EUROPEAN CHEMICALS AGENCY

Helsinki, 22 November 2019

Addressee: [redacted]

Decision number: CCH-D-2114488835-30-01/F
Substance name: 2',3-bis[[3-[3,5-di-tert-butyl-4 hydroxyphenyl]propionyl]]propionohydrazide
EC number: 251-156-3
CAS number: 32687-78-8
Registration number: [redacted]
Submission number: [redacted]
Submission date: 24/07/2018
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. **In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. / OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102 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. **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;**

4. **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;**

5. **Identification of degradation products (Annex IX, Section 9.2.3.; test method: Aerobic and anaerobic transformation in soil (OECD TG 307), or other appropriate and suitable test method, as further defined in the Appendix 1)**

You have to submit the requested information in an updated registration dossier by **29 July 2021**. You shall also update the chemical safety report, where relevant.

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 **Claudio Carlon**, 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

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

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

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA.

Other tests may be used if the conditions of Annex XI are met. More specifically, Section 1.1.2 of Annex XI provides that existing data on human health properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3) may be used if the following conditions are met:

(1) Adequacy for the purpose of classification and labelling and/or risk assessment;
(2) Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3);
(3) Exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) if exposure duration is a relevant parameter; and
(4) adequate and reliable documentation of the study is provided.

According to paragraph 13 of the current OECD TG 471 test guideline (updated 1997) at least five strains of bacteria should be used: S. typhimurium TA1535; TA1537 or TA97a or TA97; TA98; TA100; S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101). This includes four strains of *S. typhimurium* (TA1535; TA1537 or TA97a or TA97; TA98; and TA100) that have been shown to be reliable and reproducibly responsive between laboratories. These four *S. typhimurium* strains have GC base pairs at the primary reversion site and it is known that they may not detect certain oxidising mutagens, cross-linking agents and hydrazines. Such substances may be detected by *E.coli* WP2 strains or *S. typhimurium* TA102 which have an AT base pair at the primary reversion site.

You have provided a test from the year 1980 according to OECD TG 471 and GLP with an assigned reliability score of 2. The test used different strains of *S. typhimurium* TA 1535, TA 1537, TA 1538, TA 98 and TA 100 and it did not include tests with strains S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101). However, since the test was conducted, significant changes have been made to OECD TG guideline 471 so that additionally testing with S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101) is now required. Therefore, the provided study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in Annex XI, 1.1.2. of the REACH Regulation.

ECHA concludes that a test using *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 has not been submitted and that the test using one of these is required to conclude on *in vitro* gene mutation in bacteria.

In your comments on the draft decision you agreed to perform the test. You also provided a QSAR analysis using the "Ames mutagenicity S9 activated" module present in OASIS TIMES v2.27.19.13. You indicated that the prediction was negative for the parent compound and positive for the potential metabolite 3-(3,5-di -tert-butyl-4-hydroxyphenyl)propanehydrazide. However you claim that the molecule was not entirely within the applicability domain of the QSAR tool. You concluded that the QSAR prediction is considered to be "*less reliable*". Additionally, you stated that no ADME study is available for the registered suubstance and therefore it is not known if this potential metabolite is formed. Therefore, due to the remaining uncertainties you agreed to perform the study.

ECHA notes that from the documentation provided for the QSAR analysis, the description of the model found in the TIMES software and the scientific paper documenting the model, it was not possible to conclude whether the data in the training set covers the fifth strain of the Ames test. Hence, ECHA considers that the QSAR prediction cannot be considered reliable.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier and in your comments 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 bacterial reverse mutation test (test method EU B.13/14. / OECD TG 471) is appropriate to address the standard information requirement of Annex VII, Section 8.4.1. 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: Bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

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

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

An "*In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex VIII, Section 8.4.2., column 2. You provided the following justification for the adaptation "*an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study does not need to be conducted because adequate data from an in vivo cytogenicity test are available*". However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex VIII, Section 8.4.2., column 2 because the provided in vivo cytogenicity study was not deemed reliable. More specifically, in the technical dossier you have provided a study record

for an in vivo OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test) with the registered substance showing several deficiences which make the study unreliable:

- The samples seems to have been collected 24 hrs after exposure which may be too late. The bone marrow samples should have been collected between 18-24hrs. As stated in the test guideline, this required harvest time of between 18-24hrs is a consequence of the kinetics of appearance and disappearance of the micronuclei in this tissue compartment.
- At least 2000 immature erythrocytes per are animal are requsted by the testing guideline. In the provided study only 1000 cells per animal were assessed.
- The provided table does not show the PCE/NCE (polychromatic/normchromatic cells) ratio which would provide information on whether the bone marrow has been reached.

