Helsinki, 14 February 2018

Addressee: [redacted]

Decision number: CCH-D-2114392118-45-01/F
Substance name: 2-dibutylaminoethanol
EC number: 203-057-1
CAS number: 102-81-8
Registration number: [redacted]
Submission number: [redacted]
Submission date: 13/04/2017
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 information on:

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. **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;**

4. **Update of the technical dossier and the Chemical Safety Report for the endpoint of Ready biodegradability (Annex VII, section 9.2.1.1.) using as key study the study(ies) showing the highest concern according to Annex I section 3.1.5. for the endpoint *or* provide a detailed justification for not using the study(ies) giving rise to the highest concern to conclude on the endpoint.**

5. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: generate an exposure assessment for all relevant exposure scenarios and revise the risk characterisation accordingly.**

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 **21 February 2020**. 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

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.

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 XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation with respect to this adaptation.

You have provided the following justification for adaptation:

"*There is no oral sub-chronic (90 days) repeated dose study available for 2-dibutylaminoethanol. In order to assess possible effects after repeated oral exposure, 2-dibutylaminoethanol was tested in a GLP- and guideline-conform (OECD 407) subacute toxicity study ([redacted] 2004). Additionally data was obtained from Cornish et al. (1969) who described a study with 2-dibutylaminoethanol via oral application for 5 weeks. The twenty-eight day repeated dose oral (gavage) toxicity study resulted in a NOAEL of 100 mg/kg bw/day for both males and female animals and a LOAEL was set to 400 mg/kg bw due to mortality and severe clinical signs in nervous system, liver and kidney. This assessment is supported by the data published by Cornish et al. (1969).*
Hence, sufficient, valid data are available allowing assessment of the toxic potential of the test item via oral administration under long-term exposure conditions, and thus, also with regard to animal welfare, there is no need in conducting further studies", and

"*There is no sub-chronic (90 days) repeated dose study concerning inhalation exposure available for 2-dibutylaminoethanol. In order to assess possible effects after repeated exposure, 2-dibutylaminoethanol was tested via inhalation in a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test according to OECD 422 ([redacted] 2013). Additional data was obtained from Cornish et al. (1969) who described studies with 2-dibutylaminoethanol via inhalation for 6 months and 5 days, respectively. The main effects in the Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test via inhalation and according to OECD 422 were local effects, resulting in a NOAEC (local) of 20.6 mg/m³.*

As only transiently reduced food consumption, body weight and body weight gain in the highest test concentration were observed and no adverse effects concerning reproductive and developmental parameters were detected, the NOAEC for systemic effects and for reproductive and developmental effects was determined to be 236.3 mg/m³ for male and female animals (highest dose tested). These results via inhalation exposure were supported by the data published by Cornish at al. (1969). Hence, sufficient, valid data are available allowing assessment of the toxic potential of the test item via inhalation under long-term exposure conditions, and thus, also with regard to animal welfare, there is no need in conducting further studies".

To support your weight of evidence adaptation you have provided the following sources of information:

In the technical dossier you have provided study records for a "repeated dose 28-day oral toxicity study" (test method: OECD TG 407) and "Oral [...] Toxicity of 2-N-Dibutylaminoethanol (5-week, no guideline, publication from year 1969). However, these studies do not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days and the number of animals per dose group is significantly lower. Therefore, the sensitivity of a 28-day study is much lower than that of a 90-day study. You claim that the results of the 28-day study (*mortality and severe clinical signs in nervous system, liver and kidney*) are supported by *the data published by Cornish et al. (1969)".* ECHA notes that in the acute oral toxicity study similar central nervous system (CNS) effects were observed as in the OECD 407 study. However, in the 5-week oral study no such effects were observed and thus your claim "*This assessment is supported by the data published by Cornish et al. (1969)"* is not supported by the information provided.

You have also provided a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" via inhalation (test method: OECD TG 422). However, this study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days.

You have also provided study records for "[...] Inhalation Toxicity of 2-N-Dibutylaminoethanol (5 days and 6 months, no guideline, publication from year 1969). In the 5-day study CNS effects, possibly similar to the ones observed in the OECD 407 study, were observed at the highest dose 495 mg/m^3. No major adverse effects were observed in the 6-month study at 156 mg/m^3. Based on the data in the technical dossier, the 6-month study has e.g. the following shortcomings:

(i) only one dose tested,
(ii) 5 animals/dose/sex instead of 10 as recommended in the OECD TG 408/413,
(iii) no data on cage side observations and clinical observations,
(iv) histopathology was not conducted,
(v) gross pathology was conducted "*in parts*", and
(vi) limited number of haematology and clinical chemistry parameters ("*hematocrit, white blood count, serum bilirubin*") were examined.

ECHA considers that these limitations are major deviations from the OECD TG 408/413 requirements. In addition, the reporting of the study results does not allow an independent assessment of the findings, since tabular results and statistical analyses are not included and therefore ECHA considers that the study is not adequate for the purpose of hazard assessment.

