EUROPEAN CHEMICALS AGENCY

Helsinki, 20 December 2016

Addressee: [redacted]

Decision number: CCH-D-2114350104-64-01/F
Substance name: 2,2-dioctyl-1,3,2-oxathiastannolan-5-one
EC number: 239-581-2
CAS number: 15535-79-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 11.06.2015
Registered tonnage band: 100 to 1000 tonnes per year

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. **Description of the analytical methods (Annex VI, Section 2.3.7) used for the identification of the registered substance;**

   - **Identification and quantification of the main constituent(s)**

2. **Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1; test method: EU C.7/OECD TG 111) with the registered substance;**

3. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2; test method: EU B.26/OECD TG 408) in rats with the registered substance;**

4. **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;**

5. **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; provided that the study requested under item 4 (Annex VIII, Section 8.4.2.) has a negative result.**

6. **Screening for reproductive/developmental toxicity, oral route (Annex VIII, Section 8.7.1; test method: OECD TG OECD TG 421 or 422) in rats with the registered substance;**

7. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2; test method: EU B.31/OECD TG 414) in rats or rabbits, oral route with the registered substance;**

8. **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;**

9. **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;**

10. **Identification of degradation products (Annex IX, Section 9.2.3.; test method as for items 8 and 9 above) of the registered substance;**

11. **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 and/or, if relevant, with its hydrolysis products;**

12. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2; test method: Alga, growth inhibition test, EU C.3/OECD TG 201) with the registered substance and/or, if relevant, with its hydrolysis products;**

13. **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 and/or, if relevant, with its hydrolysis products;**

14. **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 and/or, if relevant, with its hydrolysis products;**

15. **Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4; test method: Respiration inhibition test, OECD TG 209) with the registered substance and/or, if relevant, with its hydrolysis products;**

16. **Exposure assessment and risk characterisation (Annex I, Sections 5 and 6) for environment using default release factors or providing a clear and detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) for any non-default ERC release factors used in the exposure estimation and revising risk characterisation accordingly.**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **27 June 2019. 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. Advice and further observations are provided in Appendix 3.

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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, shall 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/web/guest/regulations/appeals.

Authorised[1] by Kevin Pollard, Head of Unit, Evaluation E1

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

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Appendix 1: Reasons

IDENTIFICATION OF THE SUBSTANCE

In order to ensure that potential hazardous properties of the substance are not underestimated, the information that is necessary to resolve the substance identification deficiencies below, must be available to you before identifying the test sample to be used for the testing requested in the present decision.

1. **Description of the analytical methods (Annex VI, Section 2.3.7.);**

Pursuant to Article 10(a)(ii) of the REACH Regulation, the technical dossier shall contain information on the identity of the substance as specified in Annex VI, Section 2 of the REACH Regulation. In accordance with Annex VI, Section 2 the information provided shall be sufficient to enable the identification of the registered substance.

Description of the analytical methods is a formal requirement of Annex VI Section 2.3.7.

ECHA observes that you did not provide sufficient description of the analytical method used for the quantification of the constituent present in the composition of the registered substance, which is required according to Annex VI section 2.3.7.

The composition of the substance was analysed by a gas chromatographic method. In the analytical report attached in section 1.4 of the registration dossier (file [redacted]), you included a chromatographic analysis consisting of two chromatograms and one peak table with retention time, peak area and corresponding area percent. However, the identification of the peaks, the concentration of the constituents and a detailed description of the method used for the gas chromatographic analysis are missing from the dossier.

ECHA considers that for a chromatographic analysis the following information is needed to meet the requirement of a description that is sufficiently detailed to allow the method to be reproduced: the experimental set-up such as the column type, length and diameter, injection volume, mobile phase/carrier gas, GC temperature programme, flow rate, concentrations of standard solutions, detection technique and run time.

ECHA points out that the chromatographic analysis does not allow the composition of the registered substance to be verified as the results of the chromatographic analyses recorded in the peak table are not consistent with the composition provided in IUCLID section 1.2. In the reported composition one main constituent "[redacted]" with a concentration range of [redacted]% w/w and two impurities referring to "[redacted]" and "[redacted]" with typical concentration values smaller than [redacted]% w/w were reported. From the peak table provided on the chromatogram in IUCLID section 1.4, the reported composition cannot be verified.

In addition, the second chromatogram shows four main peaks which are identified, however the peak table and associated results are missing and as such the reported composition cannot be verified based on the provided analytical data. Beside the main constituent "[redacted]" there are three additional constituents, namely "[redacted]", "[redacted]" and "[redacted]" that are identified by the chromatographic analysis but not quantified.

ECHA points out that according to chapter 4.3 of the Guidance for identification and naming of substances under REACH and CLP (Version: 1.3, February 2014), you shall note that, for well-defined substances, the following applies:

- Each main constituent (i.e. the constituent present at ≥80% for mono-constituent substance or each constituent present at ≥10% and 80% for multi-constituent substance) shall be identified and reported individually; and

- Each impurity present at ≥1% or relevant for the classification and/or PBT assessment of the registered substance shall be identified and reported individually.

- For each constituent, the typical, minimum and maximum concentration levels shall be specified regardless of the substance type.

ECHA therefore concludes that the description of the analytical methods used for the quantification of the constituents and the results thereof required to be reported is currently not sufficient for the proper identification and quantification of the constituents and impurities reported in the composition of the registered substance.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you agreed to provide the missing information in an updated dossier.

You are accordingly requested to provide a description of the analytical methods used for the quantification of the constituent(s) and impurities required to be reported in the composition of the registered substance. The description shall be sufficient for the methods to be reproduced and shall therefore include details of the experimental protocol followed, any calculation made and the results obtained.

As for the reporting of the data in the registration dossier, the information shall be attached in IUCLID section 1.4.

The composition reported in the dossier must be fully consistent with the analytical results obtained.

PROPERTIES OF THE SUBSTANCE

2. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Hydrolysis as a function of pH" is a standard information requirement as laid down in Annex VIII, Section 9.2.2.1 of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement by invoking both a read-across approach and the following justification:

"According to Section 2, Annex XI of the Regulation (EC) No. 1907/2006; testing for a specific endpoint may be omitted, if it is technically not possible to conduct the study as a consequence of the properties of the substance. Furthermore, according to Annex VIII, section 9.2.2.1, Column 2 (specific rules for adaptation from Column 1), the study does not need to be conducted if the substance is highly insoluble in water. Therefore since it is not possible to develop a suitable substance specific analytical method to allow the hydrolysis of the substance to be measured and the substance was determined to be insoluble in water, testing for this endpoint has been omitted".

a) Adaptation in accordance with Annex VIII, Section 9.2.2.1. Column 2 and Annex XI Section 2

In your justification, you make reference both to the general rule for adaptation of Annex XI Section 2 of the REACH Regulation for testing that is "*technically not possible*" and to the specific rule for adaptation of Column 2 of Annex VIII 9.2.2.1. of the REACH Regulation which specifies that a hydrolysis does not need to be conducted if "*the substance is highly insoluble in water*". However, ECHA notes that the information you have provided in the registration dossier does not support that justification. In your registration dossier, you indicate a water solubility of 0.156 mg/L. ECHA considers that a hydrolysis test can still be technically feasible for a substance with this water solubility. In particular, ECHA notes that you have provided hydrolysis studies for read-across substances with even lower water solubility (*i.e.* dioctyltin dilaurate (CAS: 3648-18-8), dioctylbis(pentane-2,4-dionato-O,O')tin (CAS 54068-28-9), dioctyltin bis(2-ethylhexyl thioglycolate) (CAS: 15571-58-1) and of dioctyltin dichloride (CAS: 3542-36-7)). Furthermore, ECHA notes that, if the registered substance undergoes hydrolysis, potential hydrolysis products are dioctyltin oxide (CAS: 870-08-6) and 2-mercaptoacetic acid (CAS: 68-11-1). The latter hydrolysis product has known high water solubility and analytical data for it could for example be used as a surrogate for calculating the hydrolysis reaction rate constants and half-life values.

Therefore, ECHA concludes that neither the general rule for adaptation of Annex XI Section 2 of the REACH Regulation nor the specific rule for adaptation of Column 2 of Annex VIII 9.2.2.1. of the REACH Regulation can be accepted.

b) Read-across hypothesis

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests, "*provided that the conditions set out in Annex XI are met*". This annex proposes some general rules for adapting the standard information requirements set out in Annexes VII to X of the REACH Regulation.
In particular, Annex XI, Section 1.5. of the REACH Regulation introduces the concept of read-across. This concept is based on the identification of similar compounds. Information for one or more *source substances* or *reference substances* may be used to make a prediction for the *target substance* (*i.e.* the registered substance). For a read-across approach to be valid, the source substances shall be demonstrated to be *similar* to the target substance. According to Annex XI, Section 1.5. of the REACH Regulation, the similarities may be based on:

(1) a common functional group;
(2) the common precursors and/or the likelihood of common breakdown products via physical and biological processes, which result in structurally similar chemicals; or
(3) a constant pattern in the changing of the potency of the properties across the category.

For hydrolysis, you have proposed several read-across results with 4 different source substances: dioctyltin dilaurate (CAS: 3648-18-8), dioctylbis(pentane-2,4-dionato-O,O')tin (CAS: 54068-28-9), dioctyltin bis(2-ethylhexyl thioglycolate) (CAS: 15571-58-1) and dioctyltin dichloride (CAS: 3542-36-7).

However, you have not justified how the respective information from those source substances could predict the rate of the hydrolysis and the potential degradation products of the registered substance (target substance).

More specifically, the registered substance contains different structural elements that might cause the substance to be susceptible to hydrolysis *differently* than the source substances. The registered substance is a cyclic organotin substance whereas none of the read-across substances contains a cycle. Cyclic substances may exhibit a different stability to hydrolysis than non-cyclic substances. Furthermore, the registered substance contains a sulphur-tin bond with a different susceptibility to hydrolysis than the oxygen-tin bond.

Furthermore, the information provided for water solubility indicates that the solutions were shaken for up to 72 hours and decanted for 24 hours before being analysed by mass spectroscopy. Degradation of the substance is not mentioned in the respective study summary. This indicates that the registered substance was stable enough in water to be quantified after the time needed for sample preparation. Similarly, the data provided for the partition coefficient complements the observation for the water solubility, i.e. that there is no indication from those studies that the substance is unstable in water. Therefore, ECHA considers that the properties of the registered substance cannot be predicted from the source substances and the read-across approach cannot be accepted as the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation does not apply.

c) Outcome

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. Information on hydrolysis and the resulting potential degradation products is specifically important for the environmental risk assessment as well as for the clarification of the PBT status of the substance registered.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agreed to perform a hydrolysis study according to OECD TG 111 and to update your dossier accordingly.

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: Hydrolysis as a function of pH (test method: EU C.7/OECD TG 111).

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

A "sub-chronic toxicity study (90 day)" is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement by invoking both a 28 day study conducted according to OECD 422 with the read-across substance dioctyltin oxide (CAS: 870-08-6) ([redacted], 2004) and the specific rules in Column 2 of Annex IX Section 8.6.2. of the REACH Regulation.

a) Read-across hypothesis (Annex XI, Section 1.5.)

