ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 23 July 2019

Addressee: [redacted]

Decision number: CCH-D-2114476179-36-01/F
Substance name: N,N',N'',N'''-TETRAKIS(4,6-BIS(BUTYL-(N-METHYL-2,2,6,6-TETRAMETHYLPIPERIDIN-4-YL)AMINO)TRIAZIN-2-YL)-4,7-DIAZADECANE-1,10-DIAMINE
EC number: 401-990-0
CAS number: 106990-43-6
Registration number: [redacted]
Submission number: [redacted]
Submission date: 12/03/2014
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. **Water solubility (Annex VII, Section 7.7.; test method: EU A.6./OECD TG 105) with the registered substance;**

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

3. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) with the registered substance;**

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

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

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

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

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

9. **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;**

10. **Identification of degradation products (Annex IX, 9.2.3.) using an appropriate test method with the registered substance;**

You have to submit the requested information in an updated registration dossier by ***31 January 2022***. 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, Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

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.

1. Water solubility (Annex VII, Section 7.7.)

"Water solubility" is a standard information requirement as laid down in Annex VII, Section 7.7 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 provided a key study reporting a water solubility value of <10 mg/L at 20°, accordingly with EU Method A.6 (Water Solubility).

You have provided a remark that "the water solubility of the test substance is very low (approx. detection limit of method). Therefore the result is given as < 10 mg/L.".

You have also indicated that the flask method was used instead of the column method because a change in crystal structure might occur when the test substance is deposited on the support material.

According to ECHA guidance (Chapter R.7a: Endpoint specific guidance Version 6.0 – July 2017), and EU Method A.6, when following Flask method, you should report the pH of each sample, individual analytical determinations and the average of the values for 3 different flasks, and as a result the average of the value for the different flasks. Also any deviation from the guideline method used or any other special consideration should be reported. You have solely provided the unbound result of <10 mg/L. You did not provide further details on individual flasks results. Furthermore, you have also not reported the pH under which the test has been conducted. Therefore, ECHA considers that you did not follow the guideline, or you failed to provide reporting with the required detail.

ECHA cannot evaluate the detection limit as you have also failed to provide information regarding the analytical method. ECHA understands that under normal circumstances detection limits far below 10 mg/L can be achieved with aromatic compounds with UV/light absorbance properties. Therefore, ECHA considers that you should have used a method which would permit a lower detection limit.

ECHA notes there are no further details on which type of change in crystalline form might occur with the substance if column elution method were used. Based on information in the dossier it is not apparent that this change occurs or that it could impact a column elution study. For low water solubility substances, column elution method is recommended in the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance (Version 6.0, July 2017, p. 68).

ECHA also notes that according to ECHA guidance (Chapter R.7a: Endpoint specific guidance Version 6.0, July 2017), for ionising substances the pH-dependence of the water solubility should be known. At least the pH of the test solution needs to be reported. In the context of marine risk assessment, when the pKa is close to 8 it may be necessary to obtain realistic measurements using seawater. ECHA notes that the registered substance has ionising

properties that may impact water solubility in different pH values and you should take this into consideraton when performing the text.

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 would also like to note that for risk assessment purposes, unbound results on physicochemical properties should not be reported. This is true especially when the properties are close to a threshold limit, in this case 1 mg/L which may impact other studies.

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: Water solubility (test method: EU A.6./OECD TG 105).

Guidance for determining appropriate test methods for the water solubility is available in the ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.7a, Section R.7.1.7.

ECHA notes that this study has been requested in a draft decision to other registrants of the same substance in order to fulfil this information requirement. In this context, ECHA reminds you of the obligation imposed by Articles 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and to share the cost of required studies.

In your comments to the draft decision you indicated that the data included in the technical dossier had been obtained by the Registrant from ECHA under the "*12 years rule*". Therefore, you considered that you reported the information provided by ECHA and that the limited information available on the study, giving rise to the request for a new study, cannot be ascribed to you.

As indicated in section 4.6.3 of the ECHA Guidance on data sharing (version 3.1, January 2017), ECHA stresses that "*it is always the responsibility of the inquirer to assess the quality and relevance of the information received from ECHA so that, as a registrant, he fulfils his registration obligations. When using study summaries submitted more than 12 years earlier (e.g. in a NONS notification), it may be that these study summaries are not of sufficient quality to meet the registration obligations under the REACH Regulation*". As indicated in the draft decision, in the context of this compliance check, ECHA concluded that the documentation of the study provided to fulfil the information requirement of Annex VII, Section 7.7 on water solubility is insufficient and does not allow an independent assessment of the adequacy of the study, their results and use for hazard assessment.

