ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 21 February 2019

Addressee: [redacted]

Decision number: CCH-D-2114461478-39-01/F
Substance name: Tetrabutylammonium bromide
EC number: 216-699-2
CAS number: 1643-19-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 25 May 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. **Surface tension (Annex VII, Section 7.6.; test method: EU A.5./OECD TG 115) with the registered substance;**

2. **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) with the registered substance;**

3. **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;**

4. **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;**

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. **Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: Daphnia sp. Acute immobilisation test, EU C.2./OECD TG 202) 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. **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B) or**

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310)

    with the registered substance;

11. **Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25./OECD TG 309) at a temperature of 12 °C with the registered substance;**

12. **Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: Aerobic and anaerobic transformation in soil, EU C.23./OECD TG 307) at a temperature of 12 °C with the registered substance;**

13. **Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU C.24./OECD TG 308) at a temperature of 12 °C with the registered substance;**

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

15. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305,) with the registered substance;**

16. **Long-term toxicity to terrestrial invertebrates (Annex IX, Section 9.4.1., column 2; test method:**

    a. **Earthworm reproduction test (Eisenia fetida/Eisenia andrei), OECD TG 222, or**

    b. **Enchytraeid reproduction test, OECD TG 220, or**

    c. **Collembolan reproduction test in soil, OECD TG 232), or,**

Long-term toxicity testing on plants (Annex IX, Section 9.4.3., column 2; test method:

d. Terrestrial plants, growth test, OECD TG 208, with at least six species tested (with as a minimum two monocotyledonous species and four dicotyledonous species), or,

e. Soil Quality – Biological Methods – Chronic toxicity in higher plants, ISO 22030)

with the registered substance;

17. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21/OECD TG 216 and carbon transformation test, EU C.22/OECD TG 217) with the registered substance.

You have to submit the requested information in an updated registration dossier by **28 February 2022**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 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 C4

[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. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

0. General considerations for toxicological and ecotoxicological information

Your registration dossier contains for the endpoints addressed in this Decision (point 2, 3, 4, 5, 7-13, 15-17), adaptation arguments either in the form of a weight-of-evidence approach according to Annex XI, Section 1.2., predictions generated with the use of QSAR models under Annex XI, Section 1.3. and/or grouping and read-across approach under Annex XI, Section 1.5. of the REACH Regulation. ECHA has assessed your adaptation arguments in line with the conditions specified in Annex XI of the REACH Regulation:

(i) For the use of existing data on human health and environmental properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3), according to Annex XI, Section 1.1.2., the following conditions need to be met:

- Adequacy for the purpose of classification and labelling and/or risk assessment;
- Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(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
- Adequate and reliable documentation of the study is provided.

(ii) For the use of adaptations using Weight of Evidence (WoE) according to Annex XI, Section 1.2., it is required that there is sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion. Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to the specific standard information requirement.

(iii) For the use of QSAR models under Annex XI, Section 1.3., the following conditions shall be necessarily fulfilled: results are derived from a (Q)SAR model whose scientific validity has been established; the substance falls within the applicability domain of the model; results are adequate for the purpose of classification and labelling and/or risk assessment; adequate and reliable documentation of the applied method is provided.

(iv) For the use of read-across approach 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. Unambiguous

substance identity for both the source substance and the target substance is therefore a prerequisite for a read-across assessment. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data on reference substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[2]. This hypothesis explains why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case. Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

1. Surface tension (Annex VII, Section 7.6.)

"Surface tension" is a standard information requirement as laid down in Annex VII, Section 7.6 of the REACH Regulation.

You have waived the study with the following statement: "*In accordance with column 2 of Annex VII, surface activity is not a desired property of tetrabutylammonium bromide. Thus, this end point was considered for waiver.*"

ECHA considers the waiving not to be correct, because considering the substance structure, i.e. a charged nitrogen atom surrounded by 4 alkyl chains, surface activity cannot be disregarded without testing. Ammonium quaternary compounds with longer chains are known to be surface active, and used as detergents.

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 agreed to perform the requested test.

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: Surface tension (test method EU A.5) or surface tension of aqueous solutions (test method: OECD TG 115).

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

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.

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

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.

In your registration dossier you have provided the following:

- One experimental study report, based on publication (Kathryn M. et al., Green Chem., 2006, 8, 560–567). The test material used is quaternary ammonium cations. The study uses two *Salmonella typhimurium* strains TA98 and TA100. Results: negative with and without metabolic bioactivation. You flagged the study as "WoE".
- Weight of evidence QSAR prediction with *S. typhimurium* TA 100 with S9. In the technical dossier you provided an automated report generated with the OECD QSAR Toolbox indicating negative results.

Furthermore, you have provided the following waiver with regard to testing other strains: "*A QSAR prediction with TA100 also predicted negative genetoxicity and hence further studies using other bacterial strains were not considered mandatory as per the Column 2 of Annex VII of REACH regulation*".

Based on this information, ECHA understands that you have sought to adapt this information requirement according to Annex XI, Sections 1.2 and 1.5. of the REACH Regulation. However, ECHA notes that the experimental study (i) does not meet the information requirements, covered by OECD TG 471 (updated 1997). According to paragraph 13 of the test guideline, 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.

With regard to the waiver for testing other strains based on Column 2 of Annex VII of REACH regulation, ECHA points out that the text of column 2 says "*Further mutagenicity studies shall be considered in case of a positive result*". The text does not say anything about other strains, since as mentioned above, the initial study has to be performed in 5 strains.

For the reasons explained above, ECHA considers that 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 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.

In your comments to the draft decision you agreed to perform the requested test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit 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).

3. 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.

You have indicated "(Q)SAR" in the administrative section of the endpoint study record in the technical dossier for "in vitro cytogenicity / chromosome aberration study in mammalian cells". You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict chromosome aberration for the registered substance based on read-across.

ECHA has hence assessed your adaptation in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation and notes that:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence it is not possible to conclude whether properties could be read across.

You have further indicated within the Endpoint Study Summary for "Genetic Toxicity in vitro" that you consider the information you provided in the Endpoint Study Records for Genetic Toxicity *in vitro* to be a Weight of Evidence Approach.

