EUROPEAN CHEMICALS AGENCY

Helsinki, 16 December 2016

Addressee: [redacted]

Decision number: CCH-D-2114350591-53-01/F
Substance name: N-[3-(DIMETHYLAMINO)PROPYL]-N,N',N'-TRIMETHYLPROPANE-1,3-DIAMINE
EC number: 223-362-3
CAS number: 3855-32-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 18.11.2015
Registered tonnage band: 100-1000T

DECISION ON A COMPLIANCE CHECK

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

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

2. ***In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3; test method: OECD TG 476 or OECD TG 490) with the registered substance provided that the study requested under 1. has negative results;**

3. **Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD 421) in rats, oral route with the registered substance;**

4. **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;**

5. **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;**

6. **Robust study summary for key study, [redacted] Determination of the acute toxicity of N,N,N',N'',N''-Pentamethyldipropylentriamin to the water flea Daphnia magna STRAUS (Annex VII, Section 9.1.1. in conjunction with Annex I, Section 3.1.5**

7. **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;**

8. **Robust study summary for key study, [redacted]. N;N;N';N'';N''-Pentamethyldipropylentriamin: Acute toxicity study on the zebra fish (Brachydanio rerio HAM. and BUCH. in a static system (96 hours) (Annex VIII, Section 9.1.3. in conjunction with Annex I, Section 3.1.5)**

9. **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;**

10. **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.**

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 of the REACH Regulation. In order 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 an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **24 June 2019**. You shall also 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. Advice and further observations are provided in Appendix 3.

Appeal

Applicable only for the final decision: 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, shall 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 Kevin Pollard, Head of Unit, Evaluation E1

[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.

ECHA
EUROPEAN CHEMICALS AGENCY

Appendix 1: Reasons

1. **In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)**

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

An "*In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. 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 reading across information from an in vitro micronucleus study conducted with the analogue substance(s) [redacted].

In order to justify this read-across approach you have indicated in section 5. Human health hazard assessment of the Chemical Satefy Report that "[redacted]"

You concluded for this endpoint that "*Based on the identical predictions and the negative Ames tests available for both substances, meeting the additional genotoxicity data requirements for CAS 3855-32-1 by read-across to the studies(mouse lymphoma assay, micronucleus assay in human lymphocytes) for* [redacted] *is therefore considered to be scientifically justified*".

ECHA has evaluated the information and documentation provided in the registration dossier in light of the requirements of Annex XI, Section 1.5 of the REACH Regulation and concludes that the requirements of Annex XI, Section 1.5 are not met for the following reasons.

Impact of the structural differences on the prediction of properties

According to the provisions of Annex XI, Section 1.5 of the REACH Regulation, structural similarity is a prerequisite for applying grouping and read-across approaches. However, structurally similar substances still exhibit differences in their chemical structures.

The potential impact of these structural differences on the properties of the substances needs to be accounted for in the read-across hypothesis and justification in order to establish that the substances are likely to have similar toxicological properties, as required by the provisions of Annex XI, Section 1.5, and in turn that the toxicological properties of the target substance can be predicted from data on the source substance.

You have indicated in your read-across justification that the source and target substances are structurally similar in that they both are aliphatic tertiary amines. However, ECHA observes that despite this structural similarity, the source and target substances exhibit significant structural differences. Specifically, and as you pointed out in your read-across justification, the substances differ by "*the presence of an additional (*[redacted]" in the source substance.

Your read-across hypothesis for this endpoint is based on structural similarity, on similarities in physico-chemical and toxicological properties, on similar results in Ames tests performed with the source and target substances and on the reactivity profiles for both substances predicted by multiple expert systems. While the alert related to the formation of an iminium ion is related to a common structural feature in both substances, ECHA points out that you have not provided in your read-across hypothesis and justification, an assessment supported by scientific justifications of the impact of these structural differences between the source and the target substances on the properties of these substances. In the absence of this information, ECHA concludes that you have not provided an adequate basis for predicting the properties of the registered substance from the source substances as required by the provisions of Annex XI, section 1.5 of the REACH Regulation.

Missing supporting evidence and source studies

According to the provisions of Annex XI, Section 1.5 of the REACH Regulation, the properties of substances used in read-across approaches must be likely to be similar or follow a regular pattern. ECHA observes that no information supporting your read-across hypothesis and claim of similarity in the properties of the source and the target substances is included in the registration dossier. More specifically, for the endpoint under consideration, your read-across hypothesis is based on structural similarity, similarity in physico-chemical properties, similarities in some toxicological properties and similar toxicological fingerprints for genetic toxicity obtained from multiple expert systems.

ECHA highlights that no endpoint study record presenting a robust study summary of the study intended to be used as source study in this read-across approach, i.e. in vitro micronucleus study performed with the source substance [redacted], is provided in the technical dossier of the target substance. You state in the CSR section 5 that "*the data presented in the REACH Registration dossiers for CAS 3855-32-1 and* [redacted] *and the proposed read-across are summarised in the table below*". This suggests that the data is available in the REACH registration dossier submitted for the source substance. ECHA stresses that cross-referencing information provided in other registration dossiers is not regarded as an adequate method to document elements of a read-across approach.

