~~Confidential~~

Helsinki, 10 October 2022

Addressees
Registrant(s) of JS_75-04-7_Ethylamine as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
10/10/2019

Registered substance subject to this decision ("the Substance")
Substance name: Ethylamine
EC number: 200-834-7

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 the deadline of ***15 January 2024***.

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) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

2. Growth inhibition study 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. C/D/E/F/OECD TG 301B/C/D/F or EU C.29./OECD TG 310)

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

Information required depends on your tonnage band

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

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

How to comply with your information requirements

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

to classification and labelling, based on the newly generated information.

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

Appeal

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

Failure to comply

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

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

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

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

Appendix 1: Reasons for the decision

Contents

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 (1986) with the Substance.

1.2. Assessment of the information provided

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

1.2.1. Study not adequate for the information requirement

4 To fulfil the information requirement, the study must meet the requirements of OECD TG 471 (2020). Therefore, the following specifications must be:

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)

5 The study (i) is described as in vitro gene mutation study in bacteria. However, the following specifications are not according to the requirements of OECD TG 471 (2020):

b) Results for the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

6 The information provided does not cover one of the key parameters required by OECD TG 471.

7 Therefore, the information requirement is not fulfilled.

8 In your comments to the draft decision, you did not provide comments on this request.

1.3. Specification of the study design

9 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) should be performed using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

11 You have provided the following studies with the Substance:

(i) a non-guideline growth inhibition test on *Scenedesmus quadricauda* (1978);
(ii) an acute algal growth inhibition test according to DIN 38412, Part 9 on *Scenedesmus quadricauda* (1959).

2.2. Assessment of the information provided

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

2.2.1. The composition of the test material in the reported studies is unclear

13 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).

14 For studies (i) and (ii) above, you have identified the test material as "[redacted], without further information, including analytical purity and composition.

15 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.

16 Therefore, the information provided in studies (i) and (ii) is rejected.

2.2.2. The provided studies do not meet the information requirement

17 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:

18 Key parameter to be measured

a) the concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth at the end of the test are estimated. Growth must be expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure period;

19 Characterisation of exposure

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

20 Reporting of the methodology and results

c) the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);

d) the test conditions are reported (*e.g.*, composition of the test medium, biomass density at the beginning of the test);

e) 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;

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

21 Your registration dossier provides studies showing the following:

22 Key parameter to be measured

a) the effect values reported for study (i) and (ii) are only expressed as "t*oxicity threshold"* values (*i.e.*, equivalent to ErC3 according to you) after 8 days and 96 hours, respectively. For study (ii), the effect value is expressed on the basis of "*change in number of species groups in a community*" (*i.e.*, change in species richness);

23 Characterisation of exposure

b) no analytical monitoring of exposure was conducted in studies (i) and (ii). You have provided no justification as to why analytical monitoring is not technically feasible;

24 Reporting of the methodology and results

c) on the test design, you have not specified the number of replicates, the number of test concentrations and geometric progression used for both studies (i) and (ii);

d) on the test conditions, you have not specified the composition of the test medium and the biomass density at the beginning of the test for both studies (i) and (ii);

e) for study (i), the method used to determine algal biomass is reported as "*Extinction at 578 nm*" and no evidence of correlation between the measured parameter and dry weight are reported. For study (ii), this information is not specified;

f) tabulated data on the algal biomass determined daily for each treatment group and control are not reported for both studies (i) and (ii).

25 Based on the above,

- the key parameters of OECD TG 201 is not covered for studies (i) and (ii) as these studies does not provide information on ErC50. Furthermore, the basis of the reported effect value in study (ii), i.e. reduction in species richness, is not adequate.
- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, no analytical monitoring of exposure concentrations was conducted in studies (i) and (ii). Therefore, you have not demonstrated that exposure was satisfactorily maintained over the duration of these tests.
- the reporting of the studies (i) and (ii) is not sufficient to conduct an independent assessment of their reliability. In particular,
    - you have not provided adequate information (i.e., raw biomass data) to verify whether validity criteria equivalent to those specified in OECD TG 201 were met. Without this information, it is also not possible to verify the interpretation of the studies;
    - you have not provided adequate information on the study design and the test conditions in studies (i) and (ii). Therefore, it is not possible to verify whether these studies were conducted under conditions that are consistent with the specifications of the OECD TG 201;
    - you have not provided adequate information on the method used to determine algal biomass. Therefore the reliability of the reported effect cannot be verified.

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

27 In your comments to the draft decision, you state that you "[agree] *that the presented data on both studies do not fully comply with the requirements of the OECD TG 201. Therefore, the studies are not further used as key information for the toxicity to algae. Instead, the information requirement will be covered by a read-across to the structurally similar substance propylamine (CAS 107-10-8). The study on the growth inhibition to*

aquatic plants will be performed with propylamine according to OECD TG 201 and under GLP. The study was already ordered and the laboratory in charge dated the final study report due to the end of November 2022. This new information together with a read-across justification according to the RAAF document (ECHA, 2017) will be submitted to ECHA as soon as the study report will be available".

28 ECHA acknowledges your intentions to submit a read-across approach for this information requirement. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made.