Consequently, the validity of this test cannot be confirmed.

Therefore, your adaptation of the information requirement is rejected.

In your comments on the draft decision you agreed to perform the test. You also provided a QSAR analysis addressing in vitro cytogenicity using the "Chromosomal Aberrations S9 activated" module present in OASIS TIMES v2.27.19.13. You indicated that the prediction was negative for the parent compound and positive for the potential metabolite 3-(3,5-di - tert-butyl-4-hydroxyphenyl)propanehydrazide based on the hydrazide functional group. However you claim that the molecule was not entirely within the applicability domain of the QSAR tool. You concluded that the QSAR prediction is considered to be "*less reliable*" and that the QSAR report is not sufficient to address this endpoint. Therefore, you agreed to perform the study with the registered substance.

ECHA indeed notes that there is missing information in the QMRF regarding the endpoint and data sets and validation. Moreover, there are inconsistencies in the description of the algorithm in the peer review literature and in the QMRF and the sensitivity of the algorithm is not sufficiently defined to provide a valid data point. Therefore, ECHA does not consider that the QSAR predictions are valid.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier and in your comments 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).

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

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

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

You have sought to adapt this information requirement for the registered substance (hereafter the 'target substance') according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a Daphnia magna reproduction test (OECD TG 211) with the analogue substance thiodiethylene bis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate] (EC 255-392-8) (hereafter the 'source substance').

You have provided a read-across documentation as a separate attachment in the endpoint summary employing this approach. Furthermore you have provided within the read-across justification, data matrices comparing the ecotoxicological, environmental fate and physico-chemical properties of the target and source substances.

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

- The read-across justification is based on scenario 2 of ECHA's Read-Across Assessment Framework, i.e. the analogue approach based on different substances having qualitatively similar properties.
- You argue that *'the substances show a high degree of structural similarity. The source substance has two 3-(3,5-ditert-butyl-4-hydroxy-phenyl)propanoic acid groups connected via a carbon chain which contains an additional S atom at the center of the chain. The total chain length (including the S) is 5 atoms. Instead of the propanoic acid groups the target substance two 3-(3,5-ditert-butyl-4-hydroxy-phenyl)propenamide groups. These are directly connected at the N.'*
- Both substances are generally marketed at very high purities (>99%) and possible impurities are not expected to have any impact on the prediction.
- The physico-chemical, ecotoxicological and environmental fate properties of the substances do not show relevant variations.
- The hypothesis is that analogue substances do not have ecotoxic effects, either acute or chronic, on aquatic organisms due to limited bioavailability resulting in the absence of the chemicals at the biological targets. You state that *'The substances share very low water solubilities, high logKow values and large molecular sizes (Diammax-average 2.0 and 2.3nm, respectively) resulting in limited bioavailability in the aquatic compartments and limited uptake by organisms'*.
- The similar profiling results from the OECD (Q)SAR Toolbox are further evidence of qualitatively similar properties of the substances.

ECHA has reviewed your read across hypothesis and justification and notes the following. You rely on phyicochemical properties to demonstrate limited bioavailability of both sourece and target substances. The water solubility of registered (target) substance was determined

to be <0.05 mg/L at 20°C at pH 6.9-7.2 using the column elution method (OECD TG 105), with hplc analysis. The water solubility of the source substance is given as <1mg/l at 20°C in your read-across justification. ECHA notes that both water solubilities are limit values and the water solubility cutoff in the studies is at a rather high level such that the substances cannot be assumed to have limited bioavailability on the basis of this data alone. Additionally, there is uncertainty on which substance has higher solubility and hence higher bioavailability to aquatic organisms. Although both source and target substances would be expected to have broadly similar physicochemical properties, ECHA notes that there are significant structural differences which could influence the solubility and bioavailability of the substances. ECHA would expect that the target substance has a higher solubility and therefore a higher potential to be bioavailable in test media. Consequently, ECHA considers that at present it cannot be established that there are no effects in Daphnia at the highest attainable concentration of the target substance in test media, just because there were no effects under these conditions for the source substance. Accordingly, ECHA considers that your hypothesis that these substances do not have ecotoxic effects, either acute or chronic, on aquatic organisms due to limited bioavailability is not substantiated.