The source substance that you use for read-across is dioctyltin oxide (CAS: 870-08-6). In order to justify the read across, you claim that the registered substance would hydrolyse rapidly to dioctyltin oxide. However, as explained above under section 2 (Annex VIII, Section 9.2.2.1.) ECHA considers that you have not demonstrated that the registered substance will indeed hydrolyse rapidly to dioctyltin oxide. Furthermore, if the substance hydrolyses significantly, then every hydrolysis product should be taken into consideration. For example, one potential hydrolysis product is 2-mercaptoacetic acid (CAS: 68-11-1). ECHA notes that you have not addressed the potential toxicity of 2-mercaptoacetic acid.

Therefore, ECHA considers that the properties of the registered substance cannot be predicted from the source substances and the read-across does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. The adaptation you provided cannot be accepted.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you proposed to use available data from other di-n-octyltin compounds [DOTx] in a weight of evidence analysis to fill-in data gap for the sub-chronic toxicity study (90 day) and reproductive toxicity. Attached to your comment, a "Category definition" document was provided. ECHA notes the following with respect to this document:

"Category hypothesis"

In your justification for the "Category hypothesis" you have stated that the category covers DOTx compounds which consist of two n-octyltin groups and two ligands (containing sulphur atom or carboxylate or oxygen or chloride) covalently bound to a Sn(IV) atom and two other ligands and that the remaining two binding positions can be occupied by ligands containing a sulphur atom covalently bound to the tin (e.g. mercaptoacetates) or carboxylates (e.g. C12-C18 fatty acids), or oxygen or chlorine. You also mentioned that a grouping of octyltin substances similar or identical to what you propose has been accepted by the European Food Safety Authority (EFSA-Q-2005-016), the OECD ICCA program [SIAM 23], and the ECHA [RAC XIX] in reviewing a data set for DOTE. ECHA acknowledges your category approach and the listed references. However, ECHA notes that for an appropriate category approach, you would need to take into consideration those information, e.g., by applying appropriate classifications for the registered substance.

Within your category hypothesis you indicated that the *in vitro* metabolism of the registered substance DOTTG under simulated gastric conditions was indistinguishable from that of DOTE. However, ECHA notes that in this *in vitro* study, obviously the registered substance DOTTG dissolved in DOTE was examined. You did not provide sufficient details on this study to conclude on the metabolism of the registered substance and to support the read-across or category approach.
More specifically, the hydrolysis study for DOTTG dissolved in DOTE does not provide a proof that those breakdown products come from both DOTTG (target substance of the read-across) and DOTE. Therefore, it has not been verified that the hydrolysis products of the source and the target substances of the read-across are similar.

You further indicate that "*Independently from the hydrolytical behavior of the two ligands, the group defining Di-n-octyl tin moiety remains unchanged in any published hydrolysis study*". ECHA notes that you did not provide sufficient information to support this claim.

"Category members"

ECHA notes that you list five members of your category and the target (registered) substance. However, you did not provide information on the inclusion and/or exclusion rules for the category members.

"Target substance"

ECHA notes your following comment: "*The substance is only synthesized in the presence of DOTE. The maximum content is limited due to the poor solubility of the substance in DOTE to a maximum of < 10 %. In the real use in Dioctyltinstabilizer the concentration is typically* [redacted] *%. So an exposure to the substance is only possible when exposed to DOTE.*" ECHA notes that DOTE (EC number 239-622-4) is a member of your category and has a harmonised classification Repro 1B.
However, as required in Annex XI, 1.5., you should implement that classification for the target substance of the read-across, *i.e.* classify the registered substance as toxic to reproduction, class 2b.

"Impurities"

ECHA notes that you only mentioned in a more general statement the potential impurities of the category members but you did not provide individual information on the purity of each category member.

"Category justification"

You indicate that: "*Toxicologically the octyltins, like other alkyltin categories, have similar properties, and some patterns are generally apparent across the organotin data set: the dichloride compounds are more toxic than the diesters, and the di-[alkyl] compounds tend to be more toxic than the mono-[alkyl] compounds. Additionally, data from in vitro metabolism studies with octyltins clearly indicate that the mercaptoacetates do not hydrolyze to the dichloride, it is equally clear that the dioctyltin substructure of the molecule is stable. The in vitro metabolism suggests that gastric hydrolysis exclusively affects the ligands, never the alky-groups. More broadly, this within-category similarity of toxicological responses is observed in five additional and related categories of organotin substances, the mono and dimethyltin compounds, the mono and dibutyltin compounds, and the monooctyl compounds. Within their category each of these "families" of substances have similar toxicity endpoints. In essence, the entire data sets for organotin stabilizer compounds suggest the toxicology outcomes are in parallel with the organotin substructures of these chemicals".*

You further indicate that: "*For the octyltin compounds the existing data indicate that the target organ driving the NOEL for repeated-dose exposure to octyltins [STOT-RE] is the thymus gland; the octyltin compounds are, as a worst-case, not teratogenic but classified as Category 2 for reproductive toxicity; and not classified for mutagenicity. Conducting multiple studies with DOTTG with hundreds of test animals is unlikely to alter the worst-case classification, and are therefore unnecessary*"

ECHA acknowledges your category justification. However, ECHA notes the structural difference of the registered substance compared to the other substances of your category. As already explained in the draft decision, the registered substance is a cyclic organotin substance whereas none of the other substances in the category contains a cyclic structure. Cyclic substances may exhibit a different stability to hydrolysis than non-cyclic substances. Furthermore, the registered substance contains a sulphur-tin bond which is deemed to have a different susceptibility to hydrolysis than the oxygen-tin bond.

Hence, ECHA considers that you have not provided sufficient evidence (*e.g.*, lower tier repeated dose toxicity study with the source and target (registered) substance) to demonstrate toxicological similarity and support the read-across claim. Hence, ECHA rejects the adaptation according to Annex XI, Section 1.5. Therefore, the draft decision with respect to this request has not been amended.

"Data matrix"

ECHA notes that you attached to your comments a data matrix listing physico-chemical properties and results from eco-toxicological studies and the following four tables:

1. Summary of in vitro genotoxicity studies of DOTC, DOT(2-EHMA), and DOT(IOMA)
2. Summary of *in vitro* genotoxicity studies of the monooctyltin compounds
3. Summary of thymic toxicity in mammalian studies with octyltin substances
4. Summary of thymic toxicity in mammalian studies with methyltin and butyltin substances

ECHA notes that in order to compare results performed with different dioctyltin compounds, it might be helpful to calculate the NOAELs and LOAEOLs also with respect to mg tin/kg bw/d.

"Conclusions per endpoint for C&L, PBT/vPvB and dose descriptor"

ECHA notes that you did not provide conclusions per endpoint for C&L, PBT/vPvB and dose descriptors for the individual substances included in your proposed category.

Your summary on repeated dose toxicity provided in the comments to the draft decision

With respect to repeated dose toxicity, you provided the following conclusion in the comments: "*Two additional tables are provided to highlight the significance of the thymus as the target organ for DOTx, and for other members of the broader organotin family of substances. Table 3 is a comprehensive summary of the outcomes of repeated dose mammalian studies with dioctyltin substances. The table headings indicate the ligand type, purity, ratio of di to mono octyltin, the route and type of mammalian exposure, the study duration, the doses administered, the LOEL and NOEL for thymus toxicity, and whether the result would support a classification of STOT RE1. In essentially every instance where data are available, the thymus is a critical target organ for octyltins.*
In all of the repeated dose studies, the decrease in organ weight and histopathological effects on the thymus drive the overall NOEL for the study."

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ECHA acknowledges that for the dioctyltin compounds for which you referred to experimental data, the thymus is the critical target in rats driving the overall NOEL for the study. However, in light of the structural differences of the registered substance compared to the other dioctlytin compounds, you did not provide supporting information to demonstrate that the thymus is also the target organ for the registered substance.

Furthermore, ECHA notes that different dioctyltin compounds have different STOT RE classifications. Hence, to appropriately classify the registered substance with respect to repeated exposure, either a worst-case classification needs to be applied or information derived with the registered substance is obtained and used for its classification and labelling.

ECHA concludes that based on the additional information provided with the comments on the draft decision, supporting experimental evidence is missing to conclude if the properties and potency of the registered substance can be predicted from the source substances. Furthermore, appropriate classification and risk management measures would need to be considered and applied. Therefore, your adaptation does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. The adaptation you provided is therefore rejected.

ECHA also notes that the provided information is not sufficient to conclude according to Annex XI, Section 1.2., weight of evidence, that the "*substance has or has not a particular dangerous property*" with respect to sub-chronic toxicity. More specifically, in the absence of any information on systemic effects of the registered substance following repeated administration, it is not possible to assume/conclude that the registered substance has indeed the potential to damage the thymus and if so, with which potency. Therefore, this adaptation is also rejected.

b) Adaptation in accordance with Annex IX, Section 8.6.2. Column 2

In addition to the read-across, you have provided the following justification:

"*In accordance with point 8.6.2, Column 2 (Specific rules for adaptation from Column 1) Annex IX of Regulation (EC) No. 1907/2006, the sub-chronic toxicity study (90-days) does not need to be conducted if a reliable sub-acute (28-day) study is available showing severe toxicity effects according to the criteria for classifying the substance as R48. The existing oral data (read-across from dioctyltin oxide) is considered to adequately address the repeated dose toxicity endpoint, providing a NOAEL – 28 days suitable for extrapolation towards the NOAEL-90 days. Testing for a further 90-day study is regarded as unnecessary*".

ECHA notes that in your justification you are referring to the classification of the substance as R48 (equivalent to STOT. Rep. Exp. 1 (H372) for CLP / GHS). However, the classification you have proposed for your substance is not consistent in the different parts of your dossier. More specifically, while classification as STOT. Rep. Exp. 1 (H372) is mentioned in the chemical safety report, for the T assessment (section 2.3 of IUCLID) and in the endpoint summary for repeated dose toxicity (section 7.5 of IUCLID), you finally classify your substance as STOT Single Exp. 2 (H371) as reported in section 2.1 of IUCLID.

ECHA further notes that information on repeated dose toxicity is not available for the registered substance but for a read-across substance which ECHA considers to be not appropriately justified as explained in section 3a above. Therefore, ECHA considers that a definitive conclusion is not possible on the classification of the substance. Hence, the provided justification does not comply with the specific rules for adaptation according to Column 2 of Annex IX Section 8.6.2. of the REACH Regulation and the adaptation you provided cannot be accepted.

c) Outcome

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 4.0, July 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure and no uses with spray application are reported that could potentially lead to aerosols of inhalable size. Hence, the test shall be performed by the oral route using the test method OECD TG 408/EU B.26.

According to the test method EU B.26/OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

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

You have sought to adapt this information requirement by applying a read-across adaptation (Annex XI, Section 1.5. of the REACH Regulation). The source substance that you suggest for read-across is dioctyltin oxide (CAS no 870-08-6) and the study you have provided is an *in vivo* micronucleus assay according to OECD test guideline 474 ([redacted]). In order to justify the read across, you claim that the registered substance will hydrolyse rapidly to dioctyltin oxide. However, ECHA considers that you have not demonstrated that the registered substance will indeed hydrolyse rapidly to dioctyltin oxide (see section 2 of the decision). Furthermore, if the substance hydrolyses significantly, then every hydrolysis product should be taken into consideration.

For example, one potential hydrolysis product is 2-mercaptoacetic acid (CAS: 68-11-1). ECHA notes that you have not addressed the potential effects of 2-mercaptoacetic acid. Therefore, ECHA considers that the properties of the registered substance cannot be predicted from the source substances and the read-across justification does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. Your adaptation cannot be accepted.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you proposed to use available data from other di-n-octyltin compounds [DOTx] in a weight of evidence analysis to fill-in data gap for in vitro genotoxicity in mammalian cells. Attached to your comment, a "Category definition" document was provided. Please see ECHA's evaluation and responses with respect to this document above in Appendix 1, section 3a.