29 Based on the above, you remain responsible for complying with this decision by the set deadline.

3. Ready biodegradability

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

3.1. Information provided

31 You have provided the following studies with the Substance:

(i) a study according to OECD TG 301C (1988)
(ii) a non-testing guideline respirometric test (1968)
(iii) a study according to OECD TG 301F (1989)

3.2. Assessment of information provided

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

3.2.1. The composition of the test material in the reported studies is unclear

33 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).

34 For studies (i) to (iii) above, you have identified the test material as [redacted], without further information, including analytical purity and composition.

35 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.

36 Therefore, the information provided in studies (i) to (iii) is rejected.

37 In your comments on the draft decision, you state that for study (i), the test material is clearly identified in the full study report. You clarify that the study was conducted on "*ethylamine hydrochloride (C2H5NH2.HCl), which was used instead of ethylamine* […] *for safety reasons*". You also specified that "*the test substance had a high purity of 99.6%*". You have not provided any comment regarding this issue for study (ii) and (iii).

38 ECHA understands that study (i) was conducted on an analogue substance. The information provided as part of your comments addresses the deficiency identified above. If you intend to rely on study (i) to meet the information requirement, you should submit this information in an updated registration dossier.

3.2.2. The provided studies do not meet the information requirement

39 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 requirements must be met:

40 Technical specifications impacting the sensitivity/reliability of the test

a) For OECD TG 301C and F the concentration of the inoculum is set to reach a bacterial cell density of 10^7 to 10^8 cells/L in the test vessel. The suspended solid concentration is 30 mg/L;

41 Reporting of the methodology and results

b) the test design is described (e.g., number of replicates);

c) the results of measurements at each sampling point in each replicate is reported in a tabular form;

d) the ThOD is described and justified;

e) 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).

42 Your registration dossier provides studies showing the following:

43 Technical specifications impacting the sensitivity/reliability of the test

a) The concentration of the inoculum is described as 30 mg/l suspended solids in study (i) and (iii) but no information on inoculum density in cells/L is provided. No information on inoculum density is provided for study (ii).

44 Reporting of the methodology and results

b) for study (iii), you have not specified the number of replicates;

c) the results of measurements at each sampling point in each replicate is not reported for studies (i) to (iii);

d) the ThOD is described for studies (i) to (iii);

e) the test material in studies (i) to (iii) corresponds to a nitrogen-containing substance and it is unclear if a correction for nitrification of the theoretical oxygen demand was applied. You have provided no justification that nitrification did not occur during the test.

45 Based on the above for studies (i) to (iii),

- the reporting of the studies is not sufficient to conduct an independent assessment of their reliability. In particular,
  - you have not provided adequate information on inoculum density for any of the studies. Therefore, it is not possible to verify if the inoculum to test material ratio was consistent with the specifications of the corresponding test method.

    In your comments on the draft decision, you consider that for both OECD TG 301C and F "*The approximate number of cells in the test vessel is given in Table 2 of the guideline (OECD; 1992; p. 8) as 10^7 to 10^8 cells/L. The*

table gives these numbers for comparison between the methods, but not for verification of the inoculum density". You have provided no further information with regard inoculum density on studies (i) to (iii).

ECHA notes that the OECD TG 301 does not state that the specifications of Table 2 are provided for comparison between methods. Instead the table is entitled "test conditions" and therefore should be seen as the conditions under which the various test methods described in the test guideline must be conducted. The limit values for the inoculum density in mg/L (e.g., for sludge or soil) or mL/L (e.g., for surface water or effluent) are set to ensure that the introduction of exogeneous organic matter in the test system is within an acceptable range. Such parameter does not provide a direct estimate of bacterial biomass (as the density of bacteria in, for e.g., a sludge sample or a secondary effluent may vary by orders of magnitude). Accordingly, Appendix R.7.9-1 of ECHA Guidance on IRs and CSA specifies inoculum conditions as cell density (cells/mL) present in a relevant media (*e.g.*, surface waters, unchlorinated sewage treatment works, activated sludge). In the absence of supporting information to demonstrate that the inoculum concentrations used in study (i) to (iii) allowed reaching an adequate bacterial density, you have not demonstrated that the inoculum density was consistent with the specifications of the corresponding test method.

- you have not provided adequate information on the test design for study (iii);
- you have not provided adequate reporting of the test results for studies (i) to (iii). Therefore, it is not possible to verify whether the validity criteria of the corresponding test guideline were met. Without this information, it is also not possible to verify the interpretation of the study results

  In your comments on the draft decision, you provided the missing information for study (i).

- you have not described the ThOD calculation and you have not specified whether a correction for nitrification was applied to calculated the percentage degradation. In the absence of this information, it is not possible to verify the interpretation of the results.

  In your comments on the draft decision, you provided the missing information on ThOD calculation for study (i). Furthermore, you provided additional information showing that no significant nitrate formation was observed by the end of ths study.

46 In your comments on the draft decision, you provided additional information on study (i) that address most of the deficiencies identified above. However, you still fail to provide appropriate justification that the inoculum density was consistent with the specifications of the test guideline.

47 Therefore, the requirements of OECD 301 are not met by any of the studies.

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

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 6 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]
[redacted]	[redacted]	[redacted]
[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.

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].

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