ECHA notes that, for the reasons explained above, the information provided does not constitute relevant and reliable information in the context of a weight of evidence approach. ECHA therefore concludes that:

- The proposed adaptation is not in line neither with the conditions specified in Annex XI, Section 1.5., nor with those specified in Annex XI, Section 1.2. and is therefore rejected.
- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

In your comments to the draft decision you indicated that you already have data from a publication and you describe an *in vitro* mammalian chromosome aberration study performed with the analogue substance Benzyltriethylammonium chloride (CAS: 56-37-1). You also indicated that this information is already submitted in a recent update. You request ECHA to remove the request from the draft decision.

ECHA notes that the relevance of these studies cannot be assessed, because no data from the publication has been provided by you and no read-across justification for this endpoint was included in the comments. In any case, these studies have not been reported in the dossier subject to the draft decision. You were informed in the notification letter to the draft decision, that ECHA will not take any updates into account for the current decision making.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

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).

4. 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. Currently your dossier does not have acceptable information on the two information requirements mentioned above under points 2 and 3. Adequate information on *in vitro* gene mutation in mammalian cells will however need to be present in the technical dossier for the registered substance to meet this information requirement provided that both studies requested under 2 and 3 have negative results.

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.

In your comments to the draft decision you indicated that a test according to OECD TG 476 with the registered substance is already generated and submitted in a recent update. You request ECHA to remove the request from the draft decision.
ECHA notes that no studies according to OECD TG 476 (or 490) have been reported in the dossier subject to the draft decision. ECHA cannot assess the relevance of the data submitted in the comment by you, because the reporting of the studies is clearly inadequate. You were informed in the notification letter to the draft decision, that ECHA will not take any updates into account for the current decision making.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that both studies requested under 2 and 3 have negative results.

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.

In the technical dossier you have provided the following study records with the registered substance:

(i) Short-term (28-day) repeated dose toxicity study (OECD TG 407, GLP compliant) in rats via oral-gavage, doses: 0, 250, 500, 1000 mg/kg bw/day ([redacted] 2014). NOAEL = 1000 mg/kg bw/day

(ii) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422, GLP compliant) in rats, via oral gavage, doses: 0, 60, 180, 600 mg/kg bw/day ([redacted], 2010). NOAEL = 180 mg/kg bw/day based on effects on body weight, survival rate, organ weight, hematology, urinalysis and histopathology

(iii) Additionally, you provided a study report, flagged as "read-across", for a sub-acute (23-day) toxicity study in male mice, with N,N,N-triethylhexadecan-1-aminium bromide (CAS:13316-70-6; EC: 236-347-1), administered at a single dose of 60 mg/kg bw/day (1/10 of LD50) (publication: Hopper at al., 1949). LOEL = 60 mg/kg bw due to mortality.

ECHA has evaluated the information you have provided and notes the following:

- In the 28-day toxicity study report, in several places, including the "Executive summary" you refer to a substance *4, 4'-Methylenebis (2,6-dimethylphenol)*. For example, your conclusion of the study states: *"Therefore NOEAL for repeated dose toxicity study was considered to be 1000 mg/kg/bw/day in male and femaleSprague-Dawley rats when exposed to 4, 4'-Methylenebis (2,6-dimethylphenol) by oral route for 28 days".* Based on this, ECHA cannot conclude on which substance the study has been performed with. In any case, a 28-day toxicity study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days and the number of animals per dose group is significantly lower than in the 90 day sub-chronic toxicity study (OECD TG 408). Therefore, the sensitivity of a 28-day study is much lower than that of a 90-day study.

- The combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) does not provide the information required by Annex IX, Section 8.6.2., because the exposure duration is less than 90 days and the number of animals examined per dose group for histopathology and clinical chemistry is significantly lower than in the 90 day sub-chronic toxicity study (OECD TG 408).

- The sub-acute (23-day) toxicity study is not acceptable because it does not provide the information required by Annex IX, Section 8.6.2. Furthermore, you have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.

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

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the 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.

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 refer to an existing test according to OECD TG 407, and refer to an adaptation according to Annex VIII, Column 2.

ECHA notes that Annex VIII, Section 8.6.1., Column 2 describes the conditions under which a 28-day repeated dose toxicity study can be omitted for substances registered for 10-100 tonnes/year (Annex VIII). However, you registered your substance for 100 -1000 tonnes per year and an adaptation according to Annex VIII, Column 2 is not relevant for this endpoint.

Moreover, as explained above in the draft decision, a test according to OECD TG 407 is not sufficient to cover the information requirement for a Sub-chronic toxicity study (90-day) which is a standard information requirement in Annex IX, Section 8.6.2 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: Repeated dose 90-day oral toxicity study (test method: OECD TG 408) in rats.

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.

In the technical dossier under this endpoint you have provided the following information:

(iv) Screening study (OECD TG 422, GLP compliant) with the registered substance, administered at doses: 0, 60, 180 and 600 mg/kg bw/day, via oral gavage in SD rats. NOAEL maternal toxicity = 180 mg/kg bw/day based on high value in the stillborn index and changes in: clinical chemistry (increased AST and LDH, decreased blood urea nitrogen and creatinine); organ weight (decreased absolute weight for brain and thymus and increased weight of thyroids, heart, liver, spleen and kidneys); histopathology (diffuse hyperplasia in mucosa in the cecum, hypertrophy of perilobular hepatocytes). NOAEL offsprings = 180 mg/kg bw/day based on on low survival value

(v) One-generation reproductive toxicity study in mice with cetrimonium bromide (57-09-0/200-311-3), administered at 180 mg/kg bw/day in pregnant CD mice. The exposure period: 8-12 GD. LOEL = 180 mg/kg bw/day based on changes in live birth index and viability index

ECHA has evaluated the information you have provided and notes the following:

- Study (iv), the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422) does not provide the information required by Annex IX, Section 8.7.2. because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations. Therefore, your adaptation of the information requirement is rejected.

- For study (v), which you have flagged as Read Across (RA) in the IUCLID dossier, ECHA notes that:
  - You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
  - The study you have provided is based on publication by Robert J. et al. (1987). It is not a guideline, nor a GLP compliant study in CD mice, administered with a single dose of the source substance and consequently ECHA considers that it does not provide equivalent information to an OECD TG 414 study. . Therefore, ECHA considers that the source study does not provide the information required by Annex IX, Section 8.7.2., because it does not meet the requirements of Annex XI, Section 1.1.2. and Annex XI 1.5.

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

According to the test method 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 you refer to the Combined Repeated Dose and Reproductive Toxicity Screening Test (OECD TG 422) that is already addressed above, and you request ECHA to remove the request from the draft decision considering animal ethics.