In the absence of robust study summaries on the source studies in the technical dossier for the substance subject to this decision, ECHA considers that you have failed to establish an adequate and reliable basis according to which the properties of the registered substance can be predicted from data on the source substance, as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

Furthermore, ECHA points out that none of the predictions referred to in your read-across justification have been included in the technical dossier. Further, no endpoint study record presenting a (robust) study summary of the Ames test performed with the source substance and referred to by you as supporting of a similar toxicological profile for this endpoint has been provided. In the absence of detailed reporting of these lines of evidence, their reliability and adequacy as supporting information in this read-across approach cannot be assessed. Therefore, ECHA considers that evidence supporting essential elements of your read-across hypothesis is missing in the dossier. In the absence of such supporting information the hypothesis according to which the properties of the substances are likely to be similar for the endpoint under consideration, ECHA is of the opinion that you have not provided an adequate basis for predicting the properties of the registered substance from the source substances as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

For all the reasons set out above, ECHA considers that this grouping 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, 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 considers that the *in vitro* mammalian chromosome aberration test (test method OECD TG 473) and the *in vitro* mammalian cell micronucleus test (OECD TG 487) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

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: *In vitro* mammalian chromosome aberration test (test method: OECD TG 473) or *in vitro* mammalian cell micronucleus study (test method: OECD TG 487).

2. *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained.

ECHA notes that the registration dossier does not contain study records for the information requirement of Annex VIII, Section 8.4.2. Therefore, adequate information *on in vitro* gene mutation in mammalian cells needs to be present in the technical dossier for the registered substance to meet this information requirement provided that the study requested under 1. above has negative results.

You have sought to adapt this information requirement according to Annex XI, Section 1.5 of the REACH Regulation by reading across information from an in vitro mouse lymphoma assay conducted with the analogue substance [redacted]

In order to justify this read-across approach you have the same justification as detailed in section 1 above.

ECHA has evaluated the information and documentation provided in the registration dossier in light of the requirements of Annex XI, Section 1.5 of the REACH Regulation and concludes that the requirements of Annex XI, Section 1.5 are not met for the reasons listed under 1. above.

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 considers that the *in vitro* mammalian cell gene mutation tests using the *Hprt* and *xprt* genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.3.

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: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that the study requested under 1. has negative results.

3. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Screening for reproductive/developmental toxicity" (test method OECD TG 421 or 422) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from *in vitro* methods that the substance may be a developmental toxicant. No such evidence is presented in the dossier. Therefore, 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 screening for reproductive/developmental toxicity in the dossier that would meet the information requirement of Annex VIII, Section 8.7.1.

You have sought to adapt this information requirement according to Annex XI, Section 1.5 of the REACH Regulation by reading-across information from a 28-day repeated-dose toxicity study conducted with the analogue substance [redacted].

Your justification for this adaptation reported in the technical dossier indicates that "*Pending receipt of PC77 28-day study, a read-across is performed from the 28-day study* [redacted]" and further details the findings observed in this 28-day repeated dose toxicity study conducted with the source substance, outlining that this study "*revealed effects primarily associated with the corrosive effects of the substance*". You concluded on the basis of this data that "*The results of these studies strongly indicate that the corrosive effects of Polycat9 are the cause of all observed effects. Although a NOAEL was derived, it's relevance is questionable. Only animals in the high-dose group showed significant effects, and these are consistent with the animals being dosed with a corrosive. Thus, it is proposed to focus on a qualitative human health assessment, wherein exposure to the substance is to be avoided. Any exposure to the substance will elicit immediate irritating effects, and lead to self rremoval. The chance of chronic exposure to this substance is extremely unlikely. For this reason, and in consideration of animal welfare concerns, further vertebrate studies are not warranted*".

ECHA has evaluated the information and documentation provided in the registration dossier for this endpoint in light of the requirements of Annex XI, Section 1.5 of the REACH Regulation and concludes that the requirements of Annex XI, Section 1.5 are not met for the following reasons.

Inconsistency in the information provided in the technical dossier and CSR

ECHA understands from the following statement provided in your justification for the adaptation in the technical dossier "*Pending receipt of PC77 28-day study, a read-across is performed from the 28-day study in* [redacted]" that you are awaiting results from a 28-day repeated-dose toxicity study conducted with the registered substance. ECHA also notes that the information provided in the data matrix included in the CSR on page 31 suggests that a reproductive toxicity screening study is ongoing with the source and with the target substances. Whilst the nature of the ongoing studies remains unclear based on the information provided in the technical dossier and in the CSR, ECHA points out that a 28-day repeated dose toxicity study performed with the registered substance cannot be used to fulfil the information requirement of Annex VIII, Section 8.7.1., because it does not cover key parameters of a screening study for developmental/reproductive toxicity, with examinations of effects of a test substance on male and female reproductive performance such as gonadal function, mating behaviour, conception, development of the conceptus and parturition.

