

2.2. Assessment of the information provided

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

37 To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Reporting of the methodology and results

a) the test conditions are reported (e.g., composition of the test medium);

b) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

c) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

38 In studies (i) and (ii):

Reporting of the methodology and results

a) on the test conditions, in study (ii) you have not specified the composition of the test medium;

b) tabulated data on the algal biomass determined daily for each treatment group and control are not reported in studies (i) and (ii);

c) on the analytical method adequate information, i.e. the results of the analytically determined exposure concentrations are not provided in studies (i) and (ii). In study (ii), the concentrations of the test material were measured using phosphorus assay.

39 Based on the above, the reporting of studies (i) and (ii) is not sufficient to conduct an independent assessment of their reliability. More specifically, due to the lack of tabulated data on the algal biomass and analytically determined exposure concentrations, the fulfilment of the validity criteria of the test (i.e. exponential growth and coefficient of variation in controls) cannot be assessed. Furthermore, in study (ii), you used a non-specific analytical method (quantification of phosphorus). As the algae medium may also contain phosphorus it is unclear whether the measured concentration provide adequate estimate of

the test material concentration. Therefore, it is also important to report the composition of the test medium in this study.

40 On this basis, the specifications of OECD TG 201 are not met in any of the provided studies.

2.2.2. Read-across adaptation rejected

41 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA identified deficiencies with the reliability of the provided study on the analogue substance as already addressed above under section 3.2.1.

42 Therefore, the information requirement is not fulfilled.

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

3. Ready biodegradability

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

3.1. Information provided

45 In your dossier, you have provided:

(i) a ready biodegradability study in water based on OECD TG 301F (2015) with the source substance ITC 826, EC 422-720-8.

46 In your comments to the draft decision we understand that you indicate your intention to adapt this information requirement using Annex XI, section 1.5. (grouping and read-across approach). You provide the following justification that the Substance is not readily biodegradable: "The existing similarity between Perform STi [i.e. the Substance] and ITC 826 [i.e. the source substance], related to physicochemical properties, chemical structure, and functional groups, allows that existing data for ITC 826 can be extrapolated to Perform STi."

3.2. Assessment of the information provided in your dossier

3.2.1. Read-across adaptation rejected

47 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA identified endpoint specific issue addressed below.

3.2.1.1. The provided study on the analogue substance does not meet the specifications of the test guideline

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

Reporting of the methodology and results

a) the results of measurements at each sampling point in each replicate is reported in a tabular form;
b) the calculation of the theoretical oxygen demand (ThOD) is described and justified;
c) for nitrogen-containing test materials, correction for nitrification is applied on the theoretical oxygen demand (*i.e.* $ThOD_{NO3}$) unless it can be demonstrated that nitrification did not occur (*e.g.* by monitoring changes in concentrations in nitrite

and nitrate).

49 In study (i):

Reporting of the methodology and results

a) the results of measurements at each sampling point in each replicate is not reported in a tabular form;
b) the calculation of the ThOD is not described
c) the test material corresponds to a nitrogen-containing substance and no correction for nitrification of the theoretical oxygen demand is reported.

50 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically,

- due to the lack of detailed results for each replicate, it is not possible to assess the fulfilment of the validity criteria of the OECD 301 F.
- because no correction for nitrification is reported, the reliability of the results cannot be assessed. Furthermore, as the calculation of the ThOD was not described, the interpretation of the results cannot be assessed.

51 On this basis, the specifications of OECD TG 301 F are not met.

52 In your comments to the draft decision and in the copy of a Robust Study Summary (RSS) attached to the comments you address the study deficiencies identified above. However, as this information 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 in the decision.

3.3. Assessment of the information provided in your comments to the draft decision

53 As explained in section 0.1.1.1., the read-across justification provided with your comments address the deficiencies identified in your dossier. However, as this information is currently not available in your registration dossier, the data gap remains. You must therefore submit this information in an updated registration dossier by the deadline set in the decision.