However, a test according to OECD TG 422 is not sufficient to cover the information requirement for Pre-natal developmental toxicity (PNDT) study as explained above. ECHA also points out that a PNDT study is a standard information requirement in Annex IX 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: Pre-natal developmental toxicity study (test method: OECD TG 414) in a first species (rat or rabbit) by the oral route.

7. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)

"Short-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex VII, Section 9.1.1. of the REACH Regulation.

In the technical dossier under this endpoint you have provided the following information:

(vi) Key study (reliability 2): short-term toxicity to aquatic invertebrates study (TG other: OECD 1981, GLP not specified) with the registered substance, 24h-LC50 > 2000 mg/L (measured, arithm. mean) based on mortality of *Echinogammarus tibaldii* (mature adult male).

(vii) Supporting study (reliability 4): QSAR prediction for the registered substance using the EPI Suite ECOSAR model v1.11, 48h-LC50 = 240.875 mg/L based on mortality of *Daphnia magna*.

ECHA has evaluated the information you have provided and notes the following:

- Study (vi) is not a guideline study and the study report is based on a publication by Pantani C. et al. (1995). ECHA points out that the study does not provide equivalent information to an OECD TG 202 study (48h exposure duration for daphnids starting with < 24-hours juveniles). Due to the short exposure duration (test done on gammarids with typically longer life spans than daphnids) and due to the life stage tested (adults that might have lower sensitivity), ECHA concludes that this study does not provide the information required by Annex VII, Section 9.1.1., because it does not meet the requirements of Annex XI, Section 1.1.2..

- For study (vii), which you have flagged as QSAR calculation in the IUCLID dossier, ECHA notes that these predictions do not meet the general rules set for acceptance of QSAR models in Annex XI, Section 1.3. In particular, you do not provide documentation of the applied ECOSAR method. Therefore, ECHA cannot evaluate the reliability and adequacy of the provided results, and your adaptation of the information requirement cannot be accepted.

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Daphnia sp. acute immobilisation test (test method EU C.2. / OECD TG 202) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.1.

In your comments to the draft decision you indicate that new test data according to OECD TG 202, performed with the registered substance, is already available for this endpoint and submitted in a recent dossier update, hence you request ECHA to remove the request from the draft decision.

In your comments you describe a new study performed according to OECD TG 202 and you conclude the registered substance to be toxic and warranting classification as Aquatic Chronic 3. However, ECHA cannot currently assess the adequacy of this new study or its results and its use for the purpose of classification and labelling and risk assessment, because the the data referred to in your comments is inadequately reported and has not

been included in the dossier subject to the draft decision. In addition, ECHA reminds you that classification as Aquatic Chronic 3 is not an acceptable adaptation for this endpoint. You were informed in the notification letter to the draft decision, that ECHA will not take any updates into account for the current decision making.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

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* sp. Acute immobilisation test, EU C.2./OECD TG 202).

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.

You have sought to adapt this information requirement according to Annex XI, Section 1.3. In the technical dossier under this endpoint you have provided the following information:

- Key study (reliability 2): QSAR prediction for the registered substance using the EPI Suite ECOSAR model v1.11, NOEC (21d) = 24.077 mg/L based on immobilisation of *Daphnia magna*.

For this study, which you have flagged as QSAR calculation in the IUCLID dossier, ECHA notes that these predictions do not meet the general rules set for acceptance of QSAR models in Annex XI, Section 1.3. In particular, you do not provide documentation of the applied ECOSAR method. Therefore, ECHA cannot evaluate the reliability and adequacy of the provided results, and your adaptation of the information requirement cannot be accepted.

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) *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.

In your comments to the draft decision you refer to available test data for this endpoint on the registered substance and on "*read-across chemical*" and you conclude that the registered substance is toxic and warrants classification as Aquatic Chronic 3. You indicate that data from these existing studies is submitted in a recent dossier update, hence you request ECHA to remove the request from the draft decision.

In your comments you report two studies available in "*authoritative databases*", which were performed according to OECD TG 202 (*Daphnia sp., Acute Immobilisation Test and Reproduction Test*) and OECD TG 211 (*Daphnia magna Reproduction Test*). However, ECHA cannot assess the adequacy of the data provided and their use for the purpose of

classification and labelling and risk assessment, for the following reasons: you do not specify the test substance for either of the studies (i.e. registered substance or which read-across substance) or provide a justification for the proposed read-across. In addition, the data referred to in your comments is inadequately reported and has not been included in the dossier subject to the draft decision. You were informed in the notification letter to the draft decision, that ECHA will not take any updates into account for the current decision making.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

Furthermore, while you indicate that a long-term *Daphnia* study is not needed since data is already available, in your comments you also state that based on the chemical safety report the risks are controlled. However, there is currently no compliant information for Short-term toxicity testing on aquatic invertebrates, Long-term toxicity testing on aquatic invertebrates and Long-term toxicity testing on fish (requests 7-9, in this decision). Therefore, the Chemical Safety Assessment (CSA) cannot be used as an argument to adapt this information requirement. ECHA also reminds you that classification as Aquatic Chronic 3 is not an acceptable adaptation for this endpoint.

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).

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 9.1.6.1. of the REACH Regulation.

You have sought to adapt this information requirement according to Annex XI, Section 1.3.. In the technical dossier you have provided the following information:

- Key study (reliability 2): QSAR prediction for the registered substance using the EPI Suite ECOSAR model v1.11, NOEC (28d) = 45.553 mg/L based on fish mortality.

For this study, which you have indicated as QSAR calculation in the IUCLID dossier, ECHA notes that these predictions do not meet the general rules set for acceptance of QSAR models in Annex XI, Section 1.3. In particular, you do not provide documentation of the applied ECOSAR method. Therefore, ECHA cannot evaluate the reliability and adequacy of the provided results, and your adaptation of the information requirement cannot be accepted.

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish early-life stage (FELS) toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU

C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) 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).

In your comments to the draft decision you refer to available test data for this endpoint on the registered substance and on "*read-across chemical*" and you conclude that the registered substance is toxic and warrants classification as Aquatic Chronic 3. You indicate that data from these existing studies is submitted in a recent dossier update, hence you request ECHA to remove the request from the draft decision.