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the study/ies on behalf of all Registrant(s) within 90 days of the adoption of the decision.

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

An "*In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a

standard information requirement as laid down in Annex VIII, Section 8.4.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for an *in vivo* mammalian somatic cell study: cytogenicity / erythrocyte micronucleus (EU Method B.12, 1987, reliability 1, Key study, GLP). However, this study does not provide the information required by Annex VIII, Section 8.4.2., because the likelihood that the test substance or its metabolites reached the general circulation and the bone marrow is limited. Based on the very limited reporting of the test conditions and the results for this study in your technical dossier, there is no evidence that the test material has become systemically available after oral administration. The OECD TG 474 indicates: "*If there is evidence that the test substance, or a reactive metabolite, will not reach the target tissue, it is not appropriate to use this test*". Consequently, ECHA concludes that the *in vivo* micronucleus test is not valid and it cannot be used in order to meet the information requirement of Annex VIII, Section 8.4.2.

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

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian chromosome aberration test (test method: OECD TG 473) or *in vitro* mammalian cell micronucleus study (test method: OECD TG 487).

ECHA notes that this study has been requested in a draft decision to other registrants of the same substance in order to fulfil this information requirement. In this context, ECHA reminds you of the obligation imposed by Articles 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and to share the cost of required studies.

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the study/ies on behalf of all Registrant(s) within 90 days of the adoption of the decision.

In your comments to the draft decision you indicated that you had no comments on the requested information.

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

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

A reverse mutation assay in bacteria (Ames test, 1987, key study, reliability 1, strains: TA 1535, TA 1537, TA 98, TA 100 and TA 102; result: negative) is included in your technical dossier. As explained in Section 2 of Appendix 1 of the current decision, the registration dossier does not contain appropriate study record for the information requirement of Annex VIII, Section 8.4.2. Therefore, adequate information on *in vitro* gene mutation in mammalian cells needs to be present in the technical dossier for the registered substance to meet the information requirement of Annex VIII, Section 8.4.3 provided that the study requested under section 3 of Appendix 1 has negative results.

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

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

Therefore, you are requested to provide information derived with the registered substance subject to the present decision: *in vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that the study requested under 2. has negative results.

ECHA notes that other registrants of the same substance have already submitted in their registration dossiers information from experimental studies in order to fulfil this information requirement. In accordance with Title III of the REACH Regulation, in order to comply with the present decision where such data is already available, you may request this information from other registrants of the same substance.

In addition, you are reminded of the obligations imposed by Article 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and to share the cost of required studies.

In your comments to the draft decision you indicated that you had no comments on the requested information.

4. 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. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a screening for reproductive/developmental toxicity in the dossier that would meet the information requirement of Annex VIII, Section 8.7.1.

While you have not explicitly claimed an adaptation, you have provided information in your technical dossier and in the Chemical Safety Report (CSR) section 5.9.1.1. that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 3 Substance-tailored exposure-driven testing.

In your waiving argument you have referred to the exclusive industrial uses of the registered substance, highlighting that the substance and its formulations are not sold directly to consumers and stressed that human exposure is not expected via the environment or during service life of articles and finished products. You also considered that exposure via inhalation is negligible on the basis of physico-chemical properties of the substance. You claimed that industrial hygiene practices, safe handling procedures and personal protective equipments minimise dermal and oral exposure of workers. Eventually you referred to the absence of evidence of toxicity to the reproductive organs in repeated dose toxicity studies to conclude that there is no need to perform reproductive toxicity study.

However, ECHA notes that your adaptation does not meet the general rules for adaptation of Annex XI, Section 3 because not all the conditions listed under Annex XI, Section 3, paragraphs 3.2 (i) to (iii) are fulfilled.

According to Annex XI, Section 3, paragraph 3.2, all the following conditions need to be fulfilled to omit testing for the information requirement of Annex VIII, 8.7.1:

- Paragraph 3.2 (i): "*the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5*": based on the information included in the CSR exposure is reported for multiple uses. For Scenario 2 Plastics processing - PROC 5 Processes for formulation of preparations and articles, dermal exposure is estimated to be of 6.86 x 10^{-2} mg/kg bw/d taking into account the efficiency of personal protective equipment (95%) and estimated dermal absorption (10%). This exposure cannot be considered as not significant as it leads to a risk characterisation ratio of [redacted] for dermal long term systemic effects. Furthemore, for the same exposure scenario, you state that "*Dermal exposure, that may lead to skin damage, and direct contact to eyes are estimated from low to moderate*". This also indicates that significant dermal exposure of workers to the substance cannot be ruled out or considered non significant. Therefore ECHA considers that the criterion on the absence of or no significant exposure in all scenarios of the manufacture and all identified uses is not met.
- Paragraph 3.2(ii): "*DNEL or a PNEC can be derived from results of available test data for the substance concerned taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL or PNEC is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes*": ECHA observes that no results from test data on reproductive toxicity are available and allow for the derivation of a DNEL for this specific hazard and for risk assessment purposes. Therefore ECHA considers that the criterion on the possibility to derive a DNEL from available test data appropriate both to the information requirement to be omitted and for risk assessment purposes is not fulfilled.
- Paragraph 3.2 (iii): "*the comparison of the derived DNEL or PNEC with the results of the exposure assessment shows that exposures are always well below the derived DNEL or PNEC*": based on the information included in the CSR, all exposure levels

