~~Confidential~~

Helsinki, 07 September 2021

Addressees
Registrant(s) of JS_mDCHA as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
04/01/2021

Registered substance subject to this decision ("the Substance")
Substance name: N-cyclohexyl-N-methylcyclohexylamine
EC number: 231-453-4
CAS number: 7560-83-0

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 ***13 December 2023***.

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

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

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471)

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

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

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

2. If negative results are obtained in test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

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

4. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

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

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

2. 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)

3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII to IX of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- 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, VIII and IX to REACH, for registration at 100-1000 tpa;

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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 Christel Schilliger-Musset, Director of Hazard Assessment

[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 on Reasons common to several requests

1. **Assessment of your read-across approach under Annex XI, Section 1.5.**

You seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

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 appendices.

Grouping of substances and read-across approach

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 (addressed under 'Predictions for (eco)toxicological properties').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[2,3].

A. Predictions for (eco)toxicological properties

You have provided a read-across justification document in IUCLID, under the concerned endpoints, titled '[redacted]'.

You intend to predict the (eco)toxicological properties of your Substance using data from structurally similar substances, as follows:

- Dicyclohexyl amine (DCHA; EC No. 202-980-7; CAS No. 101-83-7), hereafter referred to as "source substance 1" – to predict both human health and environmental properties
- N-Dimethy-N-cyclohexylamine (dmCHA; EC No. 202-715-5; CAS No. 98-94-2), hereafter referred to as "source substance 2" – to predict environmental properties

You indicate that you have used OECD QSAR Toolbox (v.3.3.0) to identify structural analogues for the Substance and that "*The source substances chosen are those amines which bear the closest structural similarity to the target substance, and which have sufficiently robust datasets available which are informative for data gap filling".*

Further, you have provided the following reasoning for the prediction of (eco)toxicological properties: "*In biological and environmental settings, each of the proposed analogues is*

[2] Read-Across Assessment Framework (RAAF, March 2017)
[3] RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)

expected to elicit the same type of effects, based on a common functional group of toxicological interest (i.e., the amine group with a reactive unshared pair of electrons)." Further, you state that "*there appears to be slightly higher acute mammalian toxicity with DCHA, perhaps due to the possibility of ionisation in DCHA or effects of steric hindrance of the methyl in mDCHA",* therefore, the source substance 1 *"may represent the "worst case".*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects.

You hypothesise that the source substance 1 constitutes a worst-case for the prediction of (eco)toxicological properties of the Substance. In addition, the ecotoxicological properties of your Substance are predicted to be quantitatively equal to those of the source substance 2.

ECHA notes that with regards to prediction(s) of (eco)toxicological properties there are issues that are common to all information requirements under consideration, common to some information requirements and also issues that are specific for these information requirements individually. Altogether they result in a failure to meet the requirement of Annex XI, 1.5. The common issues are set out here, while the specific issues are set out under the information requirement(s) concerned in the Appendices below.

i. Prediction of toxicological properties

ECHA notes the following shortcoming(s) with regards to prediction(s) of toxicological properties.

a. *Missing supporting information to confirm your worst-case consideration for systemic and reproductive toxicity*

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[4]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include, among others, information to confirm your claimed worst-case prediction and bridging studies to compare properties of the Substance and source substances.

As indicated above, your read-across hypothesis is based on the assumption that the source substance 1 constitutes a worst-case for the prediction of the toxicological properties under consideration of the Substance. In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance is necessary to confirm a conservative prediction of the properties of the Substance from the data on the source substance. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).
In order to support your hypothesis you refer to the acute toxicity, skin irritation, eye irritation, skin sensitisation properties of the Substance and of the source substance 1.
You consider that the toxicological properties of the Substance and of the source substance are driven by the presence of an amine functional group, rather then by the substituents on

[4] ECHA Guidance R.6, Section R.6.2.2.1.f

the amine. To support your considerations you refer to the OECD SIDS categories of C1--13 Primary Amines (US/ICCA, 2011) and Tertiary Amines (US/ICCA, 2012).

ECHA acknowledges that the amine functional group is likely associated with common local toxicity for the Substance and the source substance 1. The reported data on the Substance and on the source substance 1, as well as the data reported for the members of the OECD SIDS categories of primary and tertiary amines, seems to support this notion. However, while the different amines may have similar local toxicity, this information is not relevant to inform on the systemic, reproductive and developmental toxicity properties of the Substance and source substance 1.

