ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 14 December 2016

Addressee: [redacted]

Decision number: CCH-D-2114350062-64-01/F
Substance name: Trioctyl benzene-1,2,4-tricarboxylate
EC number: 201-877-4
CAS number: 89-04-3
Registration number: [redacted]
Submission number: [redacted]
Submission date: 15.07.2015
Registered tonnage band: 1000+T

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information on

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

2. **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;**

3. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance;**

4. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a second species (rat or rabbit), oral route with the registered substance;**

5. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56./OECD TG 443) in rats, oral route with the registered substance specified as follows:**

   - Ten weeks premating exposure duration for the parental (P0) generation;

   - Dose level setting shall aim to induce some toxicity at the highest dose level;

   - Cohort 1A (Reproductive toxicity);

   - Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;

6. **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;**

7. **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;**

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

9. **Long-term toxicity to sediment organisms (Annex X, Section 9.5.1.; test method: Sediment-water Lumbriculus toxicity test using spiked sediment, OECD TG 225) with the registered substance.**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI 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 **22 June 2020** except for the information requested under point 2 for a sub-chronic toxicity study (90-day) which shall be submitted in an updated registration dossier by **21 December 2017**. You may only commence the extended one-generation reproductive toxicity study as requested under point 5 after **21 March 2018**, unless an indication to the contrary is communicated to you by ECHA before that date. 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.

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/regulations/appeals.

Authorised[1] by Leena Ylä-Mononen, Director of Evaluation

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

Appendix 1: Reasons

0. Grouping of substances and read-across

In your registration dossier you use a read-across approach in which the properties of the registered substance trioctyl benzene-1,2,4-tricarboxylate (hereinafter referred to as the 'target substance (TM8)') is predicted from information available on 1,2,4-benzenetricarboxylic acid, decyl octyl ester (EC No 290-754-9; CAS No 67989-23-5); hereinafter referred to as the 'source substance (TM8-10)'.

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests. Such other means include the use of information from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met".

In the registration, you have adapted the standard information requirements for:

- *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490;
- Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408): and
- Pre-natal developmental toxicity study in a first species (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414)

by applying a read-across adaptation following REACH Annex XI, Section 1.5.

Annex XI, Section 1.5. requires a structural similarity among the substances within a group or category such that relevant properties of a substance within the group can be predicted from the data on reference substance(s) within the group by interpolation. The following analysis presents your justification for the proposed grouping approach and read-across hypothesis, together with ECHA's analysis concerning the justification in both a generic and an property-specific context.

0.1 Description of your grouping and read-across approach

You have provided the following hypothesis:

> *"The source substance used as a surrogate for read-across in the registration of TM8 is considered to be sufficiently similar to supplement the registration of TM8 under REACH where environmental fate and/or (eco)toxicological data are unavailable for the registered substance. Both substances are expected to display similar effects on biological systems based upon their structural similarities and their comparable physical chemistry. As a result, the (eco)toxicological data on the surrogate are considered appropriate for use in a read-across manner when registering TM8 under REACH."*

In addition, you state the following:

> *"Overall, the defined group is made up of substances consisting of esters of 1,2,4-tricarboxylic acid. Structural differences are limited to the carbon chain length of the side chains and, by analogy wit the phthalate estsrs, those with similar carbon chain lengths are expected to exhibit very similar properties.*

While other trimellitates show greater similarity with the substance, reliable data have been located only for 1,2,4-Benzenetricarboxylic acid, mixed decyl octyl ester (TM8-10) which consisted of approximately [redacted]% didecyl monooctyl benzene-1,2,4-tricarboxylate, [redacted]% dioctyl monodecyl benzene-1,2,4-tricarboxylate, [redacted]% trioctyl benzene-1,2,4-tricarboxylate and [redacted]% tris(decyl) benzene-1,2,4-tricarboxylate. Data have also been located on tris(2-ethylhexyl) 1,2,4-benzenetricarboxylic acid (TEHTM), a trimellitate with branched C8 side chains."

ECHA understands this as the hypothesis under which you make predictions for the properties listed above.