With regard to *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study, you did not provide or refer to any *in vitro* study with any dioctyltin compound. However, in your comments, you have referred to three negative *in vivo* micronucleus studies with dioctyltin compounds, namely dioctyltin dichloride ([redacted]), dioctyltin bis(IOMA) ([redacted]) and dioctyltin oxide ([redacted]).

However, details on these studies are not provided (with the exception of the "[redacted] study, which is provided in the technical dossier and has already been considered above). Therefore, ECHA does not consider the new information on mono-, tri-, or tetraoctyltin compounds as directly supporting the read-across/category approach.

Furthermore, ECHA Secretariat notes that all members of the proposed category share the di-n-octyltin moiety, however, as already explained in the draft decision, the registered substance is a cyclic organotin substance whereas none of the other substances in the category contains a cycle. Cyclic substances may exhibit a different clastogenic activity than non-cyclic substances or may lead to metabolite of different clastogenicity.

Hence, ECHA rejects your adaptation according to Annex XI, Section 1.5.

ECHA also notes that the provided information is not sufficient to conclude according to Annex XI, Section 1.2., weight of evidence, that the "*substance has or has not a particular dangerous property*" with respect to clastogenicity in mammalian cells. More specifically, in the absence of any information on potential clastogenicity of the registered substance and its metabolism, it is not possible to assume/conclude that the registered substance does not lead to clastogenicity in mammalian cells. Therefore, this adaptation is also rejected.

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

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

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

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

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.

ECHA notes that the registration dossier contains negative results for Annex VII, Section 8.4.1 (e.g. based on the key study from [redacted], performed according to OECD Guideline 471 (Bacterial Reverse Mutation Assay)). ECHA notes further that the registration dossier does not contain appropriate information for Annex VIII, Section 8.4.2. Therefore, adequate information on *in vitro* gene mutation in mammalian cells may need to be present in the technical dossier for the registered substance to meet this information requirement provided that the study requested under point 4 of this decision for Annex VIII, Section 8.4.2. has a negative result.

You have sought to adapt this information requirement by applying a read-across adaptation (Annex XI, Section 1.5. of the REACH Regulation). The source substance that you suggest for read-across is dioctyltin oxide (CAS: 870-08-6), and the study you have provided is an *in vitro* Mouse Lymphoma Assay according to OECD test guideline 476 ([redacted]). In order to justify the read across, you claim that the registered substance will hydrolyse rapidly to dioctyltin oxide. However, ECHA considers that you have not demonstrated that the registered substance will indeed hydrolyse rapidly to dioctyltin oxide (see section 2 of the decision). Furthermore, if the substance hydrolyses significantly, then every hydrolysis product should be taken into consideration. For example, one potential hydrolysis product is 2-mercaptoacetic acid (CAS: 68-11-1). ECHA notes that you have not addressed the potential effects of 2-mercaptoacetic acid.

Therefore, ECHA considers that the properties of the registered substance cannot be predicted from the source substances and the read-across justification does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. The adaptation you provided cannot be accepted.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you proposed to use available data from other di-n-octyltin compounds [DOTx] in a weight of evidence analysis to fill-in data gap for in vitro genotoxicity in mammalian cells. Attached to your comment, a "Category definition" document was provided. Please see ECHA's evaluation and responses with respect to this document above in Appendix 1, section 3a.

With regard to *in vitro* gene mutation study in mammalian cells, ECHA notes that in Table 1 attached to your comments, you have referred to the following *in vitro* studies with dioctyltin dichloride:

- Mouse lymphoma assay with positive result without metabolic activation up to 16 µg/ml ([redacted])
- HPRT assay in V79 cells up to 90 µg/ml ([redacted])
- HPRT assay in V79 cells up to 75 µM ([redacted]).

ECHA considers that in the view of the positive result reported for the mouse lymphoma assay without metabolic activation it is not appropriate to conclude that "*the octyltin data set is overwhelmingly negative for mutagenic outcomes*".

Furthermore, ECHA Secretariat notes that all members of the proposed category share the di-n-octyltin moiety, however, as already explained in the decision, the registered substance is a cyclic organotin substance whereas none of the other substances in the category contains a cycle. Cyclic substances may exhibit a different mutagenic activity in mammalian cells than non-cyclic substances or may lead to metabolite of different mammalian mutagenicity.

Hence, ECHA rejects the adaptation according to Annex XI, Section 1.5.

ECHA also notes that the provided information is not sufficient to conclude according to Annex XI, Section 1.2., weight of evidence, that the "*substance has or has not a particular dangerous property*" with respect to gene mutation in mammalian cells. More specifically, in the absence of any information on potential mammalian gene mutation of the registered substance and its metabolism, and in view of the positive result reported from the mouse lymphoma assay with dioctyltin dichloride it is not possible to assume/conclude that the registered substance does not lead to gene mutation in mammalian cells. Therefore, this adaptation is also 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 may be necessary to provide information 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: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that the study requested under point 4 of the present decision has a negative result.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Screening for reproductive/developmental toxicity" (test method OECD TG 421 or 422) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from *in vitro* methods that the substance may be a developmental toxicant. As explained below, no such evidence is presented in the dossier. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement by applying a read-across adaptation (Annex XI, Section 1.5. of the REACH Regulation). You have provided a screening study according to test guideline OECD 422 performed with the read-across substance dioctyltin oxide (CAS: 870-08-6) ([redacted]). In order to justify the read across, you claim that the registered substance will hydrolyse rapidly to dioctyltin oxide. However, ECHA considers that you have not demonstrated that the registered substance will indeed hydrolyse rapidly to dioctyltin oxide (see section 2 of the decision). Furthermore, if the substance hydrolyses significantly, then every hydrolysis product should be taken into consideration. For example, one potential hydrolysis product is 2-mercaptoacetic acid (CAS: 68-11-1). ECHA notes that you have not addressed the potential effects of 2-mercaptoacetic acid.

Therefore, ECHA considers that the properties of the registered substance cannot be predicted from the source substances and this read-across justification does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. The adaptation you provided cannot be accepted.

In addition, you have also provided a two generation reproductive toxicity study with another read-across substance: a mixture of Dioctyltin bis (IOMA) [CAS: 26401-97-8]: Octyltintris (IOMA) [CAS: 26401-86-5] ([redacted]% mixture). While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to column 2 of Section of Annex IX, which states that the screening study does not need to be conducted if a two-generation study (B.35, OECD TG 416) is available. However, you have not provided any justification for the read-across. Hence without sufficient documentation and adequate justification for the read-across as required in Annex XI, Section 1.5. of the REACH Regulation, ECHA cannot accept that result to fulfil the information requirement for the reproductive toxicity endpoint. Therefore, your adaptation based on the existing two-generation study cannot be accepted.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you proposed to use available data from other di-n-octyltin compounds [DOTx] in a weight of evidence analysis to fill-in data gap for the sub-chronic toxicity study (90 day) and reproductive toxicity. Attached to your comment, a "Category definition" document was provided. Please see ECHA's evaluation and responses with respect to this document above in Appendix 1, section 3a.

With regard to screening for reproductive/developmental toxicity and in general (multi) generation reproductive toxicity studies, you have provided the following comments:

- *"A two generation GLP reproduction toxicity study with a related thioglycolate ester, dioctyltin di-isooctyl thioglycolate DOT[IOTG]/MOT[IOTG] mixture" [...] "The reproductive NOEL is the high dose the maternal and paternal NOEL is 20ppm (the low dose) which is driven by the effect of DOT on the thymus gland. [...]*

  This study does not meet the classification criteria of clear evidence for a reproductive effect with the DOT[IOMA] however the data can be read-across directly to DOTTG which suggests an additional study is unnecessary." ECHA notes that in the IUCLID dossier, you already provided a study summary of this study and indicated that 20 ppm are about 1.6 mg/kg bw/d. ECHA has already addressed the shortcomings of this study above.

- *"There is also a 13 week oral toxicity study in rats with DOTC, including a reproduction/developmental screening study. TNO ([redacted]). The test sample purity was 94.1 % DOTC and the study is a GLP study using OECD 408 combined to OECD 421 guideline. This study, as a worst-case assessment for DOTTG, can be used for read-across. [...] the low dose level of 10 ppm in diet (equivalent to 0.7 mg/ kg bw/day in males and 0.5-0.7 mg/kg bw/day for females) can be considered as a NOAEL for fertility and developmental effects [...] the study does not meet the classification criteria of clear evidence for a reproductive effect; [...] These data from the dichloride can be read-across to DOTTG as a worst-case outcome. When viewed within a weight-of-evidence analysis with other reproductive and developmental studies the data suggest Reproductive toxicity Category 2 may be appropriate. It follows that an additional study with DOTTG is unnecessary."* ECHA notes that this study is not included in your IUCLID dossier, that the material tested is not the substance registered and a justification for a read-across adaptation has not been provided. Furthermore, it requires clarification if the cited OECD TG 421 screening study was indeed performed in combination with a sub-chronic toxicity study according to OECD TG 408.

- ECHA notes that in the IUCLID dossier, you provided an OECD TG 422 screening study with dioctyltin oxide (DOTO, CAS number 870-08-6) by [redacted] for which you derived a NOAEL for general toxicity of 0.3-0.4 mg/kg bw/d based on decreased thymus weights.

ECHA considers that, as explained above in Appendix 1, section 3a, you did not provide an appropriate justification to support your read-across/category approach. Furthermore, you did not provide an appropriate justification for not classifying the registered substance with respect to reproductive toxicity. ECHA notes that without justification and appropriate data on the registered substance, the harmonised classification for DOTE (EC number 239-622-4) as Repro 1B (H360D) has to be applied as "worst case" classification and adequate risk mamagement measures have to be put into place.

ECHA concludes that based on the additional information provided with the comments on the draft decision, supporting experimental evidence is missing to conclude if the properties of the registered substance can be predicted from the source substances. Furthermore, appropriate classification and risk management measures would need to be considered and applied. Therefore, your adaptation still does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. The adaptation you provided is rejected.

ECHA also notes that the provided information is not sufficient to conclude according to Annex XI, Section 1.2., weight of evidence, that the "*substance has or has not a particular dangerous property*" with respect to screening for reproductive/developmental toxicity. More specifically, in the absence of any information on systemic effects of the registered substance following repeated administration, it is not possible to assume/conclude that the registered substance has indeed the potential to damage the thymus and if so, with which potency. Therefore, this adaptation is also 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 may be necessary to provide information for this endpoint.

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

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, July 2015) R.7a, chapter 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.

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 rats by the oral route: Reproductive/developmental toxicity screening test (test method: OECD TG 421) *or* Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422).

Note for your consideration

For the selection of the appropriate test, please consult ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7a, section R.7.5 and 7.6 (version 4.1, October 2015).

Column 1 of Annex VIII, Section 8.7.1. of the REACH Regulation indicates that the test needs to be provided "*if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from in vitro methods that the substance may be a developmental toxicant*". Column 2 of that Annex specifies that "*in cases where there are serious concerns about the potential for adverse effects on fertility or development, either an Extended One-Generation Reproductive Toxicity Study (Annex IX, section 8.7.3) or a pre-natal developmental toxicity study (Annex IX, section 8.7.2) may, as appropriate, be proposed by the registrant instead of the screening study*". You may therefore need to submit a testing proposal for an extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3. of the REACH Regulation) for which the test design would depend on the screening information for reproductive/developmental toxicity.

7. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

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

You have sought to adapt this information requirement by invoking both read-across (Annex XI, Section 1.5 of the REACH Regulation) and the general rule for adaptation based on substance–tailored exposure-driven testing (Annex XI, Section 3. of the REACH Regulation).

a) Read-across hypothesis (Annex XI, Section 1.5.)

You have provided a screening study according to test guideline OECD 422 performed with the read-across substance dioctyltin oxide (CAS: 870-08-6) ([redacted]). Firstly, ECHA notes that test guideline OECD 422 is not appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation. Therefore, pursuant to Article 13(3) of the REACH Regulation and Annex XI, Section 1.1.2. of the REACH Regulation, the study you provided cannot be accepted. Secondly, as explained in section 6 above of that decision, ECHA considers that your read-across approach does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. Therefore, the study of [redacted] cannot be accepted as basis for an adaptation.

In addition, you have also provided two pre-natal developmental toxicity studies, one performed with rabbits, the second with mice, according to test guideline OECD 414 with the read-across substance 2-ethylhexyl 10-ethyl-4,4-dioctyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate (CAS: 15571-58-1) ([redacted]). However, you have not provided any justification for the read-across. Hence without sufficient documentation and adequate justification for the read-across based on the Annex XI, Section 1.5, ECHA cannot assess whether the respective results fulfil the information requirement for the pre-natal developmental toxicity endpoint for the registered substance. Therefore, your adaptation based on the general rules of Annex XI, Section 1.5. of the REACH Regulation cannot be accepted.

b) Justification based on Annex XI, Section 3

With regard to your justification invoking Annex XI, Section 3. of the REACH Regulation, ECHA notes that your adaptation does not meet the general rules of that section, because your exposure assessment actually demonstrates significant exposure with risk characterisation ratios close to 1 for some of the process categories (PROCs) contrary to what is required in subparagraph 3.2(a)(i) of Annex XI. Based on the information provided in your chemical safety report, there are professional uses (e.g. handling PVC where the substance is a stabiliser) where, judging from the maximum concentration in the plastic articles, exposure is possible. There are also potential consumer exposures through contact with articles. There is some evidence of migration of the registered substance from plastic articles. Furthermore, ECHA notes that the DNELs used for your risk assessment are derived from a screening test for reproductive/developmental toxicity on a read-across substance not fulfilling the requirement in subparagraph 3.2(a)(ii) of Annex XI. As explained above, the read-across is not acceptable and cannot be used for the substance subject to this decision. Moreover, footnote 1 of Annex XI Section 3 provides that "*... a DNEL derived from a screening test for reproductive/developmental toxicity shall not be considered appropriate to omit a pre-natal developmental toxicity study ...*". Therefore ECHA considers that the adaptation you proposed cannot be accepted.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you proposed to use available data from other di-n-octyltin compounds [DOTx] in a weight of evidence analysis to fill-in data gap for the sub-chronic toxicity study (90 day) and reproductive toxicity. Attached to your comment, a "Category definition" document was provided. Please see ECHA's evaluation and responses with respect to this document above in Appendix 1, section 3a.

With regard to developmental toxicity, you have provided the following comments:

- *"Following the guidance of Annex XI, data from dioctyltin studies, particularly the dioctyltin ethylhexyl thioglycolate [DOTE] and dioctyltin dichloride [DOTC] should be part of the weight-of-evidence and data needs assessment of DOTTG."*

- *"In recent GLP OECD-414 studies with DOTE in rabbit and in mouse there is no evidence of increased developmental defects at maternally toxic doses. These new data are included in the dossier for DOTE. Therefore, the DOTE data meet the criteria in Annex XI and the RAAF, and DOTE could be expected to be equally or more developmentally toxic than DOTTG. The GLP data from OCED-414 studies clearly show DOTE is not developmentally toxic, and a similar study with DOTTG is unlikely to change the classification of DOTTG if read-across were used for this reproductive endpoint."*

ECHA notes that, as explained in Appendix 1, section 3a, you did not provide sufficient information to support your proposed read-across/category approach. ECHA further notes that you did not provide additional information on the pre-natal developmental toxicity studies performed with DOTE to which you refer above.

ECHA assumes that this is the substance with EC number 239-622-4 which has a harmonised classification Repro 1B which, as the consequence, has to be followed for this substance as well in order to successfully read-across. Furthermore, you did not provide an appropriate justification for not classifying the registered substance with respect to reproductive toxicity. ECHA notes that without appropriate data on the registered substance, the harmonised classification for DOTE (EC number 239-622-4) as Repro 1B has to be applied as "worst case" classification.

ECHA concludes that based on the additional information provided with the comments on the draft decision, supporting experimental evidence is missing to conclude if the properties and potency of the registered substance can be predicted from the source substances. Furthermore, appropriate classification and risk management measures would need to be considered and applied. Therefore, your adaptation does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. The adaptation you provided is rejected.

ECHA also notes that the provided information is not sufficient to conclude according to Annex XI, Section 1.2., weight of evidence, that the "*substance has or has not a particular dangerous property*" with respect to pre-natal developmental toxicity. More specifically, in the absence of any information on systemic effects of the registered substance following repeated administration, it is not possible to assume/conclude that the registered substance has indeed the potential to damage the thymus and if so, with which potency. Therefore, this adaptation is also rejected.

c) Outcome

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

According to the test method EU B.31/OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter 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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rats or rabbits) by the oral route.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Sediment simulation testing" is a standard information requirement as laid down in Annex IX, section 9.2.1.4. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement by using the following justification:

" In accordance with point 9.2.1.4, Column 2 (specific rules for adaptation from column 1) of Annex IX of Regulation (EC) No. 1907/2006 (REACH), sediment simulation tests do not need to be conducted as the chemical safety assessment concludes that the substance is of no immediate concern to the environment. The available data are adequate for classification and labelling purposes and PBT assessment, further testing is therefore considered inappropriate. Also direct and indirect exposure of the soil and sediment is unlikely".

a) Adaptation of the information requirement

Column 2 of Section 9.2. of Annex IX of the REACH Regulation indicates that the study needs to be conducted if the chemical safety assessment (CSA) according to Annex I of the REACH Regulation indicates the need to investigate further the degradation of the substance and its degradation products and that the choice of the appropriate test(s), which may include simulation degradation tests in appropriate media, depends of the results of the CSA. Column 2 of Section 9.2.1.4 of Annex IX of the REACH Regulation further indicates that the study does not need to be conducted if the substance is readily biodegradable or if direct and indirect exposure of sediment is unlikely.

In your justification for adaptation, you refer to the specific rule of adaptation in Section 9.2.1.4. of Column 2 in Annex IX, by claiming that direct and indirect exposure of the environment is unlikely.

Based on the information provided in the chemical safety report (CSR), ECHA however considers that the absence of exposure of the environment has not been properly demonstrated. The dossier contains 6 exposure scenarios (ES). ES1, ES2, ES3 and ES4 are industrial uses. For those 4 scenarios, you state that "*controls and risk management measures are in place to prevent losses to wastewater*" but you did not specify what those measures should be. ECHA notes that a municipal sewage treatment plant (STP) is not reported for these 4 scenarios. Therefore, the registered substance or its potential degradation products can thus be released to wastewater, e.g., adsorbed onto suspended matter.

Since no STP is assumed, the wastewater with suspended matter could then be released to the aquatic compartment where the suspended matter would settle onto the sediment. Therefore exposure to sediment is likely and the assessment of the fate of the registered substance and its potential degradation products in sediment (or in water with suspended matter) is relevant. Therefore, ECHA considers your adaptation to be inadequate.

In your justification for adaptation, you also claim that simulation testing is not needed for the PBT/vPvB assessment as you consider that the substance is not PBT/vPvB. ECHA notes that this adaptation does not comply with the adaptation possibilities in column 2 of Section 9.2. of Annex IX of the REACH Regulation for the following reasons:
For the persistence (P/vP) assessment, you state that "*although not readily biodegradable in screening tests, the substance is hydrolysed extremely rapidly (almost instantaneously) in aqueous solution. The substance therefore does not satisfy the P criteria*". ECHA cannot accept that statement. Firstly, you have not demonstrated that the substance will actually hydrolyse (see above issue on hydrolysis in section 2 of the decision). Secondly, Annex XIII of REACH on the identification of PBT and vPvB substances explicitly requires that the identification "*shall also take account of the PBT/vPvB-properties of relevant constituents of a substance and relevant transformation and/or degradation products*". Therefore, if you can demonstrate that the registered substance hydrolyses, then you must investigate the PBT/vPvB properties of the hydrolysis products and other degradation products. ECHA notes that one of the potential hydrolysis product (if hydrolysis occurs), i.e. dioctyltin oxide (CAS: 870-08-6) is not readily biodegradable and is potentially (very) persistent (P/vP).

Furthermore, it is unclear, whether the substance or its potential degradation products are bioaccumulative (B) or very bioaccumulative (vB) (see below bioaccumulation in section 11 of the decision).

As for the toxicity (T) assessment, the NOEC reported for algae is 0.00097 mg/L for the read-across substance dioctyltin oxide (CAS: 870-08-6). This value is far below the threshold of 0.01 mg/L defined in Annex XIII of REACH. Therefore, in case you are able to substantiate the respective read-across, your substance will meet the T criterion. Furthermore, ECHA notes that the substance is potentially toxic for reproduction and may induce chronic toxicity (see issues above on reprotoxicity/developmental toxicity and repeated dose toxicity).

ECHA notes that your adaptation neither meets the specific rules for adaptation of column 2 of Annex IX, Section 9.2 and of Annex IX, Section 9.2.1.4. of the REACH Regulation, nor the general rule for adaptation of Annex XI of the REACH Regulation. Therefore, ECHA considers your adaptation inadequate and you shall conduct simulations studies in particular to clarify the PBT/vPvB status of the registered substances and its potential degradation products.

b) Outcome

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.

The registered substance is deemed to be adsorptive and – once released - can adsorb onto suspended matter present in wastewater. If STP is not present (*i.e.* for exposure scenarios ES1, ES2, ES3 and ES4), the wastewater with suspended matter will be released to the aquatic compartment and the suspended matter will settle onto sediment. Therefore a simulation test in sediment (OECD 308) shall be performed.

One of the purposes of the simulation tests 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 (P) or very persistent (vP) 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 2.0, November 2014) 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*". ECHA notes that the registered substance is used in the EU. The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-9 (version 2.1 October 2012) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Therefore, the test results, and in particular the degradation rates, shall correspond to the temperature of 12°C (285K).

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 by covalent bonds or incorporated into the biomass. The amount and kind of NER is operationally defined by the extraction method employed. Strong extractions methods, for example soxhlet-extraction with apolar solvents, should be used in order to qualify the remaining NER as irreversibly bound residues. You are therefore requested to justify scientifically that the extraction method you will apply is appropriate to identify non-extractable residues (NER) as residues irreversibility bound to the sediment.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agreed to provide additional information with regard to risk management measures in place to prevent losses of the registered substance to waste water. In order to demonstrate the absence of direct or indirect exposure of sediment, you should provide in an updated dossier information on risk management measures and operational conditions for all uses and covering the whole life-cycle of the substance.

