ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 27 September 2017

Addressee: [redacted]

Decision number: CCH-D-2114370490-53-01/F
Substance name: 3-methoxypropylamine
EC number: 226-241-3
CAS number: 5332-73-0
Registration number: [redacted]
Submission number: [redacted]
Submission date: 22/04/2013
Registered tonnage band: 100-1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit:

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats with the registered substance;**

2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance;**

3. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the registered substance;**

4. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**

5. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

6. **Update of the technical dossier and the Chemical Safety Report using the study "*ISO 6341 15 (Water quality - Determination of the Inhibition of the Mobility of Daphnia magna Straus (Cladocera, Crustacea))*: [redacted] *1991/K3/Acute daphnia / HPP_MOPA_HHBV*" as key study showing the highest concern according to Annex I section 3.1.5. for the endpoint of Short-term toxicity testing on invertebrates (Annex VII section 9.1.1.) *or* provide a detailed justification for not using this study as giving rise to the highest concern.**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **4 October 2019**. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

[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

HUMAN HEALTH INFORMATION

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "sub-chronic toxicity study (90 day)" is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422, GLP) conducted with hydrochloride salt of 3-Methoxypropylamine (CAS no 18600-41-4, EC no 606-068-3). You have not provided a specific or general adaptation argument in your registration dossier. Therefore, ECHA has assessed the dossier content against the respective REACH requirement. While ECHA considers that testing with hydrochoride salt of the registered substance is acceptable because the hydrochloride salt is not considered to have an impact on toxicity, the reported study does not provide the information required by Annex IX, Section 8.6.2., because the exposure duration is less than 90 days. Moreover, the OECD TG 422 is an information requirement at a lower tonnage level prusuant to REACH Annex VIII, 8.7.1. and is not capable to meet higher tier information requirements.

Therefore, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, the exposure concentrations reported in the chemical safety report for the inhalation route are low (maximum [redacted] mg/m3) compared to the toxicity profile of the substance and according to the Chemical Safety Report, risk management measures are in place to prevent exposure of humans via inhalation.

Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

According to the test method EU B.26./OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

ECHA notes that in your comments on the draft decision you agree to conduct the study requested.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats.

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement and have provided the following justification for the adaptation:

"No prenatal developmental toxicity test was performed according to OECD Guideline 414. However, it was demonstrated in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in Wistar rats after oral administration by gavage that the NOAEL for developmental toxicity in the F1 progeny of the test substance treated groups is 1000 mg/kg body weight/day".

In the technical dossier you have provided a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422). However, this study does not provide the information required by Annex IX, Section 8.7.2. because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations.

Therefore, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.
According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

ECHA notes that in your comments on the draft decision you agree to conduct the study requested.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rat or rabbit) by the oral route.

ECOTOXICOLOGICAL INFORMATION

Grouping of substances and read-across approach for ecotoxicological information

ECHA based its decision on the evaluation of your registration dossier that contains adaptation arguments in form of a grouping and read-across approach under Annex XI, 1.5. of the REACH Regulation for the endpoints *Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)* and *Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.*). ECHA has assessed first the scientific and regulatory validity of your read-across approach in general before assessing the individual endpoints (points 3 and 4).

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests. Such other means include the use of information from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met". According to Annex XI, section 1.5. there needs to be structural similarity among the substances within a group or category and furthermore, it is required that the relevant properties of a substance within the group can be predicted from the data for the reference substance(s), and the data should be adequate for the purpose of classification and labelling and/or risk assessment. The REACH Regulation aims at promoting wherever possible the use of alternative means, where equivalent results to the prescribed test are provided on health and environmental hazards. In accordance with these objectives and the objectives of the Compliance Check process, ECHA shall assess whether a prediction of the relevant properties of the substance subject to this decision by using the results of the proposed read-across is acceptable based on the information currently available.

You propose read-across between the structurally similar substances, 2-ethoxyethylamine (EC No. 203-801-5, CAS No. 110-76-9) and 3-isopropoxypropylamine (IPOPA) (EC No. 220-816-2, CAS No. 2906-12-9), as source substances and the substance subject to this decision, 3-methoxypropylamine (MOPA) (EC No. 226-241-3, CAS No. 5332-73-0) as target substance.

