EUROPEAN CHEMICALS AGENCY

Helsinki, 16 February 2018

Addressee: [redacted]

Decision number: CCH-D-2114392720-48-01/F
Substance name: 2-[2-(dimethylamino)ethoxy]ethanol
EC number: 216-940-1
CAS number: 1704-62-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 16/01/2017
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. **Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD 421/422) in rats, oral route with the registered substance;**

3. **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;**

4. **Identification of degradation products (Annex IX, 9.2.3.) using an appropriate test method 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 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 **24 August 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 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.

Appendix 1: Reasons

TOXICOLOGICAL AND ECOTOXICOLOGICAL INFORMATION

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.

Your registration dossier contains for the endpoints repeated dose toxicity, reproductive toxicity and developmental toxicity adaptation arguments in form of a grouping and read-across approach according to Annex XI, Section 1.5. of the REACH Regulation. ECHA has assessed first the scientific and regulatory validity of your grouping and read-across approach in general before the individual endpoints (sections 1, 2 and 3).

Grouping and read-across approach for toxicological information

You have sought to adapt the information requirements for a sub-chronic toxicity (90-day) study (Annex IX, Section 8.6.2.), screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) and pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) by applying a read-across approach in accordance with Annex XI, Section 1.5. According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[2]. This hypothesis explains why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent.

[2] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.

Thus, physicochemical and degradation properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However, the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis[3]: (1) (Bio)transformation to common compound(s) - the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s) - the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common compounds).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are used as the source for the read-across prediction.

You consider to achieve compliance with the REACH information requirements for the registered substance 2-[2-(dimethylamino)ethoxy]ethanol (DMEE), (EC 216-940-1) using data of structurally similar substances (2-(2-aminoethoxy)ethanol (AEE), (EC No 213-195-4) and 2-dimethylaminoethanol (DMAE), (EC No 203-542-8) (hereafter the 'source substances').

You have provided a read-across documentation as a separate attachment.

You use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group:

"For this assessment we relied on the hypothesis that the chemical structure drives the phys-chem properties as well as the biological responses. This is the fundamental basis of the analog approach [ECHA 2015a]. Since no specific mechanism of action was identified for DMEE, the structural similarity hypothesis was determined to be the most appropriate."

"Due to the similarity in carbon chain lengths, dissociation constant, partition coefficient and solubility, it should be expected that DMEE, AEE, and DMAE would have similar biological properties. This is easily confirmed by the available acute toxicity data of DMEE as listed in Table 2. All of the above acute toxicity results of DMEE within the corresponding AEE and DMAE values. This is also true for the aquatic toxicity endpoints."

As an integral part of this prediction, you assume that the source and registered substance(s) have similar properties for the above-mentioned information requirements. ECHA considers that this information is your read-across hypothesis.

[3] Please see ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

ECHA's evaluation and conclusion

Your proposed adaptation argument is that the similarity in chemical structure and in some of the physico-chemical and toxicological properties between the source and target substances is a sufficient basis for predicting the properties of the target substance subject to this decision for other endpoints.

Structural similarity is a prerequisite for applying the grouping and read-across approach. However similarity in chemical structure and similarity of some of the physico-chemical parameters does not necessarily lead to predictable or similar human health properties, *i.e.* lead to similarity in other endpoints. Therefore, your justification based on structural similarity and similar physico-chemical properties is not sufficient to establish why the prediction is reliable for the human health end-points for which the read across is used. When turning to the provided toxicological information, ECHA notes that you have provided results from the following supporting studies using the target substance:

- Dimethylaminoethoxyethanol (DMEE): Nine-Day Vapor Inhalation Study in Rats and
- 2-(2-(Dimethylamino)-Ethoxy)Ethanol (DMEE): Nine-Day Repeated Dose Percutaneous Toxicity Study in Albino Rabbits.

Preceding your comments ECHA considered that the results from these supporting studies suggest different toxic properties for the target and source substances in terms of i) *type of toxic effects* and ii) *adverse effect levels*. Hence, ECHA found that the information on the selected source substances do not support the assumption that similarity in chemical structure results in similar toxicological properties and, therefore, do not seem to be suitable for predicting human health effects for the target substance.

Type of toxic effect: In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you state that "*OECD-member state experts concluded, based on the publication attached (CoCAM 6, 2014), that the haematological changes are likely secondary to the corrosive and local effects on the skin barrier (i.e. severe inflammation, damage to the epidermal layer, loss of integrity of the barrier function, and subsequent bacterial infection.)... The hematological effects included increased in lymphocyte and leucocyte values which are common responses to inflammation.*" As a conclusion, you disagree with the argument that the differences in hematology between source and target substance originate from a difference in systemic toxicity.