0.2 Information you submitted to support of the grouping and read-across approach

You have provided a read-across justification as a separate attachment in in IUCLID, Section 13. In addition, you provide the following information to support the read-across approach:

Target (registered) substance (TM8)

- Acute oral toxicity study (OECD TG 401); 2001; GLP; Rel. 1
- Acute dermal toxicity study (OECD TG 402); 2009; GLP; Rel. 2
- Bacterial reverse mutation assay (OECD TG 471); 2001; GLP; Rel. 1
- *In vitro* mammalian chromosome aberration test (OECD TG 473); 2001; GLP; Rel. 1
- Several QSAR predictions (see below); Rel. 2
- Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test (OECD TG 422; 'OECD TG 422 screening study'); 2001; GLP; Rel. 1

Source substance (TM8-10)

- Acute oral toxicity study (OECD TG 401); 1989; GLP; Rel. 2
- Acute dermal irritation/corrosion (OECD TG 404); 1989; Rel. 2
- Acute eye irritation/corrosion (OECD TG 405); 1989; GLP; Rel. 2
- Skin sensitisation (OECD TG 406); 1989; GLP; Rel. 2
- Bacterial reverse mutation assay (OECD TG 471); 1987; GLP; Rel. 2
- *In vitro* mammalian chromosomal aberration test (OECD TG 473); 2009; GLP; Rel. 2
- *In vitro* mammalian cell gene mutation test (OECD TG 476); 2009; GLP; Rel. 2
- 28-day oral repeated dose toxicity study (OECD TG 407); 2010; GLP; Re. 2
- 90-day oral repeated dose toxicity study (OECD TG 408); 2014; GLP; Rel. 2
- Pre-natal developmental toxicity study (OECD TG 414); 2010; GLP; Rel. 2

Furthermore, you provided information on toxicokinetics (OECD TG 417) on another source substance tri-(2-ethylhexyl)trimellitate (CAS 3319-31-1).

0.3 ECHA analysis of your grouping and read-across approach in light of the requirements of Annex XI, 1.5.

With regard to the proposed predictions ECHA has the following observations:

(i) Structural similarity and dissimilarities

You claim that *"Overall, the defined group is made up of substances consisting of esters of 1,2,4-tricarboxylic acid. Structural differences are limited to the carbon chain length of the side chains and, by analogy wit the phthalate estsrs, those with similar carbon chain lengths are expected to exhibit very similar properties.*

While other trimellitates show greater similarity with the substance, reliable data have been located only for 1,2,4-Benzenetricarboxylic acid, mixed decyl octyl ester (TM8-10) which consisted of approximately [redacted]*% didecyl monooctyl benzene-1,2,4-tricarboxylate,* [redacted]*% dioctyl monodecyl benzene-1,2,4-tricarboxylate,* [redacted]*% trioctyl benzene-1,2,4-tricarboxylate and* [redacted]*% tris(decyl) benzene-1,2,4-tricarboxylate. Data have also been located on tris(2-ethylhexyl) 1,2,4-benzenetricarboxylic acid (TEHTM), a trimellitate with branched C8 side chains."*

ECHA concludes that you have not addressed the obvious compositional and structural differences between the target and the source substances (mono constituent and multi constituent substances, respectively) in context of the read-across hypothesis. Furthermore, you did not explain why those differences would not lead to differences in the toxicokinetic profiles of target and source substances (see point (iv) below).

(ii) Physico-chemical properties

You state that *"The target substance and the structural analogue TM8-10 appear show no significant differences in their physico-chemical properties, being liquids of very low vapour pressure and water solubility and high partition coefficient."*

ECHA notes that the fact that physico-chemical parameters do not show significant differences may support the similar toxicokinetic and toxicity profile, but cannot be used alone to justify a prediction of properties related to human health in absence of other supporting information as described under (i), (iii), (iv) and (v).

(iii) Experimental data on systemic toxicity

ECHA notes that you have provided the following studies on sytemic toxicity performed with the target and source substances:

Target (registered) substance (TM8):

- OECD TG 422 screening study in rats;
  You derived a NO(A)EL of 30 mg/kg bw/day for female animals based on increased liver weight and reduced red blood cell count at 125 and 500 mg/kg bw/day. For male animals you derived a NOAEL of 125 mg/kg bw/d based on hepatocellular hypertrophy in the centrilobular region of the liver observed at 500 mg/kg bw/d. You indicated that no reproductive effects occurred at the highest dose tested of 500 mg/kg bw/day.

Source substance (TM8-10):

- 28-day repeated dose toxicity study in rats (OECD TG 407):
  You derived a NOAEL of 300 mg/kg bw/day based on hypertrophy of the adrenal gland in male animals at 1000 mg/kg bw/d;

- 90-d repeated dose toxicity study in rats (OECD TG 408):
  You derived a NOAEL of 500 mg/kg bw/day based on no adverse effects at this dose which was the highest dose tested; and

- Pre-natal developmental toxicity study (OECD TG 414);
  You derived a NOAEL for maternal toxicity of 300 mg/kg bw/day based on decreased body weight, reduced body weight gain, and reduced food consumption. For developmental toxicity you derived a NOAEL of 1000 mg/kg bw/d (highest dose tested); ECHA notes that you indicated significantly reduced foetal and litter weights.