3.4. Study design and test specification

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

55 The revised introduction to the OECD Guidelines For Testing Of Chemicals, Section 3 Part I states that ready biodegradability tests are intended for pure substances but may also be relevant, on a case-by-case basis, to mixtures of structurally similar chemicals (i.e. which are composed of constituents expected to show similar degradation kinetics). However, such tests are not generally applicable for complex mixtures or substances (i.e. UVCB or multi-constituent substances) containing different types of constituents. For complex substances, a single ready biodegradability test does not allow to conclude on the ready biodegradability of all constituents and therefore, does not fulfil the information requirement. In section 1.2 you describe the Substance as "Reaction product of tetrakis(hydroxymethyl)phosphonium chloride, urea and distilled 1-tetradecylamine (Monomer) - solution in water". The main constituents are tetrakis(hydroxymethyl)phosphonium chloride, THPC-Urea ([(carbamoylamino)methyl]-[tris(hydroxymethyl)]phosphonium chloride), 2THPC-1UREA (1,9-dihydroxy-2,2,8,8-tetrakis(hydroxymethyl)-5-oxo-4,6-diaza-2,8-diphosphonianonane, N-tetradecyl amino-methyl trishydroxymethyl phosphonium chloride, Reaction products of tris(hydroxymethyl)-

phosphine and urea and Reaction products of tris(hydroxymethyl) phosphine oxide and urea.

56 Therefore, the Substance is a complex substance and contains constituents with significant structural differences described above.

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

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

Reasons related to the information under Annex VIII of REACH

4. In vitro micronucleus study

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

4.1. Information provided

60 You have adapted this information requirement by using Annex VIII, Section 8.4., Column 2. To support the adaptation, you have provided the following information:

(i) an *in vivo* cytogenicity study in mammalian cells according to the OECD TG 474 (1996) with the source substance ITC 826, EC 422-720-8.

4.2. Assessment of the information provided

4.2.1. The provided adaptation does not meet the criteria of Annex VIII, Section 8.4., Column 2

61 Under Annex VIII, Section 8.4., Column 2, the study usually does not need to be conducted "if adequate data from an in vivo cytogenicity test are available". The Guidance on IRs and CSA, Section R.7.7.6.3 and Table R.7.7–3 clarifies that the in vivo somatic cell cytogenicity test must be either a micronucleus test or a chromosomal aberration test, performed according to the OECD TG 474 or 475, respectively.

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

d) a clear negative outcome is concluded when the data available shows that bone marrow exposure to the Substance or its metabolite(s) occurred;

e) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control database.

63 However, in study (i):

a) you did not demonstrate that bone marrow exposure to the Substance, or its metabolite(s), occurred;

b) the negative control did not show a response within the historical control range of the laboratory.

64 Therefore, the information provided does not cover the specifications required by the OECD TG 474.

65 Furthermore, independent on the reliability issues with the study you provided, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected for the reasons explained in Section 0.1.

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

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

4.3. Study design

68 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the in vitro mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the in vitro mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate

chromosomal aberrations in vitro. However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2). Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential in vitro. Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

4.3.1. Assessment of aneugenicity potential

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

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

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

5. *In vivo* mammalian genetic toxicity study

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

5.1. Triggering of the information requirement

72 Your dossier contains positive results for the in vitro gene mutation study in mammalian cells [redacted]) which raise the concerns for gene mutations.

73 Therefore, the information requirement is triggered.

5.2. Information requirement not fulfilled

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

6. Short-term toxicity testing on fish

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

6.1. Information provided

76 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on the following experimental data from the source substances:

(i) a short-term toxicity study on fish (1995) based on EU method C.1 with the source substance ITC 826, EC 422-720-8.

6.2. Assessment of the information provided

6.2.1. Read-across adaptation rejected

77 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA identified the endpoint specific issue addressed below.