Your comments that the haematology effects can be explained by the infection, which is due to severe skin damage, is plausible. This view is supported by the article of Hermansky et al (provided by you), which demonstrates that elevated leukocytes, increase of platelets and decrease haemoglobin and haematocrit can be caused by cutaneous application of skin irritating substances. Note that there may be a species difference which supports this conclusion. According to the Hermansky et al, increase of platelet count was seen in rabbits only. The study with the registered substance was made with rabbits, whereas the 90-day study with RA substances was made in rat. Furthermore, as you point out in your comment, the doses administered in the 9-day dermal study with the registered substances were higher than the doses in the read-across study. This may explain, why haematology effects were seen in the 9-day study but not in the 90-day study.

Adverse effect levels: However, ECHA disagrees with your comments on the higher toxicity for the target substance. You have commented on this as follows "*This difference in exposure methods (whole body versus nose only) could easily account for the apparent difference in potencies. It is concluded that remaining uncertainties due to the correct uptake of the target substance by inhalation can be compensated by application of a safety factor in the DNEL derivation.*"

ECHA notes that the difference in potency is 10 fold as indicated by the NOAECs in the inhalation studies, and the explanation provided by you basically is that in the whole body exposure, the test animals will get an additional exposure by licking the fur/skin, which would lead to the difference. ECHA considers that this explanation is unlikely to fully cover the difference. Because of this difference, the LOAELs/NOAECs derived from the RA substances studies are not likely to provide correct DNELs and may lead to underestimation of the risk caused by the registered substance.

Furthermore, you have not compensated for the uncertainty caused by the read-across by applying an additional (adequate) assessment factor when calculating the DNEL.

Because the information available suggests that the target substance is more systemically toxic than the source substances, and because of the implications of this to the risk assessment the overall read-across is considered not adequate for risk assessment and classification and labelling.

Additionally, ECHA has taken into account all of your arguments together. ECHA firstly notes that you have not provided a reasoning as to why these arguments add to one another to provide sufficient basis for read-across. Secondly, the defects of each individual argument are not mitigated by the other arguments you have provided, and so ECHA considers that the arguments when taken all together do not provide a reliable basis for predicting the properties of the registered substance.

A Member State Competent Authority (MSCA) submitted a Proposal for Amendment (PfA) for this aspect of the draft decision. In the MSCA's PfA, it was pointed out that for the read-across in general, the draft decision, did not mention whether a sound comparison of the structural differences between the target and source substances is given.

In your comments on the MSCA's PfA, you have claimed that your arguments on the toxicokinetic behaviour of DMEE, as well as your read across justification and your comments on the draft decision sent in August 2017 have not been taken into account.

ECHA notes that only the studies concerning the toxicokinetic behaviour of DMEE have not been mentioned in Appendix 1 of the draft decision. Indeed, ECHA considered that there was no need to address these studies concerning the toxicokinetic behaviour of DMEE in the read across assessment. In ECHA's understanding your read-across hypothesis is primarily built on the structural similarity and similar physico-chemical and toxicological properties, not on transformation to common compounds. Moreover, you have not provided any relevant information on the metabolites and bio-transformation of the source substances (you have only provided theoretical claims, which is not substantiated with substance-specific information).

The QSAR data, which you have provided in your response to the PfA and also on your comments on the draft decision, only covers the target substance and is therefore not relevant for human metabolism as it only predicts the degradation products produced by environmental microbes (e.g. microbes present in sewage sludge). As this metabolites prediction relies on documented pathways of microbial catabolism, it can predict how a substance will metabolise (degrade) in the environment but it does not predict how the substance will metabolise in the human body (or in mammals).

In additon, ECHA also notes that there are structural differences between the target and source substances. More notably one of the source substances, AEE has a primary amino group, whereas in the target substance DMEE, there is a tertiary amino group. For the other source substance DMAE, the difference is that the target substance has an ether group, whereas that is absent in the source substance. ECHA also notes that the information of the metabolism of the source and target substances is incomplete.

Therefore, ECHA considers that this grouping and read-across approach does not provide a reliable basis whereby the human health effects of the registered substance may be predicted from data for reference substance(s) within the group. Hence, this approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation.

ECHA notes that there are specific considerations for the individual endpoints which also result in a failure to meet the requirement of Annex XI, Section 1.5., and these are set out under the endpoint concerned.

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

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 providing study records for the following sub-chronic toxicity studies marked as key studies:

- 90-day inhalation study (OECD TG 413) with 2-dimethylaminoethanol (EC No 203-542-8) and
- 90-day dermal toxicity study in rats (OECD TG 411) with 2-(2-aminoethoxy)ethanol (EC no 213-195-4).