In your comments you report two studies from secondary sources (test guidelines not reported). However, ECHA cannot assess the adequacy of the data provided and their use for the purpose of classification and labelling and risk assessment, for the following reasons: you do not specify the test substance for either of the studies (i.e. registered substance or which read-aross substance) or provide a justification for the proposed read-across. In addition, the data referred to in your comments is inadequately reported and has not been included in the dossier subject to the draft decision. You were informed in the notification letter to the draft decision, that ECHA will not take any updates into account for the current decision making.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

Furthermore, while you indicate that a long-term fish study is not needed since data is already available, in your comments you also state that based on the chemical safety report the risks are controlled. However, there is currently no compliant information for Short-term toxicity testing on aquatic invertebrates, Long-term toxicity testing on aquatic invertebrates and Long-term toxicity testing on fish (requests 7-9, in this decision). Therefore, the Chemical Safety Assessment (CSA) cannot be used as an argument to adapt this information requirement. ECHA also reminds you that classification as Aquatic Chronic 3 is not an acceptable adaptation for this endpoint.

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 for requests 7-9

Before conducting the tests requested above under points 8. and 9., you shall consult the ECHA Guidance on information requirements and chemical safety assessment (version 4.0,

June 2017), Chapter R.7b, Section R.7.8.5 to determine the necessity to conduct the long-term toxicity testing on aquatic invertebrates and on fish.

Concerning the order of studies to be conducted, you may first carry out the short-term toxicity test on aquatic invertebrates (Annex VII, Section 9.1.1.) requested under point 7 and subsequently update the CSA according to Annex I of the REACH Regulation.
If you come to the conclusion that no further investigation of chronic effects on aquatic organisms is required, you shall update your technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, 9.1.5 and 9.1.6. taking into account the new data generated by the short-term toxicity test on aquatic invertebrates requested by the present decision and exposure assessment and risk characterisation.
On the other hand, if after the update of the CSA you come to the conclusion that the long-term toxicity tests are still required to refine the risk assessment, you should further consider Integrated Testing Strategy (ITS) for aquatic toxicity as described in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b (Section R.7.8.5., including Figure R.7.8-4).

According to the ITS, if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially less sensitive than other trophic levels (i.e. fish, invertebrates, algae), long-term studies may be required on both fish and invertebrates. In such case, according to the ITS, the long-term *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

Due to the substance being ionised, 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 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).

10. Ready biodegradability (Annex VII, Section 9.2.1.1.)

"Ready biodegradability" is a standard information requirement as laid down in Annex VII, section 9.2.1.1. of the REACH Regulation.

In the technical dossier under this endpoint you have provided the following information:

(viii) Key study (reliability 2): QSAR prediction for the registered substance using the EPI Suite BIOWIN model v4.10, result: "*Ready Biodegradability Prediction: NO*".

(ix) Supporting study (reliability 2): Ready Biodegradability: Modified MITI Test (I) (OECD TG 301C, GLP not specified) with the analogue substance N,N,N-tripropylpropan-1-aminium bromide (CAS no 1941-30-6, EC no 217-727-6), 0% biodegradation (BOD) in 28 days.

ECHA has evaluated the information you have provided and notes the following:

- For study (viii), which you have flagged as QSAR calculation in the IUCLID dossier, ECHA notes that these predictions do not meet the general rules set for acceptance

of QSAR models in Annex XI, Section 1.3. In particular, you do not provide documentation of the applied method. Therefore, ECHA cannot evaluate the reliability and adequacy of the provided results, and your adaptation of the information requirement cannot be accepted.

- For study (ix), which you have flagged as RA in the IUCLID dossier, ECHA notes that:
  - You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
  - You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
  - The study submitted does not provide the information required by Annex IX, Section 9.1.5., because, contrary to Article 3(28) of the REACH Regulation, the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment. In particular, the following elements are missing: details on inoculum, details on test conditions, initial substance concentration, information on controls and blank system used, assessment of inhibition, oxygen uptake of the inoculum blank, degradation % of the reference compound by day 7 and by day 14.

ECHA therefore concludes that the proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.5. and is therefore 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.

Regarding the test method, depending on the substance profile, you may conclude on ready biodegradability, by applying the most appropriate and suitable test guideline among those listed in the ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) and in the paragraph below. The test guidelines include the description of their applicability domain.

In your comments to the draft decision you indicated your agreement to perform the requested test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to perform one of the following tests with the registered substance subject to the present decision:

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B)
or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C)
or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D)
or

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F)
or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310) with the registered substance.

11. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.)

"Simulation testing on ultimate degradation in water" is a standard information requirement as laid down in Annex IX, section 9.2.1.2. of the REACH Regulation.

In the technical dossier under this endpoint you have provided the following information:

(x) Key study (reliability 2): QSAR prediction for the registered substance using the PBT profiler database, result: "*8.7 days (half-life)*" in water.
(xi) Supporting study (reliability 2): QSAR prediction for the registered substance using the Fugacity Model by EPI Suite estimation database, result: "*8.66 days (half-life)*" in water.

ECHA has evaluated the information you have provided and notes that for the studies (x) and (xi), which you have flagged as QSAR calculations in the IUCLID dossier, these predictions do not meet the general rules set for acceptance of QSAR models in Annex XI, Section 1.3. In particular, you do not provide documentation of the applied method. Therefore, ECHA cannot evaluate the reliability and adequacy of the provided results, and your adaptation of the information requirement cannot be accepted.

Furthermore, ECHA notes that you have sought to adapt this information requirement according to column 2 of Annex IX, Section 9.2.1.2.. You provided the following justification for the adaptation: "*According to the standard information requirements in Annex IX point 9.2.1.3 column 2, this endpoint is considered for waiver,since direct and indirect exposure of Tetrabutylammonium bromide to water and sediment is unlikely.*"

ECHA has assessed this adaptation and concludes that based on the information in the technical dossier your adaptation does not meet the specific rules for adaptation of Column 2 of Annex IX, Sections 9.2 and 9.2.1.2 due to the following.

According to Annex IX, Section 9.2.1.2, column 2 of the REACH Regulation, simulation testing on ultimate degradation in surface water does not need to be conducted if the substance is highly insoluble in water or is readily biodegradable. Hence, ECHA notes first that the statement in your adaptation that "*direct and indirect exposure of Tetrabutylammonium bromide to water and sediment is unlikely*" is not a valid adaptation based on column 2 of Annex IX, Section 9.2.1.2.. In addition, ECHA considers that direct and/or indirect exposure of the aquatic compartment cannot be excluded based on the substance uses reported in the CSR (e.g. widespread professional and consumer uses in plant protection products for exposure scenarios ES9 and ES12). Furthermore, ECHA notes that this information requirement cannot be adapted based on column 2 of Annex IX, Section 9.2.1.2, since information compliant with Annex VII Section 9.2.1.1 on ready biodegradability is currently not present in the technical dossier, as discussed under point 10. above. In addition, ECHA notes that the registered substance is not highly insoluble in water (water solubility = 1000g/L).