Waiving of the information requirement based on corrosive properties

As indicated above, your adaptation is based on postulated similarity in effects between the source substance [redacted]) and the target substance subject to this decision. You indicated in your justification of this adaptation that you consider that the effects observed in this study are "*primarily associated with the corrosive effects of the substance*".

ECHA understands that you intend to use this read-across approach to establish that the toxicological response to repeated oral exposure to the target substance would be of a similar nature as that observed with the source substance, i.e. that it would also be primarily associated with effects caused by the corrosive properties of the target substance. On this basis, you propose to address these hazards in a qualitative risk assessment rather than by conducting further testing for the endpoint under consideration.

ECHA recognises the merits of a qualitative risk assessment in controlling the risks associated with the corrosive properties of the substance subject to this decision. However, ECHA points out that the identification of corrosive properties and the development of a qualitative risk assessment do not constitute, by themselves, valid reasons for waiving the information requirement of Annex VIII, section 8.7.1 for a screening study for reproductive/developmental toxicity. In addition ECHA points out that increases in the relative weights of kidneys, ovaries, uterus in females of the high dose group have been reported in this study, together with increased relative weight of the pituitary gland in treated satellite females and decreased weight of epididymides in treated satellite males. These observations may suggest that the source substance causes systemic toxicity which may not be secondary to its corrosive properties.

ECHA notes that you have not provided a read-across hypothesis and justification to establish that reproductive toxicity properties of the registered substance can be predicted from data obtained from the source substance. In the absence of an endpoint-specific hypothesis, ECHA concludes that you have not provided, in this read-across approach, an adequate basis for predicting the properties of the registered substance from the source substances for the endpoint under consideration as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

Furthermore, Annex XI, Section 1.5 requires that the source study(ies) used in a read-across approach should provide results that are adequate for classification and labelling, should have an adequate and reliable coverage of the key parameters and an exposure duration at least matching these parameters in the corresponding test method according to Article 13(3) of the REACH Regulation. The read-across approach for this endpoint, as currently reported in the technical dossier, refers to information on local and systemic toxicity observed in a 28-day repeated dose toxicity study. No evidence of toxicity to the reproductive organs is reported from this study. This source study does not provide the information required by Annex VIII, Section 8.7.1., because it does not cover key parameters of a screening study for developmental/reproductive toxicity, with examinations of effects of a test substance on male and female reproductive performance such as gonadal function, mating behaviour, conception, development of the conceptus and parturition.

Therefore ECHA considers that the source study that you have reported in this read-across approach does not constitute an adequate and reliable basis for predicting the properties of the registered substance from data on the analogue substance for the endpoint under consideration as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

For all the reasons set out above, ECHA considers that this grouping 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, 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 methods OECD TG 421, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

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 4.1, October 2015) R.7a, chapter 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.

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: Reproductive/developmental toxicity screening test (test method: OECD TG 421) in rats by the oral route.

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH 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.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by reading across information from a 28-day repeated dose toxicity study (EU Method B.7) conducted via the oral route with the analogue substance [redacted].

In order to justify this read-across approach you have indicated in section 5. Human health hazard assessment of the Chemical Safety Report that "[redacted] *CAS 3855-32-1* [redacted].

You further provided the following endpoint-specific information: *"The available toxicological data for CAS 3855-32-1 and* [redacted] *indicate irritation/corrosivity as the predominant effect. The 28-day toxicity study performed with* [redacted] *identifies a NOAEL of 200 mg/kg bw/d based on effects at the highest dose level of 400 mg/kg bw/d. Findings in this study were limited to local effects on the gastrointestinal tract (or secondary findings) and are consistent with the corrosive nature of the substance. The results of a range-finding study performed with CAS 3855-32-1 showed no effects at a dose level of 100 mg/kg bw/d, marked toxicity and local effects on the stomach at 600 mg/kg bw/d and less marked effects at 300 mg/kg bw/d"* and you concluded on this basis that *"A comparable level of toxicity and a similar predominance of local effects and an absence of systemic toxicity can be predicted for CAS 3855-32-1; read-across to the 28-day study performed with* [redacted] *is therefore scientifically justified and also is clearly in the interests of animal welfare"*

ECHA has evaluated the information and documentation provided in the registration dossier in light of the requirements of Annex XI, Section 1.5 of the REACH Regulation and concludes that the requirements of Annex XI, Section 1.5 are not met for the following reasons.