6.2.1.1. The provided study on the analogue substance does not meet the specifications of the test guideline

78 To fulfil the information requirement, a study must comply with OECD TG 203 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Reporting of the methodology and results

c) the test procedure is reported (e.g. composition of the test medium, fish loading);

d) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided.

79 In study (i):

Reporting of the methodology and results

a) on the test procedure, you have not specified the composition of the test medium;

b) on the analytical method, adequate information, i.e. the results of the analytically determined exposure concentrations are not provided.

80 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, the lack of results of the analytical measurements hinders the confirmation of the exposure during the experiment. This is especially relevant because the LC50 is close to the Limit of Quantification and NOEC below it. Furthermore, you used the non-specific analytical method (quantification of phosphorus). As the test medium may also contain phosphorus it is unclear whether the measured concentration provide adequate estimate of the test material concentration. Therefore, it is also important to report the composition of the test medium in this study.

81 On this basis, the specifications of OECD TG 203 are not met.

82 Therefore, the information requirement is not fulfilled.

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

Reasons related to the information under Annex IX of REACH

7. In vivo mammalian genetic toxicity study

84 Under Annex IX, Section 8.4.4., an appropriate in vivo mammalian somatic cell genotoxicity study is an information requirement if there is a positive result in any of the in vitro genotoxicity studies referred to in Annex VII or VIII, which gives rise to concern. The in vivo mammalian somatic cell genotoxicity study must address the chromosomal aberration concern or the gene mutation concern or both, as appropriate.

7.1. Information provided

85 You have provided:

(i) an *in vivo* Unscheduled DNA Synthesis in Rat Hepatocytes (2005) with the Substance.

7.2. Assessment of the information provided

7.2.1. The provided study does not meet the information requirement

86 In order to be appropriate, according to the Guidance on IRs and CSA, Section R.7.7.6.3., the in vivo somatic cell genotoxicity study must address the specific concern raised by the in vitro positive result.

87 However, the in vivo study provided is not addressing the gene mutation concern raised by the in vitro data. Therefore, the provided in vivo test is not appropriate.

88 ECHA considers that an appropriate in vivo follow up genetic toxicity study is necessary to address the concern identified in vitro.

89 Therefore, the information requirement is not fulfilled.

90 ECHA considers that an appropriate in vivo follow up genetic toxicity study is necessary to address the concern identified in vitro.

7.3. Test selection

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

92 As explained above, under request 5, in the dossier there is no adequate information from an in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study, according to the requirements of Section 8.4.2., Annex VIII to REACH as the provided waiver and in vivo micronucleus study are not considered adequate/valid and the information requirement is not fulfilled. Therefore, by this decision, ECHA also requests an in vitro micronucleus study, which may raise a concern for chromosomal aberration in the case of positive results.

93 If there is also a concern for chromosomal aberration, the comet assay can be combined with an in vivo mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) in a single study (see OECD TG 489 paragraph 33; OECD TG 474 paragraph 37c; Guidance on IRs & CSA, Section R.7.7.6.3.). While the comet assay can detect primary DNA damage that may lead to gene mutations and/or structural chromosomal aberrations, the MN test can detect both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy). A combined study will thus address both the identified concerns for chromosomal aberration as well as gene mutation.

94 The combined study, together with the results of the in vitro mutagenicity studies, can be used to make definitive conclusions about the mechanism(s) inducing in vivo mutagenicity and lack thereof. Furthermore, the combined study can help reduce the number of tests performed and the number of animals used while addressing (structural and numerical) chromosomal aberrations as well as gene mutations.

95 Therefore, you must wait for the results of the in vitro test requested under request 5 and, depending on these results, to conduct either a) the TGR assay or Comet assay if the test results of request 5 are negative; or b) Comet assay combined with MN test if the test results of request 5 are positive. The deadline set in this decision allows for sequential testing.

96 ECHA understands that you agree to perform the appropriate requested study based on the results of request 4.

7.4. Study design

*7.4.1. Comet assay (if the test results of request 4 are **negative**)*

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

98 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.