In agreement with the proposal for amendment submitted by the Competent Authority of [redacted], you have indicated your intention to further strengthen the read-across arguments in your dossier by further investigating the hydrolysis potential of the registered substance. You have also attached the study report[2] for a hydrolysis study performed under simulated mammalian gastric conditions (0.1 M HCl / pH 1.2 / 37 °C). However, ECHA notes that this study is not relevant for investigating hydrolysis under environmentally relevant conditions. It is therefore neither appropriate to fulfil the information requirements for hydrolysis nor can it be used to justify the read-across approach for the degradation endpoint.

You also indicate the fact that that the registered substance "*is manufactured solely in situ together with DOTE or DOTI and marketed in concentrations of typically* [redacted] *% (max* [redacted] *%) and DOTE / DOTI are well examined substances, The registrant believes further vertebrate testing is not justified*". However, ECHA notes that the relevance of this fact in the further justification of the proposed read-across is not clear nor substantiated with evidence.

In summary, ECHA notes that in your comments to the proposal for amendment, you have not provided relevant evidence to conclude whether the registered substance will actually hydrolyse under environmental conditions and if yes how fast and to what hydrolysis products.

ECHA notes following the performance of the hydrolysis study (OECD TG 111) which you have indicated you will undertake, the results may potentially strengthen or weaken your proposed read-across approach. However, as this information, which should have already been present in your initial registration, is not available ECHA can but only conclude that your adaptation does not comply with this standard information requirement.

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 aquatic sediment systems (test method: EU C.24./OECD TG 308). The test results shall correspond to the temperature of 12°C (285K).

Note for your consideration:
You are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11.4. and Figure R.11—3 on the PBT/vPvB assessment for further information on the integrated testing strategy for the persistence assessment of the registered substance. You shall revise the PBT/vPvB assessment when information on persistence is available.

9. Soil simulation testing (Annex IX, Section 9.2.1.3.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

[2] 2,2-dioctyl-1,3,2-oxathiastannolan-5-one [DOTTG], CAS number: 15535-79-2: In-vitro Metabolism Study. Final Report. Author: [redacted]

"Soil simulation testing" is a standard information requirement as laid down in Annex IX, section 9.2.1.3. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement by using the following justification:

"In accordance with point 9.2.1.3, Column 2 (specific rules for adaptation from column 1) Annex IX of Regulation (EC) No. 1907/2006 (REACH), Soil Simulation testing does not need to be conducted as the chemical safety assessment concludes that the substance is of no immediate concern to the environment. The available data are adequate for classification and labelling purposes and PBT assessment, so no further testing is required. Also direct and indirect exposure of the soil is unlikely".

a) Adaptation of the information requirement

Column 2 of Section 9.2. of Annex IX of the REACH Regulation indicates that the study needs to be conducted if the chemical safety assessment (CSA) according to Annex I of the REACH Regulation indicates the need to investigate further the degradation of the substance and its degradation products and that the choice of the appropriate test(s), which may include simulation degradation tests in appropriate media, depends of the results of the CSA. Column 2 of Section 9.2.1.3 of Annex IX of the REACH Regulation further indicates that the study does not need to be conducted if the substance is readily biodegradable or if direct and indirect exposure of soil is unlikely.

In your justification for adaptation, you claim that direct and indirect exposure of the environment is unlikely. Based on the information provided in the chemical safety report (CSR), ECHA however considers that the absence of exposure of the environment has not been demonstrated. More specifically, the dossier contains 6 exposure scenarios (ES). ES5 and ES6 are for professional and consumer uses, respectively. Further, there is evidence of migration of the registered substance out of plastic articles (e.g. study of [redacted] cited in the CSR). For ES5, you claim that "*controls will also be in place to prevent losses to the environment*" but you did not specify what those controls should be. Therefore, the registered substance or its potential degradation products can be released to wastewater, e.g. adsorbed onto suspended matter. For both scenarios, you assume in your exposure assessment that STP is present. Suspended matter will then most likely settle onto STP sludge. Based on your exposure assessment, the STP sludge will be applied onto agricultural soil. Therefore, ECHA concludes that exposure of soil is likely and, as consequence, the assessment of the fate of the registered substance and its potential degradation products in soil is relevant. Therefore, ECHA considers your adaptation to be inadequate.

In your justification for adaptation, you also claim that simulation testing is not needed for the PBT/vPvB assessment as you consider that the substance is not PBT/vPvB. ECHA notes that this adaptation does not comply with the adaptation possibilities in column 2 of Section 9.2. of Annex IX of the REACH Regulation for the following reasons:

For the persistence (P/vP) assessment, you state that "*although not readily biodegradable in screening tests, the substance is hydrolysed extremely rapidly (almost instantaneously) in aqueous solution. The substance therefore does not satisfy the P criteria*". ECHA disagrees with that statement. Firstly, you have not demonstrated that the substance will actually hydrolyse (see above issue on hydrolysis in section 2 of the decision). Secondly, Annex XIII of REACH on the identification of PBT and vPvB substances explicitly requires that the identification "*shall also take account of the PBT/vPvB-properties of relevant constituents of a substance and relevant transformation and/or degradation products*".

Therefore if you can demonstrate that the registered substance hydrolyses, then you must investigate the PBT/vPvB properties of the hydrolysis products and other degradation products should. ECHA notes that one of the potential hydrolysis product (if hydrolysis occurs), i.e. dioctyltin oxide (CAS: 870-08-6) is not readily biodegradable and is potentially (very) persistent (P/vP).

Furthermore, it is unclear, whether the substance or its potential degradation products are bioaccumulative (B) or very bioaccumulative (vB) (see below bioaccumulation in section 11 of the decision).

As for the toxicity (T) assessment, the NOEC reported for algae is 0.00097 mg/L for the read-across substance dioctyltin oxide (CAS: 870-08-6). This value is far below the threshold of 0.01 mg/L defined in Annex XIII of REACH. Therefore, in case you are able to substantiate the respective read-across, your substance will meet the T criterion. Furthermore, ECHA notes that the substance is potentially toxic for reproduction and may induce chronic toxicity (see issues above on reprotoxicity/developmental toxicity and repeated dose toxicity).

ECHA notes that your adaptation neither meets the specific rules for adaptation of column 2 of Annex IX, Section 9.2 and of Annex IX, Section 9.2.1.3. of the REACH Regulation, nor the general rule for adaptation of Annex XI of the REACH Regulation. Therefore, ECHA considers your adaptation inadequate and you shall conduct simulation studies in particular to clarify the PBT/vPvB status of the registered substance and its potential degradation products.

b) Outcome

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.

The registered substance is deemed to be adsorptive and – once released - can adsorb onto suspended matter present in wastewater. If STP is present (*i.e.* for ES5 and ES6), suspended matter will mostly settle onto STP sludge which might be applied to agricultural soils. Therefore a simulation test in soil (OECD 307) shall be performed.

One of the purposes of the simulation tests 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 (P) or very persistent (vP) 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 2.0, November 2014) 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*". ECHA notes that the registered substance is used in the EU. The Guidance on information requirements and chemical safety assessment
Chapter R.16 on Environmental Exposure Estimation, Table R.16-9 (version 2.1 October 2012) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Therefore, the test results, and in particular the degradation rates, shall correspond to the temperature of 12°C (285K).

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 by covalent bonds or incorporated into the biomass. The amount and kind of NER is operationally defined by the extraction method employed. Strong extractions methods, for example soxhlet-extraction with apolar solvents, should be used in order to qualify the remaining NER as irreversibly bound residues. You are therefore requested to justify scientifically that the extraction method you will apply is appropriate to identify non-extractable residues (NER) as residues irreversibility bound to the soil.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agreed to provide additional information with regard to risk management measures in place to prevent losses of the registered substance to waste water. In order to demonstrate the absence of direct or indirect exposure of soil, you should provide in an updated dossier information on risk management measures and operational conditions for all uses and covering the whole life-cycle of the substance.

In agreement with the proposal for amendment submitted by the Competent Authority of [redacted], you have indicated your intention to further strengthen the read-across arguments in your dossier by further investigating the hydrolysis potential of the registered substance. You have also attached the study report[3] for a hydrolysis study performed under simulated mammalian gastric conditions (0.1 M HCl / pH 1.2 / 37 °C). However, ECHA notes that this study is not relevant for investigating hydrolysis under environmentally relevant conditions. It is therefore neither appropriate to fulfil the information requirements for hydrolysis nor can it be used to justify the read-across approach for the degradation endpoint.

You also indicate the fact that that the registered substance "*is manufactured solely in situ together with DOTE or DOTI and marketed in concentrations of typically* [redacted] *% (max* [redacted] *%) and DOTE / DOTI are well examined substances, The registrant believes further vertebrate testing is not justified*". However, ECHA notes that the relevance of this fact in the further justification of the proposed read-across is not clear nor substantiated with evidence.

In summary, ECHA notes that in your comments to the proposal for amendment, you have not provided relevant evidence to conclude whether the registered substance will actually hydrolyse under environmental conditions and if yes how fast and to what hydrolysis products.

[3] 2,2-dioctyl-1,3,2-oxathiastannolan-5-one [DOTTG], CAS number: 15535-79-2: In-vitro Metabolism Study. Final Report. Author [redacted]

ECHA notes following the performance of the hydrolysis study (OECD TG 111) which you have indicated you will undertake, the results may potentially strengthen or weaken your proposed read-across approach. However, as this information, which should have already been present in your initial registration, is not available ECHA can but only conclude that your adaptation does not comply with this standard information requirement.

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.23./OECD TG 307). The test results shall correspond to the temperature of 12°C (285K).

Note for your consideration:
You are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11.4. and Figure R.11—3 on the PBT/vPvB assessment for further information on the integrated testing strategy for the persistence assessment of the registered substance. You shall revise the PBT/vPvB assessment when information on persistence is available.

10. Identification of degradation products (Annex IX, Section 9.2.3.)

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Identification of degradation products" is a standard information requirement as laid down in Annex IX, Section 9.2.3. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement. Column 2 of Section 9.2. of Annex IX of the REACH Regulation indicates that the study needs to be conducted if the chemical safety assessment (CSA) according to Annex I of the REACH Regulation indicates the need to investigate further the degradation of the substance and its degradation products and that the choice of the appropriate test(s), which may include simulation degradation tests in appropriate media, depends of the results of the CSA. Column 2 of Section 9.2.3. of Annex IX of the REACH Regulation further states that the identification of degradation products does not need to be provided if the substance is readily biodegradable.

ECHA notes that you have not provided information on the degradation products of the registered substance. However, ECHA notes that:

- The substance is not readily biodegradable.

- Pursuant to Annex XIII of the REACH Regulation "*the identification* [of PBT and vPvB substances] *shall also take account of the PBT/vPvB-properties of relevant constituents of a substance and relevant transformation and/or degradation products*". Your CSA does not contain any information on the degradation products and on whether they could be PBT/vPvB or not.

- Information on degradation products shall also be taken into account for the exposure assessment (Annex I 5.2.4. of the REACH Regulation) and for the hazard assessment (e.g. column 2 of Annex X 9.4 and Annex X 9.5.1 of the REACH Regulation). Finally, information on degradation products is required for the preparation of Section 12 of the safety datasheet (Annex II of the REACH Regulation).