Impact of the structural differences on the prediction of properties

According to the provisions of Annex XI, section 1.5 of the REACH Regulation, structural similarity is a prerequisite for applying grouping and read-across approaches. However, structurally similar substances still exhibit differences in their chemical structures. The potential impact of these structural differences on the properties of the substances needs to be accounted for in the read-across hypothesis and justification in order to establish that the substances are likely to have similar toxicological properties, as required by the provisions of Annex XI, section 1.5, and in turn that the toxicological properties of the target substance can be predicted from data on the source substance.

You have indicated in your read-across justification that the source and target substances are structurally similar in that they both are aliphatic tertiary amines. However, ECHA observes that despite this structural similarity, the source and target substances exhibit significant structural differences. Specifically, and as you pointed out in your read-across justification, the substances differ by "*the presence of an additional (*[redacted]" in the source substance.

Your read-across hypothesis for this endpoint is based on structural similarity, on similarities in physico-chemical and toxicological properties, on similar effects observed in a 28-day repeated dose toxicity study performed with the source substance and in a dose-range finding study performed with the target substance. ECHA points out that you have not provided in your read-across hypothesis and justification, an assessment supported by scientific justifications of the impact of the identified structural differences between the source and the target substances on the properties of these substances. In the absence of this information ECHA concludes that you have not provided an adequate basis for predicting the properties of the registered substance from the source substances as required by the provisions of Annex XI, section 1.5 of the REACH Regulation.

Missing supporting evidence

According to the provisions of Annex XI, Section 1.5 of the REACH Regulation, the properties of substances used in read-across approaches must be likely to be similar or follow a regular pattern. ECHA notes that no information supporting your read-across hypothesis and claim of similarity in the properties of the source and the target substances is included in the registration dossier. More specifically, for the endpoint under consideration, your read-across hypothesis is based on structural similarity, similarity in physico-chemical properties, similarities in some toxicological properties and on similar effects observed in a 28-day repeated dose toxicity study performed with the source substance and in a dose-range finding study performed with the target substance.

ECHA points out that no endpoint study record presenting a (robust) study summary of the range-finding study conducted with the target substance and referred to as supporting evidence of a similar toxicological profile for this endpoint has been provided. In the absence of information on this study, its reliability and adequacy as supporting information in this read-across approach cannot be assessed. ECHA considers that evidence supporting essential elements of your read-across hypothesis for the endpoint repeated-dose toxicity is missing in the dossier.

In the absence of such information, the hypothesis according to which the properties of the substances are likely to be similar for the endpoint under consideration cannot be verified. Therefore, ECHA considers that you have not provided an adequate basis for predicting the properties of the registered substance from the source substances as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

Adequacy of the source study

Annex XI, Section 1.5 requires that the source study(ies) used in a read-across approach should provide results that are adequate for classification and labelling, should have an adequate and reliable coverage of the key parameters and an exposure duration at least matching these parameters in the corresponding test method according to Article 13(3) of the REACH Regulation.

ECHA observes that the source study that you have used in your read-across approach, *PURAMCAT, 2012, Read-across* is a 28-day repeated dose toxicity study performed according to the OECD TG 407. This study does not provide the information required by Annex IX, Section 8.6.2., because the exposure duration is less than 90 days and the number of animals per dose group is significantly lower than in a sub-chronic (90-day) repeated toxicity study performed according to the OECD TG 408.

Therefore, the sensitivity of a 28-day study is much lower than that of a 90-day study. On that basis, ECHA considers that this source study does not fulfil the requirement of Annex XI, Section 1.5 of the REACH Regulation for an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) and therefore that it does not constitute an adequate and reliable basis for predicting the properties of the registered substance from data on the analogue substance as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

For all the reasons set out above, ECHA considers that this grouping 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, 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. The substance is a corrosive liquid. Based on the information reported in the dossier, the industrial uses include industrial spraying (PROC 7) and the professional uses include non-industrial spraying (PROC 11). Therefore exposure of the respiratory tract and local respiratory effects cannot be excluded. Local respiratory effects have been addressed by a qualitative risk assessment; therefore ECHA considers that further investigations of the systemic toxicity of the substance subject to this decision should be conducted via the oral route.

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.

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.

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH 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 according to Annex XI, Section 1.5. of the REACH Regulation by reading-across information from a 28-day repeated-dose toxicity study conducted with the analogue substance [redacted].

Your justification for this adaptation reported in the technical dossier indicates that "*Pending receipt of PC77 28-day study, a read-across is performed from the 28-day study in* [redacted]" and further details the findings observed in this 28-day repeated dose toxciity study conducted with the source substance, outlining that this study "*revealed effects primarily associated with the corrosive effects of the substance*". You concluded on the basis of this data that "*The results of these studies strongly indicate that the corrosive effects of Polycat9 are the cause of all observed effects. Although a NOAEL was derived, it's relevance is questionable. Only animals in the high-dose group showed significant effects, and these are consistent with the animals being dosed with a corrosive. Thus, it is proposed to focus on a qualitative human health assessment, wherein exposure to the substance is to be avoided. Any exposure to the substance will elicit immediate irritating effects, and lead to self rremoval. The chance of chronic exposure to this substance is extremely unlikely. For this reason, and in consideration of animal welfare concerns, further vertebrate studies are not warranted*".