99 In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver, as primary site of xenobiotic metabolism, and from 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 analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

7.4.1.1. Germ cells

100 You may consider collecting the male gonadal cells from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

*7.4.2. TGR assay (if the test results of request 4 are **negative**)*

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

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

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

104 According to the test method OECD TG 488, the test must be performed by analysing tissues from liver, as slowly proliferating tissue and primary site of xenobiotic metabolism, and from 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 analyse both tissues to ensure a sufficient evaluation of the potential for mutagenicity at the site of contact in the gastro-intestinal tract. However, duodenum must be stored (at or below −70 ºC) until the analysis of liver and glandular stomach is completed; the duodenum must then be analysed, only if the results obtained for the glandular stomach and for the liver are negative or inconclusive.

7.4.2.1. Germ cells

105 You must collect the male germ cells (from the seminiferous tubules) at the same time as the other tissues, to limit additional animal testing. According to the OECD TG 488, the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 ºC). This duration is sufficient to allow you or ECHA to decide on the need for assessment of mutation frequency in the collected germ cells. This type of evidence is relevant under Annex IX, Section 8.4.5. in case of positive result in the in vivo genotoxicity test on somatic cells and for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

*7.4.3. Comet assay combined with MN test (if the test results of request 4 are **positive**)*

106 According to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified. According to the test method OECD TG 474, the test may be performed in mice or rats. Therefore, the combined study must be performed in rats, or if justified, in mice.

107 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.

108 In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver, as primary site of xenobiotic metabolism, and from 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 analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

109 According to the test method OECD TG 474, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen (OECD TG 474, paragraph 25, Table 1).

110 The combination of OECD TGs 489 and 474 should not impair the validity of and the results from each individual study. Careful consideration should be given to the dosing, and tissue sampling for the comet analysis alongside the requirements of tissue sampling for the mammalian erythrocyte micronucleus test (see OECD TG 489, e.g. Bowen et al. 2011 [1]).

[1] Bowen DE *et al.* (2011) Evaluation of a multi-endpoint assay in rats, combining the bone-marrow micronucleus test, the comet assay and the flow-cytometric peripheral blood micronucleus test. *Muta Res*;722:7–19.

7.4.3.1. Assessment of aneugenicity potential

111 If the result of the in vivo MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance unless the aneugenic potential has been conclusively investigated in the in vitro micronucleus study requested under Section 5. In line with the OECD TG 474 (paragraph 42), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

7.4.3.2. Investigation of target tissue exposure

112 The applicable test method OECD TG 474 states that "If there is evidence that the test substance(s), or its metabolite(s), will not reach the target tissue, it may not be appropriate to use this test". Additionally, a negative test result can be considered reliable only if "Bone marrow exposure to the test substance(s) occurred".

113 Therefore, to ensure that the data generated are adequate for hazard identification, you must take blood samples at appropriate times and measure plasma levels of the Substance and/or its metabolites (OECD TG 474, paragraph 40), unless exposure of the bone marrow can be demonstrated through other means, e.g. by showing a depression of immature to mature erythrocyte ratio (OECD TG 474, paragraph 48).

114 If the Substance is negative in this test, but it is not possible to demonstrate that bone marrow exposure to the Substance occurred, then ECHA will consider any remaining uncertainty concerning the mutagenic potential of the Substance and whether to request any further information.

7.4.3.3. Germ cells

115 You may consider collecting the male gonadal cells from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

8. Analysis of male germ cells

116 Under Annex IX, Section 8.4.5., an appropriate in vivo mammalian germ cell genotoxicity study is an information requirement if there is a positive result in an available in vivo mammalian somatic cell genotoxicity study, which gives rise to concern. The in vivo mammalian germ cell genotoxicity study must address the chromosomal aberration concern or the gene mutation concern or both, as appropriate.