Furthermore, ECHA notes that column 2 of Annex IX, Section 9.2. requires that the simulation study shall be conducted if indicated by the chemical safety assessment (CSA) according to Annex I, including PBT assessment. You have not provided any justification in your chemical safety assessment (CSA) or in the technical dossier for why there is no need to investigate further the degradation of the substance and its degradation products. As explained further below, ECHA considers that the information is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment. In addition, ECHA notes that information on the related PBT endpoints of aquatic toxicity and bioaccumulation is missing and has been requested in this decision. On this basis, you have not demonstrated that there is no need to investigate further the degradation of the substance and its degradation products.

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

For the reasons explained above, ECHA considers that 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) Aerobic mineralisation in surface water – simulation biodegradation (test method EU C.25. / OECD TG 309) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.2.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of the REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 4.0, June 2017) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-8 (version 3.0 February 2016) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 309. Therefore, the test should be performed at the temperature of 12°C.

In the OECD TG 309 Guideline two test options, the "pelagic test" and the "suspended sediment test", are described. ECHA considers that the pelagic test option should be followed as that is the recommended option for P assessment. The amount of suspended solids in the pelagic test should be representative of the level of suspended solids in EU surface water. The concentration of suspended solids in the surface water sample used should therefore be approximately 15 mg dw/L. Testing natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable. Furthermore, when reporting the 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.

In your comments to the draft decision, you indicated that based on the preliminary results of an ongoing ready biodegradability test, the substance is considered to be inherently biodegradable and therefore, a Simulation study in surface water does not need to be conducted. You request ECHA to remove the request from the draft decision.

ECHA notes that the data referred to in your comments is not available in the dossier subject to the draft decision, hence ECHA cannot assess its reliability and adequacy. Furthermore, ECHA notes that the substance being inherently biodegradable is not a valid adaptation according to Annex IX, Section 9.2.1.2., Column 2. ECHA points you to the ECHA Guidance on information requirements and chemical safety assessment indicated in the *Notes for your consideration for requests 11-14* below for guidance on how to conclude on persistence based on reliable screening information and on the integrated testing strategy on persistence to determine the necessity to conduct simulation testing.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

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: Aerobic mineralisation in surface water – simulation biodegradation test (test method: EU C.25./OECD TG 309).

12. Soil simulation testing (Annex IX, Section 9.2.1.3.) and

13. Sediment simulation testing (Annex IX, Section 9.2.1.4.)

"Soil simulation testing" and "sediment simulation testing" are standard information requirements as laid down in Annex IX, sections 9.2.1.3. and 9.2.1.4 of the REACH Regulation for substances with a high potential for adsorption to soil and to sediment. The registered substance is ionic, indicating high potential for adsorption.

In the technical dossier for the endpoint "soil simulation testing" you have provided the following information:

(xii) Key study (reliability 2): QSAR prediction for the registered substance using the PBT profiler database, result: "*17 days (half-life)*" in soil.
(xiii) Supporting study (reliability 2): QSAR prediction for the registered substance using the Fugacity Model by EPI Suite estimation database, result: "*17.33 days (half-life)*" in soil.

In the technical dossier for the endpoint "sediment simulation testing" you have provided the following information:

(xiv) Key study (reliability 2): QSAR prediction for the registered substance using the PBT profiler database, result: "*78 days (half-life)*" in sediment.
(xv) Supporting study (reliability 2): QSAR prediction for the registered substance using the Fugacity Model by EPI Suite estimation database, result: "*77.91 days (half-life)*" in sediment.

ECHA has evaluated the information you have provided and notes that for the studies (xii), (xiii), (xiv) and (xv), which you have flagged as QSAR calculations in the IUCLID dossier,

these predictions do not meet the general rules set for acceptance of QSAR models in Annex XI, Section 1.3. In particular, you do not provide documentation of the applied method. Therefore, ECHA cannot evaluate the reliability and adequacy of the provided results, and your adaptation of the information requirement cannot be accepted.

Furthermore, ECHA notes that you have sought to adapt these information requirements according to column 2 of Annex IX, Sections 9.2.1.3. and 9.2.1.4. You provided the following justifications for the adaptation: *"According to the standard information requirements in Annex IX point 9.2.1.3 column 2, this endpoint is considered for waiver,since direct and indirect exposure of Tetrabutylammonium bromide to soil is unlikely"*. and "(..) *since direct and indirect exposure of Tetrabutylammonium bromide to water and sediment is unlikely."*

ECHA has assessed this adaptation and concludes that based on the information in the technical dossier your adaptation does not meet the specific rules for adaptation of Column 2 of Annex IX, Sections 9.2, 9.2.1.3. and 9.2.1.4 due to the following.

According to Annex IX, Sections 9.2.1.3./9.2.1.4, column 2 of the REACH Regulation, simulation testing on sediment does not need to be conducted if the substance is readily biodegradable or if direct or indirect exposure of soil/sediment is unlikely. However, information compliant with Annex VII Section 9.2.1.1 on ready biodegradability is currently not present in the technical dossier, as discussed under point 10. above. In addition, regarding soil and sediment exposure, the substance has high potential for adsorption as described above and ECHA considers that direct and/or indirect exposure of the soil and sediment compartments cannot be excluded based on the substance uses reported in the CSR (e.g. widespread professional and consumer uses in plant protection products for exposure scenarios ES9 and ES12). ECHA therefore considers that you have not demonstrated that soil/sediment exposure is unlikely.
ECHA notes further that column 2 of Annex IX, Section 9.2. requires that the simulation study shall be conducted if indicated by the chemical safety assessment (CSA) according to Annex I, including PBT assessment. For the reasons explained under point 11. above, you have not demonstrated that there is no need to investigate further the degradation of the substance and its degradation products.

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

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. 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) Aerobic and anaerobic transformation in soil (test method EU C.23. / OECD TG 307) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.3.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Aerobic and anaerobic transformation in aquatic sediment systems (test method EU C.24. / OECD TG 308) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.4.
One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with

Annex XIII of REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 4.0, June 2017) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-8 (version 3.0 February 2016) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 308. Therefore, the test should be performed at the temperature of 12°C.