ECHA has evaluated the information and documentation provided in the registration dossier for this endpoint in light of the requirements of Annex XI, Section 1.5 of the REACH Regulation and concludes that the requirements of Annex XI, Section 1.5 are not met for the following reasons.

As indicated above, your adaptation is based on postulated similarity in effects between the source substance [redacted] and the target substance subject to this decision. You indicated in your justification of this adaptation that you consider that the effects observed in this study are "*primarily associated with the corrosive effects of the substance*".

ECHA understands that you intend to use this read-across approach to establish that the toxicological response to repeated oral exposure to the target substance would be of a similar nature as that observed with the source substance, i.e. that it would also be primarily associated with effects caused by the corrosive properties of the target substance. On this basis, you propose to address these hazards in a qualitative risk assessment rather than by conducting further testing for the endpoint under consideration.

ECHA recognises the merits of a qualitative risk assessment in controlling the risks associated with the corrosive properties of the substance subject to this decision. However, ECHA points out that the identification of corrosive properties and the development of a qualitative risk assessment do not constitute, by themselves, valid reasons for waiving the information requirement of Annex IX, section 8.7.2 for a pre-natal developmental toxicity study. In addition ECHA points out that increases in the relative weights of kidneys, adrenal glands, ovaries, uterus in females of the high dose group have been reported in this study, together with increased relative weight of the pituitary gland in treated satellite females and decreased weight of epididymides in treated satellite males. These observations may suggest that the source substance causes systemic toxicity which may not be secondary to its corrosive properties.

ECHA notes that you have not provided a read-across hypothesis and justification to establish that developmental toxicity properties of the registered substance can be predicted from data obtained from the source substance. In the absence of an endpoint-specific hypothesis, ECHA concludes that you have not provided, in this read-across approach, an adequate basis for predicting the properties of the registered substance from the source substances for the endpoint under consideration as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

Furthermore, Annex XI, Section 1.5 requires that the source study(ies) used in a read-across approach should provide results that are adequate for classification and labelling, should have an adequate and reliable coverage of the key parameters and an exposure duration at least matching these parameters in the corresponding test method according to Article 13(3) of the REACH Regulation. ECHA observes that the read-across approach for this endpoint, as currently reported in the technical dossier, refers to information on local and systemic toxicity observed in a 28-day repeated dose toxicity study. No evidence of toxicity to the reproductive organs is reported from this study. ECHA points out that this source 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 ECHA considers that the source study that you have reported in this read-across approach does not constitute an adequate and reliable basis for predicting the properties of the registered substance from data on the analogue substance for the endpoint under consideration as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

For all the reasons set out above, ECHA considers that this grouping 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, your adaptation of the information requirement is rejected. 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 4.1, October 2015) R.7a, chapter 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.

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.

6. **Robust study summary for key study, [redacted]. Determination of the acute toxicity of N,N,N',N'',N''-Pentamethyldipropylentriamin to the water flea Daphnia magna STRAUS (Annex VII, Section 9.1.1. in conjunction with Annex I, Section 3.1.5);**

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

Pursuant to Articles 10(a)(vii) of the REACH Regulation, the information set out in Annex VII to XI must be provided in the form of a robust study summary, if required under Annex I. Article 3(28) defines a robust study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report. Guidance on the preparation of the robust study summaries is provided in the ECHA Practical Guide 3: 'How to report robust study summaries' (Version 2.0, November 2012).

"Short-term toxicity testing on aquatic invertebrates", is a standard information requirement as laid down in Annex VII, Section 9.1.1. 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. Furthermore, pursuant to Article 10(a)(vii) and Annex I, Section 3.1.5. if there are several studies addressing the same effect, then, the study or studies giving rise to the highest concern shall be used to draw the conclusion and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment.

In the technical dossier you have provided a study record for "*Determination of the acute toxicity of N,N,N',N'',N''-Pentamethyldipropylentriamin to the water flea Daphnia magna STRAUS*" (key study, GLP, [redacted]) according to EU Method C.2 (Acute Toxicity for Daphnia) and GLP, to meet the information required by Annex VII, Section 9.1.1. ECHA notes the following:

a) In your robust study summary, you have reported that pH varied from 7.0 to 9.5 during duration to test. According to EU Method C.2 quality criteria the pH should not vary more than one unit.