ECHA's evaluation and conclusion of the information provided

An adaptation pursuant to Annex XI, Section 1.2. requires sufficient weight of evidence from several independent sources of information leading to the assumption/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.

Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to a sub-chronic toxicity study (EU B.26/OECD TG 408). Relevant elements are in particular route of exposure, exposure duration and levels, two genders, sensitivity and of investigations to detect specific organ toxicity. For the reasons explained above (in particular shorter duration of the available studies compared to the required duration of 90 days and major shortcomings in the 6-month study) the sources of information you provided, together with your justification for the adaptation, do not allow to conclude on the dangerous (hazardous) property of the registered substance with respect to the information requirement for Annex IX, Section 8.6.2.

Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and 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 default 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, potential inhalation-specific effects are already addressed by providing a screening study by the inhalation route and by deriving a long-term DNEL for inhalation, local effects. 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.

In your comments to the draft decision you agree to fulfil the request. However, you further indicate that the inhalation route is preferred taking into account the existing OECD 422 inhalation study with the registered substance and the uses of the substance by industrial and professional users.

ECHA notes that the current decision does not question the applicability of the OECD 422 study with the registered substance for the purpose of hazard and risk assessment. ECHA has already indicated in the decision for this endpoint that: "More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, potential inhalation-specific effects are already addressed by providing a screening study by the inhalation route and by deriving a long-term DNEL for inhalation, local effects."

ECHA further notes that although some of the uses reported in the Chemical Safety Report include applications for industrial and professional spraying (PROCs 7 and 11), this cannot be taken as a sole criterion for choosing the most appropriate route of exposure. ECHA also notes that industrial and professional spraying are not the only applications reported in the CSR.

ECHA further considers that the properties of the registered substance indicate that the substance is a respiratory irritant and has corrosive properties (STOT Single Exp.3 and Skin Corr. 1C). In this context, the local effects for the inhalation route and the relevant risk management measures have been addressed in the registration dossier and the Chemical Safety report with the use of the existing animal studies performed via the inhalation route. Therefore, ECHA concluded that for the purpose of risk assessment for local effects via the inhalation route no additional information is required. However, for the purpose of classification and labelling additional information is required and according to ECHA Guidance on Information Requirements and Chemical Safety Assessment (R.7.5.6.3.4) "*Concerning repeated dose toxicity testing, the oral route is the default one because it is assumed to maximise systemic availability (internal dose) of most substances*".

In addition, ECHA considers that further testing via the inhalation route with a respiratory irritant and corrosive substance will limit the usefulness of the test results for the purpose of classification and labelling since they are likely to be confounded by the presence of local effects. It is likely that not adequate concentrations will be achievable for testing via the inhalation route taking into account animal welfare considerations.

You have also indicated the potential use of read-across with other structural analogues that are being or will be tested and provided an overview of the existing available studies with the analogues. As you indicate in your comments, Diethylethanolamine (DEEA) will be tested via the oral route with the EOGRTS OECD TG 443 test protocol, and before the OECD TG 443 test, a range-finding study will be conducted, which according to you "*can serve as a basis for read-across approach from DBEA* [the registered substance] *to DEEA*", and "*This study can then serve as the basis for comparing the systemic effects of both compounds DBAE and DEEA and allow a proper decision if read-across among these chemicals is applicable or not*".

In addition, you refer to an ongoing OECD TG 422 study with Dimethylethanolamine (DMAE), which "*is being performed as well to decide on possible read-across or serve as*

a range-finding study for an DMAE-own OECD 443,". ECHA notes that the request for the OECD 443 for DMAE is also via the oral route.
ECHA cannot assess at this stage relevance and adequacy of the planned read-across approaches but identifies that planned testing with structural analogues will also be made by the oral route. Therefore, in order to allow better comparison of the requested test results between structural analogues, ECHA considers that the data derived to address the information requirement for the registered substance should also be from testing via 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: 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.

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, inhalation). You have also provided the following justification: "*The Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test according to OECD TG 422 ([redacted] 2013) with 2-dibutylaminoethanol covers reproductive performance, developmental toxicity and offspring observations until day 4. No effects on reproduction and development were observed at any dose-level. The NOAEC for reproduction / developmental toxicity was considered to be 236.3 mg/m³/day (highest dose tested).*
It was therefore concluded that an additional Developmental Toxicity / Teratogenicity study is not necessary as no adverse effects were detected in the Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test".

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.

In your comments to the draft decision you agree to fulfil the request. ECHA understands that you propose the inhalation route also for the request for the pre-natal developmental toxicity study, and you have provided the same arguments as for the request for the sub-chronic (90-day) toxicity study. Therefore, please see the ECHA responses under endpoint 2, sub-chronic (90-day) toxicity which address these comments.

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.