Simulation tests performed in sediment or in soil possibly imply the formation of non-extractable residues (NER). These residues (of the parent substance and/or transformation products) are bound to the soil or to the sediment particles. NERs may potentially be re-mobilised as parent substance or transformation product unless they are irreversibly bound or incorporated into the biomass. When reporting the 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.

In your comments to the draft decision, you indicated that based on the preliminary results of an ongoing ready biodegradability test, the substance is considered to be inherently biodegradable and therefore, Simulation studies in soil and sediment do not need to be conducted. You also state that exposure to soil compartment is unlikely. You request ECHA to remove the request from the draft decision.

ECHA notes that the data referred to in your comments is not available in the dossier subject to the draft decision, hence ECHA cannot currently assess its reliability and adequacy. Furthermore, ECHA notes that the substance being inherently biodegradable is not a valid adaptation according to Annex IX, Sections 9.2.1.3 and 9.2.1.4., Column 2. ECHA points you to the ECHA Guidance on information requirements and chemical safety assessment indicated in the *Notes for your consideration for requests 11-14* below for guidance on how to conclude on persistence based on reliable screening information and on the integrated testing strategy on persistence to determine the necessity to conduct simulation testing.

In addition, as described above, in your dossier you report substance uses including agriculture, forestry and use as an active substance in plant protection products. Therefore, exposure of the soil and sediment compartment is likely and the studies cannot be adapted on this basis.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

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:

Aerobic and anaerobic transformation in soil (test method: EU C.23./OECD TG 307) and

Aerobic and anaerobic transformation in aquatic sediment systems (test method: EU C.24./OECD TG 308).

14. 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.

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

According to Annex IX, Section 9.2.3., column 2 of the REACH Regulation, identification of degradation products is not needed if the substance is readily biodegradable. ECHA notes that information compliant with Annex VII Section 9.2.1.1 on ready biodegradability is currently not present in the technical dossier, as discussed in point 10. above.

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. ECHA considers that this information is needed in relation to the PBT/vPvB assessment and risk 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 appropriate and suitable test method, the methods will have to be substance-specific. When analytically possible, identification, stability, behaviour, molar quantity of metabolites relative to the parent compound should be evaluated. In addition, degradation half-life, log Kow and potential toxicity of the metabolite may be investigated. You may obtain this information from the relevant degradation studies also requested in this decision, or by some other measure. You will need to provide a scientifically valid justification for the chosen method.

In your comments to the draft decision, you indicate that based on the preliminary results of an ongoing ready biodegradability test, the substance is considered to be inherently biodegradable and therefore, a simulation study does not need to be conducted. You request ECHA to remove the request from the draft decision.

ECHA notes that the data referred to in your comments is not available in the dossier subject to the draft decision, hence ECHA cannot currently assess its reliability and adequacy. Furthermore, ECHA notes that the substance being inherently biodegradable is not a valid adaptation according to Annex IX, Sections 9.2.3., Column 2.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision:

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

Notes for your consideration for requests 11-14

Before conducting the tests requested under points 11-14, you may conduct the ready biodegradability study requested under point 10. above. If the registered substance is shown to be readily biodegradable (with or without fulfilling the 10-d window) there is no need to provide the information requested in points 11-14. However, if the registered substance is shown not to be readily biodegradable, before conducting the simulation tests requested under points 11-13 you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4 and R.7.9.6 (version 4.0, June 2017) and Chapter R.11, Section R.11.4.1.1 (version 3.0, June 2017) on PBT assessment to determine the sequence in which the simulation tests are to be conducted and the necessity to conduct all of them. The order in which the simulation biodegradation tests are performed needs to take into account the intrinsic properties of the registered substance and the identified use and release patterns which could significantly influence the environmental fate of the registered substance.

In addition, before providing the information on degradation products requested under point 14 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 results of the tests detailed above is available. 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.

15. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.)

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2.of the REACH Regulation.

In the technical dossier under this endpoint you have provided the following information:

(xvi) Key study (reliability 2): QSAR prediction for the registered substance using the EPI Suite BCFBAF model v3.01, BCF = 70.79 L/kg whole body w.w. ([redacted] (including biotransformation rate estimates, upper trophic)), "*result based on measured log Pow of: 1.71*".

(xvii) Supporting study (reliability 2): QSAR prediction for the registered substance using PBT profiler database, BCF = 71 L/kg (basis not specified).

(xviii) Supporting study (reliability 2): bioaccumulation in aquatic species: fish (TG: "*other*", GLP not specified) with the analogue substance N,N,N-tripropylpropan-1-aminium bromide (CAS no 1941-30-6, EC no 217-727-6), BCF = 0.3 L/kg whole

body w.w., *Cyprinus carpio*, lipid content 4.4%.

ECHA has evaluated the information you have provided and notes the following:

- For studies (xvi) and (xvii), which you have flagged as QSAR calculations in the IUCLID dossier, ECHA notes that these predictions do not meet the general rules set for acceptance of QSAR models in Annex XI, Section 1.3. In particular, you do not provide documentation of the applied method. Therefore, ECHA cannot evaluate the reliability and adequacy of the provided results, and your adaptation of the information requirement cannot be accepted.

  Furthermore, ECHA notes that you use the Log Kow of the registered substance (Log Kow = 1.6 as reported in the CSR) to predict the BCF. However, since the substance is ionised, LogKow is not a good descriptor to predict the BCF, nor to conclude on the bioaccumulation of the registered substance, as explained in the following. According to the ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7c. (version 3.0, June 2017) "*for certain types of substances (e.g. surface-active agents and those which ionise in water), the log Kow might not be suitable for calculation of a BCF value. [...] the classification of the bioconcentration potential based on hydrophobicity measures (such as log Kow) should be used with caution. [...] Measured BCF values are preferred.*" and according to *Guidance on information requirements and chemical safety assessment*, Chapter R.11. (version 3.0, June 2017) "*for some groups of substances, such as organometals, ionisable substances and surface active substances, log Kow is not a valid descriptor for assessing the bioaccumulation potential. Information on bioaccumulation of such substances should therefore take account of other descriptors or mechanisms than hydrophobicity.*"

- For study (xviii), which you have flagged as RA in the IUCLID dossier, ECHA notes that:

  - You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
  - You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
  - The study submitted does not provide the information required by Annex IX, Section 9.1.5., because, contrary to Article 3(28) of the REACH Regulation, the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment. In particular, the following elements are missing: complete description of all chemical analysis procedures employed including limits of detection and quantification, variability and recovery; tabulated test substance concentration data in fish and water for all sampling times; curves showing growth, uptake and depuration of the test chemical in the fish; steady-state and kinetic bioconcentration factor and derived uptake and depuration rate constants; concentration of dissolved oxygen; mortality of the control fish and the fish in each exposure chamber and any observed abnormal behaviour.