Your dossier contains read-across documentation as a separate attachment in Section 13 of the technical dossier in IUCLID "[redacted]".
You use the following arguments to support the prediction of properties of the registered substance from data for the source substances:

- Target and source substances have high purity and impurities are not expected to influence the prediction (section 3 of your read-across justification document).
- On the basis of structural similarity and similarity in physico-chemical, environmental fate and pathways and environmental toxicity, it is possible to predict the ecotoxicological properties of the registered substance (section 4 of your read-across justification document).

You propose that the target and the source substances have similar properties for the above-mentioned information requirements. Furthermore, you consider that "*IPOPA is concluded to be most toxic to aquatic organisms within the group of three substances*

presented". Therefore, you propose that using information on the source substance IPOPA would constitute a worst-case approach in the prediction of aquatic toxicity of the target substance.

ECHA considers that this information is your read-across hypothesis, which provides the basis whereby you predict the properties of the registered substance from the source substances.

In the following, ECHA examines whether the substances have indeed similar properties and whether algae toxicity for the target substance can be predicted from the source substance.

ECHA agrees that the two substances are structurally similar. However, ECHA does not accept in general or this specific case that structural similarity *per se* is sufficient to enable the prediction of eco-toxicological properties of a substance, since structural similarity does not always lead to predictable or similar eco-toxicological properties. In reviewing whether a read-across approach can be accepted, a comparatative analysis of the data for the properties of target and source substances is needed in order to establish whether indeed they are similar or follow a regular pattern.

ECHA acknowledges that you have provided a data matrix in Table 5 of the read-across document to allow comparison of physicochemical, environmental fate and pathway and ecotoxicity properties between the target and the source substances.

ECHA agrees that the target and source substances have similar physico-chemical properties and that in water they are expected to dissociate at environmentally relevant pHs and to be stable to hydrolysis. At the same time, regarding the ecotoxicity data ECHA notes that in the data matrix you have not included the following result on short-term toxicity to aquatic invertebrates on the registered substance present in the technical dossier:

Supporting study on the registered substance according to "*ISO 6341 15 (Water quality - Determination of the Inhibition of the Mobility of Daphnia magna Straus (Cladocera, Crustacea))*": "[redacted] *1991/K3/Acute daphnia / HPP_MOPA_HHBV*". Reliability 3 (not reliable), result 48-h EC50 of 13.73 mg/L.

Based on the information provided in the Robust Study Summary (RSS) for this study, ECHA considers that the validity criteria of this study have been fulfilled. At the same time, you have not provided an adequate justification on why you consider this study, which is the one giving rise to the highest concern as non reliable, as addressed in more detail below under point 6. This study shows that for short-term toxicity to aquatic invertebrates, the target substance (48-h EC50 of 13.73 mg/L) is more toxic than the source substances (48-h EC50 above 100 mg/L for 2-ethoxyethylamine and 48-h EC50 of 65 mg/L for IPOPA). The source substance indicates "*a relatively low toxicity to aquatic organisms.*" Hence, the data on short-term toxicity to aquatic invertebrates, available for the target and source substances respectively, show that the ecotoxicological properties of the substances differ.

In summary, even if the physico-chemical and environmental fate and pathway properties of most relevance for the prediction of ecotoxicological properties are similar, ECHA concludes that based on the short-term toxicity to aquatic invertebrates data available for the target and source substances, you have not demonstrated that the substances would have similar properties or they would follow a regular pattern in their properties regarding aquatic toxicity.

As a consequence, there is not an adequate basis for predicting the properties of the target substance from the data obtained with the source substances and read-across approach does not comply with the general rules of adaptation as set out in Annex XI, 1.5. of the REACH Regulation. Therefore, ECHA concludes that you have not demonstrated the aquatic toxicities of the target and source substances are similar.