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

In your comments to the draft decision, you agree to perform the study.

ECHA also notes that the registered substance is poorly water soluble (WS<0.05mg/l). ECHA Guidance on information requirements and chemical safety assessment Chapter R7b (Version 4.0, June 2017) further explains why short-term tests may not give a true measure of toxicity for poorly soluble substances. Poorly water soluble substances require longer time to be significantly taken up by the test organisms and, consequently, the duration of short-term toxicity test is likely to be insufficient to reach steady state conditions. For this reason, short-term tests may not give a true measure of toxicity for poorly soluble substances. Accordingly, long-term toxicity cannot be excluded and should be investigated.

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

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

Notes for your consideration

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

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 /REV1 (6 July 2018) and ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

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

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

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

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation: *'According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of the substance reveals neither a need to classify the substance as dangerous to the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Therefore, and for reasons of animal welfare, a long-term toxicity study in fish is not provided.'*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2.

ECHA Guidance on information requirements and chemical safety assessment Chapter R7b (Version 4.0, June 2017) explains in section R.7.8.4.3 "Exposure considerations for aquatic pelagic toxicity requirements" the context of this Annex IX, Section 9.1.6., column 2 adaptation rule. The need to conduct further testing is confirmed in a number of different instances, one of which is when there is a qualitative risk assessment and a possible risk needs to be confirmed/rejected e.g. when due to low water solubility of a substance, short term toxicity tests do not reveal any toxicity, long-term tests should be performed.

ECHA notes that the registered substance is poorly water soluble (WS<0.05mg/l). ECHA Guidance on information requirements and chemical safety assessment Chapter R7b (Version 4.0, June 2017) further explains why short-term tests may not give a true measure of toxicity for poorly soluble substances. Poorly water soluble substances require longer time to be significantly taken up by the test organisms and, consequently, the duration of short-term toxicity test is likely to be insufficient to reach steady state conditions. For this reason, short-term tests may not give a true measure of toxicity for poorly soluble substances. Accordingly, long-term toxicity cannot be excluded and should be investigated.

Additionally, as explained in section 3 above, your read-across adaptation for long term toxicity to aquatic invertebrates is rejected. Consequently, ECHA considers that there is currently no information available which would enable an adaptation in line with Annex IX, Section 9.1.6., column 2. The chemical safety assessment does not contain any reliable information on aquatic toxicty to invertebrates and fish therefore it is not possible to determine the relative sensitivity of the species.

As a consequence, the Integrated testing strategy (ITS) outlined in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4), is not applicable in this case and long-term studies on both invertebrates and fish are required to be conducted.

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.

In your comments to the draft decision, you agree to perform the study.

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).

Notes for your consideration

nce 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 the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6/REV1 (6 July 2018) and ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

5. Identification of degradation products (Annex IX, Section 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.

In the technical dossier you have provided some information on potential degradation products. You have indicated that according to CATALOGIC 301C (v.09.13) prediction submitted under the endpoint of ready biodegradation (IUCLID section 5.2.1) 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionic acid (CAS 20170-32-5, EC 243-556-1) is the main metabolite of the registered substance. In the QPRF of the CATALOGIC prediction a number of other potential metabolities has been identified by their structure and SMILES codes alone.

However, this information does not provide the information required by Annex IX, Section 9.2.3., because of the following.

Based on the information available, the metabolities have been identified by the CATALOGIC model alone. However, the registered substance is significantly (by 20 %) out of the structural domain of the model used. Also the transformation reliability was low for most of the metabolites identified. The low reliabilities (between 0.01 to 0.37) indicate that in the Catalogic 301C these transformations are not well supported by available biodegradation data. Hence, it is unclear what metabolites would be formed in quantities >=0.1% and at what rate they would be formed. Furthermore, the substance's low water solubility and potential for microbial toxicity flagged by the model further hamper the reliability of the prediction of the metabolities.