are always below the derived DNEL. This condition is considered as fulfilled.

For the reasons presented above, ECHA considers that not all the conditions listed under Annex XI, Section 3, paragraphs 3.2 (i) to (iii) are fulfilled. Therefore, your adaptation of the information requirement is rejected. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test methods OECD TGs 421/422, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

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

In your comments to the draft decision you indicated that you see it contradictory that in the context of this *in vivo* micronucleus study, ECHA questioned the systemic availability of the registered substance after oral administration whilst also requesting a screening for reproductive/developmental toxicity study and a pre-natal developmental toxicity study to be conducted via the oral route. You are of the opinion that the substance does not reach the systemic compartment after oral administration and that *in vivo* studies conducted via the oral route will not provide meaningful results.

In Appendix 1 – Section 2 of the draft decision, ECHA indicated that "*the likelihood that the test substance or its metabolites reached the general circulation and the bone marrow is limited*" and concluded that "*there is no evidence that the test material has become systemically available after oral administration*". ECHA stresses that the identified absence of information on the systemic bioavailability of the substance in this *in vivo* mammalian somatic cell study does not imply that the substance is not systemically bioavailable at all. Furthermore, in a sub-chronic (90-day) repeated dose toxicity study conducted in rats via the oral route with the registered substance ([redacted] 1998) and reported in the joint submission for this substance, effects in the mesenteric lymph nodes and in the spleen have been observed, leading to the self-classification of the registered substance as STOT RE 2. These findings suggest that constituents of the registered substance or their metabolites may give rise to significant toxicological findings. Therefore, ECHA considers that your views that conducting *in vivo* studies via the oral route is not meaningful are not supported by the existing data on the registered substance.

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 consideration

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 6.0, July 2017).

You should also carefully consider the order of testing of the requested screening (OECD TG 421/422) and the developmental toxicity studies (OECD TG 414) to ensure that unnecessary animal testing is avoided, paying particular attention to the ECHA Guidance[2].

In addition, ECHA also notes that an extended one-generation reproductive toxicity study (EOGRTS) has been requested in a separate decision to other registrants of the same substance in order to fulfil the information requirement of Annex X, 8.7.3. Once an EOGRTS is available, according to Column 2 of Annex VIII, Section 8.7.1. and in order to prevent unnecessary animal testing, a screening for reproductive/developmental toxicity does not therefore need to be conducted. In this context, ECHA reminds you of the obligations imposed by Articles 11 and Title III of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly.

5. 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. Furthermore, pursuant to Article 10 (a)(vii) and Annex I, Section 1.1.4. if there are several studies addressing the same effect, then, having taken into account possible variables (e.g. conduct, adequacy, relevance of test species, quality of results, etc.), normally the study or studies giving rise to the highest concern shall be used to establish the DNELs and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment.

You have provided a study record for a 90-day repeated dose toxicity study conducted in 1987 using the registered substance according to an unspecified test guideline and without compliance with the good laboratory practices to meet the standard information requirement of Annex IX, Section 8.6.2.

However, ECHA notes that, contrary to Article 3(28) of the REACH Regulation the information provided in the robust study summary is insufficient to allow an independent assessment of the study.

In this regard, ECHA notes that the robust study summary does not include critical information required in the OECD TG 408 and in ECHA's Practical Guide 3 "*How to report robust study summaries*". This critical information concerns in particular the following elements: rationale for the selection of the test doses, details on the preparation of the test doses, details of the scope of the observations and examinations performed during the study (general clinical observations, functional observation battery, haematology, clinical biochemistry), scope of the investigations conducted after sacrifice (gross necropsy and histopathology) in accordance with the recommendations of the OECD TG 408 and detailed presentation of the results for each of these investigations.

Without this critical information, the robust study summary cannot be relied on for an independent assessment of the properties of the registered substance. Hence, the information provided on this endpoint for the registered substance in the technical dossier

[2] ECHA Guidance R7a, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017 https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf

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 reported to occur as a dust but no significant proportion (>1% on weight basis) of particles are of inhalable size (MMAD < 50 µm). Hence, the test shall be performed by the oral route using the test method OECD TG 408.