3. 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 sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation "*In Annex IX of Regulation (EC) No 1907/2006, it is laid down that chronic tests shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on fish. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB.*

The hazard assessment of the substance reveals neither a need to classify the substance as dangerous to the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Therefore, and for reasons of animal welfare, a chronic test in fish is not provided."

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2 because of the following. You consider that the Chemical Safety Assessment (CSA) has not indicated the need to conduct chronic testing in fish since the substance is not classified for environment nor is it considered a PBT/vPvB substance. ECHA notes that as you have not submitted the environmental EA/RC sections in your CSA, you cannot refer to the CSA to claim that there are no risks to the environment and that further aquatic testing would not be necessary.

Also, contrary to your claim, there are indications of an environmental hazards, and as discussed in detail under section 5 of this decision, the need for carrying out EA/RC for environment is triggered for your substance.

In your comments on the draft decision (DD), you state that based on the new exposure assessment and risk characterisation (EA/RC) performed for environment (following request 5. below), the CSA indicates no risks for the registered substance (RCRs below 1). In addition, you propose a *"weight-of-evidence approach to justify the adaptation of the information requirement (..)."*

ECHA notes that while on one hand you still intend to adapt the current standard information requirement according to Annex IX, Section 9.1.5., column 2., you have on the other hand also submitted a weight of evidence approach (WoE), according to Annex XI section 1.2., to justify why no long-term fish testing is needed.

ECHA notes that a WoE adaptation pursuant to Annex XI, Section 1.2. requires sufficient WoE 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. In all cases, adequate and reliable documentation shall be provided.

ECHA notes that while you have indicated that a WoE approach has been submitted, you have not provided an explicit explanation or justification on how the sources of information/studies that you have provided enable to conclude on the endpoint of long-term toxicity testing on fish based on a WoE approach. ECHA considers that you have used the WoE approach to justify that the fish is not the most sensitive species and therefore long-term toxicity testing on fish is unnecessary. ECHA has assessed the individual sources of information and considers that they cannot be used to adapt the present standard information requirement in a WoE approach, according to Annex XI section 1.2., or individually, as described below.

To support the weight-of-evidence adaptation you have used the following sources of individual information:

- Acute-to-chronic approach by ECETOC (2003)

In your comments on the DD you provide five estimations of NOECs for long-term toxicity to fish (all above 1mg/L) by "*dividing the available experimental 96-h LC50 of > 100 mg/L*" for the registered substance, with the 90%-ile of the acute-to-chronic ratios (ACR) derived from 5 different ECETOC databases. ECHA notes that you have not provided adequate and reliable documentation for the proposed estimations, including justification on their reliability, it is therefore not possible for ECHA to assess their reliability.

Nevertheless, ECHA notes that extrapolation from acute to chronic toxicity is hardly possible, as shown by the analysis of a large number of validated data on new and existing chemicals described in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R.7b (Section R.7.8.5.). The analysis revealed that acute data have only limited predictive value for long-term effects in aquatic ecosystems. For any of the three trophic levels, the acute/chronic ratio correlates neither with acute toxicity nor with baseline toxicity as modelled through log Kow. In addition, no acute/chronic ratio correlation is found across trophic levels. Based on the above and in the absence of documentation on the estimation method, ECHA considers the provided NOEC estimations for long-term toxicity to fish as not adequate or reliable. As a consequence, for the current endpoint ECHA cannot accept the proposed information on its own or as part of a weight of evidence approach.

- Relative species sensitivity

In your comments on the DD you also provide information on relative species sensitivities derived from the available acute aquatic toxicity studies on the registered substance, from QSAR models and from "*information on general trends of the toxicity of aliphatic amines*" in order to justify why you consider that further testing on fish is not needed.

Regarding the available aquatic data, ECHA notes that the results of the valid acute aquatic toxicity studies available in the current technical dossier show that algae is the most sensitive species in acute tests, but there is no substantial difference (i.e. at least 10 times) between fish and *Daphnia*.

The QSAR predictions provided to support your approach are developed using the EPI Suite ECOSAR model v1.11 for "aliphatic amines" with measured physicochemical data as input (LogKow = 1.86 and WS = 4000 mg/L). ECHA notes that these predictions do not meet the general rules set for acceptance of QSAR models in Annex XI, section 1.3. due to the absence of adequate and reliable documentation, since no (Q)SAR prediction reporting format (QPRF) and (Q)SAR model reporting format (QMRF) have been submitted.

However, since the models are publicly available, even in the absence of documentation, ECHA was able to assess the predictions provided and notes that the QSAR predictions for acute toxicity endpoints (short-term fish, short-term Daphnia and algae growth inhibition), are valid. The predictions support the available experimental data in showing that algae is the most sensitive species in short-term tests (predicted 96h LC50 = 4.1 mg/L) and that there is no substantial difference in the sensitivities of *Daphnia* (predicted 48h EC50 = 4.8 mg/L) and fish (predicted 96h EC50 = 41 mg/L) as also acknowledged by you in your comments.