In your comments on the draft decision you consider that "*a comparative analysis of the ecotoxicity data for the properties of target and source substances indicate that they are similar or follow a regular pattern*", and justify why the ISO 6341 15 short-term toxicity to aquatic invertebrates study ([redacted], 1991) should be disregarded. As indicated above ECHA considered that the source and target had different toxicities based on this study and consequently rejected your read-across approach. ECHA has addressed the justification for disregarding the ISO study under the endpoint specific request 6. below and acknowledges that with the information provided in the comments on the draft decision the study cannot be considered reliable. While ECHA acknowledges that with this information the read-across adaptation may be considered as acceptable, ECHA notes that this information should be included in the technical dossier and reflected in the read-across justification. While for the purpose of this decision making, ECHA does not take into account any dossier updates after the notification of this draft decision under Article 50(1) of the REACH Regulation, ECHA notes that dossier updates and any adaptations therein will be evaluated by ECHA at the follow up stage.

3. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.
You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a Alga, Growth Inhibition Test (OECD TG 201) with the analogue substance 3-isopropoxypropylamine (EC no 220-816-2) However, as explained above in the section 'Grouping of substances and read-across approach for ecotoxicological information', your adaptation of the information requirement cannot be accepted.

In your comments on the draft decision you maintain that this standard information requirement can be fulfilled with the data on the analogue substance 3-isopropoxypropylamine (EC no 220-816-2). ECHA refers to their reply in the 'Grouping of substances and read-across approach for ecotoxicological information' section above and notes that the read-across adaptation may be supported by the information provided in the comments on the draft decision. Nevertheless, the information needs to be included in the technical dossier. While for the purpose of this decision making, ECHA does not take into account any dossier updates after the notification of this draft decision under Article 50(1) of the REACH Regulation, ECHA notes that dossier updates and any adaptations therein will be evaluated by ECHA at the follow up stage.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Algae growth inhibition test, EU C.3./OECD TG 201).

4. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.
"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a long-term toxicity on aquatic invertebrates in the dossier that would meet the information requirement of Annex IX, Section 9.1.5.

You have sought to adapt this information requirement by providing the following justification for the adaptation: "*In accordance with Regulation (EC) No. 1907/2006, Annex 1, Section 6.4, the chemical safety assessment for MOPA demonstrates that 1) the exposure levels estimated in all relevant scenarios do not exceed the appropriate PNEC, 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 characterization ratios are under 1.0; and there are no physicochemical hazards identified for this substance in the aquatic environment. Therefore, long-term aquatic toxicity testing on invertebrates is not indicated.*" While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex IX, Section 9.1.5., column 2.

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2. The results of short-term studies included in the technical dossier cannot be used to conclude on the risks of the registered substance in the aquatic environment for the following reasons. First, the result for Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.) used in your Chemical Safety Assessment (CSA) to derive the PNEC is not valid, as discussed in point 3. above. Second, in the current PNEC derivation you have not used the study giving rise to the highest concern, i.e. the short-term toxicity testing on invertebrates (IUCLID section 6.1.3) study, on the registered substance, where the lowest effect value was observed (48-h EC50 of 13.73 mg/L). As discussed in point 6. below, you have not adequately justified why you have considered this study giving rise to the highest concern as not reliable. As a result, the PNEC derivation and consequent risk characterisation are not reliable.

Therefore, the CSA cannot be used to adapt the information requirement. Finally, ECHA notes that as the risk characterisation is not reliable you have not shown that all risks are controlled as given in Annex 1, section 6.4.

In your comments on the draft decision you maintain that there is no need to provide information for the present endpoint. You provide further justification as to why the short-term aquatic invertebrates study should be disregarded, and consider the read-across approach and the current risk characterisation reliable. ECHA refers to the replies given in the 'Grouping of substances and read-across approach for ecotoxicological information' section above and request 6. below and notes that the read-across adaptation may be supported by the information provided in the comments on the draft decision. Nevertheless, the information needs to be included in the technical dossier. While for the purpose of this decision making, ECHA does not take into account any dossier updates after the notification of this draft decision under Article 50(1) of the REACH Regulation, ECHA notes that dossier updates and any adaptations therein will be evaluated by ECHA at the follow up stage.

