~~Confidential~~

Helsinki, 10 October 2022

Addressee
Registrant of JS_111-26-2_SSS as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
05/12/2018

Registered substance subject to this decision ("the Substance")
Substance name: Hexylamine
EC number: 203-851-8

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 ***17 October 2023***.

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

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: OECD TG 471, 2020)

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

The reasons for the requests are explained in Appendix 1.

Information required depends on your tonnage band

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

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

How to comply with your information requirements

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

You must follow the general requirements for testing and reporting new tests under

REACH, see Appendix 4.

Appeal

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

Failure to comply

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

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

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

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

Appendix 1: Reasons for the decision

Contents

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

1 An in vitro gene mutation study in bacteria is an information requirement under Annex VII to REACH, Section 8.4.1.

1.1. Information provided

2 You have provided:

i. *In vitro* gene mutation study in bacteria (2016) with the Substance.

3 In addition, you have also adapted this information requirement by using a Grouping of substances and read-across approach based on experimental data from the following substance:

ii. *In vitro* gene mutation study in bacteria (1986) with Pentylamine, EC No. 203-780-2.

1.2. Assessment of the information provided

1.2.1. The provided study (i) does not meet the information requirement

4 To fulfil the information requirement, a study must comply with OECD TG 471 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the test is 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 induces 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 corresponds to 5 mg/plate or 5 µl/plate;
c) at least 5 doses are evaluated, in each test condition;
d) triplicate plating is used at each dose level;
e) one positive control is included in the study and the positive control substance produces a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control;
f) the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory;
g) the mean number of revertant colonies per plate is reported for the treated doses and the controls.

5 The study (i) is described as an in vitro gene mutation study on bacteria.

6 However, the following specifications are not according to the requirements of the OECD TG 471:

a) the test was performed with the strains TA98, TA100, TA1535 and TA97 (i.e., the strain TA102 or E.coli WP2 uvrA or E.coli WP2 uvrA (pKM101) is missing);
b) the maximum dose tested as you do not report whether it induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance, and whether it was less than 5 mg/plate

or 5 ml/plate;

c) you do not report how many doses were evaluated in absence and in presence of metabolic activation (i.e., the required 5 doses or less than 5 doses);
d) triplicate plating was not used at each dose level;
e) a positive control was not included in the study;
f) you do not show that the number of revertant colonies per plate for the concurrent negative control are inside the historical control range of the laboratory;
g) the mean number of revertant colonies per plate for the treated doses and the controls was not reported.

7 The information provided does not cover the key parameter(s) required by the OECD TG 471.

1.2.2. Read-across adaptation rejected

8 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.

9 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).

10 You have not provided any reasoning for the prediction of this information requirement

11 In the absence of supporting justification, ECHA presumes that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

12 We have identified the following issues with the prediction of in vitro gene mutation in bacteria:

1.2.2.1. Absence of read-across documentation

13 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 include an explanation why the properties of the Substance may be predicted from information on the source substance(s).

14 You have provided robust study summary for study(ies) conducted with another substance than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation as to why this information is relevant for the Substance and thus why the properties of the Substance may be predicted from information on the source substance(s).

15 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substance.

1.2.2.2. Adequacy and reliability of the study (ii) on the source substance

16 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 471. Therefore, the following specifications must be met:

a) the test is 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 induces 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 corresponds to 5 mg/plate or 5 µl/plate;
c) at least 5 doses are evaluated, in each test condition;
d) triplicate plating is used at each dose level;
e) one positive control is included in the study and the positive control substance produces a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control;
f) the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory;
g) the mean number of revertant colonies per plate is reported for the treated doses and the controls.

17 Your registration dossier provides a study similar to an OECD TG 471 showing the following: Negative in S. typhimurium TA98, TA100, TA1535 and TA1537 with and without metabolic activation.

18 However, the following specifications are not according to the requirements of the OECD TG 471:

a) the test was performed with the strains TA98, TA100, TA1535 and TA1537 (i.e., the strain TA102 or E.coli WP2 uvrA or E.coli WP2 uvrA (pKM101) is missing);
b) the maximum dose tested did not induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance and it was less than 5 mg/plate or 5 ml/plate;
c) you do not show that positive controls included in the study produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control;
d) you do not show that the number of revertant colonies per plate for the concurrent negative control are inside the historical control range of the laboratory;
e) the mean number of revertant colonies per plate for the treated doses and the controls was not reported.