Regarding the EPI Suite QSAR predictions for chronic toxicity endpoints (long-term fish and long-term *Daphnia*), ECHA notes that they cannot be considered valid for the following reasons. First, ECHA notes that the applied ECOSAR models are built only on few data points (n= 5+2 for chronic *Daphnia*, and n = 3+1 for chronic fish) leading to unreliable predictions, as you also acknowledge in your comments on the DD regarding the chronic fish model. Second, while ECHA agrees that the registered substance falls within the applicability domains (AD) of the models used as described by an upper limit of log Kow, ECHA notes that the registered substance does not fall within the structural domains of these two models due to the following. The ECOSAR model used for chronic toxicity to fish is built on three data points, of which one is confidential and hence it is not possible to confirm how and whether it relates to the registered substance. The other two data points are for pesticides with structures that are very different to the registered substance. In addition to these data sources, the ECOSAR model for long-term *Daphnia* includes only one additional non-confidential data point, however, that data point is for a substance very dissimilar to the registered substance. In addition, the Log Kow of these three non-confidential source substances is over 4, while the registered substance has a much lower log Kow of 1.86 adding more uncertainty to the result. Therefore, the results do not meet the general rules set for acceptance of QSAR models in Annex XI, section 1.3 because first the predictions are not derived from a (Q)SAR model whose scientific validity has been established and second the substance does not fall within the structural applicability domain of the QSAR models. ECHA hence considers that the QSAR data provided could not be used to fulfill the current standard information requirement.

Finally, you provide information on relative species sensitivities derived from general toxicity trends of aliphatic amines, in order to justify why you consider that further testing on fish is not needed. You indicate that "*Descriptions of the toxicity of aliphatic amines can be found in the environmental toxicity profile of the aliphatic amines category described in the definition of the chemical categories of the Toxic Substances Control Act (TSCA) New Chemical Program (August, 2010* [link to document provided]) *and the description contained in the OECD QSAR Toolbox.*"

Based on the information described in this document, you conclude that "*the trends for aliphatic amines are in accordance with the analysis of the relative species sensitivity with regard to the relations between fish and invertebrates to algae*".

However, ECHA notes that you provide no explanation nor a scientific justification on how and why the toxicity trends described in the TSCA document for the aliphatic amines category, which includes a wide array of structurally different amines with different substituents and insertions on the alkyl chain (e.g. halogens, hydroxyls, ethoxys, ethers, disulfides, etc.), are applicable to the registered substance. In the absence of such a documented justification, you have not shown how these general trends support the relative species sensitivities for the registered substance. Nevertheless, ECHA understands that you intend to use this information only to support the other data on the registered substance showing that algae is the most sensitive species.

As discussed above, ECHA considers that the information provided on relative species sensitivity based on the available acute aquatic toxicity studies on the registered substance and on QSAR models shows that algae is the most sensitive species, however there is no significant difference in the sensitivities of *Daphnia* and fish. According to the integrated testing strategy (ITS) described in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R.7b (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 needed on both. Hence, according to the ITS the long-term studies on fish on the registered substance cannot be adapted based on relative species sensitivities alone.

However, if based on the results of the available aquatic toxicity studies 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. ECHA acknowledges that you indicate that you have performed an exposure assessment and risk characterisation (EA/RC) for the environment (as per request 5. below) and that the CSA indicates no risk to the environment. However, ECHA notes that in your comments on the DD you do not specify the assessment factor (AF) used for the RC and you indicate that the EA/RC will be provided in an update of the technical dossier. Consequently, with the current information it is not possible for ECHA to assess whether a long-term fish study is needed.

You are in this context reminded that ECHA does not take into account dossier updates submitted after the notification of the draft decision under Article 50(1) of the REACH Regulation for the purpose of this decision. However, ECHA will examine the information submitted in later updates of the registration dossier at the stage of the follow-up to the dossier evaluation in accordance with Article 42 of the REACH Regulation.

In conclusion, on the basis of the information available, 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 R.7b, 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 R.7b,* 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).

Notes for your consideration

Before conducting the chronic fish test requested above, you may first update the CSA according to Annex I of the REACH Regulation as discussed in section 5 below. 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, 9.1.6. taking into account the new exposure assessment and risk characterisation for environment.

On the other hand, if after the update of the CSA you come to the conclusion that further hazard data is required to refine the risk assessment the long-term fish study needs to be conducted. You may also consult the ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b, Section R.7.8.5 to determine the necessity to conduct the long-term toxicity testing on fish. Once results of the test on long-term toxicity to fish are available, you shall again revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

4. Update of the technical dossier and the Chemical Safety Report for the endpoint of Ready biodegradability (Annex VII, section 9.2.1.1.) using as key study the study(ies) showing the highest concern according to Annex I section 3.1.5. for the endpoint *or* provide a detailed justification for not using the study(ies) giving rise to the highest concern to conclude on the endpoint.