Furthermore, you have sought to adapt this information requirement according to Annex XI, Section 1.3. You provided the following justification for the adaptation: *"QSAR prediction using the most recent version of ECOSAR (2011) - can be used as key information in a weight-of-evidence approach."*

However, ECHA notes that your adaptation does not meet the general rule for adaptation of Annex XI, Section 1.3., and notes the following concerning the validity of the predictions submitted. According to the requirements set for acceptance of QSAR models in Annex XI, section 1.3., results obtained must be adequate for the purpose of classification and labelling and/or risk assessment. According to ECHA *Practical Guide - How to use and report (Q)SARs* (version 3.1, July 2016), section 3.3., (Q)SAR predictions cannot be accepted for the prediction of higher-tier endpoints since they cannot fully cover the complexity of these endpoints.

ECHA hence considers that (Q)SAR results for long-term aquatic toxicity are not adequate for the purpose of classification and labelling and/or risk assessment as required by Annex XI, section 1.3. Nevertheless, ECHA notes the following regarding the other requirements set for acceptance of QSAR models in Annex XI, section 1.3. Firstly, you have not provided adequate and reliable documentation of the QSAR method, since for the ECOSAR prediction you have not submitted a (Q)SAR prediction reporting format (QPRF) nor a (Q)SAR model reporting format (QMRF). In particular, the QPRF is prediction-specific and should be prepared using the information in the software report and manual (*ECHA Practical Guide 5 How to use and report (Q)SARs* (version 3.1. July 2016)). Secondly, the results are not derived from a (Q)SAR model whose scientific validity has been established, since the ECOSAR model for aliphatic amines used for the prediction of chronic toxicity is built only on few data points leading to unreliable prediction.

In conclusion, the (Q)SAR information submitted is not sufficient to fulfil the requirements of Annex XI, section 1.3.

Furthermore, ECHA notes that you have indicated that this study is submitted in a weight of evidence approach. However, ECHA notes that an adaptation pursuant to Annex XI, Section 1.2. requires sufficient weight of evidence from several independent sources of information leading to the conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion.

Since you have provided only this source of information, ECHA considers that weight of evidence approach according to Annex XI, section 1.2 is not justified.

In your comments on the draft decision you acknowledge that the QSAR predictions cannot be used as key information in a WoE approach and that they do not provide reliable information for higher tier endpoints and that the information is not acceptable for the purposes of classification and labelling. However, you consider that the QSAR data support the rationale that no effects will be observed and no further testing is needed. ECHA acknowledges your comments on the draft decision and notes that as indicated above, a WoE approach as now submitted in the technical dossier with single point of information cannot be accepted to fulfil the standard information requirement of the present endpoint. As indicated above ECHA does acknowledge that based on the information provided in your comments on the draft decision on the read-across approach, this information gap may be considered as fulfilled. However, the information provided in the comments need to be included in the technical dossier and reflected in the read-across justification.

Therefore, your adaptations of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *Daphnia magna* reproduction test (test method: EU C.20./OECD TG 211).

Once results of the proposed test on long-term toxicity to aquatic invertebrates are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

5. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a long-term toxicity on fish in the dossier that would meet the information requirement of Annex IX, Section 9.1.6.1 / 9.1.6.2 / 9.1.6.3.

You have sought to adapt this information requirement by providing the following justification for the adaptation: "*Taking into consideration results from short-term toxicity tests on fish, Daphnia and algae there is a high probability that the most sensitive species (algae, daphnia) has already been examined and that a further long-term result from fish would not be lower than the data already available. Therefore, and for reasons of animal welfare, a chronic test on fish is not provided. Moreover, the chemical safety assessment for MOPA demonstrates that 1) the exposure levels estimated in all relevant scenarios do not exceed the appropriate PNEC, 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 characterization ratios are under 1.0; and there are no physicochemical hazards identified for this substance in the aquatic environment.*"
While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex IX, Section 9.1.6., column 2.

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2. As already discussed in point 4. above, the PNEC derivation and consequent risk characterisation are currently not reliable. Therefore, the CSA cannot be used at this stage to adapt the current information requirement. ECHA notes further that as the risk characterisation is not reliable you have not shown that all risks are controlled as given in Annex 1, section 6.4.