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 degradation products can be identified when performing the tests already required above under points 8 and 9 of the present decision (test methods EU C.7/OECD TG 111, EU C.24./OECD TG 308 or EU C.25./OECD TG 309, and EU C.23./OECD TG 307). Thus, there is no need for other tests in order to provide information for this endpoint.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agreed to conduct a hydrolysis study according to OECD test guideline 111. However the requirement of Annex IX, Section 9.2.3 of REACH is to identify degradation products not only from abiotic degradations as hydrolysis but also from biodegradation. The identification of hydrolysis products only would therefore not meet the information requirements of Annex IX, Section 9.2.3 of REACH. You further indicated that information is available on the in-vitro metabolism of dioctyltin compounds. However, ECHA notes that this study was conducted to mimic gastric conditions, under low pH, and cannot be used to predict the environmental fate of the substance. You also indicated that the analytical determination of degradation products may not be feasible. ECHA notes that radio-labelling may be used as a very sensitive method for identifying and quantifying degradation products. If radio-labelling is not technically possible either, you may then adapt the information requirement by invoking Annex XI of REACH.

In agreement with the proposal for amendment submitted by the Competent Authority of [redacted], you have indicated your intention to further strengthen the read-across arguments in your dossier by further investigating the hydrolysis potential of the registered substance. You have also attached the study report[4] for a hydrolysis study performed under simulated mammalian gastric conditions (0.1 M HCl / pH 1.2 / 37 °C). However, ECHA notes that this study is not relevant for investigating hydrolysis under environmentally relevant conditions. It is therefore neither appropriate to fulfil the information requirements for hydrolysis nor can it be used to justify the read-across approach for the degradation endpoint.

You also indicate the fact that that the registered substance "*is manufactured solely in situ together with DOTE or DOTI and marketed in concentrations of typically* [redacted] *% (max* [redacted] *%) and DOTE / DOTI are well examined substances, The registrant believes further vertebrate testing is not justified*". However, ECHA notes that the relevance of this fact in the further justification of the proposed read-across is not clear nor substantiated with evidence.

[4] 2,2-dioctyl-1,3,2-oxathiastannolan-5-one [DOTTG], CAS number: 15535-79-2: In-vitro Metabolism Study. Final Report. Author [redacted]

In summary, ECHA notes that in your comments to the proposal for amendment, you have not provided relevant evidence to conclude whether the registered substance will actually hydrolyse under environmental conditions and if yes how fast and to what hydrolysis products.

ECHA notes following the performance of the hydrolysis study (OECD TG 111) which you have indicated you will undertake, the results may potentially strengthen or weaken your proposed read-across approach. However, as this information, which should have already been present in your initial registration, is not available ECHA can but only conclude that your adaptation does not comply with this standard information requirement.

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 degradation products (Annex IX, Section 9.1.3.; test method as for points 8 and 9 above) of the registered substance.

11. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD 305, aqueous exposure).

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"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. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement by applying a read-across adaptation. In addition, ECHA notes that you have submitted a QSAR (Quantitative Structure Activity Relationship) result that you have disregarded because the model used (BCFWIN, v. 2.15) is not validated for organometallic compounds.

a) Read-across hypothesis (Annex XI, Section 1.5.)

You have provided a bioaccumulation study ([redacted]) on the read-across substance dioctyltin bis(2-ethylhexyl thioglycolate) (DOT(EHTG)$_2$, CAS: 15571-58-1). In order to justify that read across, you claim that both the registered substance and DOT(EHTG)$_2$ will hydrolyse very rapidly to dioctyltin oxide (CAS: 870-08-6). From that read-across study, you claim that the bioconcentration factor (BCF) of the registered substance is less than 100.

However, ECHA has several reservations about your read-across approach:

- You have not demonstrated that the registered substance will actually hydrolyse rapidly to dioctyltin oxide as already explained above under section 2 (Annex VIII, Section 9.2.2.1.

- You assume that the read-across substance, i.e. DOT(EHTG)$_2$, hydrolyses very rapidly to dioctyltin oxide, but you have not provided actual evidence to support this claim either. The only information available on hydrolysis of DOT(EHTG)$_2$ is from the study of [redacted] in section 5.1.2 of IUCLID, but that study does not provide a hydrolysis rate or a half-life value. Because of analytical issues with the test substance, the bioaccumulation study of [redacted] was designed to detect the test substance itself, i.e. DOT(EHTG)$_2$, and any degradation products or impurities that contain the octyltin group. It is therefore not possible to conclude to what moiety, be it the parent substance or one of its degradation products, the BCF actually pertains.

- The BCF value reported in the study of [redacted] is questionable, because it is not possible to ascertain based on the provided information whether or not steady state was reached during that study.

Therefore, ECHA considers your adaptation to be inadequate and not complying with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation and the properties of the registered substance cannot be predicted from the proposed source substance.

b) QSAR (Quantitative Structure Activity Relationship)

ECHA notes that the model used has not been validated for organometallic substances (such as the registered substance) and that you have consequently disregarded this result. ECHA agrees that this information cannot be used to assess the properties of the substance and does therefore not assess this adaptation further.

c) Outcome

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 considers the OECD 305 test guideline (Bioaccumulation in Fish: Aqueous and Dietary Exposure) to be appropriate to meet the information requirement of Annex IX, Section 9.3.2.of the REACH Regulation.

According to ECHA guidance R7c, chapter R.7.10.3.4, where the hydrolysis half-life is less than 12 hours at environmentally relevant pH values (4-9) and temperature, it can be assumed that the rate of hydrolysis is greater than the rate for uptake by the exposed organisms. Hence, in such cases it may be appropriate to perform a BCF test on the hydrolysis products, instead of the parent substance.

ECHA Guidance defines 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 you should investigate whether it is possible to keep a constant concentration of the test substance (i.e. the registered substance, or, if relevant, the hydrolysis products) in the aqueous phase before deciding whether an aqueous BCF study or a dietary bioaccumulation study will provide the most reliable and useful results for the PBT/vPvB assessment.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you referred to in-vitro metabolism studies on dioctyltin compounds to justify your read-across approach. However, ECHA notes that this study was conducted under simulated gastric conditions, at low pH, whereas bioconcentration refers to uptake from water across the gills of aquatic organisms and therefore occurs at environmental pH. ECHA considers that you have not provided evidence that the registered substance will hydrolyse quickly under environmental conditions and therefore that you have failed to justify the proposed read-across.

Furthermore, you disagreed with ECHA's assessment of the study of [redacted] and considered that this study could be used without reservation. As already indicated previously in the draft decision, ECHA considers that the BCF value reported for the study of [redacted] is difficult to interpret in itself, regardless of the read-across issue. This study was designed to detect any substance containing the octyltin group, it is therefore not possible to conclude to what extent the BCF value pertains to the test substance itself or to potential degradation products or impurities. Moreover, no time trend data on the actual concentration of the substance in the fish is provided, therefore it is not possible to establish whether steady state was reached during the test. ECHA notes that in the PBT factsheet prepared by the UK competent authorities for substituted mono- and dioctyltin compounds, the very same reservations are mentioned for the interpretation of the study of Bouwman, 2010.

In agreement with the proposal for amendment submitted by the Competent Authority of [redacted], you have indicated your intention to further strengthen the read-across arguments in your dossier by further investigating the hydrolysis potential of the registered substance. You have also attached the study report[5] for a hydrolysis study performed under simulated mammalian gastric conditions (0.1 M HCl / pH 1.2 / 37 °C). However, ECHA notes that this study is not relevant for investigating hydrolysis under environmentally relevant conditions. It is therefore neither appropriate to fulfil the information requirements for hydrolysis nor can it be used to justify the read-across approach for the bioaccumulation endpoint.

You also indicate the fact that that the registered substance "*is manufactured solely in situ together with DOTE or DOTI and marketed in concentrations of typically* [redacted] *% (max* [redacted] *%) and DOTE / DOTI are well examined substances, The registrant believes further vertebrate testing is not justified*". However, ECHA notes that the relevance of this fact in the further justification of the proposed read-across is not clear nor substantiated with evidence.

In summary, ECHA notes that in your comments to the proposal for amendment, you have not provided relevant evidence to conclude whether the registered substance will actually hydrolyse under environmental conditions and if yes how fast and to what hydrolysis products.

ECHA notes following the performance of the hydrolysis study (OECD TG 111) which you have indicated you will undertake, the may potentially strengthen or weaken your proposed read-across approach. However, as this information, which should have already been present in your initial registration, is not available ECHA can but only conclude that your adaptation does not comply with this standard information requirement.

[5] 2,2-dioctyl-1,3,2-oxathiastannolan-5-one [DOTTG], CAS number: 15535-79-2: In-vitro Metabolism Study. Final Report. Author: [redacted]

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 and/or, if relevant, with its hydrolysis products: Bioaccumulation in fish (test method: OECD TG 305).

Note for your consideration:

You are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11.4. and Figure R.11—4 on the PBT/vPvB assessment for further information on the integrated testing strategy for the bioaccumulation assessment of the registered substance. The bioaccumulation or bioconcentration potential of degradation products shall also be investigated when conducting the required test to be used for the PBT/vPvB assessment. You shall revise the PBT/vPvB assessment when information on bioaccumulation is available as part of revising the chemical safety report.

Because of uncertainties on whether hydrolysis actually occurs for the registered substance and on how fast it is, it is not possible to judge at this stage, whether the bioaccumulation study should be performed on the parent substance or on the potential hydrolysis products. The bioaccumulation test shall therefore be performed after the results of the requested hydrolysis study (see section 2 of the decision) are available.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex IX, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

Toxicity testing on algae is necessary for the PNEC derivation and for the PBT assessment and shall be considered for classification and labelling of the substance.

You have sought to adapt this information requirement by applying a read-across adaptation (Annex XI, Section 1.5. of the REACH Regulation). You have provided an Algae Growth Inhibition Test (OECD 201) performed with the read-across substance dioctyltin oxide (CAS: 870-08-6). In order to justify the read across, you claim that the registered substance would hydrolyse rapidly to dioctyltin oxide. However, as explained above under section 2 (Annex VIII, Section 9.2.2.1.) ECHA considers that you have not demonstrated that the registered substance will indeed hydrolyse rapidly to dioctyltin oxide (see section 2 of the decision). Furthermore, if the substance hydrolyses significantly, then every hydrolysis product should be taken into consideration. For example, one potential hydrolysis product is 2-mercaptoacetic acid (CAS: 68-11-1). ECHA notes that you have not addressed the potential effects of 2-mercaptoacetic acid.

Furthermore, ECHA notes that the information provided in the dossier on the read-across substance indicates the need for classifying the substance as hazardous to the aquatic environment "Acute Category 1" and "Chronic Category 1". However, you have not classified the substance accordingly and thus implicitly considered that the results are not adequate for classification and labelling and thus the provision "*In all cases results should ... be adequate for classification and labelling ...*" of Annex XI, Section 1.5 of the REACH Regulation is not met.

Therefore ECHA considers that the read-across justification does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation and the adaptation you provided 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 R7b, Appendix R.7.8—1, Table R.7.8—3 (pages 85-86) if the hydrolysis half-life is less than 1 hour, then the test should be performed on the hydrolysis products. However, if the hydrolysis half-life is more than 3 days, the test should be performed on the parent substance. If the hydrolysis half-life is more than 1 hour but less than 3 days, then testing of either parent and/or hydrolysis products should be considered on a case-by-case basis.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you referred to in-vitro metabolism studies on dioctyltin compounds to justify your read-across approach. However, ECHA notes that this study was conducted under simulated gastric conditions, at low pH, which are not relevant for assessing the ecotoxicity of the substance under environmental conditions. ECHA considers that you have not provided evidence that the registered substance will hydrolyse quickly under environmental conditions and therefore that you have failed to justify the proposed read-across.