However, as explained above in Appendix 1, section "*Grouping and read-across approach for toxicological information*" of this decision, your read-across approach using the analogue substances 2-dimethylaminoethanol and 2-(2-aminoethoxy)ethanol is rejected.

Furthermore, the sub-chronic toxicity study (90-day) by the dermal route performed with the source substance 2-(2-aminoethoxy)ethanol is considered as a not appropriate source study to fulfill a standard information requirement of Annex IX, Section 8.6.2., because the criteria of Annex IX, Section 8.6.2., column 2 for the appropriateness of testing by the dermal route are not fulfilled.

More specifically, (1) skin contact in production and/or use is not likely and has to be avoided since the substance is corrosive to the skin; (2) the physico-chemical properties of this substance (high water solubility and very low log k_{ow}) does not suggest significant absorption through the skin; however, destruction of the membrane barriers of the skin due to the corrosive property of the substance may increase the uptake through the skin in a non-quantifyable manner; and (3) significant dermal absorption was not observed and skin irritation is observed as the leading effect of this substance in studies with acute and repeated dermal exposure; in the dermal sub-chronic toxicity study study, the NOAEL for local irritating effects was 17 mg/kg bw/d, whereas no systemic effects were observed at 175 mg/kg bw/d (the highest dose tested).

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

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 5.0, December 2016) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure. Uses with industrial and professional spray application are reported in the chemical safety report. However, the reported concentrations are low ([redacted] %). 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.

You provided comments on the draft decision according to Article 50(1) of the REACH Regulation, which have been discussed under Appendix 1, section 'Grouping of substances and read-across approach'.

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

"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 sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) via inhalation route with the analogue substance 2-(2-aminoethoxy)ethanol (EC No 213-195-4).

You provided the following justification for the adaptation: *"In accordance with Section 1 of REACH Annex XI, the extended one generation reproductive toxicity study EOGRTS does not need to be conducted due to the following reasons: Based on the structural similarity 2-(2-aminoethoxy)ethanol, AEE, CAS# is proposed as read-across to DMEE for the reproduction toxicity endpoints (see Annex 13 Read across Justification). For AEE, an OECD 422 inhalation study was performed with screening for development and reproduction toxicity effects. No treatment related effects on development and reproduction were noted. The NOAEC for reproductive performance and fertility was 0.04 mg/L (highest concentration tested). Following Annex VIII No. 8.7.3 Column 2 of REACH the existing information caused by substances structurally analogous to the substance being studied, suggesting a similar mechanism. In consequence, there are no triggers for an EOGRTS study. It is proposed that the reproduction/developmental toxicity study can be waived."*

A Member State Competent Authority (MSCA) submitted a Proposal for Amendment (PfA) for this endpoint of the draft decision. In the MSCA's PfA, it was pointed out that this test with AEE is not suitable for read-across, also as it has not applied high enough doses. (And also the MSCA's PfA does not find it suitable for compliance of the registration of AEE itself.).

Concerning the relevance of this test, ECHA notes that there is a deficiency, which may limit the use of this study for the read-across. The highest dose is comparable to around 10 mg/kg bw/d of an oral dose (a rat inhales [redacted] m^3/kg bw/6h). However, the OECD TG 422 states "*The highest dose level should be chosen with the aim of inducing toxic effects but not death nor obvious suffering*". In this case, accordingly the study summary states no systemic toxicity, but local signs of toxicity, presumably due to corrosivity, were observed at the medium dose. Since it seems likely that these local effects have limited the maximum concentration administered, inhalation route does not seem to be the most appropriate route of administration. When applying the oral route, systemic effects, which have not been seen in the inhalation study, could potentially be observed, because higher doses can be used. Therefore, ECHA considers that the relevance of this OECD 422 study is limited.

However, as explained above in Appendix 1, section "*Grouping and read-across approach for toxicological information*" of this decision, your read-across approach using the analogue substances 2-(2-aminoethoxy)ethanol is rejected.

Hence, 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 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 5.0, December 2016) 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 on the draft decision according to Article 50(1) of the REACH Regulation

you state that you will submit robust study summary of screening study OECD TG 421 made on 2-dimethylaminoethanol (DMAE). The read-across approach is discussed under Appendix 1, section 'Grouping of substances and read-across approach'. Also, the robust study summary has not yet been submitted and, therefore, cannot be assessed by ECHA. According to our current policy, ECHA does not for the purpose of decision making take into account dossier updates after the date when the draft decision was notified to you.

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) *or* Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route.