In your comments on the draft decision you maintain that there is no need to provide information for the present endpoint. You provide further justification as to why the short-term aquatic invertebrates study should be disregarded, and consider the read-across approach and the current risk characterisation reliable. ECHA refers to the replies given in the 'Grouping of substances and read-across approach for ecotoxicological information' section above and request 6. below and notes that the read-across adaptation may be supported by the information provided in the comments on the draft decision. Nevertheless, the information needs to be included in the technical dossier and reflected in the read-across justification. While for the purpose of this decision making, ECHA does not take into account any dossier updates after the notification of this draft decision under Article 50(1) of the REACH Regulation, ECHA notes that dossier updates and any adaptations therein will be evaluated by ECHA at the follow up stage.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish early-life stage (FELS) toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), *Chapter R7b, Figure R.7.8-4).*

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA *Guidance Chapter R7b,* version 4.0, June 2017).
Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Once results of the proposed test on long-term toxicity to fish are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

6. **Update of the technical dossier and the Chemical Safety Report using the study *"ISO 6341 15 (Water quality - Determination of the Inhibition of the Mobility of Daphnia magna Straus (Cladocera, Crustacea))*: [redacted] *1991/K3/Acute daphnia / HPP_MOPA_HHBV"* as key study showing the highest concern according to Annex I section 3.1.5. for the endpoint of Short-term toxicity testing on invertebrates (Annex VII section 9.1.1.) *or* provide a detailed justification for not using this study as giving rise to the highest concern.**

In accordance with Articles 10(b) and 14(1) of the REACH Regulation, the registration must contain a chemical safety report (CSR) which documents the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I to the REACH Regulation.

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Annex I, Section 3.1.5. of the REACH Regulation requires that the study or studies giving rise to the highest concern shall normally be used to draw a conclusion and a robust study summary shall be prepared for that study or studies and included in the technical dossier. In addition, Annex I, Section 3.1.5. requires that if a study giving rise to the highest concern is not used, then this shall be fully justified.
You have provided the following three study summaries to fulfill the Annex VII section 9.1.1. information requirement of Short-term toxicity testing on invertebrates (IUCLID section 6.1.3):

1. Key study on the analogue substance 3-isopropoxypropan-1-amine (EC No 220-816-2) according to OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test): "*RA CAS 2906-12-9_Short-term toxicity to aquatic invertebrates_*[redacted]". Reliability 2, result: 48-h EC50 of 65 mg/L;

2. Supporting study on the analogue substance 2-ethoxyethanamine (EC No 203-801-5) according to "*the EU Directive 79/831/EEC, Annex V, part C, which is comparable to the OECD guideline 202*": "*RA CAS 110-76-9_BAS F96/0079/50/1.Short-term toxicity to aquatic invertebrates*". Reliability 2,result 48-h EC50 > 100 mg/L;
3. Supporting study on the registered substance according to "*ISO 6341 15 (Water quality - Determination of the Inhibition of the Mobility of Daphnia magna Straus (Cladocera, Crustacea))*": "[redacted] *1991/K3/Acute daphnia / HPP_MOPA_HHBV*". Reliability 3 (not reliable), result 48-h EC50 of 13.73 mg/L.

ECHA notes that you have sought to adapt the information requirement for short-term toxicity testing on invertebrates according to Annex XI, Section 1.5. of the REACH Regulation by providing study No. 1. above as the key study. However, as explained above in the section 'Grouping of substances and read-across approach for ecotoxicological information', your adaptation of the information requirement cannot be accepted.

ECHA notes further that study No. 3 listed above is a study on the registered substance carried out according to guideline ISO 6341 15. You have set this study as a supporting study and assigned it a reliability score of 3 "*not reliable*". You have indicated "*Documentation insufficient for assessment*" as the reason for the low reliability. However, in the Endpoint Study Record you have indicated that the validity criteria of the study were fulfilled.