19 Therefore, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG.

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

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

1.3. Specification of the study design

22 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) is considered suitable.

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

2. Growth inhibition study aquatic plants

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

2.1. Information provided

25 You have provided:

i. a study according to OECD Guideline 201 (Freshwater Alga and Cyanobacteria, Growth Inhibition Test) (2017) with the Substance

ii. a study according to OECD Guideline 201 (Freshwater Alga and Cyanobacteria, Growth Inhibition Test) (2015) with the Substance

2.2. Assessment of the information provided

2.2.1. The identity of the test material used in the source studies is unclear

26 To comply with this information requirement, the test material in a study must be representative for the Substance (Article 10 and Recital 19 of REACH; ECHA Guidance R.4.1).

27 For the studies (i) and (ii) you have not provided any information on the composition, including their purity profile and the presence of impurities.

28 In the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the substance that was intended to be tested. Therefore, the studies (i) and (ii) provided are rejected.

2.2.2. The provided studies do not meet the information requirement

29 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:

30 Validity criteria

a) exponential growth in the control cultures is observed over the entire duration of the test;

31 Technical specifications impacting the sensitivity/reliability of the test

b) three replicates at each test concentration and at least three replicates for controls (including solvent controls, if applicable) are included;

32 Characterisation of exposure

c) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

33 Reporting of the methodology and results

d) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported. Algal biomass is normally determined based on dry weight per volume, or alternatively as cell counts or biovolume using microscopy or an electric particle counter. If an alternative method is used (*e.g.,* flow cytometry, *in vitro* or *in vivo* fluorescence, or optical density), a satisfactory correlation with biomass must be demonstrated over the range of biomass occurring in the test;

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

34 Your registration dossier provides OECD TG 201 studies showing the following:

35 Validity criteria

a) exponential growth in the control cultures was not observed over the entire duration of the test in study (ii). The average growth rate was only 0.33 and 0.32 for 24-48h and 48-72h, respectively;

36 Technical specifications impacting the sensitivity/reliability of the test

b) the number of replicates was 2 in each test concentration for the study (ii);

37 Characterisation of exposure

c) no analytical monitoring of exposure was conducted in study (i) and (ii);

38 Reporting of the methodology and results

d) you report that algal biomass was determined using spectrophotometer in study (ii). However, you have not reported evidence of correlation between the measured parameter and dry weight or cell numbers over the range of biomass occurring in the test;
e) tabulated data on the algal biomass determined daily for each treatment group and control are not reported for study (i).

39 Based on the above,

- the validity criteria of OECD TG 201 are not met for study (ii);
- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically,
  - the number of replicates in study (ii) was too low;
  - no analytical monitoring of exposure concentrations was reported in any of studies (i) to (ii). Therefore, you have not demonstrated that exposure was satisfactorily maintained over the duration of these tests;
- the reporting of the study (i) and (ii) is not sufficient to conduct an independent assessment of their reliability. More specifically,
  - for study (i) you have not provided adequate information (i.e., raw biomass data) to verify whether the validity criteria of the OECD TG 201 were met. Without this information, it is also not possible to verify the interpretation of the study;
  - you have not provided adequate information on the method used to determine algal biomass in study (ii). Therefore, the reliability of the reported effect values cannot be verified.

40 Therefore, the requirements of OECD TG 201 are not met.

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

42 In your comments to the draft decision, you state that you intend to update your registration dossier by providing a study "*following OECD 201 and Some modification of the ISO 8692 method*". You provide a brief decription of the test methodology and effect values.

43 As you have not provided a robust study summary providing a detailed summary of the objectives, methods, results and conclusions for this new study (i.e. a robust study summary as per Article 3(28)), the information from your comments is not sufficient for ECHA to make an assessment of this new information. You remain responsible for complying with this decision by the set deadline.

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).

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

Read-across assessment framework (RAAF)

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

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

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

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

Appendix 2: Procedure

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

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

The compliance check was initiated on 06 July 2021.

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

ECHA took into account your comments and did not amend the requests.

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.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 6 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

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

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

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

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[2].

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

1.2. Test material

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

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

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

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[3].

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