ECHA therefore concludes that the proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.5. and is therefore 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.7c* (version 3.0, June 2017) bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2. ECHA Guidance defines further that results obtained from a test with aqueous exposure can be used directly for comparison with the B and vB criteria of Annex XIII of REACH Regulation and can be used for hazard classification and risk assessment. Comparing the results of a dietary study with the REACH Annex XIII B and vB criteria is more complex and has higher uncertainty. Therefore, the aqueous route of exposure is the preferred route and shall be used whenever technically feasible. If you decided to conduct the study using the dietary exposure route, you shall provide scientifically valid justification for your decision. You shall also attempt to estimate the corresponding BCF value from the dietary test data by using the approaches given in Annex 8 of the OECD 305 TG and in OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation, ENV/JM/MONO (2017)16. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG.

In your comments to the draft decision you refer to various data available confirming that the registered substance is not bioaccumulative. This data includes QSARs and tests according to OECD TG 305, available on the registered substance and on "*read-across substance*". You also state that the data reported in your comments is already available and submitted in a recent update. You request ECHA to remove the request from the draft decision.

ECHA notes that some of the reported data refers to studies already addressed by ECHA in the draft decision (i.e. studies xviii, xviiii and xviii described above), but in your comments you do not address the deficiencies indicated by ECHA above.

In addition, in your comments you report QSAR predictions on the registered substance (CompTox Chemistry Dashboard), but you do not provide documentation of the applied method. You also report details of a bioaccumulation study from an authoritative database, but you do not specify the test substance (i.e. registered substance or which read-aross substance) or provide a justification for the proposed read-across. Consequently, ECHA cannot currently assess the adequacy of the data provided, because the data referred to in your comments is inadequately reported, it has not been included in the dossier subject to the draft decision, and you have not provided any read-across justification or QSAR documentation. You were informed in the notification letter to the draft decision, that ECHA will not take any updates into account for the current decision making.

Furthermore, in your comments you propose to adapt this information requirement based on Annex IX, Section 9.3.2., Column 2. by stating that the substance has a low potential for bioaccumulation because the partition coefficient value (log Kow) of is ≤ 3. However, logKow cannot be used to adapt this information requirement because the substance is ionised and, as also described above, log Kow is not a valid descriptor for assessing the bioaccumulation potential of such substances.

Any new data will be evaluated for compliance at the follow-up evaluation according to Article 42 of the REACH Regulation once the deadline set in this decision has expired.

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: Bioaccumulation in fish: aqueous or dietary bioaccumulation fish test (test method: OECD TG 305)

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11.4. and Figure R.11-4 on the PBT assessment for further information on the integrated testing strategy for the bioaccumulation assessment of the registered substance. In particular, you are advised to first conclude whether the registered substance may fulfil the REACH Annex XIII criteria of being persistent or very persistent, and then to consult the PBT assessment for Weight-of-Evidence determination and integrated testing strategy for bioaccumulation assessment. You should revise the PBT assessment when information on bioaccumulation is available.

In addition, you are advised to consult the ECHA Guidance on the information requirements and chemical safety assessment (version 2.0, November 2014), Chapters R.4, 5, 6, R.7b and R.7c. Where you decide to adapt the testing requested according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation, ECHA refers you to the advice provided in practical Guides 4, 5 and 6.

16. Long-term toxicity to terrestrial invertebrates (Annex IX, Section 9.4.1., column 2), or Long-term toxicity testing on plants (Annex IX, Section 9.4.3., column 2);

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX, Section 9.4. of the REACH Regulation. Column 2 of Annex IX, Section 9.4 specifies that long-term toxicity testing shall be considered by the Registrant instead of short-term, in particular for substances that have a high potential to adsorb to soil or that are very persistent.

In the technical dossier for the endpoints "toxicity to soil macroorganisms except arthropods: short-term" and "toxicity to terrestrial arthropods: short-term" you have provided the following information:

(xix) Key study (reliability 2): QSAR prediction for the registered substance using the QSAR Toolbox version 2.3, 48h-LC50 = 414.8 AI ug/cm2, mortality of *Eisenia fetida* (annelids).
(xx) Key study (reliability 2): QSAR prediction for the registered substance using the QSAR Toolbox version 2.3, NOEL (48h) = 373.0167 mg/L, mortality of *Neoseiulus fallacis* (arthropods).
(xxi) Supporting study (reliability 2): QSAR prediction for the registered substance using the QSAR Toolbox version 2.3, NOEL (24h) = 373.0167 mg/L, mortality of *Neoseiulus fallacis* (arthropods).

In the technical dossier for the endpoint "toxicity to terrestrial plants: short-term" you have provided the following information:

(xxii) Key study (reliability 2): QSAR prediction for the registered substance using the QSAR Toolbox version 2.3, 72h-EC50 = 87.19575 mg/L, reproduction of *Lactuca sativa*.

You have indicated the provided information as "(Q)SAR" in the administrative section of the endpoint study records in the technical dossier. In the technical dossier you provided automated reports generated with the OECD QSAR Toolbox and it is indicated within these reports that they are used to predict the endpoint values for the registered substance based on read-across.

ECHA has hence assessed your adaptation in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation and notes that:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence concluding whether properties could be read across.

ECHA therefore concludes that:

- The proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.5. and is therefore rejected.
- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

Furthermore, ECHA notes that you indicate the results listed above are for short-term terrestrial toxicity endpoints, whereas due to the adsorptive properties of the registered susbtance, the effect of long-term exposures should be estimated.

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.

According to section R.7.11.5.3., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), substances that are ionisable or have a log K_{ow}/K_{oc} >5 are considered highly adsorptive, whereas substances with a half-life >180 days are considered very persistent in soil. According to the evidence presented within the Registration dossier, the substance has a high potential to adsorb to soil since it is ionic. Therefore ECHA considers that the column II adaptation for Annex IX,

section 9.4 regarding long-term testing instead of short-term testing, is applicable to this substance.