With regard to the general toxicity of your Substance and the source substance, you further claim that "*it is the chemical activity of nitrogen which characterises the toxicity of this category of amines rather than the substituents on the amine*". As indicated above, you refer to conclusions derived in the context of OECD categories on amines to support this consideration. However, ECHA notes that the information reported in these OECD SIDS categories on systemic and reproductive toxicity, contradicts your claim. More specifically, evidence of systemic, reproductive and developmental toxicity is reported for some members of the two categories for which data investigating these properties is available while no such evidence of toxicity is reported for other amines for which comparables studies are available. As these substances are all amines which differ in the number and type of alkyl substituent, this suggests that the different alkyl substituents may impact the toxicity of these substances.

With regard to your Substance and the source substance 1, you consider that the source substance 1 represents a worst-case for the Substance. However, you have not established that the differences in the chemical structures between these substances do not influence their toxicological properties. The data set reported in the technical dossier does not include any experimental data of comparable design and duration for the Substance to compare the systemic toxicity and reproductive toxicity properties between the Substance and the source substance 1. In the absence of such information it is not possible to compare the subchronic toxicity, reproductive toxicity and pre-natal developmental toxicity properties of the Substance and the source substance 1.

Therefore, based on the above, you have not established that the source substance 1 constitutes a worst-case for the prediction of the systemic and reproductive toxicity properties of the Substance.

ii. Prediction of ecotoxicological properties

ECHA notes the following general shortcoming(s) with regards to prediction(s) of aquatic toxicity.

a. Missing supporting information to compare properties of the substances and to substantiate worst-case consideration for aquatic toxicity

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[1]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include, among others, information to confirm your claimed worst-case prediction and bridging studies to compare properties of the Substance and source substances.

As indicated above, your read-across hypothesis is based on the assumption that (i) the source substance 2 causes the same type of effect(s) and (ii) that the source substance 1 constitutes a worst-case for the prediction of aquatic toxicity of the Substance. In this context, relevant, reliable and adequate information allowing to compare the properties of the source substances is necessary to confirm that (i) the source substance 1 cause the same type of effects and (ii) the prediction of the aquatic toxicity properties of the Substance is conservative from the data on source substance 1. Such information can be obtained, for example, from bridging studies of comparable design and duration for the source substance(s).

You have provided aquatic toxicity studies on the source substances, as described in point b. below.The data set reported in the technical dossier does not include any experimental data with the Substance for the aquatic toxicity properties under consideration (acute toxicity to fish and to aquatic invertebrates and algae growth inhibition). In the absence of data with the Substance, it is not possible to compare the aquatic toxicity properties for the Substance and the source substances. Furthermore, as explained in point b. below, there are also no adequate short-term toxicity studies on aquatic invertebrates for source substance 1 nor adequate data on algae growth inhibition provided for any of the source substances.

Based on the above, it is not possible to compare aquatic toxicity for your Substance and the source substances, e.g. bridging studies of comparable design and duration.
In the absence of this information, you have not established that the Substance and the source substance 2 are likely to have similar properties nor that properties prediction from source substance 1 to the Substance is conservative. Therefore, you have not provided sufficient supporting information to strengthen the rationale for your read-across.

b. Adequacy and reliability of source studies for aquatic toxicity

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

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

For short-term toxicity to aquatic invertebrates, you have provided two studies on source ssubstance 1 and one study on source substance 2.
For toxicity to algae, you have provided one study on source substance 2.
For short-term toxicity to fish, you have provided two studies on each source substance.

Specific reasons why your source study/ies do not meet these criteria are explained further below under the relevant information requirement sections A.1. A.2 and B.2. In particular, the short-term study on aquatic invertebrates on source substance 1 and the algae toxicity study on source substance 2 are not adequate for the purpose of classification and labelling and/or risk assessment. Therefore, no reliable predictions can be made for these information requirements.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substances. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected already for these general reasons.

As indicated above, ECHA notes that there are issues that are common to all information requirements under consideration and also issues that are specific for these information requirements individually. Altogether they result in a failure to meet the requirement of Annex XI, 1.5. The common issues are set out in the above, while the specific issues are set out under the information requirement(s) concerned in the Appendices below.

Appendix A: Reasons to request information required under Annex VII of REACH

1. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

You have provided a key study in your dossier:

i. Bacterial reverse mutation test (equivalent to OECD TG 471 and TG 480, GLP, 1975) with the following strains: S. typhimurium TA 1535, TA 1537, TA 98 and TA 100, Saccharomyces cerevisiae D4, which all gave negative results.