ECHA notes that the source and target substances seem to have different toxicity profiles. More specifically, you have not made a detailed and systematic comparison of the toxicological findings of the provided OECD TG 422 screening study (with the registered substance) and the findings of the repeated dose toxicity studies and the pre-natal developmental toxicity studies (with the analogue substance). Furthermore, no attempt has been made to explain the lower NO(A)EL in the study conducted with the registered substance as compared to the NO(A)ELs of the studies conducted with the analogue substance. Furthermore, your claim of low absorption of phthalates in general after oral administration is in contradiction with the results of the OECD TG 422 screening study with the target substance as ECHA does not consider a NOAEL of 30 mg/kg bw/day as indicative of low absorption.

ECHA observes that the NO(A)EL obtained with the target substance in the OECD TG 422 screening study with regard to systemic toxicity is significantly different from those observed in the sub-acute and sub-chronic toxicity studies with the source substance. You have not explained how and why the properties of the potential more toxic target substance can be accurately predicted by using data obtained with a less toxic source substance.

ECHA concludes that the presented evidence in the data matrix does not support a similar or regular pattern of toxicity as a result of structural similarity. Therefore it cannot be verified that the presented information from analogue substance(s) can be used to predict properties of the registered substance.

(iv) Experimental data on mutagenicity

ECHA notes that you have provided the following information on genotoxicity performed with/on the target and source substances:

Target (registered) substance (TM8):

- Tests
  - Bacterial reverse mutation assay (OECD TG 471); negative
  - *In vitro* mammalian chromosome aberration test (OECD TG 473); negative

- QSAR predictions flagged as 'weight of evidence':
  - *"Genetic toxicity in vitro (Ames test) estimated via (Q)SAR Toolbox"*; negative
  - *"MultiCASE commercial model A2H for Ames test, Danish National Food Institute"*; negative
  - *"MultiCASE commercial model A61 for in vitro chromosomal aberrations (CHO), Danish National Food Institute"; negative*
  - *"MultiCASE model for Syrian Hamster Embryo (SHE) in vitro cell transformation, Danish National Food Institute"*; negative
  - *"MultiCASE model for unscheduled DNA synthesis (UDS) in Rat hepatocyte cells in vitro, Danish National Food Institute"*; negative

Source substance (TM8-10):

- Tests (flagged as 'weight of evidence' and 'read-across'):
  - Bacterial reverse mutation assay (OECD TG 471); negative
  - *In vitro* chromosomal aberrations in human lymphocytes (OECD TG 473); negative
  - *In vitro* mammalian cell gene mutation test (OECD TG 476); negative

ECHA notes that based on the provided information you conclude that "*The target substance and the structural analogue TM8-10 are not genotoxic*".

However, ECHA notes that for "*in vitro* gene mutation test in mammalian cells" you provided a test with the source substance, but no appropriate information on gene mutation in mammalian cells for the target (registered) substance. In light of the potential higher toxicity of the target (registered) substance compared to the source substance as explained above (see "(iii). *Experimental data on systemic toxicity*"), ECHA considers that you have not explained how and why the outcome of the *in vitro* gene mutation test in mammalian cells with the source substance can be used to predict the outcome of the same test for the target (registered) substance.

ECHA concludes that the presented evidence on *in vitro* gene mutation in mammalian cells does not support a similar or regular pattern of toxicity as a result of structural similarity. Therefore it cannot be verified that information for the proposed analogue substance(s) can be used to predict properties of the registered substance.

(v) Toxicokinetics

ECHA notes that you suggest a similar toxicokinetic behaviour leading to "*likelihood of common breakdown products*" for the phthalate esters in general based on various reviews of different phthalate esters by the Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Furthermore, ECHA notes that you have provided a toxicokinetic study on tri-(2-ethylhexyl)trimellitate (CAS 3319-31-1) and suggest based on the toxicokinetic data that the "*target substance is expected to be similarly poorly absorbed through the gastro-intestinal tract following oral administration. If absorbed, elimination is expected to be relatively rapid and to occur mainly via the urine as polar metabolites.*"

ECHA notes further that you did not provide factual evidence from the substance subject to this decision (target) to support the suggested similarities of the toxicokinetic bahaviour including common metabolites.