Based upon the available aquatic toxicity information and the physico-chemical properties of the substance and in relation to section R.7.11.6., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), ECHA considers that the substance would fall into soil hazard category 3. In the context of an integrated testing strategy for soil toxicity, the Guidance advocates performing an initial screening assessment based upon the Equilibrium Partitioning Method (EPM), together with a confirmatory long-term soil toxicity test. The PNECscreen is calculated through EPM on the basis of aquatic toxicity data only.

The earthworm reproduction test (OECD TG 222), Enchytraeid reproduction test (OECD TG 220), and Collembolan reproduction test (OECD TG 232) are each considered capable of generating information appropriate for the fulfilment of the information requirements for long-term toxicity testing to terrestrial invertebrates. ECHA is not in a position to determine the most appropriate test protocol, since this decision is dependent upon species sensitivity and substance properties. You are to apply the most appropriate and suitable test guideline among those listed above.

OECD TG guideline 208 (Terrestrial plants, growth test) considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing shall be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208 guideline. You should consider if testing on additional species is required to cover the information requirement.

In your comments to the draft decision you indicate that direct or indirect exposure of the soil compartment is unlikely based on the substance's uses. Further, you state that even if exposure of the soil compartment happens, the substance is likely not to adsorb due to an experimental logKoc value of <1.5. You request ECHA to remove the request from the draft decision.

ECHA notes that, as also described above, in your dossier you have reported use in agriculture, forestry and as active substance in plant protection products. Therefore, exposure of the soil compartment is likely. In addition, you have not reported an experimental logKoc value in your registration dossier, but you report a QSAR prediction for logKoc of 4.2 at 25 C, and you conclude that the substance has strong adsorption potential to soil. Furthermore, as also described above, the substance has a high potential to adsorb to soil since it is ionic.

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: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) (test method: OECD TG 222), or Enchytraeid reproduction test (test method: OECD TG 220), or Collembolan reproduction test in soil (test method: OECD TG 232), or, Terrestrial plants, growth test (test method: OECD TG 208), with at least six species tested (with as a minimum two monocotyledonous species and four dicotyledonous species), or, Soil Quality – Biological Methods – Chronic toxicity in higher plants (test method: ISO 22030).

17. Effects on soil micro-organisms (Annex IX, Section 9.4.2.)

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX, Section 9.4. of the REACH Regulation. Column 2 of Annex IX, Section 9.4 specifies that long-term toxicity testing shall be considered by the Registrant instead of short-term, in particular for substances that have a high potential to adsorb to soil or that are very persistent.

In the technical dossier for the endpoint "toxicity to soil microorganisms" you have provided the following information:

(xxiii) Key study (reliability 2): QSAR prediction for the registered substance using the QSAR Toolbox version 2.3, LOEL (168h) = 6539.882 mg/L, growth of *Beauveria bassiana*.

You have indicated the provided information as "(Q)SAR" in the administrative section of the endpoint study records in the technical dossier. In the technical dossier you provided automated reports generated with the OECD QSAR Toolbox and it is indicated within these reports that they are used to predict the endpoint values for the registered substance based on read-across.

ECHA has hence assessed your adaptation in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation and notes that:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence concluding whether properties could be read across.

ECHA therefore concludes that:

- The proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.5. and is therefore rejected.
- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard 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.

ECHA notes that the test requested under point (16) above is not sufficient to address this standard information requirement. ECHA concludes that the effects on soil microorganisms need to be ascertained by performing a relevant test.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), Chapter R.7C, Section R.7.11.3.1., the nitrogen transformation test is considered sufficient for most non-agrochemicals. However, as the substance has known agrochemical uses (e.g. uses in plant protection products for exposure scenarios ES9 and ES12 are reported in the CSR), ECHA considers that both the nitrogen and carbon transformation tests should be performed simultaneously.

In your comments to the draft decision you indicate that direct or indirect exposure of the soil compartment is unlikely based on the substance's uses. Further, you state that even if exposure of the soil compartment happens, the substance is likely not to adsorb due to an experimental logKoc value of <1.5. You request ECHA to remove the request from the draft decision.

ECHA notes that, as also described above, in your dossier you have reported use in agriculture, forestry and as active substance in plant protection products. Therefore, exposure of the soil compartment is likely. In addition, you have not reported an experimental logKoc value in your registration dossier, but you report a QSAR prediction for logKoc of 4.2 at 25 C, and you conclude that the substance has strong adsorption potential to soil. Furthermore, as also described above, the substance has a high potential to adsorb to soil since it is ionic.

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: Soil microorganisms: nitrogen transformation test (test method: EU C.21./OECD TG 216), and Soil microorganisms: carbon transformation test (test method: EU C.22./OECD TG 217).

Notes for your consideration

As the Guidance advocates performing an initial screening assessment based upon the EPM, together with a confirmatory long-term soil toxicity test (the long-term terrestrial toxicity test, specified above), which you are requested to carry out by the present decision, ECHA considers that at this stage it is not possible to determine whether a test will be required to fulfil the remaining standard information requirements of section 9.4 of Annex IX, of the REACH Regulation.

Therefore, once results of the requested terrestrial toxicity test are available, you should consider whether there is a need to investigate further the effects on terrestrial organisms in order to fulfil the information requirements of section 9.4 of Annex IX, and if necessary, submit testing proposals for additional terrestrial toxicity tests. If you conclude that no further investigation of effects on terrestrial organisms is required, you should update your technical dossier by clearly stating the reasons for adapting the information requirements of Annex IX, section 9.4. of the REACH Regulation.

ECHA emphasises that the intrinsic properties of soil microbial communities are not addressed through the EPM extrapolation method and therefore the potential adaptation possibility outlined for the information requirement of Annex IX, Section 9.4. does not apply for the present endpoint.

Deadline to submit the requested information

In the draft decision communicated to you the time indicated to provide the requested information was 36 months from the date of adoption of the decision. In your comments on the draft decision you state that the given timeline is "*very limited considering the data requirements identified by ECHA*" and that the "*timeline should also be reconsidered mentioned in draft report*". ECHA notes that you have not proposed a more suitable timeline or justified the request for a longer deadline in any way. ECHA requested documentary evidence from you to support your request for an extension of the deadline. However, you did not provide any documentary evidence by the deadline 11 September 2018.

The deadline indicated in the draft decision follows ECHA's standard deadlines and it allows sequential testing, where applicable. Therefore, ECHA has not modified the deadline of the decision.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 9 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.

ECHA took into account your comments and did not amend the requests.

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

ECHA received proposal for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment.

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-63 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.