b) Your reporting is contradictory: only the following four test concentrations are reported to be sampled: 100 mg/L, 25 mg/L; 3.13 mg/L; 0 mg/L while the following test concentrations are reported: control; 3.13. mg/L (nominal); 6.25 mg/L (nominal); 12.5 mg/L (nominal); 25 mg/L (nominal); 50 mg/L (nominal); 50 mg/L neutralised (nominal); 100 mg/L (nominal); 100 mg/L neutralised (nominal).
c) You did not report the age of the test species, *Daphnia magna Straus*. According to the EU Method C.2 they shall be less than 24 hours old at the beginning of the test, laboratory bred, free from overt disease and with a known history (e.g. breeding -any pre-treatments, etc.).
d) In your robust study summary you have not provided a table showing the cumulative immobilisation at each concentration and the control (and control with the auxiliary substance if required) at each of the recommended observation times (24 and 48 h). However, in the Applicant's summary and conclusion you have stated that the validity criteria was fulfilled and that "*In the control, immobilisation was less than or equal to 10%.*"

Overall, the quality criteria regarding the EU C.2 is not fulfilled and the reporting is not adequate. ECHA considers this lack of information undermines the reliability of the test results on algal growth inhibition.

Therefore, ECHA notes that, contrary to Article 3(28) of the REACH Regulation the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment. In particular, the above mentioned elements regarding the quality criteria are missing.

Since the outcome of this study is used in your chemical safety assessment and as a result also to adapt the information requirements for long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5) and long-term toxicity testing on fish (Annex IX, Section 9.1.6.1) pursuant to Article 41(1) and (3) of the REACH Regulation you are requested to provide a complete robust study summary with the above missing elements for this study.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information: Robust study summary for the key study, [redacted]. Determination of the acute toxicity of N,N,N',N'',N''-Pentamethyldipropylentriamin to the water flea Daphnia magna STRAUS.

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

Pursuant to Articles 10(a) (vi) and 12(1)(e) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH 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 read-across information from an algal growth inhibition study (EU Method C.3) conducted with the analogue substance [redacted]

In order to justify this read-across approach you have indicated in section 7. Environmental hazard assessment of the Chemical Safety Report that "*The substances are structurally similar aliphatic tertiary amines. Structurally,* [redacted] *differs only in* [redacted] and that "*Both substances are highly water-soluble and have similar partition coefficients. Both substances have the same physical state (liquid) with comparable surface tensions, boiling points and melting points. Given this close similarity,behaviour in the environment driven by physicochemical properties (such as organic carbon binding, fugacity, partitioning and bioavailability)is expected to be highly similar. (...)*"

You further provided the following endpoint-specific information: "*non-target environmental organism toxicity data indicates broadly the same ecotoxicology profiles for each substance. In all cases equivalent endpoints for core aquatic toxicity studies are within one order of magnitude. For example in a Daphnia acute toxicity study the acute EC50 is 34.4 mg/L for CAS 3855-32-1 and 48 mg/L for* [redacted]*. Acute endpoints for fish are more difficult to compare directly, as the testing of each substance was conducted with different species and different test durations. A 96-hour test in zebra fish was conducted for CAS3855-32-1, while a 48-hour test in Medaka was conducted for* [redacted] *Nevertheless, the derived endpoint values were within the expected range of interspecies variability at LC50 = 92.5 mg/L and TLM = 430 mg/L, respectively. Given the above it is considered that the environmental behaviour and ecotoxicology profiles for CAS 3855-32-1 and* [redacted] *are sufficiently equivalent for the purposes of read across.*"

ECHA has evaluated the information and documentation provided in the registration dossier in light of the requirements of Annex XI, Section 1.5 of the REACH Regulation and concludes that the requirements of Annex XI, Section 1.5 are not met for the following reasons.

Impact of the structural differences on the prediction of properties

According to the provisions of Annex XI, section 1.5 of the REACH Regulation, structural similarity is a prerequisite for applying grouping and read-across approaches. However, structurally similar substances still exhibit differences in their chemical structures. The potential impact of these structural differences on the properties of the substances needs to be accounted for in the read-across hypothesis and justification in order to establish that the substances are likely to have similar fate and ecotoxicological properties, as required by the provisions of Annex XI, section 1.5, and in turn that the fate and ecotoxicological properties of the target substance can be predicted from data on the source substance.

You have indicated in your read-across justification that the source and target substances are structurally similar in that they both are aliphatic tertiary amines. However, ECHA observes that despite this structural similarity, the source and target substances exhibit significant structural differences. Specifically, and as you pointed out in your read-across justification, the substances differ by "*the presence of an additional (*[redacted]" in the source substance.

Your read-across hypothesis for this endpoint is based on structural similarity; on similarities in physico-chemical, fate and ecotoxicological properties; on similar EC50 values ("*within one order of magnitude*") observed in a *Daphnia* acute toxicity study performed with the source and target substances and on similar endpoint values ("*within the expected range of interspecies variability*") observed in fish acute toxicity studies performed with the source and target substances on different species and with different test durations. ECHA points out that you have not provided in your read-across hypothesis and justification, an assessment supported by scientific justifications of the impact of the identified structural differences between the source and the target substances on the properties of these substances. In particular for this endpoint, you did not explain how the difference in structure between target and source substances would affect algae growth inhibition toxicity and how the source study can be used as a worst case scenario. In the absence of this information ECHA concludes that you have not provided an adequate basis for predicting the properties of the registered substance from the source substances as required by the provisions of Annex XI, section 1.5 of the REACH Regulation.