According to the test method 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 indicated that the data included in the technical dossier had been obtained by the Registrant from ECHA under the "*12 years rule*". Therefore, you considered that you reported the information provided by ECHA and that the limited information available on the study, giving rise to the request for a new study, cannot be ascribed to you.

As indicated in section 4.6.3 of the ECHA Guidance on data sharing (version 3.1, January 2017), ECHA stresses that "*it is always the responsibility of the inquirer to assess the quality and relevance of the information received from ECHA so that, as a registrant, he fulfils his registration obligations. When using study summaries submitted more than 12 years earlier (e.g. in a NONS notification), it may be that these study summaries are not of sufficient quality to meet the registration obligations under the REACH Regulation*". As indicated in the draft decision, in the context of this compliance check, ECHA concluded that the documentation of the study provided to fulfil the information requirement of Annex IX, Section 8.6.2 for a sub-chronic (90-day) is insufficient and does not allow an independent assessment of the adequacy of the study, their results and use for hazard assessment.

In accordance with Article 26(3) ECHA informs you that other registrants of the same substance have already submitted in their registration dossiers information from experimental studies involving vertebrate animals in order to fulfil the relevant information requirements. In accordance with Title III of the REACH Regulation, namely the obligations to request access to available information of studies on vertebrate animals (Articles 27 and 30 of the REACH Regulation), you shall not perform new testing involving vertebrate animals in order to comply with the present decision where such data is already available. Under these provisions you are compelled to request this information from other registrants of the same substance. All the registrants concerned shall make every effort to reach an agreement on the fair, transparent and non-discriminatory sharing of the cost.

In addition, you are reminded of the obligations imposed by Article 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and to share the cost of required studies.

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation. 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[3]. 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. 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[4]- (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

[3] 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.
[4] 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).

quality of the studies which are to be read-across.

You consider to achieve compliance with the REACH information requirements for the registered substance using data of structurally similar substance 1,3,5-Triazine-2,4,6-triamine (Melamine) (hereafter the 'source substance').

You provided the following documentation for the adaptation in the technical dossier and in the CSR section 5.9.2.1: "*1,3,5-Triazine-2,4,6-triamine (or Melamine) was identified as a potential toxophore in a substance similar to HALS11, the* [redacted] *by Derek analysis. Therefore the literature search for assessing reproductive toxicity of this compound was undertaken and summarized below*". You have then provided descriptions of the results of studies conducted with melamine administered to rats via the diet or by gavage during gestation days 6-15 or 6-20 respectively. Data from single intraperitoneal administration of melamine to rats on specific gestation days is also reported. Based on this information, you conclude that "*from these data it can be concluded that* [redacted] *would not require a reproductive toxicity classification*".

You have provided documentation of the read-across adaptation, but the documentation that you provided in your dossier does not contain any specific justification whereby relevant human health properties of the registered substance may be predicted from data for the source substances. Specifically, your dossier does not address why such prediction would be possible.

In the absence of this information, ECHA cannot verify that the properties of the registered substance can be predicted from the data on the source substance.

Hence, you have not established that relevant properties of the registered substance can be predicted from data on the analogue substance. Since your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5., it is rejected and it is necessary to perform testing on the registered substance.

According to the test method 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 solid, ECHA concludes that testing should be performed by the oral route.

In your comments to the draft decision you indicated that you see it contradictory that in the context of this *in vivo* micronucleus study, ECHA questioned the systemic availability of the registered substance after oral administration whilst also requesting a screening for reproductive/developmental toxicity study and a pre-natal developmental toxicity study to be conducted via the oral route. You are of the opinion that the substance does not reach the systemic compartment after oral administration and that *in vivo* studies conducted via the oral route will not provide meaningful results.

In Appendix 1 – Section 2 of the draft decision, ECHA indicated that "*the likelihood that the*

test substance or its metabolites reached the general circulation and the bone marrow is limited" and concluded that "*there is no evidence that the test material has become systemically available after oral administration*". ECHA stresses that the identified absence of information on the systemic bioavailability of the substance in this *in vivo* mammalian somatic cell study does not imply that the substance is not systemically bioavailable at all.

Furthermore, in a sub-chronic (90-day) repeated dose toxicity study conducted in rats via the oral route with the registered substance ([redacted] 1998) and reported in the joint submission for this substance, effects in the mesenteric lymph nodes and in the spleen have been observed, leading to the self-classification of the registered substance as STOT RE 2. These findings suggest that constituents of the registered substance or their metabolites may give rise to significant toxicological findings. No information on the pre-natal developmental toxicity of the registered substance is available. Therefore, ECHA considers that your views that conducting *in vivo* studies via the oral route is not meaningful are not supported by the existing data on the registered substance.