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 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.

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 four study summaries to fulfill the Annex VII, section 9.2.1.1. standard information requirement of Ready biodegradability (IUCLID section 5.2.1.):

1. Key study according to OECD 301 B (Ready Biodegradability: CO2 Evolution Test): "*Key.* [redacted] *Biodegradation in water: screening tests_2012*", Reliability 1, GLP, non adapted inoculum, 80-90 % degradation in 28 d, 10-d window criteria and other validity criteria fulfilled.
2. Adequacy of study "*other information*" according to OECD 301 A (Ready Biodegradability: DOC Die Away Test): "[redacted]. *Biodegradation in water: screening tests.OECD 301A_2005*", Reliability 1, GLP, adaptation of inoculum not specified, < 10 % degradation in 28 d, not indicated whether validity criteria fulfilled
3. Adequacy of study "*other information*" according to OECD Guideline 301 C (Ready Biodegradability: Modified MITI Test (I)): "[redacted]", Reliability 2, adaptation of inoculum not specified, "*under test conditions no biodegradation observed*", validity criteria fulfilled, poor reporting however reliable database as also indicated by you.
4. Supporting study according to OECD Guideline 302 B (Inherent biodegradability: Zahn-Wellens/EMPA Test) "[redacted].*Biodegradation in water: screening tests.Zahn-Wellens_1985*", Reliability 2, non GLP, adaptation of inoculum not specified, 60 % degradation in 10 days, 72 % in 21 d, 91 % degradation in 28 d, not indicated whether validity criteria fulfilled.

In the Endpoint summary under IUCLID section 5.2.1. "*Biodegradation in water: screening tests*" you have indicated that based on Study No 1., the key study carried out according to the OECD TG 301 B, the registered substance is readily biodegradable and that this conclusion is supported by data obtained from Study 4., the OECD TG 302 B inherent biodegradation study.

In the summary you also include the results from Studies 2. and 3., the OECD 301 A (< 10 % degradation in 28 d) and OECD 301 C (no biodegradation observed in 28d) ready biodegradation studies, but you provide no discussion on why you have not used them in the CSA to conclude on this endpoint. Since these two studies showing very low biodegradation are the ones giving rise to highest concern, ECHA considers that a justification on why you consider them not relevant is needed, as required by Annex I, Section 3.1.5.

ECHA notes that the results provided in your dossier are in fact conflicting. According to ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b, Section R.7.9.4. "*when conflicting test results are reported, it is recommended to consider such differences in stringency and to check the origin of the inoculum in order to check whether or not differences in the adaptation of the inoculum may be the reason (OECD, 2006).*" Furthermore, according to the Guidance on the Application of the CLP Criteria (version 5.0, July 2017) conflicting test results could be interpreted in a weight-of-evidence (WoE) approach and "*the data of the highest quality and the best documentation should be used for determining the ready biodegradability of the substance.*" ECHA guidance does also state that due to the stringency of the ready biodegradation tests consistent positive results may supersede negative results. Similarly, according to the CLP Guidance "*positive results in ready biodegradability tests could be considered valid, irrespective of negative results, when the scientific quality is good and the test conditions are well documented, i.e. guideline criteria are fulfilled, including the use of non-pre-exposed (non-adapted) inoculum.*" In summary, ECHA notes that while positive ready biodegradation results may supersede negative results, it is necessary to consider the conflicting results in, for example, a weight-of-evidence approach and to determine whether the test design may have influenced the results obtained. 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.

Based on the information provided ECHA agrees that Study 1 is valid and reliable. ECHA notes that you consider both Studies 2. and 3. as reliable and in the ESR of Study 3. have indicated that the validity criteria were fulfilled. While you have not indicated whether the validity criteria have been fulfilled in Study 2, based on the information provided in the ESR ECHA considers the study valid. While studies 2. and 3. showing negligent degradation are valid, you provide no discussion on why it is acceptable to not to use these studies to conclude on the endpoint. Rather, you consider that the conclusion of ready biodegradation, provided by the key study, is supported by the data obtained from the inherent biodegradation study (Study 4). However, ECHA notes that while ready biodegradation studies may be used to prove that a substance is inherently biodegradable, inherent biodegradation studies cannot be used to fulfil the standard information requirement of ready biodegradation. ECHA hence considers that with the current information the results from the OECD 302 B study alone cannot support the conclusion of ready biodegradation.

In conclusion, ECHA considers that due to the conflicting results and no discussion on why the single positive result can be used to conclude on the endpoint, ECHA considers that you have not justified why the studies showing the highest concern have not been used to conclude on the endpoint. Consequently, your dossier does not fulfil the requirements of Annex I, section 3.1.5.

In your comments on the draft decision (DD), you maintain that the registered substance is ready biodegradable and that the OECD TG 301 B study (Study 1, 87% in 28d, non-adapted inoculum) should remain as the key study.