ECHA concludes that you did not address important aspects such as the toxicokinetics of the substances and their metabolic fate / (bio)tranformation and the resulting possible difference in the metabolite profile. Furthermore, you have not provided any information on how these toxicokinetic differences may impact the toxicity of the substances and thus affect the possibility to predict the properties of the registered substance from the data of the analogue substance. The provided explanation is not considered as valid to establish a scientific credible link between the structural similarity and the prediction. Therefore, it is not possible to verify the substances which are likely to govern the toxicity profiles of source and target substances. In the absence of such information there is not an adequate basis for predicting the properties of the registered substance from the data obtained with the source substance.

0.4 Conclusion on your read-across approach

ECHA considers that structural similarity alone is not sufficient for predicting toxicological properties. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation.

ECHA concludes that in view of the issues listed above it has not been demonstrated that the source and target substances have the same properties or follow a similar pattern with regard to studies on sub-chronic toxicity study (90-day), *in vitro* mammalian cell gene mutation study, pre-natal developmental toxicity study (first species) and extended one-generation reproductive toxicity study. Hence you have failed to meet the requirement of Annex XI, Section 1.5. that human health effects may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach).

In your comments following the procedure set out in Article 50(1) of the REACH Regulation, you have agreed that the read-across justification provided for the endpoints subject of the current draft decision contained insufficient detail for ECHA to be able to accept that adaptation from the standard information requirements.

ECHA notes your intention to update the read-across justification addressing the issues highlighted above in an update of the registration dossier. However, ECHA reminds you that such an update will only be evaluated after the deadline established in the present decision has passed.

Pursuant to Article 41(1)(b) of the REACH Regulation, ECHA concludes that the adaptation of the standard information requirements for the endpoints repeated dose toxicity, genetic toxicity, reproductive toxicity and developmental toxicity in the technical dossier based on the proposed read-across approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, ECHA rejects all adaptations in the technical dossier that are based on Annex XI, 1.5.

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

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

An "*In vitro* gene mutation study in 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 both these information requirements. Therefore, adequate information *on in vitro* gene mutation in mammalian cells needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a *in vitro* mammalian cell gene mutation test (OECD TG 476) with the analogue substance 1,2,4-benzenetricarboxylic acid, mixed decyl and octyl triesters (EC no 290-754-9) and a related justification. However, as explained above in Appendix 1, Section 0 of this decision, your adaptation of the information requirement is rejected.

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

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

Therefore, 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).

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same 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.

In the technical dossier you have provided a study record for a Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (according to OECD 422). However, this study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days.

In addition, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for a 28-day repeated dose toxicity study (OECD TG 407) and 90-d repeated dose toxicity study (OECD TG 408) with the analogue substance 1,2,4-benzenetricarboxylic acid, mixed decyl and octyl triesters (EC no 290-754-9) and a related justification. However, as explained above in Appendix 1, Section 0 of this decision, your adaptation of the information requirement is rejected.

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

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 4.1, October 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, the available oral study indicate a concern for systemic toxicity. More specifically, the OECD TG 422 screening study provided in the dossier indicate some toxicity that requires further information on repeated dose toxicity by the oral route. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

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

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.

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

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

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing (a) study record(s) for a pre-natal developmental toxicity study (OECD TG 414) with the analogue substance 1,2,4-benzenetricarboxylic acid, decyl octyl ester (EC no 290-754-9) and a related justification.

However, as explained above in Appendix 1, Section 0 of this decision, your adaptation of the information requirement is rejected.

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

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

According to 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 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

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

4. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

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

Pre-natal developmental toxicity studies (test method EU B.31./OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

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

- Based on an OECD TG 422 screening study performed with the registered substance and a pre-natal developmental toxicity study (OECD TG 414) performed with the analogue substance 1,2,4 -benzenetricarboxylic acid with mixed C8 and C10 linear side chains you conclude that *"These studies demonstrate that the substance does not impact developmental toxicity in rats."*

- Furthermore, you refer to preliminary results of a comparative analysis of data on pharmaceutical compounds that suggest that the 2nd species does not add significant information for the assessment of developmental effects (*Theunissen, P.T. et al. (2014) Reproductive Toxicol. 47: 27-32)*. Based on this information you conclude *"Therefore, referring to Regulation (EC) No. 1907/2006, Annex IX, 8.7.2 Column 2, performing a prenatal developmental toxicity study in a 2nd species is considered not to add new information for hazard assessment and therefore is scientifically and, considering concerns regarding the use of vertebrate animals for experimental purposes, morally unjustified."*

However, ECHA observes that at the tonnage band registered (1000 tonnes or more) information on pre-natal developmental toxicity in a second species is a standard information requirement according to Annex X, Section 8.7.2.. ECHA notes that this information is missing from the registration and cannot be substituted by a screening study or by generic arguments such as those provided by you.