Missing supporting evidence

According to the provisions of Annex XI, Section 1.5 of the REACH Regulation, the properties of substances used in read-across approaches must be likely to be similar or follow a regular pattern. ECHA notes that there is insufficient information supporting your read-across hypothesis and claim of similarity in the properties of the source and the target substances in the registration dossier. More specifically, for the endpoint under consideration, your read-across hypothesis is based on structural similarity; on similarities in physico-chemical, fate and ecotoxicological properties; on similar EC50 values ("*within one order of magnitude*") observed in a *Daphnia* acute toxicity study performed with the source and target substances and on similar endpoint values ("*within the expected range of interspecies variability*") observed in fish acute toxicity studies performed with the source and target substances on different species and with different test durations.

ECHA points out that the results of the short-term fish toxicity tests conducted with the target and source substances cannot be compared, because, as you indicated, different fish species and different durations exposures have been used. In addition, ECHA notes that the validity of the bridging study on *Daphnia* acute toxicity conducted with the target and source substances cannot be established, because, as explained above in section 6, there is insufficient evidence in the RSS to establish whether the test performed on the registered substance is valid. In the absence of such information, the hypothesis according to which the properties of the substances are likely to be similar for the endpoint under consideration cannot be verified. Therefore, ECHA considers that you have not provided an adequate basis for predicting the properties of the registered substance from the source substances as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

Adequacy of the source study

Annex XI, Section 1.5 requires that the source study(ies) used in a read-across approach should provide results that are adequate for classification and labelling, should have an adequate and reliable coverage of the key parameters and an exposure duration at least matching these parameters in the corresponding test method according to Article 13(3) of the REACH Regulation.

ECHA observes that in your read-across approach you have used the study "POLYCAT 9 Catalyst - Alga, Growth Inhibition Test" (key study, [redacted] (2012), [redacted] dated on 2012-10-18, owner [redacted] according to EU Method C.3. (Algal Inhibition Test) and GLP with the analogue substance [redacted], purity 98,5 % (w/w). For this analogue source data, you have reported the following deviations from the EU Method C.3 test guideline: *"Nominal concentrations were used for three test concentrations (6, 10, and 16 mg/L) for which the measured concentrations were below the LOQ and for which geometric mean concentrations could not be calculated."*

ECHA notes, that in your robust study summary you have reported that the following test validity criteria was fulfilled: *"1) biomass in the controls increased ≥16x within the 72-h test; 2) mean coefficient of variation (Cv) for specific growth rates in the controls was ≤ 35 %; and 3) Cv of avg sp. growth rate in repl. controls was ≤7%."* In addition, according to EU Method C.3, the concentrations of the test substance shall be maintained to within [redacted] % of the initial concentrations/throughout a time corresponding to the duration of the test. Also evidence shall be presented that the concentrations have been maintained throughout the test and that the quality criteria have been satisfied. ECHA notes, that in your robust study summary you have not provided any such evidence, and therefore the test quality criteria cannot be considered as fulfilled. Furthermore, in your preliminary test you have noted that *"The analytical results showed that the test substance was not stable in test medium under the conditions of testing."*

ECHA also notes that, the pH varied from 7.9 to 9.5 in the test vessels during the conduct of the full test. You did not explain this variability in pH in your robust study summary. According to EU Method C.3. test guideline, the explanation should be provided if pH deviations of more than 1.5 units are observed.

In general, in your robust study summary, you have not provided all the information and results possible to report with EU Method C.3, including graphical presentation of the concentration effect relationship or NOEC.

Overall, the quality criteria regarding the EU Method C.3 is not fulfilled and the reporting is not adequate. On that basis, ECHA considers that this source study does not fulfil the requirement of Annex XI, Section 1.5 of the REACH Regulation and therefore that it does not constitute an adequate and reliable basis for predicting the properties of the registered substance from data on the analogue substance as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

For all the reasons set out above, ECHA considers that this grouping 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, 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 3.0, February 2016) 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).

8. **Robust study summary for key study, [redacted]. N;N;N';N'';N''-Pentamethyldipropylentriamin: Acute toxicity study on the zebra fish (Brachydanio rerio HAM. and BUCH. in a static system (96 hours) (Annex VIII, Section 9.1.3. in conjunction with Annex I, Section 3.1.5);**

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

Pursuant to Articles 10(a)(vii) of the REACH Regulation, the information set out in Annex VII to XI must be provided in the form of robust study summary, if required under Annex I. Article 3(28) defines a robust study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report. Guidance on the preparation of the robust study summaries is provided in the ECHA Practical Guide 3: 'How to report robust study summaries' (Version 2.0, November 2012).