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

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[5] (1997). Four of the key parameters of this test guideline include:

a) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)
b) The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate or 5 ml/plate.
c) At least 5 doses must be evaluated, in each test condition.
d) Triplicate plating must be used at each dose level.

The reported data for the study you have provided did not include the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101). You also reported that your test procedures did not permit exact quantitation of the number of cells surviving chemical treatment and the highest tested concentration was 10.0 µL/plate. You reported that at least 4 dose levels of the test chemical were used but at least 5 dose levels are required. Furthermore, you have reported a single instead of triplicate plating at each dose level.

The information provided does not cover four of the key parameters required by OECD TG 471. Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agree to conduct the requested test as specified in the decision.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

2. Short-term toxicity testing on aquatic invertebrates

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests above.

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

You have provided the following information:

i. OECD TG 202 key study with source substance 1 ([redacted], 1999);
ii. OECD TG 202 key study with source substance 2 [redacted]., 1989);
iii. US-EPA (1992) 40 CFR 797-1300 supporting study (similar or equivalent to OECD TG 202) with source substance 1 ([redacted]., 1999).

We have assessed this information and identified the following issues:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of some of the source studies.

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

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

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;
- the effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also ECHA Guidance R.7b, Section R.7.8.4.1);

Reporting of the methodology and results

- the test design is reported (*e.g.* static or semi-static test, number of replicates, test concentrations, age and feeding of daphnids);
- the test procedure is reported (*e.g.* composition of the test medium, loading in number of *Daphnia* per test vessel);
- 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;
- the dissolved oxygen and pH measured at least at the beginning and end of the test is reported;

Validity criteria

- the percentage of immobilised daphnids is ≤ 10% at the end of the test in the controls (including the solvent control, if applicable);
- the dissolved oxygen concentration is ≥ 3 mg/L in all test vessels at the end of the test;

Your registration dossier provides two OECD TG 202 studies (studies i. and ii.) and one study similar (or equivalent) to OECD TG 202 (study iii.) with source substances, two of which (studies i. and iii. with source substance 1) showing the following:

Reporting of the methodology and results

- on the test design, for study iii. you have not specified test type (e.g. static or semi-static) and test concentrations, and for studies i. and iii. you have not specified number of replicates and age and feeding of daphnids;
- on the test procedure, for studies i. and iii. you have not specified loading in number of *Daphnia* in each test vessel, and for study iii. you have not provided information on test medium;
- tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported for studies i. and iii.;
- the dissolved oxygen and pH measured at least at the beginning and end of the test is not reported for study iii.;

Characterisation of exposure
- in study iii you have not specified if analytical monitoring of exposure was conducted;
- in study iii, effect values are based on nominal concentration;

Validity criteria
- for studies i and iii you have not specified if the validity criteria were met;

Based on the above, there are major deficiencies impacting studies i. and iii. with source substance 1, including the following:

- *Reporting of the methodology and results*: In the absence of information on the study design (for instance on age of daphnids) and on the test procedure for both studies, ECHA is not in a postion to make an independent assessment of the reliability of methodology and results.
- *Characterisation of exposure*: in the absence of information on analytical monitoring for study (iii.), you have not demonstrated the stability of the test substance.
- *Validity criteria*: as you have not provided tabulated data on the number of immobilised daphnids for any of the studies nor information on dissolved oxygen for study iii., it is not possible to verify that the validity criteria are met.

As the requirements of OECD TG 202 are not met for studies i and iii., your adaptation is rejected. On this basis, the information requirement is not fulfilled.

In your comments to the draft decision, you indicate your intention to use the long-term toxicity study on aquatic invertebrates, yet to be generated, to fulfil this information requirement. Should you decide to pursue this strategy, ECHA will assess its compliance in the follow-up to the dossier evaluation. You remain responsible for complying with this decision by the set deadline.

3. Growth inhibition study aquatic plants

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the Appendix on Reasons common to several requests above.

You have provided a study according to German Standard DIN 38412, Part 9 (and OECD TG 201) with source substance 2

We have assessed this information and identified the following issues:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of the source study.

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

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:

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;
- The results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test;

Your registration dossier provides a study similar (or equivalent) to OECD TG 201 with source substance 2 showing the following:

Characterisation of exposure

- no analytical monitoring of exposure was conducted and no justification is provided whether analytical monitoring was not technically feasible;
- effect values are based on nominal concentration.

Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically in the absence of analytical monitoring of effective exposure concentration, you have not demonstrated the stability of the test substance. As the requirements of OECD TG 201 are not met, your adaptation is rejected. On this basis, the information requirement is not fulfilled.

In your comments to the draft decision, you agree to conduct the requested test as specified in the decision.

Appendix B: Reasons to request information required under Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

You have sought to adapt this information requirement according Section 8.4.2., Column 2, Annex VIII by providing the following justification: "*an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study does not need to be conducted because adequate data from an in vivo cytogenicity test are available*". Further, in the IUCLID dossier (7.6.2. Genetic toxicity *in vivo*) you provided the following *information* to support your adaptation:

i. Mammalian Bone marrow chromosome aberration (equivalent to OECD Guideline 475, not GLP, 1981), which gave negative results.
ii. Germ cell chromosomal aberration (equivalent to OECD Guideline 478 (, not GLP, 1981), which gave negative results.
iii. Sex-linked Recessive Lethal Test in Drosophila (equivalent to OECD Guideline 477, not GLP, 1981), which gave negative results.
iv. Spermatogonial Chromosome Aberration (equivalent to OECD Guideline 483, not GLP 1981), which gave negative results.

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

Under Section 8.4.2., Column 2, first indent, Annex VIII to REACH, the study may be omitted "if *adequate data from an in vivo cytogenicity test are available*". ECHA Guidance[6] clarifies that the *in vivo* study must be either a micronucleus test or a chromosomal aberration test, performed according to OECD TG 474 or 475, respectively[7].

For the data from an *in vivo* cytogenicity test to be considered adequate, the *in vivo* study you submitted has to meet the requirements of OECD TG 475, and the specifications/conditions of this test guideline include:

a) The study must include a minimum of three doses/groups of treated animals, as well as a negative control group and a positive control group.
b) The highest dose studied must be the maximum tolerated dose (MTD), i.e. the highest dose that is tolerated without evidence of toxicity (e.g. body weight depression or hematopoietic system cytotoxicity, but not death or evidence of pain, suffering or distress necessitating humane euthanasia). The highest dose can also be a dose that produces toxicity in the bone marrow.
c) The mitotic index must be determined as a measure of cytotoxicity in at least 1000 cells per animal for all treated animals (including positive controls), untreated or vehicle/solvent negative control animals.
d) At least 200 metaphases must be analysed for each animal for structural chromosomal aberrations including and excluding gaps.
e) The mitotic index and the mean number of cells with aberrations per group must be reported for each group of animals.

The reported data for the *in vivo* study/ies you submitted did not include:

[6] ECHA Guidance R.7a, R.7.7.6.3, p.568
[7] ECHA Guidance R.7a, Table R.7.7–3, p.558

a) the appropriate number of doses - only two doses are administered.
b) a maximum studied dose that is a MTD or induces toxicity - you report that the toxicity to the animals was so severe that the Principal Investigator lowered the target concentration from the planned 50 ppm while the animals were still in the chambers, therefore the maximum studied dose is unclear.
c) the analysis of the adequate number of metaphases - only 50 cells with a minimum of 41 well spread chromosomes were examined and scored.
d) data on the mitotic index and the mean number of cells with aberrations per group for each group of animals.

The information provided does not cover specifications/conditions required by the OECD TG 475.

Further, studies (ii), (iii) and (iv) are not performed according to the OECD TG 474 or 475.

In addition, as specified in the test guidelines for an *in vivo* cytogenicity investigation (OECD TG 474 and TG 475, the *in vivo* studies referred to in Annex VIII, section 8.4.2., column 2, should be performed on rodents or other species with the most relevant metabolism for humans. Since the study (iii) has been performed on insects, which metabolism differs to the one of humans, it is not considered as being acceptable.

Based on the above, the requirements of Section 8.4.2., Column 2, first indent, Annex VIII to REACH are not met.

In your comments to the draft decision you agree to conduct the requested test as specified in the decision.

Study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

i. Triggering of the study

Your dossier contains data for an *in vitro* gene mutation study in bacteria, and an adaptation for an in vitro cytogenicity study in mammalian cells or *in vitro* micronucleus study.