In your comments to the draft decision, you requested the possibility to submit an updated adaptation for this information requirement before considering testing.
As indicated in the notification letter accompanying the draft decision, ECHA does not take into account any dossier updates after the notification of this draft decision under Article 50(1) of the REACH Regulation. Any such updates will be examined by ECHA after the deadline set in the adopted decision has passed.

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: OECD TG 414) in a first species (rat or rabbit) by the oral route.

ECHA notes that this study has been requested in a draft decision to other registrants of the same substance in order to fulfil this information requirement. In this context, ECHA reminds you of the obligation imposed by Articles 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and to share the cost of required studies.

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the study/ies on behalf of all Registrant(s) within 90 days of the adoption of the decision.

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

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.
Furthermore, pursuant to Article 10 (a)(vii) and Annex I, Section 3.1.5. if there are several studies addressing the same effect, then, the study or studies giving rise to the highest concern shall be used to draw the conclusion and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust study summaries will be required of all key data used in the hazard assessment.

Under Article 3(28) of the REACH Regulation, a Robust study summary "*means a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report*".

You have provided a study record for a growth inhibition study aquatic plants conducted in 1987 (reliability 1) using the registered substance according to ISO 8692 test guideline (OECD TG 201/EU Method C.3) and with compliance with the good laboratory practices to meet the standard information requirement of Annex VII, Section 9.1.2.

However, ECHA notes that, contrary to Article 3(28) of the REACH Regulation the information provided in the robust study summary is insufficient to allow an independent assessment of the study.

In this regard, ECHA notes that the Robust study summary does not include critical information required in the OECD TG 201 and in ECHA's Practical Guide 3 "*How to report robust study summaries*". This critical information concerns in particular:

- Information to assess the validity and reliability of the study.

  In particular, in the robust study summary you do not report details on sampling and on analytical monitoring of the test concentrations, details on the preparation of the test solutions (the robust study summary only indicates that WAFs were used), description of test design (e.g. test type), details on test conditions (e.g. temperature, pH), details on nominal and measured test concentrations and on replicates, detailed presentation of the results (e.g. observations in the controls and treated cultures, determination of growth rates in the controls and treated cultures, determination of the mean coefficient of variation for section-by-section specific growth rates in the control, determination of the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures).

- Details on test material

  The robust study summary does not include details on the test material (e.g. content and identity of impurity) nor a justification to support that the test material is representative of the registered substance including its 5 unknown impurities, as given in ECHA's Practical Guide 3.

Without this critical information, the robust study summary cannot be relied on for an independent assessment of the properties of the registered substance. 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 ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

In your comments to the draft decision you indicated that the data included in the technical dossier had been obtained by the Registrant from ECHA under the "*12 years rule*". Therefore, you considered that you reported the information provided by ECHA and that the

limited information available on the study, giving rise to the request for a new study, cannot be ascribed to you.

As indicated in section 4.6.3 of the ECHA Guidance on data sharing (version 3.1, January 2017), ECHA stresses that "*it is always the responsibility of the inquirer to assess the quality and relevance of the information received from ECHA so that, as a registrant, he fulfils his registration obligations. When using study summaries submitted more than 12 years earlier (e.g. in a NONS notification), it may be that these study summaries are not of sufficient quality to meet the registration obligations under the REACH Regulation*". As indicated in the draft decision, in the context of this compliance check, ECHA concluded that the documentation of the study provided to fulfil the information requirement of Annex VII, Section 9.1.2 for a growth inibition study on aquatic plants is insufficient and does not allow an independent assessment of the adequacy of the study, their results and use for hazard assessment.

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

ECHA notes that other registrants of the same substance have already submitted in their registration dossiers information from experimental studies in order to fulfil this information requirement. In accordance with Title III of the REACH Regulation, in order to comply with the present decision where such data is already available, and if such data is considered as acceptable to be used to fulfill this information requirement, you may request this information from other registrants of the same substance.

In addition, you are reminded of the obligations imposed by Article 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and the share the cost of required studies.