A Member State Competent Authority (MSCA) submitted a Proposal for Amendment (PfA) for this endpoint. The PfA considers that it is likely that the inoculum used in the OECD TG 301 B study (Study 1) is adapted as the sewage treatment plant (STP; [redacted]) where it originates from, is located in the vicinity of several industrial sites.

As given in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b., OECD guidance on testing of chemicals specifies that results based on adapted inocula are generally regarded as inappropriate. An inoculum is considered adapted, for example, if the inoculum used has been exposed to the substance or structurally similar substances (e.g. in an industrial STP, in a contaminated site or in municipal waste water treatment plants (WWTPs) receiving releases from sites using the substance). It is also given that "*inocula from WWTPs influenced by point sources must not be used, e.g. if effluents from an industrial site using the substance are connected to the municipal WWTP.*" Therefore, origin of the inocula should be examined to verify whether adaptation may have caused differences in results. It is also acknowledged that substances that are widely used and continuously emitted to WWTPs (e.g. if they are ubiquitous in consumer products), pre-exposure of the degrading microorganisms may not be avoided (ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b). In light of the information above provided above, ECHA considers it necessary for you to explain whether indeed pre-adaptation may have caused the high degradation in the key study.

You also provide the following scientific explanation for the negative ready biodegradability results obtained from the other two valid ready biodegradability studies included in the technical dossier as "*other information*". Regarding the OECD TG 301 C study (Study 3, no biodegradation observed in 28d), you explain that the negative results may have been caused by the long pre-treatment of the inoculum and the very high test substance concentration of 100 mg/L, both as specified in the guideline.

ECHA notes that as described in Section R.7.9.4 of ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b., pre-treatment of the inoculum as given in OECD TG 301C (par. 10) may lower the diversity and biodegradation capacity of the microbes. Furthermore, ECHA acknowledges that the very high test concentrations used for the OECD TG 301C test (par. 11) may have increased the probability of inhibition, as described in Section R.7.9.4 of ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b. However, ECHA notes that as no information on inhibition control (containing both the test substance and a reference compound) was included in the RSS, the latter is difficult to prove for this study.

Also, ECHA notes that in the other 2 ready biodegradability studies (Study 1 according to OECD TG 301 B and Study 2 according to OECD TG 301 A), inhibition controls were included and the test substance was not inhibitory to the inoculum. ECHA also notes that, as indicated in your comments on the DD, no inhibition of the microorganisms occurred in the short-term respiration inhibition test (OECD TG 209, 30min EC20>1000mg/L). Nevertheless, ECHA accepts that the probability of inhibition in the OECD TG 301 C (Study 3) may have been higher than in the other two ready biodegradability Studies 1 and 2, where lower test substance concentrations of about 30 mg/L were used, and in the respiration inhibition study, due to the different inoculum source and cultivation.

For the study according to OECD TG 301 A (Study 2, < 10 % degradation in 28 d) you consider that the negative result can be explained by the low test volume used in the study (1L) compared to the higher test volume of 1.5L used in the OECD TG 301B study (Study 1) showing positive results. ECHA agrees that the lower test volume used in Study 2 lead to lower total number, and possibly also type, of microorganisms introduced into the test compared to Study 1 where otherwise similar test substance and inoculum concentrations were used.

As a consequence, ECHA accepts that the lower test volume used in Study 2 may have decreased the probability of introducing competent microorganisms into the test vessel, as also discussed in Section R.7.9.4 of ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b.

In their PfA the MSCA agrees that the low degradation observed in the OECD 301 A study (Study 2) may have been caused by small test volume as discussed above. However, the PfA also indicates that the inoculum in this study originates from a STP where preadaptation of the inoculum for the test substance may have been lower. ECHA agrees with the PfA that there are a number of variables which could influence the degradation rate, which should be considered further by you in your justification.

Furthermore, in your comments on the DD you agree that the inherent biodegradability test (OECD 302 B, 91% after 28d, industrial inoculum) cannot be used to fulfil the ready biodegradation information requirement. You also indicate that this study does not fulfil the specific criteria for the assessment of ultimate degradation and that it also cannot be used for the purposes of classification and labelling.

In their PfA the MSCA agrees that the OECD 302 B study cannot be used to fulfil the information requirement of ready biodegradation nor to conclude on persistence due to adapted inoculum being used in the study. The PfA notes that according to ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11., the conclusion on "not P" on the basis of screening information from tests on inherent biodegradation is only allowed in case the inoculum was not pre-adapted to the test substance or structural similar substances. ECHA notes that in the respective endpoint study record the adaptation is not specified however it is given that the "*activated sludge from* [redacted] *sewage works*" was used. The adaptation of the inoculum may hence be a concern and may have contributed to the high degradation rate.

