~~Confidential~~

Helsinki, 08 November 2023

Addressee(s)
Registrant(s) of JointSubmission_MOPA as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
08 December 2022

Registered substance subject to this decision ("the Substance")
Substance name: 3-methoxypropylamine
EC/List number: 226-241-3

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 17 November 2025***.

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

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

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

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

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

[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.

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Appendix 1: Reasons for the request(s)

Reasons common to several requests

0.1. Substance-tailored exposure-driven testing adaptation rejected

1 ECHA understands that you have adapted the following standard information requirement(s) under Annex XI, Section 3.2 (a) substance-tailored exposure-driven testing, for the following information requirements:

- Long-term toxicity to aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity to fish (Annex IX, Section 9.1.6.)

2 In your dossier you refer to the results of short-term toxicity tests indicating that "*according to the results obtained from those studies i.e. Short-term toxicity on fish, aquatic invertebrate and algae, the observed effects are affected by the pH increasing effect of the substances. Although some results indicate that a direct intrinsic toxic effect (apart from the pH effect) cannot be excluded, it is not considered necessary to perform long-term toxicity tests studies*". You explain that "*based on the worst case effect concentrations for PNEC derivation (i.e. the effect concentrations obtained in test solutions in which the pH was not adjusted), the chemical safety assessment demonstrates that 1) the exposure levels estimated in all relevant scenarios do not exceed the PNEC under consideration, and 2) the likelihood and severity of an event occurring due to the physicochemical properties of the substance in the aquatic environment are negligible. Therefore, the criteria for adaptation are met. Specifically, all risk characterisation ratios are below 1 and there are no relevant physicochemical hazards identified for this substance in the aquatic environment*".

0.1.1. Exposure always well below PNEC not demonstrated

3 The results of the exposure assessment must show that exposures are always well below the PNEC, i.e. RCRs must always be well below 1. This means that a high level of confidence is needed to demonstrate that every RCR is low enough to ensure that the risks are always controlled, under every plausible condition of the manufacture and all identified uses of the Substance. For this purpose, the possible sources of variability and uncertainty must be considered in the assessment of exposure (Guidance on IRs and CSA Chapter R.16, page 68).

4 Uncertainty must be taken into account, either by carrying out the environmental exposure assessment using conservative assumptions and default values, which are provided in Guidance on IRs and CSA Chapters R.16. (Guidance on IRs and CSA Chapter R.19).

5 Alternatively, when the environmental exposure assessment is not based on these generic assumptions, a stepwise, tiered approach including an uncertainty analysis must be conducted. This analysis can be qualitative, deterministic, or probabilistic, to demonstrate that the risk is adequately controlled (Guidance on IRs and CSA Chapter R.19 provides a framework for carrying out a stepwise, tiered approach to uncertainty analysis). The results must be provided in the dossier to demonstrate that the application of such tiered uncertainty analysis gives a clear indication that the risk is adequately controlled (e.g. an increased belief that the (distribution of the) RCR is less than 1).

6 You have provided an exposure assessment reporting several exposure scenarios (ES) with quantitative exposure assessment and risk characterisation for each of them.

7 All exposure assessments are not based on the generic assumptions recommended in Guidance on IRs and CSA Chapter R.16, but you have used less conservative input parameters, in particular for the release factors. For example for some of the ES the release factors used for the assessment are generally a factor 100 or even 1000 lower than the default values recommended in ECHA Guidance R.16, and the justification provided for risk

management measures for some of the ES is either not substantiated and/or not supported by evidence.

8 In addition, ECHA notes that using the default input parameters recommended in ECHA Guidance R.16, for almost all the ES a much higher RCR values (above > 1) can be calculated.

9 Based on the above, using input parameters for all the the exposure assessments that differ considerably from those in ECHA guidance R.16, you have not demonstrated that the worst case conditions are covered by those parameters. Potential sources of variability and uncertainty under every plausible condition of uses of the Substance have not been presented. You have not provided results of the uncertainty analysis for the environmental exposure assessment ensuring a high level of confidence that the risk is always adequately controlled.

10 Therefore, you have not demonstrated that your exposure assessment is always conservative enough and the RCRs always low enough to cover the possible sources of variability and uncertainty. Thus, exposures cannot be regarded as being always well below the PNEC.

0.1.2. Conclusion on the substance-tailored exposure driven testing adaptation

11 Based on the above, your substance-tailored exposure driven testing adaptation under Annex XI, Section 3. is rejected.