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

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.5., column 2 and Annex XI, Section 3 Substance-tailored exposure-driven testing. You provided the following justification for the adaptation: "*In accordance with column 2 of REACH annex IX, long-term toxicity testing on aquatic invertebrates does not need to be conducted as the chemical safety assessment does not indicate a need for further investigation. In accordance with Section 3 of REACH Annex XI, Substance-tailored exposure- driven testing, long-term toxicity testing on aquatic invertebrates (information requirement 9.1.5 in Annex IX) may be omitted based on the exposure scenarios developed in the Chemical Safety Report. Justification and documentation are provided in Chapter 9.*"

However, for the reasons explained below, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2 and the general rule

for adaptation of Annex XI; Section 3.

i. Annex IX, Section 9.1.5., column 2, adaptation

In your adaptation you propose that the chemical safety assessment (CSA) does not indicate the need to investigate further the effects on aquatic organisms. However, ECHA considers that your assessment of the need for further investigations based on the CSA is highly uncertain as the current information in your Chemical Safety Report (CSR) and your technical dossier is not complete for the following reasons:

(1) Aquatic toxicity data used as basis for PNEC derivation in the CSA cannot currently be considered reliable.

ECHA notes that all short-term studies available in the technical dossier cannot currently be considered reliable, since, contrary to Article 3(28) of the REACH Regulation, the information provided in their robust study summaries is insufficient to allow an independent assessment of the study. This is discussed in section 7 above for the study provided for the endpoint algae growth inhibition and it is discussed in the following paragraph on for short-term aquatic invertebrates and on short-term fish endpoints (not requested in this draft decision, as explained in the Notes for consideration below).

For aquatic invertebrates, you have provided a study record for a short-term toxicity study conducted in 1987 (reliability 1) using the registered substance according to OECD TG 202, and with compliance with the good laboratory practices. For fish, you have provided a study record for a short-term toxicity study conducted in 1987 (reliability 1) using the registered substance according to OECD TG 203. However, the robust study summaries of both studies do not include critical information required in the in the standard TGs (OECD TG 202 for *Daphnia* and OECD TG 203 for fish) and in ECHA's Practical Guide 3 "*How to report robust study summaries*", such as details on test material, details on sampling and on analytical monitoring of the test concentrations, description of test design, details on test conditions (e.g. temperature, pH), details on nominal and measured test concentrations and on replicates, observations in the controls and treated cultures. As a consequence, for the same reasons as for the algae study addressed under section 7 above, ECHA considers that the available short-term studies for aquatic invertebrates and fish cannot be relied on for an independent assessment of the properties of the registered substance.

Since the aquatic toxicity data you have used as basis for PNEC derivation cannot currently be considered reliable, the CSA cannot be used to adapt the current information requirement.

(2) Long-term aquatic studies are necessary for a meaningful risk assessment of the registered substance.

ECHA notes that long-term aquatic studies on *Daphnia* (current request) and on fish (request 9 below) are not available in the technical dossier and are required for a meaningful PNEC derivation and consequently risk assessment of the registered substance, as explained in the following.

Although the water solubility of the registered substance is currently not clear (as described in request 2. above), there are indications that the registered substance is poorly water soluble. For instance, the test solutions of the algae growth inhibition study (request 8 above) were prepared with WAFs indicating that the test substance is difficult to test, considered to be partially soluble in water and may dissociate at environmentally relevant pH. In addition, the registered substance has a high log Kow (4.5 at pH 7, as reported in the study summary of IUCLID section 4.7).

For difficult to test substances with these properties (i.e. poorly water soluble and with a high log Kow), the Integrated testing strategy (ITS) outlined 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), is not applicable. ECHA notes that poorly soluble and hydrophobic substances require longer time to be taken up by test organisms and therefore steady-state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, Chapter R.7b (Version 4.0, June 2017) of ECHA Guidance indicates that short-term tests may not give a true measure of toxicity for poorly soluble and hydrophobic substances and toxicity may actually not even occur at the water solubility limit of the substance during an acute study of short duration. In the present case, no effects were for example observed in the short-term fish study since effect values of LC50 > 119 mg/L and NOEC > 119 mg/L were derived ("initial measured concentrations"). Therefore, ECHA considers that it is not possible to derive a reliable PNEC for a poorly water soluble substance with acute data alone and long-term aquatic studies are necessary to clarify the toxicity of the substance to aquatic organisms and in order to support a meaningful risk assessment. For the derivation of PNECaquatic, reliable information on three trophic levels is required. In the absence of reliable aquatic plants (as addressed in request 7 above) and in the absence of information on long-term toxicity to *Daphnia* (current request) and fish (request 9 below), you currently have no reliable long-term data available to enable you to derive a reliable PNEC and to carry out a risk assessment.