To further support the conclusion of the substance being readily biodegradable in your comments you also provide QSAR results for ready biodegradability calculated with different QSAR models (i.e. six aerobic models from EPISuite BIOWIN v4.10, three ready biodegradability models from OASIS Catalogic v5.11.19 and the ready biodegradability model v1.0.9 from VEGA v1.1.3,).

ECHA notes that these predictions do not meet the general rules set for acceptance of QSAR models in Annex XI, section 1.3. due to the absence of adequate and reliable documentation, since (Q)SAR prediction reporting format (QPRF) and (Q)SAR model reporting format (QMRF) have not been submitted. However, even in the absence of documentation, ECHA was able to assess the predictions provided and notes that the QSAR predictions are valid. ECHA agrees that the registered substance falls within the applicability domains (AD) of all of the models submitted. All six aerobic models from EPISuite BIOWIN v4.10 predict that the registered substance will biodegrade fast; in particular the BIOWIN5 and BIOWIN6 models predict that the registered substance is readily biodegradable. Regarding the predictions with the three CATALOGIC models, based on three different OECD guidelines (i.e. 301B, 301C and 301F), only two out of three predict that the registered substance is readily biodegradable (i.e. 301B and 301F). ECHA agrees that the negative result from the 301C model is due to the fact that the training set of this model includes the OECD TG 301 C study (Study 3, no biodegradation observed in 28d), which ECHA accepts should be disregarded, as explained above.

Finally, the prediction with the ready biodegradability model of VEGA yields a result of "Possible readily biodegradable", with good reliability. Hence, ECHA considers that these QSAR predictions are reliable and the results support the conclusion of the substance being readily biodegradable.

In conclusion, ECHA acknowledges that in your comments on the draft decision you have adequately justified why the two ready biodegradability studies (Studies 2. and 3.) showing the highest concern have not been used to conclude on the endpoint. As a consequence, ECHA accepts that the positive ready biodegradability result obtained in the valid key study (Study 1.) can be used to conclude on the endpoint. This is further supported by the QSAR data submitted as part of your comments, even if the required QPRF and QMRF have not been submitted as part of your comments.

In your comments on the DD, you indicate that you will update the registration dossier with a justification for considering the registered substance as ready biodegradable. ECHA agrees that this information needs to be included in the technical dossier in the formats requested by the REACH Regulation. 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, the request(s) remains in the draft decision.

ECHA acknowledges that in the respective endpoint study record in IUCLID of the OECD 301 B study (Study 1 showing substance to be readily biodegradable) you have indicated that Study 1 was conducted *"using non-adapted activated sludge from a municipal sewage treatment plant as inoculum"*. However, ECHA notes that as discussed above there is a concern raised by the variability of the results obtained from the experimental studies

available. Above, ECHA has acknowledged that the argumentation and additional adaptations provided by you during the registrant's commenting phase on the initial DD supports your conclusion of ready biodegradation. As stated above, in their PfA the MSCA raises concerns with possible adaptation of the inoculum used in the OECD 301 B study. ECHA agrees with the PfA that the potential adaptation of the inoculum used in the key study needs to be addressed and as stated below, you need to justify why you consider it acceptable to not use the study showing the highest concern to conclude on the endpoint is required to fulfil the requirements of Annex I, section 3.1.5.

In your comments on the PfA, you acknowledge that preadaptation of the inocolumn in the OECD 301 B study, the key study, cannot be fully excluded due to the STP [redacted] being located in a highly industrialised region. However, you note that the preadaptation of the inocolumn from STP [redacted] in the OECD 301 A study with low degradation could similarly be questioned. You however state that a difference in the potential adaptation of the two STPs as you note that STP [redacted] receives sewage potentially also from industrial point sources. You indicate that to clarify the conflict of different inocula of different origin you propose to conduct two new OECD 301 B studies using activated sludge from the STPs [redacted] and [redacted]. You also emphasise that this substance being readily biodegradable is confirmed by the QSAR models you referred to in your comments on the initial DD.
ECHA acknowledges your intention to conduct new ready biodegradation studies to further clarify the impact of the source of the inocula on the ready biodegradation status of the registered substance. ECHA considers it is your responsibility if you wish to carry out further studies to clarify the ready biodegradation status of the registered substance and to use as key study, the study(ies) showing the highest concern according to Annex I section 3.1.5. for the endpoint *or* provide a detailed justification for not using the study(ies) giving rise to the highest concern to conclude on the endpoint.
However, ECHA would like to emphasise that as discussed above and given in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b., "*inocula from WWTPs influenced by point sources must not be used, e.g. if effluents from an industrial site using the substance are connected to the municipal WWTP.*"

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 the study showing the highest concern as key study according to Annex I section 3.1.5. for the endpoint of Ready biodegradation (Annex VII, section 9.2.1.1.) or provide a detailed justification for not using the studies giving rise to the highest concern to conclude on the endpoint.

5. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment

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.