In your comments on the Proposal for Amendment (PfA), based on which this request was added to the decision, you consider the CATALOGIC prediction reliable eventhough you also acknowledge that the substance is outside the structural fragments domain. As given above ECHA agrees that the substance fulfils the parametric domain of the model, including the range of water solubility as its lower threshold in the model is zero. Nevertheless, the low solubility of the registered substance affects the reliability of the prediction and makes it questionable whether the transformation products would be formed in the predicted quantities in the context of a 28 days MITI study set up (OECD 301C) used in the prediction. Regarding the metabolic domain, ECHA notes that as given above the transformation reliability is low (between 0.01 to 0.37). Hence, even if the substance is within the applicability domain, meaning that it has been recognised and matched by the training set of the model, some transformation reactions are not well supported by available biodegradation data. Due to this and the fact that the registered substance is significantly out of the structural domain of the model used the prediction is of low reliability. As discussed in more detail below it is necessary to have reliable information on the degradation products formed, and in particular on whether they are formed under relevant conditions.

The information on predicted transformation/degradation products are hence not adequate for the purpose of risk assessment, and hence does not fulfil the requirements for acceptance of QSARs set in Annex XI section 1.3.

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, the registered substance is not readily biodegradable (OECD TG 301B 1 % degradation in 28 days).

Furthermore, ECHA considers that information on transformation and/or degradation products is needed in relation to the PBT/vPvB assessment and risk assessment that also need to cover its relevant transformation and/or degradation products.

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 conditions and methods, as the substance has a water solubility of < 10 µg/l, and is also highly adsorptive (log Koc = 6.5-8.9), adsorption to soil and sediment is likely. Therefore, soil and sediment simulation test (OECD TG 307 and TG 308) can be considered as appropriate test methods to study degradation of the registered substance. Based on the uses reported in the technical dossier, soil exposure cannot be excluded [redacted]
The aerobic and anaerobic transformation in soil (test method: OECD TG 307) is therefore the preferred test to cover this endpoint and to obtain information on degradation products. Due to the high adsorption potential of the registered substance formation of Non Extractable Residues might occur. Therefore in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

In the test each relevant transformation/degradation product shall be assessed. This can be done simultaneously during the same study. Assessment of relevant degradation/transformation products is described in ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11 PBT/vPvB assessment.

You may also use other appropriate and suitable test methods to provide information on the the degradation products for example by enhanced screening level degradation test or modelling tools. In any case 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. You will need to provide a scientifically valid justification for the chosen method.

Providing accurate information on the transformation and/or degradation products of the registered substance is particularly important since the main metabolite identified by you is in ECHA's Annex III inventory identified as likely to meet criteria for category 1A or 1B carcinogenicity, mutagenicity or reproductive toxicity and may hence fulfil the T-criterion of Annex XII of REACH. Nevertheless it is necessary to emphasise that the present information requirement of identification of degradation products is not yet adequately fulfilled and it is unknown whether the main and other relevant degradation products are formed in relevant conditions.

In section 2.3 of your IUCLID dossier (PBT assessment) you have indicated that the possible main transformation/degradation product(s) do not qualify as bioaccumulative. You also indicate this in your comments on the PfA. However, ECHA considers this information as not yet sufficient to conclude the PBT/vPvB assessment of the substance and/or its degradation/transformation products since as discussed above the information provided on transformation/degradation products is not yet sufficient to fulfil the present standard information requirement. If it is shown that this suspected degradation product is formed during the study, also its bioaccumulation potential as that of any other relevant transformation/degradation products formed, would need to be fully assessed.

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.) OECD TG 307, or other appropriate and suitable test method, as described above. ECHA recommends to use OECD TG 307, as specified above.

Deadline to submit the requested information in this decision

The deadline indicated in the draft decision to provide the information requested was 12 months from the date of adoption of the decision.

In your comments on the draft decision, you requested an extension of the deadline to 20 months. You justified your request stating that preliminary testing is necessary to determine the conditions for the main studies for this poorly-water soluble and adsorptive substance. You also provided a letter from the ecotoxicological lab which details the need for an extended period to conduct the study due to lab capacity and experimental challenges.

ECHA has considered your arguments and has granted the request for extension of the deadline to 20 months.

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 04 May 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.

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the requests but amended the deadline.

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.

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

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-66 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 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.