In conclusion, for all reasons listed above, the Chemical Safety Assessment (CSA) cannot currently be considered reliable. Consequently, the CSA cannot be used to adapt this information requirement.

ii. Annex XI, Section 3 adaptation

ECHA notes that your adaptation does not meet the general rules for adaptation of Annex XI, Section 3 because not all the conditions listed under Annex XI, Section 3, paragraphs 3.2 (i) to (iii) are fulfilled. According to Annex XI, Section 3, paragraph 3.2, all the following conditions need to be fulfilled to comply with the information requirement of Annex IX, Section 9.1.5.:

- Under Paragraph 3.2 (i): "*the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5*". Based on the information included in the CSR exposure is reported for multiple scenarios. For instance, in Scenario 1 Manufacturing of the substance –ERC 1, the environmental exposure

concentration is estimated to be of 1.64 x 10^{-4} mg/L in surface water (annual average local PEC), of 1.34 x 10^{-1} mg/kgdwt in freshwater sediment (local PEC during emission episode) and of 6.54 x 10^{-2} mg/kgdwt in soil (local PEC averaged over 30 days). Thus, exposure cannot be considered as absent or not significant. Therefore ECHA considers that the criterion on the absence of or no significant exposure in all scenarios of the manufacture and all identified uses is not met.

- Under Paragraph 3.2(ii): "*DNEL or a PNEC can be derived from results of available test data for the substance concerned taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL or PNEC is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes*". However, ECHA observes that the robust study summaries of the short-term aquatic toxicity studies submitted in your dossier cannot be relied on for an independent assessment of the properties of the registered substance, as discussed in point i) above. As a result, the PNEC derivation and consequent risk characterisation are currently not reliable. Furthermore, as described above, long-term aquatic studies are not available in the technical dossier and are required for a meaningful PNEC derivation and consequent risk characterisation of the registered substance (poorly water soluble with a high log Kow). Therefore, the dossier does not contain information that can be used to calculate the PNEC. Therefore ECHA considers that the criterion on the possibility to derive a PNEC from available test data appropriate both for the information requirement to be omitted and for risk assessment purposes is not fulfilled.

- Under Paragraph 3.2 (iii): "*the comparison of the derived DNEL or PNEC with the results of the exposure assessment shows that exposures are always well below the derived DNEL or PNEC*". Based on the information included in the CSR, all exposure levels are always below the derived PNEC. However, due to the unreliable PNEC derivation as described above, this condition is considered as not fulfilled.

In conclusion, for the reasons presented above, your adaptation of the information requirement is rejected.

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

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

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

ECHA notes that other registrants of the same substance have already submitted in their registration dossiers information from experimental studies in order to fulfil this information

requirement. In accordance with Title III of the REACH Regulation, in order to comply with the present decision where such data is already available, and if such data is considered as acceptable to be used to fulfill this information requirement, you may request this information from other registrants of the same substance.

In addition, you are reminded of the obligations imposed by Articles 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and the share the cost of required studies.

In your comments to the draft decision you indicated that you had no comments on the requested information.

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

"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 9.1.5., column 2 and Annex XI, Section 3 Substance-tailored exposure-driven testing. You provided the following justification for the adaptation: "*In accordance with column 2 of REACH annex IX, long-term toxicity testing on fish does not need to be conducted as the chemical safety assessment does not indicate a need for further investigation. In accordance with Section 3 of REACH Annex XI, Substance-tailored exposure- driven testing, long-term toxicity testing on fish (information requirement 9.1.6 in Annex IX) may be omitted based on the exposure scenarios developed in the Chemical Safety Report. Justification and documentation are provided in Chapter 9.*"

ECHA notes that your justification is identical to the adaptation justification provided for "Long-term toxicity testing on aquatic invertebrates" addressed under section 8 above.

For the same reasons as those identified under Section 8, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6.1., column 2 and the general rule for adaptation of Annex XI, Section 3.

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 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) can be performed to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Section R.7.8.4.1.

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA Guidance Chapter R7b, version 4.0, June 2017).

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

ECHA notes that this study has been requested in a draft decision to other registrants of the same substance in order to fulfil this information requirement. In this context, ECHA reminds you of the obligation imposed by Articles 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and to share the cost of required studies.

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the study/ies on behalf of all Registrant(s) within 90 days of the adoption of the decision.

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapters R.4 (v.1.1, December 2011), R.5 (v.2.1, December 2011), R.6 (May 2008), R.7b (v 4.0, June 2017) and R.7c (v 3.0, June 2017). If you decide to adapt the testing requested according to the specific rules outlined in Annexes VI to X and/or according to general rules contained in Annex XI of the REACH Regulation, you are referred to the advice provided in practical guides on "How to use alternatives to animal testing to fulfil your information requirements for REACH registration".

ECHA emphasises that any testing strategy or adaptation is your responsibility. ECHA notes that given its physico-chemical and environmental fate properties (e.g. logKow, ionisability, water solubility), the substance is very likely to fall outside the applicability domain of most commercially available QSAR models predicting ecotoxicity.