"Short-term toxicity testing on fish", is a standard information requirement as laid down in Annex VIII, Section 9.1.3. 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. Furthermore, pursuant to Article 10 (a)(vii) and Annex I, Section 3.1.5. if there are several studies addressing the same effect, then, the study or studies giving rise to the highest concern shall be used to draw the conclusion and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment.

In the technical dossier you have provided a study record for a N;N;N';N'';N''-Pentamethyldipropylentriamin: Acute toxicity study on the zebra fish (Brachydanio rerio HAM. and BUCH. in a static system (96 hours) (key study, [redacted]) according to OECD TG 203 (Fish, Acute Toxicity Test) and GLP, with the registered substance, to meet the standard information requirement of Annex VIII, Section 9.1.3.For a test according to OECD TG 203 to be valid the following conditions should be fulfilled:

1) the mortality in the control(s) should not exceed 10% (or one fish if less than 10 fish are used) at the end of the test;
2) constant conditions should be maintained as far as possible throughout the test and, if necessary, semi-static or flow-through procedures should be used;
3) the dissolved oxygen concentration must have been at least 60 per cent of air saturation value throughout the test;

4) there must be evidence that the concentration of the substance being tested has been satisfactorily maintained, and preferable it should be at least 80 per cent of the nominal concentration throughout the test. If the deviation from the nominal concentration is greater than 20 per cent, results should be based on the measured concentration.

In your robust study summary, you have not reported the results of the mortality of the control. Also, you have not provided any information regarding the keeping of the constant conditions and that the concentration of the test substance has been satisfactorily maintained during the test. You have only reported the nominal values for the static test. Also you have not reported the dissolved oxygen concentrations; you only mention that "no aeration" was done during the test. Furthermore, the average zebra fish length at the study initiation 3.4 cm (range 2.7 - 3.7 cm), that you reported, is higher than the OECD 203 test guideline recommendation for the zebra fish (2.0 ± 1.0 cm).However, you have not provided any explanation or justification for this or any other possible deviations from the OECD 203 test guideline's recommendations.

Therefore, ECHA notes that, contrary to Article 3(28) of the REACH Regulation the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment. In particular, the above mentioned elements regarding the quality criteria are missing.

Since the outcome of this study is used in your chemical safety assessment and as a result also to adapt the information requirements for long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5) and long-term toxicity testing on fish (Annex IX, Section 9.1.6.1) pursuant to Article 41(1) and (3) of the REACH Regulation you are requested to provide a complete robust study summary with the above missing elements for this study.

Therefore pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information: Robust study summary for key study, [redacted] N;N;N';N'';N''-Pentamethyldipropylentriamin: Acute toxicity study on the zebra fish (Brachydanio rerio HAM. and BUCH. in a static system (96 hours).

9. and 10. 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), and 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).

"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. "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 these endpoints need to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt these information requirements according to Annex IX, Sections 9.1.5. and 9.1.6 column 2 . You provided the following justification for both adaptations: "*According to Regulation (EC) No.1907/2006, Annexes VIII and IX, Column 2, long-term aquatic toxicity testing shall be conducted if the substance is poorly soluble in water, or if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. The substance is soluble in water, and the chemical safety assessment indicated that aquatic exposures do not require further investigation; the risk characterisation ratios for surface water are below one. Therefore, in accordance with Annex I, the risks are considered to be controlled, and long-term toxicity testing of aquatic invertebrates / fish is not indicated.*" However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Sections 9.1.5 and 9.1.6 since no valid information on short or long-term toxicity to aquatic invertebrates and fish is available in the registration dossier. In the absence of valid information on short-term toxicity to aquatic invertebrates, algae and fish, it cannot be concluded if fish or invertebrates or aquatic plants are shown to be substantially more sensitive.

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

As explained above, the information provided on these endpoints 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 3.0, February 2016):

- the *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.
- the fish early-life stage 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.

Regarding the long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6.1, ECHA considers that the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Figure R.7.8-4). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 3.0, February 2016). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as most appropriate and suitable.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, based on the results of the short-term toxicity tests in sections 2 – 3 above, you are you are requested to submit the following information derived with the registered substance subject to the present decision: Long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211) and/or Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.; test method: Fish, early-life stage toxicity test, OECD 210).

Note for consideration for aquatic testing:

Due to the ionising properties of the registered substance you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

Notes for your consideration for long-term aquatic testing

Before conducting any of the tests mentioned above in points 9 -10 you shall consult the ECHA *Guidance on information requirements and chemical safety assessment (version 3.0, February 2016)*, Chapter R7b, Section R.7.8.5 to determine the sequence in which the aquatic long-term toxicity tests are to be conducted and the necessity to conduct long-term toxicity testing on fish.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the *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.

If you come to the conclusion that no further investigation of 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 short-term toxicity studies requested by the present decision.

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 14 April 2016.

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 did not receive any comments by the end of the commenting period.

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 request(s) in this decision, or to fulfil otherwise the information requirement(s) 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 test(s) 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 test(s) 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 test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.