Notes for your considerations

For the selection of the appropriate test, please consult ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7a, Section R.7.5 and 7.6 (version 5.0, December 2016).

The registrant should also carefully consider the order of testing especially the requested screening (OECD TG 421/422) and the developmental toxicity studies (OECD TG 414) to ensure unnecessary animal testing is avoided, paying particular attention to the end point specific guidance (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf) p 461 - 462.

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

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 (OECD TG 422) via inhalation route with the analogue substance 2-(2-aminoethoxy)ethanol (EC no 213-195-4). 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.

In the data matrix of your read-across justification document, you also referred to existing prenatal developmental toxicity study with 2-dimethylaminoethanol (DMAE), but respective study summaries were not provided in the dossier. REACH requires adequate and reliable documentation of the applied method (Annex XI, Section 1.5, last indent).

You should thus provide a robust study summary in IUCLID for information that is most relevant to support the read-across approach. For information supporting the read-across, either detailed information on the results should be provided in the read-across justification document or a study summary with appropriate reference to publicly available information.

In addition, as explained above in Appendix 1, section "*Grouping and read-across approach for toxicological information*" of this decision, your read-across approach using the analogue substances 2-(2-aminoethoxy)ethanol is rejected.

Hence, 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 rat or rabbit 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 5.0, December 2016) 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 on the draft decision according to Article 50(1) of the REACH Regulation you state that you will submit robust study summaries of OECD 414 and screening study OECD TG 421 made on 2-dimethylaminoethanol (DMAE). The read-across approach is discussed under Appendix 1, section 'Grouping of substances and read-across approach'. Also, the robust study summary has not yet been submitted and, therefore, cannot be assessed by ECHA and, according to our current policy, ECHA does not assess the dossier updates after the date when the draft decision was notified to you.

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.

4. Identification of degradation products (Annex IX, 9.2.3.)

The identification of the degradation products is a standard information requirement according to column 1, Section 9.2.3. of Annex IX 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.

The biodegradation section in the technical dossier does not contain any information in relation to the identification of degradation products, nor an adaptation in accordance with column 2 of Annex IX, Sections 9.2 or 9.2.3. or with the general rules of Annex XI for this standard information requirement.

According to Annex IX, Section 9.2.3., column 2 of the REACH Regulation, identification of degradation products is not needed if the substance is readily biodegradable. ECHA notes that based on the information in the technical dossier, you have concluded that the substance subject to this decision is not readily biodegradable.

Furthermore, ECHA notes that you have not provided any justification in your chemical safety assessment or in the technical dossier for why there is no need to provide information on the degradation products. Therefore, ECHA considers that this information is needed in relation to the chemical safety assessment (*e.g.* PBT/vPvB assessment).

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

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you provided results of the prediction of identity of degradation products by Qualitative or Quantitative structure-activity relationship (QSAR) model as well as results of PBT assessment for the identified degradation products. Furthermore, you noted intention to report above mentioned results in the registration dossier.

ECHA acknowledges that you intend to adapt the information requirements using QSAR predictions. However, ECHA is at this moment unable to assess appropriately the validity, applicability and adequacy of the results provided in the absence of a scientific justification, referring and conforming to the appropriate rules of Annex XI, Section 1.3 of the REACH Regulation. More specifically, you have not explained how the scientific validity of the model has been stablished, how the substance falls within the applicability domain, and provide adequate and reliable documentation of the applied method addressing those issues. Therefore, your adaptation does not meet the conditions of Annex XI, Section 1.3 of the REACH Regulation and is thus rejected.

ECHA notes that you can find further information in the Practical Guide on How to use and report (Q)SARs (https://echa.europa.eu/documents/10162/13655/pg_report_qsars_en.pdf)

Regarding appropriate and suitable test method, the methods will have to be substance-specific. When analytically possible, identification, stability, behaviour, molar quantity of metabolites relative to the parent compound should be evaluated. In addition, degradation half-life, log Kow and the potential toxicity of the metabolite may be investigated. You will need to provide a scientifically valid justification for the chosen method.

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: Identification of the degradation products (Annex IX, Section 9.2.3.) by using an appropriate and suitable test method, as explained above in this section.

Notes for your consideration:

Before providing the above information you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R.7b., Sections R.7.9.2.3 and R.7.9.4. These guidance documents explain why the information on degradation products following primary degradation is required and how this information is used in order to complete the chemical safety assessment. Section R.7.9.4. further clarifies also that when a substance is not fully degraded or mineralised, the degradation products may be determined by chemical analysis.

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 15 March 2017.

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

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

ECHA took into account your comments and did not amend the request(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

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.

In addition, you provided comments on the draft decision. These comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

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.