As indicated above there are no reliable short-term studies available on aquatic invertebrates and fish, hence it is not possible to determine the sensitivity of species. Additionally the registered substance has low water solubility and high log Kow value. For the substances with these properties, the Integrated testing strategy (ITS) outlined 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), is not applicable and the long-term studies on both invertebrates and fish are needed. Since short-term studies are in any case not recommended for a poorly water soluble substance with a high log Kow and

long-term aquatic testing is requested in this decision, short-term aquatic studies are not requested.

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

Due to high adsorption potential and ionising properties you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R.7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

If the test proves to be unfeasible because of the physicochemical properties of the substance you may decide, based on preliminary test results or laboratory assessment, that the test is technically not possible and then stop testing. The information as to why the tests were stopped and the reasons for them not being technically possible should be explicitly included in the registration dossier.

In your comments to the draft decision you indicated that you had no comments on the requested information.

10. 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 on the degradation products, nor an acceptable adaptation for this standard information requirement 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 in your Chemical Safety Assessment (CSA) you have concluded that the registered substance is not readily biodegradable based on the results of the ready biodegradability study provided in the technical dossier (6% biodegradation after 28 days, Ready Biodegradabilty: Modified AFNOR Test).

Furthermore, ECHA notes that you have not provided any justification in your chemical safety assessment (CSA) 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 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.

Regarding the appropriate and suitable test method to provide further information on degradation/transformation products, you may obtain this information from the OECD TG 309 "pathway part" or by some other measures. ECHA considers that in this case you are recommended to perform the "pathway part" of the OECD TG 309 test. ECHA also notes that to overcome the potential analytical limitations in the identification and quantification of major transformation products you may use higher concentrations of the test substance (e.g. >100 µg/L) as specified in the OECD 309 test guideline. Furthermore, when reporting the role of non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER as described in Guidance on information requirements and chemical safety assessment R.7b (version 4.0, June 2017) and R.11 (version 3.0, June 2017).

You may also use other appropriate and suitable test methods to provide information on the identity of the degradation products for example by enhanced screening level degradation test. You will need to provide a scientifically valid justification for the chosen method. The provided information should include, identification, stability, behaviour, molar quantity of metabolites relative to the parent compound. In addition, degradation half-life, log Kow and potential toxicity of the metabolites may be investigated.

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, including each relevant impurity present in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable. ECHA recommends to use Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25./OECD TG 309, with higher initial concentration of the test material as specified above.

ECHA notes that this information has been requested in a draft decision to other registrants of the same substance in order to fulfil this information requirement. In this context, ECHA reminds you of the obligation imposed by Articles 11 and Title II of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly and to share the cost of required studies.

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the study/ies on behalf of all Registrant(s) within 90 days of the adoption of the decision.

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 4.0, June 2017), Chapter R.7b., Sections R.7.9.2.3 and R.7.9.4. These guidance documents explain that the data on degradation products is only required if information on the degradation products following primary degradation is required in order to complete the chemical safety assessment. Section R.7.9.4. further states that when substance is not fully degraded or mineralised, degradation products may be determined by chemical analysis.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when the information requested is available. ECHA notes that the PBT assessment currently does not include any information on the PBT/vPvB properties of the potential degradation products and of the 6 impurities (5 of which are unknown) present in the registered substance in concentration of ≥ 0.1% (w/w). In this regard, ECHA reminds you that Annex XIII of the REACH Regulation explicitly requires that PBT/vPvB properties of relevant constituents and relevant degradation products need to be taken into account. ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11.4.1. further specifies that *"constituents, impurities and additives should normally be considered relevant for the PBT/vPvB assessment when they are present in concentration of ≥ 0.1% (w/w). This limit of 0.1% (w/w) is set based on a well-established practice rooted in a principle recognised in European Union legislation."* and that *"the PBT/vPvB assessment should normally be carried out for each relevant transformation or degradation product"*. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

If you decide to adapt the testing requested according to the specific rules outlined in Annexes VI to X and/or according to general rules contained in Annex XI of the REACH Regulation, ECHA emphasises that any testing strategy or adaptation is your responsibility. ECHA also notes that given its physico-chemical and environmental fate properties (e.g. logKow, ionisability, water solubility), the substance is very likely to fall outside the applicability domain of most commercially available QSAR models predicting degradability.

In your comments to the draft decision you indicated that you had no comments on the requested information.

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 2018.

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 proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments.

ECHA referred the draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-65 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 carrying out the tests required by the present decision, it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new tests must be suitable to assess these.

   Furthermore, 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.