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 and/or, if relevant, with its hydrolysis products: Growth inhibition study aquatic plants (test method: EU C.3/OECD TG 201).

Notes for your consideration:

You are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11.4. and Figure R.11—5 on the PBT/vPvB assessment for further information on the integrated testing strategy for the toxicity assessment of the registered substance. The toxicity of degradation products shall also be investigated when conducting the required test to be used for the PBT/vPvB assessment. You shall revise the PBT/vPvB assessment when information on toxicity is available as part of revising the chemical safety report.

Because of uncertainties on whether hydrolysis actually occurs for the registered substance and on how fast it is, it is not possible to judge at this stage whether the study should be performed on the parent substance or on the potential hydrolysis products. The test should therefore be performed after the result of the requested hydrolysis study is available (see section 2 of the decision). If the substance hydrolyses rapidly, then every hydrolysis product should be taken into account for the assessment.

Furthermore, due to the low solubility of the substance in water, you should consult the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA Guidance, Chapter R7b, table R. 7.8-3 for choosing the design of the requested test and for calculation and expression of the results of this test.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

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

Toxicity testing on aquatic invertebrates is necessary for the PNEC derivation and for the PBT assessment and shall be considered for classification and labelling of the substance.

You have sought to adapt this information requirement by applying a read-across adaptation (Annex XI, Section 1.5.) and the specific adaptation in Annex IX, Section 9.1.of Column 2.

a) Read-across hypothesis (Annex XI, Section 1.5.)

You have provided two *Daphnia* sp. Acute Immobilisation Test (OECD 202) studies both performed with the read-across substance dioctyltin oxide (CAS: 870-08-6). In order to justify the read across, you claim that the registered substance would hydrolyse rapidly to dioctyltin oxide. However, as explained above under section 2 (Annex VIII, Section 9.2.2.1.) ECHA considers that you have not demonstrated that the registered substance will indeed hydrolyse rapidly to dioctyltin oxide. Furthermore, if the substance hydrolyses significantly, then every hydrolysis product should be taken into consideration. For example, one potential hydrolysis product is 2-mercaptoacetic acid (CAS: 68-11-1). ECHA notes that you have not addressed the potential effects of 2-mercaptoacetic acid.

Furthermore, ECHA notes that the information provided in the dossier on the read-across substance indicates the need for classifying the substance as hazardous to the aquatic environment "Acute Category 1" and "Chronic Category 1". However, you have not classified the substance accordingly and thus implicitly considered that the results are not adequate for classification and labelling and thus the provision "*In all cases results should ... be adequate for classification and labelling ...*" of Annex XI, Section 1.5 of the REACH Regulation is not met.

Therefore ECHA considers that the read-across justification does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation and the adaptation you provided cannot be accepted.

b) Justification based on the specific adaptation of Annex IX, Section 9.1.5. Column 2.

Concerning the requirement to conduct a long term toxicity test, you adapted the standard testing regime also based on the following consideration: "*In accordance with point 9.1.5, Column 2 (Specific rules for Adaption from Column 1) of Regulation (EC) No. 1272/2008 (REACH) Annex IX, the long-term testing on aquatic invertebrates does not need to be conducted as the chemical safety assessment concludes that the substance is of no immediate concern to the environment. The available data are adequate for classification and labelling purposes and PBT assessment, so no further testing is required*".

According to the Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b, Section R.7.8.5.3, the Chemical Safety Assessment (CSA) is to be based on all available toxicity information, and that the information used for the derivation of the predicted no effect concentration (PNEC) for water should at least cover species of three trophic levels: algae/aquatic plants, invertebrates (Daphnia preferred), and fish, irrespective of the term of the studies (whether short-term or long-term).

However, as explained above in section 13 a, ECHA considers that no adequate information is available for aquatic toxicity to *Daphnia* and therefore there is not sufficient information available for the PNEC derivation. Moreover, aquatic toxicity to *Daphnia* is necessary for the PBT assessment and shall be considered for classification and labelling of the substance.

ECHA notes that short-term toxicity testing on *Daphnia* is a standard information requirement of Annex VII, Section 9.1.1. of the REACH Regulation. However, Column 2 of that Annex also states that long-term aquatic toxicity on Daphnia shall be considered if the substance is poorly water soluble. ECHA notes that the reported value for water solubility of the registered substance is relatively low (0.156 mg/L). Therefore, ECHA understands that the substance is poorly water soluble and, pursuant to Column 2 of Annex VII, Section 9.1.1. of the REACH Regulation, that long-term toxicity on Daphnia shall be considered instead of short-term toxicity on Daphnia.

Therefore, ECHA considers that the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms and your adaptation based on Column 2 of Annex IX, Section 9.1 cannot be accepted.

c) Outcome

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 R7b, Appendix R.7.8—1, Table R.7.8—3 (pages 85-86) if the hydrolysis half-life is less than 1 hour, then the test should be performed on the hydrolysis products. However, if the hydrolysis half-life is more than 3 days, the test should be performed on the parent substance. If the hydrolysis half-life is more than 1 hour but less than 3 days, then testing of either parent and/or hydrolysis products should be considered on a case-by-case basis.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you referred to in-vitro metabolism studies on DOTE and DOTTG dissolved in DOTE to justify your read-across approach. However, ECHA notes that the read-across proposed in the dossier for addressing aquatic toxicity to *Daphnia* is based on DOTO, not DOTE. ECHA further notes that the *in-vitro* metabolism studies were conducted under simulated gastric conditions, at low pH, which are not relevant for assessing the ecotoxicity of the substance under environmental conditions. ECHA considers that you have not provided evidence that the registered substance will hydrolyse quickly under environmental conditions and therefore that you have failed to justify the proposed read-across.

ECHA also notes that the read-across studies that you have proposed can only address short-term toxicity. As already explained in the draft decision, the registered substance is deemed to be poorly soluble in water. Substances that are poorly soluble require longer time to be significantly taken up by the aquatic organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for poorly soluble substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. Still, long-term toxicity cannot be excluded and should be investigated. Annex VIII 9.1.3. and Annex VII 9.1.1. of the REACH Regulation explicitly recommend that long-term aquatic toxicity tests be considered if the substance is poorly water soluble.

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 and/or, if relevant, with its hydrolysis products: *Daphnia magna* reproduction test (test method: EU C.20./OECD TG 211).

Notes for your consideration:

You are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11.4. and Figure R.11—5 on the PBT/vPvB assessment for further information on the integrated testing strategy for the toxicity assessment of the registered substance. The toxicity of degradation products shall also be investigated when conducting the required test to be used for the PBT/vPvB assessment. You shall revise the PBT/vPvB assessment when information on toxicity is available as part of revising the chemical safety report.

Because of uncertainties on whether hydrolysis actually occurs for the registered substance and on how fast it is, it is not possible to judge at this stage whether the study should be performed on the parent substance or on the potential hydrolysis products. The test should therefore be performed after the result of the requested hydrolysis study (see section 2 of the decision) is available. If the substance hydrolyses rapidly, then every hydrolysis product should be taken into account for the assessment.

Furthermore, due to the low solubility of the substance in water, you should consult the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA Guidance, Chapter R7b, table R. 7.8-3 for choosing the design of the requested test and for calculation and expression of the results of this test.

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

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

Toxicity testing on fish is necessary for the PNEC derivation and for the PBT assessment and shall be considered for classification and labelling of the substance.

You have sought to adapt this information requirement by applying a read-across adaptation (Annex XI, Section 1.5.) and the specific adaptation in Annex IX, Section 9.1. Column 2.

a) Read-across hypothesis (Annex XI, Section 1.5.)

You have provided a Fish, Acute Toxicity Test (OECD 203) study performed with the read-across substance dioctyltin oxide (CAS: 870-08-6). In order to justify the read across, you claim that the registered substance would hydrolyse rapidly to dioctyltin oxide. However, as explained above under section 2 (Annex VIII, Section 9.2.2.1.) ECHA considers that you have not demonstrated that the registered substance will truly hydrolyse rapidly to dioctyltin oxide. Furthermore, if the substance hydrolyses significantly, then every hydrolysis product should be taken into consideration. For example, one potential hydrolysis product is 2-mercaptoacetic acid (CAS: 68-11-1). ECHA notes that you have not addressed the potential effects of 2-mercaptoacetic acid.

Furthermore, ECHA notes that the information provided in the dossier on the read-across substance indicates the need for classifying the substance as hazardous to the aquatic environment "Acute Category 1" and "Chronic Category 1". However, you have not classified the substance accordingly and thus implicitly considered that the results are not adequate for classification and labelling and thus the provision "*In all cases results should ... be adequate for classification and labelling ...*" of Annex XI, Section 1.5 or the REACH Regulation is not met.

Therefore ECHA considers that the read-across justification does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation and the adaptation you provided cannot be accepted.

b) Justification based on the specific adaptation of Annex IX, Section 9.1.6. Column 2.

Concerning the requirement to conduct a long term toxicity test, you adapted the standard testing regime based on the following consideration: "*In accordance with point 9.1.6, Column 2 (Specific rules for Adaption from Column 1) of Regulation (EC) No. 1272/2008 (REACH) Annex IX, the long-term testing on fish study does not need to be conducted as the chemical safety assessment concludes that the substance is of no immediate concern to the environment. The available data are adequate for classification and labelling purposes and PBT assessment, so no further testing is required*".

According to the Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b, Section R.7.8.5.3, the Chemical Safety Assessment (CSA) is to be based on all available toxicity information, and that the information used for the derivation of the predicted no effect concentration (PNEC) for water should at least cover species of three trophic levels: algae/aquatic plants, invertebrates (Daphnia preferred), and fish, irrespective of the term of the studies (whether short-term or long-term).

However, as explained above in section 14 a, ECHA considers that no adequate information is available for aquatic toxicity to fish and therefore there is not sufficient information available for the PNEC derivation. Moreover, aquatic toxicity to fish is necessary for the PBT assessment and shall be considered for classification and labelling of the substance.

ECHA notes that short-term toxicity testing on fish is a standard information requirement of Annex VIII, Section 9.1.3. of the REACH Regulation. However, Column 2 of that Annex also states that long-term aquatic toxicity on fish shall be considered if the substance is poorly water soluble. ECHA notes that the reported value for water solubility of the registered substance is relatively low (0.156 mg/L). Therefore, ECHA understands that the substance is poorly water soluble and, pursuant to Column 2 of Annex VIII, Section 9.1.3. of the REACH Regulation, that long-term toxicity on fish shall be considered instead of short-term toxicity on fish.

Therefore, ECHA considers that the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms and your adaptation based on Column 2 of Annex IX, Section 9.1 cannot be accepted.

c) Outcome

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 long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6.1, ECHA considers that the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R7b, Figure R.7.8-4).

The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 2.0, November 2014). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as appropriate and suitable.