The information for the *in vitro* gene mutation study in bacteria and for the *in vitro* cytogenicity study in mammalian cells provided in the dossier are rejected for the reasons provided in Appendix A, section 1 and Appendix B, section 1.

The result of the requests for information in Appendix A, section 1 and Appendix B, section 1 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

ii. Assessment of information provided

In your dossier, you have provided the following *in vitro* study, relevant for this endpoint:

i. *In vitro* unscheduled DNA synthesis in mammalian cells (EU Method B.18, not GLP, 1981), which gave negative results.

In addition, you have provided the following justification: "*an in vitro gene mutation study in mammalian cells does not need to be conducted because adequate data from a reliable in vivo mammalian gene mutation test are available*". Further, in the IUCLID dossier (7.6.2. Genetic toxicity *in vivo*) you provided the following *information* to support your adaptation

ii. Germ cell chromosomal aberration (equivalent to OECD Guideline 478, not GLP, 1981), which gave negative results.
iii. Mammalian Bone marrow chromosome aberration (equivalent to OECD Guideline 475, not GLP, 1981), which gave negative results
iv. Sex-linked Recessive Lethal Test in Drosophila (equivalent to OECD Guideline 477, not GLP, 1981), which gave negative results.
v. Spermatogonial Chromosome Aberration (equivalent to OECD Guideline 483, not GLP 1981), which gave negative results.

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

A. Regarding the source of information (i)

To fulfil the information requirement, a study must be an *in vitro* gene mutation study in mammalian cells and comply with the OECD TG 476 or 490 (Article 13(3) of REACH and ECHA Guidance R.7, Table R.7.7-2).

The source (i) of information provided does not cover the key parameter(s) required by the OECD TG 476 or 490. Therefore, the information requirement is not fulfilled.

B. Regarding the sources of information (ii) – (v)

ECHA understands that you want to adapt the information requirement according to Section 8.4.3., Column 2, Annex VIII

Under Section 8.4.3., Column 2, Annex VIII to REACH, the study may be omitted if adequate data from a reliable *in vivo* mammalian gene mutation test are available. ECHA Guidance[8] clarifies that the *in vivo* study must be a Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay (TGR), performed according to the OECD TG 488. This test investigates gene mutations using reporter genes.

The studies (ii) – (iv), you have provided are not performed according to the OECD TG 488.

In addition, as specified in the test guidelines for an *in vivo* mammalian gene mutation investigation (OECD TG 488), the *in vivo* studies referred to in Annex VIII, section 8.4.3., Column 2, should be performed on rodents or other species with the most relevant metabolism for humans. Since the study (iv) has been performed on insects, which metabolism differs to the one of humans, it is not considered as being acceptable.

Based on the above, the requirements of Section 8.4.3., Column 2, first indent, Annex VIII to REACH are not met.

Consequently, you are required to provide information for this endpoint, if the *in vitro* gene

[8] ECHA Guidance R.7a, R.7.7.6.3, p. 568

mutation study in bacteria, the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provides a negative result.

In your comments to the draft decision you agree to conduct the tests requested under A.1 and B.1 in this decision and you specify that if these tests provide negative results "*further In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) will be proposed*" using the Substance. ECHA stresses that the *in vitro* gene mutation study in mammalian cells is an information requirement of Annex VIII of the REACH Regulation. Proposals for testing are only applicable for information requirements listed in Annex IX and X. No testing is to be proposed to comply with the information requirement of Annex VIII, Section 8.4.3. This decision requires an *in vitro* gene mutation study in mammalian cells (test method: OECD TG 476 or TG 490) to be performed provided that the conditions listed above are met.

Study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

3. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. You have provided the following information:

i. Screening for reproductive/developmental toxicity study (key study; equivalent to OECD TG 421, non GLP) performed with source substance 1

As explained in the Appendix of Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agree that the Screening for reproductive/developmental toxicity study is a standard information requirement, You indicate your intention to use the pre-natal developmental toxicity study (Annex IX, Section 8.7.2; OECD TG 414), requested in the current draft decision, to adapt this information requirement.

ECHA points out that when the pre-natal developmental toxicity study is available, you may adapt this information requirement according to Annex VIII, Section 8.7.1, Column 2, first paragraph, fourth indent of REACH ("the study does not need to be conducted if a pre-natal developmental toxicity study (OECD TG 414) is already available"). However, at this point of time, the study is still to be conducted, therefore, the information requirement is not fulfilled.

Information on study design

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 with oral[9] administration of the Substance.