8.1. Triggering of the information requirement

117 The results of request 3 will determine if an appropriate in vivo mammalian germ cell genotoxicity study is triggered. If triggered, this study must address the gene mutation concern.

8.2. Data in the dossier

118 Your dossier does not contain any in vivo mammalian germ cell genotoxicity study.

119 Therefore, this information requirement, if triggered, is not fulfilled.

8.3. Study selection and design

120 In case you will perform the TGR assay (OECD TG 488) to fulfil the information requirement for an in vivo mammalian somatic cell genotoxicity study and if the analysis of somatic cell is positive, you must analyse the male germ cells from the seminiferous tubules, collected and stored as specified in section 7.4.2.1 above. The analysis must be performed according to the OECD TG 488.

121 ECHA notes that if you decide to carry out a different test on somatic cells than the TGR assay and the test is positive, a subsequent germ cell genotoxicity study (TGR/OECD TG 488) may still be required under Annex IX, Section 8.4.5.

9. Long-term toxicity testing on aquatic invertebrates

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

9.1. Information provided

123 In your dossier, you have provided:

(i) a long-term toxicity study on *Daphnia magna* (1998) based on OECD TG 211 with ITC 826, EC 422-720-8;

124 In your comment to the draft decision, we understand that you intent to adapt this information requirement. You mention that long-term toxicity test on daphnids with the registered Substance is not necessary because: "the classification for this substance will be derived from the surrogate system based on (…) three trophic levels (acute studies on daphnids and fish and a study on algae) and the outcome regarding biodegradation".

9.2. Assessment of the information provided in your dossier

9.2.1. Read-across adaptation rejected

125 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA identified endpoint specific issue addressed below.

9.2.1.1. The provided study on the analogue substance does not meet the specifications of the test guideline

126 To fulfil the information requirement, a study must comply with the OECD TG 211 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Reporting of the methodology and results

a) the nominal test concentrations and the results of all analyses to determine the concentration of the test substance in the test vessels are reported;

b) the full record of the daily production of living offspring during the test by each parent animal is provided;

c) the number of deaths among the parent animals (if any) and the day on which they occurred is reported;

d) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

127 In study (i):

Reporting of the methodology and results

a) the results of the analytical determination of exposure concentrations in the test vessels are not reported;

b) the full record of the daily production of living offspring during the test by each parent animal is not provided;

c) the number of deaths among the parent animals (if any) and the day on which they occurred is not reported.

d) on the analytical method adequate information, i.e. performance parameters of the method and the results of the analytical determination of exposure concentrations is not reported;

128 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, due to the lack of detailed information on the results of both analytical and biological measurements, it is not possible to assess the fulfilment of the validity criteria of the test and the reliability of the derived endpoints.

129 On this basis, the specifications of OECD TG 211 are not met.

130 In your comments to the draft decision you disagree with the request. You have attached a copy of a Robust Study Summary (RSS) which includes the information listed above as missing in the dossier. However, as this information is currently not available in your registration dossier, the data gap remains. You must therefore submit this information in an updated registration dossier by the deadline set in the decision.

131 Therefore, the information requirement is not fulfilled.

9.3. Assessment of the information provided in your comments to the draft decision

132 A registrant may only adapt this information requirement based on the specific rules for adaptation set out in Annex XI. Your argumentation to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH, nor to any specific rules set out in Annex IX, Column 2 for this endpoint.

10. Long-term toxicity testing on fish

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

10.1. Information provided

134 In your dossier, you have provided:

(i) a long-term toxicity study on fish (1999) based on OECD TG 215 with ITC 826, EC 422-720-8.

135 In your comment to the draft decision, we understand that you intent to adapt this information requirement. You mention that long-term toxicity test on fish with the registered Substance is not necessary because: "the classification for this substance will be derived from the surrogate system based on (…) three trophic levels (acute studies on daphnids and fish and a study on algae) and the outcome regarding biodegradation".