According to ECHA guidance R7b, Appendix R.7.8—1, Table R.7.8—3 (pages 85-86) if the hydrolysis half-life is less than 1 hour, then the test should be performed on the hydrolysis products. However, if the hydrolysis half-life is more than 3 days, the test should be performed on the parent substance. If the hydrolysis half-life is more than 1 hour but less than 3 days, then testing of either parent and/or hydrolysis products should be considered on a case-by-case basis.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you referred to in-vitro metabolism studies on DOTE and DOTTG dissolved in DOTE to justify your read-across approach. However, ECHA notes that the read-across proposed in the dossier for addressing aquatic toxicity to fish is based on DOTO, not DOTE. ECHA further notes that the in-vitro metabolism studies were conducted under simulated gastric conditions, at low pH, which are not relevant for assessing the ecotoxicity of the substance under environmental conditions. ECHA considers that you have not provided evidence that the registered substance will hydrolyse quickly under environmental conditions and therefore that you have failed to justify the proposed read-across.
ECHA also notes that the read-across study that you have proposed can only address short-term toxicity. As already explained in the draft decision, the registered substance is deemed to be poorly soluble in water. Substances that are poorly soluble require longer time to be significantly taken up by the aquatic organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for poorly soluble substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. Still, long-term toxicity cannot be excluded and should be investigated. Annex VIII 9.1.3. and Annex VII 9.1.1. of the REACH Regulation explicitly recommend that long-term aquatic toxicity tests be considered if the substance is poorly water soluble.

In agreement with the proposal for amendment submitted by the Competent Authority of [redacted], you have indicated your intention to further strengthen the read-across arguments in your dossier by further investigating the hydrolysis potential of the registered substance. You have also attached the study report[6] for a hydrolysis study performed under simulated mammalian gastric conditions (0.1 M HCl / pH 1.2 / 37 °C). However, ECHA notes that this study is not relevant for investigating hydrolysis under environmentally relevant conditions. It is therefore neither appropriate to fulfil the information requirements for hydrolysis nor can it be used to justify the read-across approach for the aquatic endpoint.

You also indicate the fact that that the registered substance "*is manufactured solely in situ together with DOTE or DOTI and marketed in concentrations of typically* [redacted] *% (max* [redacted] *%) and DOTE / DOTI are well examined substances, The registrant believes further vertebrate testing is not justified*". However, ECHA notes that the relevance of this fact in the further justification of the proposed read-across is not clear nor substantiated with evidence.

In summary, ECHA notes that in your comments to the proposal for amendment, you have not provided relevant evidence to conclude whether the registered substance will actually hydrolyse under environmental conditions and if yes how fast and to what hydrolysis products.

ECHA notes following the performance of the hydrolysis study (OECD TG 111) which you have indicated you will undertake, the results may potentially strengthen or weaken your proposed read-across approach. However, as this information, which should have already been present in your initial registration, is not available ECHA can but only conclude that your adaptation does not comply with this standard information requirement.

[6] 2,2-dioctyl-1,3,2-oxathiastannolan-5-one [DOTTG], CAS number: 15535-79-2: In-vitro Metabolism Study. Final Report. Author: [redacted]

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 and/or, if relevant, with its hydrolysis products: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Notes for your consideration:

You are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11.4. and Figure R.11—5 on the PBT/vPvB assessment for further information on the integrated testing strategy for the toxicity assessment of the registered substance. The toxicity of degradation products shall also be investigated when conducting the required test to be used for the PBT/vPvB assessment. You shall revise the PBT/vPvB assessment when information on toxicity is available as part of revising the chemical safety report.

Because of uncertainties on whether hydrolysis actually occurs for the registered substance and on how fast it is, it is not possible to judge at this stage whether the study should be performed on the parent substance or on the potential hydrolysis products. The test should therefore be performed after the result of the requested hydrolysis study (see section 2 of the decision) is available. If the substance hydrolyses rapidly, then every hydrolysis product should be taken into account for the assessment.

Furthermore, due to the low solubility of the substance in water, you should consult the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA Guidance, Chapter R7b, table R. 7.8-3 for choosing the design of the requested test and for calculation and expression of the results of this test.

15. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Activated sludge respiration inhibition testing" is a standard information requirement as laid down in Annex VIII, Section 9.1.4. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement by applying a read-across adaptation (Annex XI, Section 1.5. of the REACH Regulation).

You have provided an Activated Sludge, Respiration Inhibition Test (OECD 209) performed with the read-across substance dioctyltin oxide (CAS: 870-08-6). In order to justify the read across, you claim that the registered substance would hydrolyse rapidly to dioctyltin oxide. However, as explained above under section 2 (Annex VIII, Section 9.2.2.1.) ECHA considers that you have not demonstrated that the registered substance will indeed hydrolyse rapidly to dioctyltin oxide. Furthermore, if the substance hydrolyses significantly, then every hydrolysis product should be taken into consideration. For example, one potential hydrolysis product is 2-mercaptoacetic acid (CAS: 68-11-1). ECHA notes that you have not addressed the potential effects of 2-mercaptoacetic acid.

Therefore ECHA considers that the properties of the registered substance cannot be predicted from the source substances and the read-across justification does not comply with the general rule for adaptation of Annex XI, Section 1.5. of the REACH Regulation. The adaptation you provided 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 R7b, Appendix R.7.8—1, Table R.7.8—3 (pages 85-86) if the hydrolysis half-life is less than 1 hour, then the test should be performed on the hydrolysis products. However, if the hydrolysis half-life is more than 3 days, the test should be performed on the parent substance. If the hydrolysis half-life is more than 1 hour but less than 3 days, then testing of either parent and/or hydrolysis products should be considered on a case-by-case basis.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you referred to in-vitro metabolism studies on DOTE and DOTTG dissolved in DOTE to justify your read-across approach. However, ECHA notes that the read-across proposed in the dossier for addressing toxicity to activated sludge is based on DOTO, not DOTE. ECHA further notes that the in-vitro metabolism studies were conducted under simulated gastric conditions, at low pH, which are not relevant for assessing the ecotoxicity of the substance under environmental conditions. ECHA considers that you have not provided evidence that the registered substance will hydrolyse quickly in sewage treatment plants and therefore that you have failed to justify the proposed read-across.

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 and/or, if relevant, with its hydrolysis products: Activated sludge respiration inhibition testing, test method (OECD 209).

Notes for your consideration:
Because of uncertainties on whether hydrolysis actually occurs for the registered substance and on how fast it is, it is not possible to judge at this stage whether the study should be performed on the parent substance or on the potential hydrolysis products. The test should therefore be performed after the result of the requested hydrolysis study (see section 2 of the decision) is available.

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

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report (CSR) which shall document the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Based on Article 14(4), if the substance fulfils the criteria for any of the hazard classes listed in that provision or is assessed to be a PBT or vPvB, the CSA shall include exposure assessment and risk characterisation. The registered substance is classified for health hazards therefore the CSA shall include exposure assessment and risk characterisation.

Pursuant to Annex I, Section 5.2.1 of the REACH Regulation the exposure estimation as part of the exposure assessment entails three elements: emission estimation, assessment of chemical fate and pathways and estimation of exposure levels. Emission estimation shall be performed under the assumption that the risk management measures (RMMs) and operational conditions (OCs) described in the exposure scenario (ES) have been implemented. These RMMs and OCs should be included in the ESs provided in the CSR.

According to the *Guidance on information requirements and chemical safety assessment* Chapter R.16: Environmental Exposure Estimation (ECHA, version: 2.1, October 2012), operational conditions "*consist of a set of actions, tools, parameters such as amount of substance, process temperature and pH, duration and frequency of release, type of use (e.g. indoor or outdoor), containment of process (open or closed), continuous or batch process (leading to an intermittent release), capacity of surroundings, etc. having, as a side effect, an impact on the release and the exposure*". Risk management measures "*consist of technologies and procedures aimed at either reducing the releases and/or preventing a release pathway.*

Examples of risk management measures intended to reduce release are filters, scrubbers, biological or physico-chemical wastewater treatment plants etc." Both OCs and RMMs have an impact on the type and amount of release and the resulting exposure. ECHA guidance R.16 specifically provides default release factors associated with different Environmental Release Categories (ERCs). These default release factors can be used for a first tier assessment of the emissions. However, better information may be available that could then be used instead. In particular, release factors can be refined by taking into account RMMs and OCs. In this case, it is important to explicitly link such RMMs and OCs to the release factors and communicate them properly to the downstream users in the exposure scenarios.

In the present case, in the CSR you have provided 6 ESs:

- ES1) Manufacture;
- ES2) Formulation of preparations;
- ES3) Formulation of the substance in dry-blend preparations;
- ES4) Use at industrial site - Processing of polymers containing DOTTG as stabilizer through calendering, extrusion, injection moulding and low energy manipulation of plastic articles;
- ES5) Use by professional worker - Processing of polymer containing DOTTG as a stabiliser through low energy manipulation of plastic articles;
- ES6) Service life (consumers) - Service Life of DOTTG contained in articles.

You have stated for ES1, ES2, ES3 and ES4 (industrial uses) that "*controls and risk management measures are in place to prevent losses to wastewater*". However, ECHA notes that you have not specified what those measures should be.

For scenarios ES5 and ES6 you have indicated that "*the substance is highly insoluble and will be bound within a matrix (e.g. silicones, plastics, polymers). Loss of the compound during use of the products containing the substance will therefore be very low*". Thus, you have assumed a release factor to water and soil of 0.0001%. However, ECHA notes that you have also indicated that based on a study by [redacted] the quantity of organotin compound that can migrate from the surface of octyltin-stabilised PVC can be estimated to be 0.22% of the total mass of dioctyltin contained in PVC after a 10-day period at 40% in 95% ethanol. This percentage is much higher than the release factor used for scenarios ES5 and ES6 (i.e. 0.0001%).

[redacted]

You have claimed in addition that "*controls will also be in place to prevent losses to the environment*". However, again ECHA notes that you have not specified what those controls should be.

ECHA also notes that you have claimed that "*the substance is also very unstable in water hydrolysing almost immediately to DOTO* [i.e. dioctyltin oxide (CAS: 870-08-6)]. *DOTO is highly insoluble and is unlikely to dissolve in water to any extent. Releases to surface water are therefore expected to be negligible and thus very little to no waste will be lost via this route*". However, ECHA highlights that, as explained above under section 2 (Annex VIII, Section 9.2.2.1.), you have failed to demonstrate that the registered substance indeed hydrolyses rapidly to dioctyltin oxide.

Furthermore, the registered substance or its potential degradation products may be released to wastewater adsorbed onto suspended matter. Thus, where STP is present (*i.e.* for ES5 and ES6), suspended matter will mostly settle onto STP sludge which may be applied to agricultural soils. Therefore, an appropriate risk assessment for soil is needed for ES5 and ES6. Where no STP is present (*i.e.* for ES1, ES2, ES3 and ES4), the wastewater with suspended matter will be released to the aquatic compartment and the suspended matter will settle onto sediment. In this case, an appropriate risk assessment for sediment is needed for ES1, ES2, ES3 and ES4.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agreed to provide additional information on exposure scenarios and exposure assessment.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested either to use default release factors and other recommendations of ECHA Guidance R.16 and revise the risk characterisation accordingly *or* to provide a detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) for deviating from the recommendations of ECHA Guidance R.16 for estimation of environmental exposure.

Notes for your consideration:
The revised risk assessment shall take into account not only the revised information on the exposure assessment but also new information for the hazard assessment requested above in 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 30 October 2015

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

ECHA notified you of the draft decision and invited you to provide comments. ECHA took into account your comments, which were sent within the commenting period, and they are reflected in the Reasons (Appendix 1).

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment(s).

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

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

ECHA referred the draft decision to the Member State Committee.

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

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

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-51 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 fulfil otherwise the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In carrying out the tests required by the present decision it is important to ensure that the particular sample of substance tested is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured. If the registration of the substance covers different grades, the sample used for the new tests must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.