2. Short-term toxicity testing on fish

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

You have adapted this information requirement under Section 1.5, Annex XI to REACH (Grouping of substances and read-across approach), providing the justification examined in the the Appendix on Reasons common to several requests above.

You have provided the following information:

i. EU Method C.1 key study with source substance 1 ([redacted] 1992);
ii. DIN 38 412 L15 (1982) key study with source substance 2 ([redacted] 1988);
iii. OECD TG 203 supporting study with source substance 1 (Environmental Agency, Japan, 1999);
iv. OECD TG 203 supporting study with source substance 2 ([redacted] 1989).

We have assessed this information and identified the following issues:

Whilst your read-across adaptation is rejected for the reasons explained in the Appendix on Reasons common to several requests, ECHA has also identified the following endpoint specific issue with the adequacy and reliability of some of the source studies.

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

To fulfil the information requirement, a study must comply with OECD TG 203 (Article 13(3) of REACH) or with acceptable alternatives to OECD TG 203 (as listed in ECHA Guidance R.7b, Appendix R.7.8-2). Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

- the test is conducted on juveniles of similar age (or size);

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;

Reporting of the methodology and results

- mortalities and sub-lethal effects (*e.g.* with regard to equilibrium, appearance, ventilator and swimming behaviour) are reported. The frequency of observations includes at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4;
- size of the fish is reported. If fish of sizes other than those recommended are used, this must be reported together with developmental stage (juvenile, sub-adult, adult stage) and the rationale.

Validity criteria

- mortality in the control(s) is ≤ 10% (or one fish, if fewer than 10 control fish are tested) at the end of the test;

[9] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Your registration dossier provides one study according to EU method C.1 (study i.), one according to DIN 38 412 L15 (study ii.) and two studies according to OECD TG 203 (studies iii. and iv.) with source substances, two of which (i.e. study i. and study ii.) showing the following:

Technical specifications impacting the sensitivity/reliability of the test

- for study i., the size of fish was 2.5-3.5 cm, which does not correspond to juveniles for *Danio rerio* (1-2 cm);
- for study ii., the mean size of fish was 5.3 cm (4.7-5.7 cm) for *Leuciscus idus L.*;

Characterisation of exposure

- for study ii no analytical monitoring of exposure was conducted;

Reporting of the methodology and results

- for study i., tabulated data on mortalities and sub-lethal effects (*e.g.* with regard to equilibrium, appearance, ventilator and swimming behaviour) for each treatment group and control are not reported;
- for studies i. and ii. developmental stage and rationale are not reported.

Validity criteria

- for study i. you have not specified if the validity criteria were met.

Based on the above, there are major deficiencies impacting study i. with source substance 1 and study ii. with source substance 2, conducted according to acceptable alternatives to the OECD TG 203, including the following:

- *Technical specifications impacting the sensitivity/reliability of the test*: the size of fish used in study i. is above the test guideline recommendations and you have not reported developmental stage and rationale, therefore it is considered that fish used was not juvenile. The fish species used in study ii. (*Leuciscus idus L*) is not one of the standard species listed in the OECD TG 203 and you have not reported developmental stage and rationale, therefore you have not demonstrated that fish used was juvenile.
- *Characterisation of exposure*: for study ii, in the absence of analytical monitoring of effective exposure concentration, you have not demonstrated the stability of the test substance.
- *Validity criteria*: as you have not provided tabulated data on mortalities for study i., it is not possible to verify that the validity criteria are met.

Therefore, the requirements of the OECD TG 203 are not met for both key studies (studies i and ii) and your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

In your comments to the draft decision, you indicate your intention to use the long-term toxicity study on fish, yet to be generated, to fulfil this information requirement. Should you decide to pursue this strategy, ECHA will assess its compliance in the follow-up to the dossier evaluation.

Appendix C: Reasons to request information required under Annex IX of REACH

1. Sub-chronic toxicity study (90-day)

A Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX to REACH.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. You have provided the following information:

(i) Sub-chronic (90-day) repeated dose toxicity study in rats (according to OECD TG 408, GLP), performed with the source substance 1.

As explained in the Appendix of Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

Study design

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because although the information indicates that human exposure to the Substance by the inhalation route is likely (PROC 7) potential inhalation-specific effects are already addressed by deriving a long-term DNEL for inhalation 0.7 mg/m³. The calculated RCR = 0.105 (PROC 7, scenario 4) and RCR = 0.209 (PROC 7, scenario 8) are well-below the derived DNEL.