Reasons related to the information under Annex IX of REACH

1. Long-term toxicity testing on aquatic invertebrates

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

1.1. Information provided

13 You have adapted this information requirement by using Annex XI, Section 3. (substance-tailored exposure-driven testing). To support the adaptation, you have provided the following information:

14 *"[…] To conclude, the chemical safety assessment for the test substance demonstrates that the exposure levels estimated in all relevant scenarios do not exceed the appropriate PNEC, and the likelihood and severity of an event occurring due to the physicochemical properties of the substance in the aquatic environment are negligible […] Based on the above, and for reasons of animal welfare, a chronic test on fish and Daphnia is not provided*".

15 Furthermore, under Section 6.1.2 you add that *"A testing proposal to assess the chronic toxicity to aquatic invertebrates (Daphnia magna) is included*". ECHA understands that you intended to submit a testing proposal for the standard information requirement of Long-term toxicity testing on aquatic invertebrates.

1.2. Assessment of the information provided in your registration dossier

1.2.1. Substance-tailored exposure-driven testing adaptation rejected

16 As explained in Section 0.1., your adaptation based on exposure-based waiving under Annex XI, Section 3. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

1.2.2. Your justification to omit the study for reasons of animal welfare has no legal basis

17 A registrant may only adapt this information requirement based on the general rules set out in Annex XI.

18 Your justification to omit this information for reasons of animal welfare does not refer to any legal ground for adaptation under Annex XI to REACH. Furthermore, the testing proposal that you are referring to for chronic toxicity to aquatic invertebrates is not included in the dossier.

19 Therefore, you have not demonstrated that this information can be omitted and the information requirement is not fulfilled.

20 In your comments to the draft decision, you do not agree to perform the requested study. Instead, you indicate your intention to adapt this information requirement using QSAR Toolbox (v. 4.5) prediction based on Annex XI Section 1.3 ((Q)SAR).

1.3. Assessment of the information provided in your comments

1.3.1. (Q)SAR adaptation rejected

21 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(1) the prediction needs to be derived from a scientifically valid model,
(2) the substance must fall within the applicability domain of the model,

(3) results need to be adequate for the purpose of risk assessment or classification and labelling, and
(4) adequate and reliable documentation of the method must be provided.

1.3.1.1. Inadequate documentation of the prediction (QPRF)

22 Guidance on IRs and CSA R.6.1.6.3. states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others that the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

23 You provided the following information about the prediction: A trend analysis (i.e. the model) that is derived using information from a category of analogue substances, which consequently represent the training set used to develop the model.

24 The Substance contains a primary amine and an ether function. However, the training set (i.e. category of analogues substances) does not contain primary amines. Further, there is only one substance in the training set that contains both an amine (although it is a secondary amine) and the ether functions, but its structure is cyclic while the Substance has a linear structure. You have not provided any justification to explain the (lack of) impact on the toxicity of the structural differences of the close analogues used to build the trend.

25 In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

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

1.4. Study design

27 The Substance is difficult to test due to the its ionisation properties (pKa of 10.4 ± 0.5). OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 211. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

2. Long-term toxicity testing on fish

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

2.1. Information provided

29 You have adapted this information requirement by using Annex XI, Section 3. (substance-tailored exposure-driven testing). To support the adaptation, you have provided the following information:

30 *"[…] To conclude, the chemical safety assessment for the test substance demonstrates that the exposure levels estimated in all relevant scenarios do not exceed the appropriate PNEC, and the likelihood and severity of an event occurring due to the physicochemical properties of the substance in the aquatic environment are negligible […] Based on the above, and for reasons of animal welfare, a chronic test on fish and Daphnia is not provided*".

2.2. Assessment of the information provided

2.2.1. Substance-tailored exposure-driven testing adaptation rejected

31 As explained in Section 0.1., your adaptation based on exposure-based waiving under Annex XI, Section 3. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

2.2.2. Your justification to omit the study for reasons of animal welfare has no legal basis

32 A registrant may only adapt this information requirement based on the general rules set out in Annex XI.

33 As already explained under request 1, your justification to omit this information for reasons of animal welfare does not refer to any legal ground for adaptation under Annex XI to REACH.

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

35 Therefore, the information requirement is not fulfilled.

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

2.3. Study design

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

38 OECD TG 210 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under request 1.

References

The following documents may have been cited in the decision.

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

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

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2023).
Guidance on intermediates; ECHA (2010).
All Guidance 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 10 August 2022.

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

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

ECHA took into account your comments and 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.

Appendix 3: Addressee(s) 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;

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

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

Appendix 4: Conducting and reporting new tests for REACH purposes

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

1.1 Test methods, GLP requirements and reporting

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

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

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

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

1.2 Test material

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.

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

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