10.2. Assessment of the information provided in your dossier

10.2.1. Read-across adaptation rejected

136 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. In addition, ECHA identified endpoint specific issue addressed below.

10.2.1.1. The provided study on the analogue substance does not meet the specifications of the test guideline

137 To fulfil the information requirement, a study must comply with OECD TG 210 or OECD TG 215 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Reporting of the methodology and results

a) the test design is reported (e.g. semi-static or flow-through, number of test chambers and replicates);

b) the test procedure is reported (e.g. number of fish per replicate, composition of the test medium, fish loading);

c) data on mortality measured daily and cumulative mortality are reported;

d) the number of healthy fish at end of test is reported;

e) data for length (specify either standard or total) and weight of surviving animals at the end of the test are reported;

f) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

138 In study (i):

Reporting of the methodology and results

a) on the test design, you have not specified the number of test chambers and replicates;

b) on the test procedure, you have not specified the number of fish per replicate and the fish loading;

c) data on mortality measured daily and cumulative mortality are not reported;

d) the number of healthy fish at end of test is not reported;

e) data for length and weight of surviving animals at the end of the test are not reported;

f) on the analytical method adequate information, i.e. performance parameters of the method are not reported and the results of the analytically determined exposure concentrations are not provided.

139 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, the lack of information concerning the test design and test procedure hinders the assessment of the validity of the test. The lack of

raw data on the results hinders the assessment of the reliability of the test and the independent calculation of the endpoints. Finally, the lack of information concerning the analytical methods and results hinders the assessment of the reliability of the derived endpoints.

140 On this basis, the specifications of OECD TG 210 are not met.

141 In your comments to the draft decision you disagree with the request. You have attached a copy of a Robust Study Summary (RSS) which includes the information listed above as missing in the dossier. However, as this information is currently not available in your registration dossier, the data gap remains. You must therefore submit this information in an updated registration dossier by the deadline set in the decision.

142 Therefore, the information requirement is not fulfilled.

10.3. Assessment of the information provided in your comments to the draft decision

143 A registrant may only adapt this information requirement based on the specific rules for adaptation set out in Annex XI. Your argumentation to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH, nor to any specific rules set out in Annex IX, Column 2 for this endpoint.

10.4. Study design

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

References

The following documents may have been cited in the decision.

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

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

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2023).
***Guidance on intermediates*;** ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

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

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

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

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

Appendix 2: Procedure

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

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

The compliance check was initiated on 22 February 2023.

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

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

ECHA took into account your comments and amended the request(s).

You have provided comments during the decision-making phase which were found to address the incompliance(s) identified in the draft decision. Therefore, the original request for skin sensitisation was removed.

As a result of one or more changes of registration tonnage band or registration type, the request for pre-natal developmental toxicity study in a second species and extended one-generation reproductive toxicity study were removed from the decision.

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

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

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

You provided comments agreeing with the proposed amendment(s), which were taken into account by the Member State Committee.

In addition, you provided comments on the draft decision, regarding the studies to be conducted to follow-up the concerns identified in the *in vitro* mutagenicity tests, which do not address the proposal(s) for amendment(s). Therefore, these comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5). In any event, the current decision follows the approach agreed during the MSC-70 meeting for cases where both concerns, chromosomal aberrations and gene mutation, are identified. The minutes of the MSC-70 meeting are available at https://echa.europa.eu/documents/10162/2200431/MinutesofMSC-70_adopted-1.pdf/

The Member State Committee unanimously agreed on the draft decision in its MSC-86 written procedure. ECHA adopted the decision under Article 51(6) of REACH.

Appendix 3: Addressee 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]

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

Appendix 4: Conducting and reporting new tests for REACH purposes

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

1.1 Test methods, GLP requirements and reporting

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

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

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries (https://echa.europa.eu/practical-guides).

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

1.2 Test material

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

(2) Information on the Test Material needed in the updated dossier

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).