Pursuant to Article 14(4), if the substance fulfils the criteria for any of the hazard classes listed in that provision or is assessed to be a PBT (persistent, bioaccumulative and toxic) or

vPvB (very persistent and very bioaccumulative), the CSA shall include exposure assessment and risk characterisation.

Annex I, Section 5 of the REACH Regulation requires the Registrant to generate exposure scenarios and exposure estimations for the registered substance. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards.

Annex I, Section 6 of the REACH Regulation requires you to characterise the risk for each exposure scenario and to consider the human population (exposed as workers, consumer or indirectly via the environment and if relevant a combination thereof) and the environmental spheres for which exposure to the substance is known or reasonable foreseeable, under the assumption that the risk management measures described under exposure scenario in Section 5 of the same Annex have been implemented. In addition, the overall environmental risk caused by the substance shall be reviewed by integrating the results for the overall releases, emissions and losses from all sources to all environmental compartments.

ECHA notes that you have classified the substance as Acute Tox. 4 (H302), Acute Tox. 4 (H312), Skin Corr. 1C (H314) and Eye Damage 1 (H318) thus, fulfilling the criteria set out in Article 14(4) of the REACH Regulation to require an exposure assessment and a risk characterisation in the chemical safety assessment.

With regard to the scope of the required exposure assessment, as stated above and in accordance with Annex I, section 5.0., it has to cover all hazards that have been identified according to sections 1 to 4 of Annex I of REACH Regulation.

In the CSR you provided, the exposure assessment for the environment is missing. You claimed that no exposure assessment is necessary for the environment by stating that "*As no environmental hazard was identified no environmental-related exposure assessment and risk characterization was performed.*"

ECHA however notes that adverse effects were observed in some environmental toxicity studies. In particular, in the short-term and long-term toxicity studies to aquatic invertebrates an EC50 of 73.7 mg/L and an NOEC of 4.38 mg/L were obtained, respectively. Furthermore, in an algae study an EC50 of 21.6 mg/L and a NOEC of 3.2 mg/L were obtained and you have used this NOEC value for the derivation of the aquatic PNEC. Therefore, exposure assessment and risk characterisation for environment are needed to address the hazards identified for the environment. As further outlined in Guidance *on information requirements and chemical safety assessment*, Part B: Hazard Assessment, Section B.8.1. (version 2.1, December 2011), such identified hazards (among others) necessitating exposure assessment are the *"hazards for which there are classification criteria and there is information on these properties of the substance showing that it does have these properties, but the severity of the effects is lower than the criteria for classification and so the substance is not classified".* Moreover, the above mentioned guidance specifies further (in Section 8.4.2.2.) that *"If there are ecotoxicity data showing effects in aquatic organisms, but the substance is not classified as dangerous for the aquatic environment, an aquatic PNEC can nevertheless be derived thus indicating a hazard to the aquatic environment.(...) Hence quantitative exposure assessment, i.e. derivation of PECs, is mandatory for the water, sediment and soil environmental compartments."*

In your comments on the draft decision, you agree to perform this request. You indicate that the exposure assessment and risk characterisation (EA/RC) for environment has already been performed for all relevant uses. You further specify that the RC shows no risks for the environment since all RCRs are below 1 (RCRmax = [redacted]). You indicate that this information will be provided in an update of the technical dossier.

ECHA notes that any new information should be submitted in a form of a dossier update. 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 new information/adaptations therein will be evaluated by ECHA at the follow up stage.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to generate an environmental exposure assessment for all relevant exposure scenarios and subsequently perform the risk characterisation for each exposure scenario to demonstrate the safe use of the substance, and update the dossier accordingly.

6. Deadline to submit the requested Information

In the draft decision communicated to you the time indicated to provide the requested information was 24 months from the date of adoption of the decision. In your comments on the draft decision, you have indicated a potential use of a read-across approach with structural analogues that are being (OECD TG 422 with DMEA) or may be tested (range-finding study with DEEA; for details see Appendix 1, section 1 of this decision). You asked ECHA to "*to wait for these range-finding results in order to enable a possible read-across approach based on solid oral data*".

ECHA notes that you have not provided a read-across hypothesis and/or supporting data to support the potential read-across approach. In fact, you have the intention to use the ongoing/future studies to verify if the read-across approach between these substances is acceptable: "*data and read-across justification will be elaborated in greater in details in case the before mentioned read-across approach appears applicable* ".

Therefore, ECHA understands that you are in a process of exploring whether a possible future read-across approach can be made and that at this stage it is not possible to prove if the approach is acceptable. ECHA reminds you that it is your responsibility to update your dossier, including the read-across justification and supporting information, when new data becomes available, and that ECHA cannot delay the decision-making process to await that such data to become available. ECHA notes that the deadline in the current decision may allow you to take into consideration the data generated on the analogue substances.

Therefore, ECHA has not modified the deadline of the 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 23 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 proposal(s) for amendment.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-58 written procedure and ECHA took the decision according to Article 51(6) 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.