In your comments to the draft decision you agree that the sub-chronic toxicity study is a standard information requirement and you state you "*will submit a testing proposal in accordance with Article 12 and Annex IX introductory paragraph 1, with emphasis on the conduct of an adequate dose-range finding study*". You explain the reason for performing the range-finding study is the corrosivity properties of the Substance and that "*no explicit guidance is provided on how to manage the testing of corrosive substances in repeat-dose oral studies*" apart from REACH Annex IX fourth introductory paragraph and the OECD TG 408, paragraph 20. For this reason, you further indicate your intention to "*defer to the expertise of the performing laboratory in order to define what is a non-corrosive dose to be used in the main study, and how such a dose should be administered (i.e. via oral gavage or by diet)".*

Firstly, ECHA points out that there is no need to submit a testing proposal for this endpoint because it is already subject to the current compliance check and decision requesting the information.

Secondly, ECHA acknowledges your intention to take the expertise of the performimg laboratory in defining the appropriate dose range for the main study. In addition, information on how to manage the testing of corrosive substances is provided in the ECHA Guidance on information requirements and chemical safety assessment (Chapter R7a; section R.7.6.2.3.2.): "*It is to be noted that corrosive or highly irritating substances should be tested preferentially via the oral route, however it must be noted that in vivo testing with corrosive substances at concentration/dose levels causing corrosivity must be avoided (see REACH Annex VII-X preamble). The vehicle should be chosen to minimise gastrointestinal irritation. For some substances dietary administration may allow adequate dosing without irritation compared with oral gavage dosing".*

ECHA further points out that as explained in paragraph 15 of the OECD TG 408: "[…] *Unless limited by the physical-chemical nature or biological effects of the test substance, the highest dose level should be chosen with the aim to induce toxicity but not death or severe suffering*."

Therefore the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

2. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. You have provided the following information:

(i) Pre-natal developmental toxicity study in rats (according to OECD TG 414, GLP), performed with the source substance 1.

As explained in the Appendix of Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agree that the pre-natal developmental toxicity study is a standard information requirement and you state you "*will submit a testing proposal in accordance with Article 12 and Annex IX introductory paragraph 1, with emphasis on the conduct of an adequate dose-range finding study*". You explain that the reason for performing the range-finding study is the corrosivity properties of the Substance and that "*no explicit guidance is provided on how to manage the testing of corrosive substances in PNDT studies*". Further, you refer to the OECD TG 414, stating *that "the highest dose should be chosen with the aim to induce some developmental and/or maternal toxicity (clinical signs or a decrease in body weight) but not death or severe suffering".*For this reason, you further indicate your intention to "*defer to the expertise of the performing laboratory in order to define what is a non-corrosive dose to be used in the main study, and how such a dose should be administered (i.e. via oral gavage or by diet)".*

As ECHA already pointed out in Appendix C, section 1, there is no need to submit a testing proposal for this endpoint because it is already subject to the current compliance check and decision requesting the information.

ECHA acknowledges your intention to take the expertise of the performimg laboratory in defining the appropriate dose range for the main study. Further, with regards to the information on how to manage the testing of corrosive substances, in Appendix C, section 1 above, ECHA has already provided you the Guidance where this information can be found.

Study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[10] administration of the Substance.

3. Long-term toxicity testing on fish

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

[10] ECHA Guidance R.7a, Section R.7.6.2.3.2.

You have omitted this information and you provided the following justification: "After *assessment of information from acute test results, the applicant suggests to perform long-term testing on aquatic invertebrates as the most sensitive species instead on fish.*".

We have assessed this information and identified the following issue:

A registrant may only adapt this information requirement based on the general rules set out in Annex XI. It is noted that Column 2 of Annex IX, Section 9.1, does not allow omitting the need to submit information on long-term toxicity to fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

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

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

On this basis, the information requirement is not fulfilled.

In your comments to the draft decision, you agree to conduct the requested test as specified in the decision.

Study design

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

Appendix D: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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[11].

B. 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.

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[12].

[11] https://echa.europa.eu/practical-guides
[12] https://echa.europa.eu/manuals

Appendix E: 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 06 August 2020.

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

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

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

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

Appendix F: List of references - ECHA Guidance[13] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[14]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[15]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[16]

[13] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[14] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[15] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[16] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

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

You must provide the information requested in this decision for all REACH Annexes applicable to you.

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