Concerning the validity of the study on the registered substance, ECHA notes the following: Based on ECHA's Guidance on information requirements and chemical safety assessment Chapter R4 (version 1.1, December 2011) a Klimisch score 3 (unreliable) may be assigned, for example, for studies or data "*which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for assessment and which is not convincing for an expert judgment*". ECHA notes that according to ECHA's Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, the ISO guideline used in your registration dossier (TG ISO 6341 15) is an acceptable alternative to the OECD TG 202 and can thus be used to fulfil the standard information requirement of short-term toxicity testing on invertebrates (Annex VII section 9.1.1.). Furthermore, while ECHA acknowledges that the reporting of the study could be improved, and for example information on test substance concentrations are not reported in detail, based on the information provided it is possible to determine that the validity criteria set in the TG ISO 6341 15 have been met.

Study No 3 carried out on the registered substance is the one showing the highest concern. As indicated above, if the study showing the highest concern is not used to draw conclusion for an endpoint, a full justification shall be provided. Your justification of "*Documentation insufficient for assessment*" does not constitute a sufficient justification for not using this study because it does not provide the elements in the study documentation or any other explanation allowing to verify the claim of the study being "non reliable". Consequently, your justification does not fulfil the requirements of Annex I, section 3.1.5.

In your comments on the draft decision you provide further justification as to why study No. 3 above cannot be considered valid. Most importantly you consider that the daphnids were weakened in the study due to there being no pH adjustment and monitoring (not required in the ISO test guideline) and the oxygen level was 2.2 mg/L which is acceptable by the ISO standard but below the required level of 3 mg/L in the OECD TG 202. You consider that high pH and low oxygen level may have overestimated the toxicity of the registered substance.

You also note that in the ESR the validity criteria were accidently set as "fulfilled". ECHA accepts that the toxicity may have been enhanced by pH conditions which were however not monitored and have hence not been reported in the ESR. Nevertheless ECHA notes that based on the other, valid, aquatic studies, it is clear that adjustment of pH is necessary in studies conducted with the registered substance.

ECHA hence acknowledges that in your comments on the draft decision you have justified that study 3. cannot be considered valid, however it is also necessary to include this information in the technical dossier. While for the purpose of this decision making, ECHA does not take into account any dossier updates after the notification of this draft decision under Article 50(1) of the REACH Regulation, ECHA notes that dossier updates and any adaptations therein will be evaluated by ECHA at the follow up stage. With regards to your comments on the draft decision on the acceptability of the read-across approach, ECHA has assessed those in the section 'Grouping of substances and read-across approach for ecotoxicological information' above.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to update the technical dossier and the Chemical Safety Report using this study showing the highest concern as key study according to Annex I section 3.1.5. for the endpoint of Short-term toxicity testing on invertebrates (Annex VII section 9.1.1.) or provide a detailed justification for not using the study giving rise to the highest concern.

Note for your consideration for requests 3-6

Before conducting the tests requested above under points 4. and 5., you shall consult the ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Section R.7.8.5 to determine the necessity to conduct the long-term toxicity testing on aquatic invertebrates and on fish.

Concerning the order of studies to be conducted, you may first complete the requirements on short-term aquatic studies requested under points 3 and 6 in this decision, and subsequently update the CSA according to Annex I of the REACH Regulation. When updating your CSA, you need to consider which data to use as the starting point for PNEC derivation as given in Annex I, Sections 3.3.1. and 6.

If you come to the conclusion that no further investigation of chronic effects on aquatic organisms is required, you shall update your technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, 9.1.5 and 9.1.6. taking into account the new data generated by the growth inhibition study requested by the present decision and exposure assessment and risk characterisation.

On the other hand, if after the update of the CSA you come to the conclusion that the long-term toxicity tests are still required to refine the risk assessment, you should further consider Integrated Testing Strategy (ITS) for aquatic toxicity as described in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4). According to the ITS, if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially less sensitive than other trophic levels (i.e. fish, invertebrates, algae), long-term studies may be required on both fish and invertebrates. In such case, according to the ITS, the long-term *Daphnia* study is to be conducted first.

If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 01 March 2017.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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 took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.