Therefore, your adaptation of the information requirement is rejected.

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

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 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

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 second species (rabbit or rat) by the oral route.

5. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

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

The basic test design of an extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Further detailed guidance on study design and triggers is provided in the ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015).

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

a) The information requirement

In the technical dossier you have provided a study record for a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422). However, this study does not provide the information required by Annex X, Section 8.7.3., because it does not cover key elements, such as exposure duration, life stages and statistical power of an extended one-generation reproductive toxicity study.

More specifically, the main missing key elements are: 10 weeks pre-mating exposure duration, at least 20 pregnant females per group, and an extensive postnatal evaluation of the F1 generation. Therefore, your adaptation of the information requirement is rejected.

Hence, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint. Thus, an extended one-generation reproductive toxicity study according Annex X, Section 8.7.3. is required. The following refers to the specifications of this required study.

b) The specifications for the study design

Information from studies to be conducted before the extended one-generation reproductive toxicity study

The sub-chronic toxicity study shall be conducted before the extended one-generation reproductive toxicity study and the results from that study shall be used, among other relevant information, to decide on the study design of the extended one-generation reproductive toxicity study following ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015). The sub-chronic toxicity study may provide information on effects that is relevant for triggers (e.g. weight changes and histopathological observations of organs as indication(s) of one or more modes of action related to endocrine disruption which may meet the toxicity-trigger for extension of Cohort 1B or as evidence of specific mechanism/modes of action and/or neurotoxicity and/or immunotoxicity which may meet the particular concern criteria for developmental neurotoxicity and/or developmental immunotoxicity cohorts).

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015). Ten weeks exposure duration is supported also by the lipophilicity of the substance to ensure that the steady state in parental animals has been reached before mating. You state that "*the partition coefficient, determined using the HPLC method in accordance with EPA, OECD and EU test methods, has been determined as: Log10 Pow = 9.3 (T= 55 deg C).*"

The highest dose level shall aim to induce some toxicity to allow comparison of effect levels and effects of reproductive toxicity with those of systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

If there is no existing relevant data to be used for dose level setting, it is recommended that results from a conducted range-finding study (or range finding studies) are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Species and route selection

According to the test method EU B.56./ OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in 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 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

c) Outcome

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: Extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce some toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;

Currently, the extension of Cohort 1B and the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) are not requested. **However, the sub-chronic toxicity study (90-day) requested in this decision (request 2) and/or any other relevant information may trigger changes in the study design.** Therefore, the sub-chronic toxicity study (90-day) is to be conducted first and the study results submitted to ECHA in a dossier update by **21 December 2017**. If, on the basis of this update and/or other relevant information, a need for changes to the study design is identified, ECHA will inform you by **21 March 2018** (i.e. within three months after expiry of the 12-month deadline to provide the sub-chronic toxicity study (90-day)) of its intention to initiate a new decision making procedure under Articles 41, 50 and 51 of the REACH Regulation to address the design of the extended one-generation reproductive toxicity study. If you do not receive a communication from ECHA by **21 March 2018**, the request of the present decision for the extended one-generation reproductive toxicity study remains effective and you may commence the conduct of the study and the results will need to be submitted by the deadline given in this decision **22 June 2020.**

Notes for your consideration

When submitting the study results of the sub-chronic toxicity study (90-day) you are invited to also include in the registration update your considerations whether changes in the study design are needed (see also *ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.6 (version 4.1, October 2015)*).

Furthermore, after having commenced the extended one-generation reproduction toxicity study in accordance with the ECHA decision, you may also expand this study to address a concern identified during the conduct of it and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the changes in the study design must be documented. The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/ triggers must be documented.

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

"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 according to Annex IX, Section 9.2.1.3., column 2. You provided the following justification for the adaptation: *"In accordance with REACH Regulation 1907/2006/EC (Annex IX - 9.2.1.3 - column 2) simulation tests of biodegradation in soil do not need to be conducted as the substance can be regarded as biodegradable via common microbial pathways although the rate of degradation is likely to be limited due to limited bioavailability as a result of low water solubility."*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.2.1.3., column 2, because ECHA observes that in the registration dossier you have concluded that the substance is not readily biodegradable. In addition, based on how the uses have been reported in the technical dossier, ECHA considers that soil exposure cannot be excluded, e.g. Environmental Release Category (ERC) 8c, 8f, 9a and 9b. ECHA therefore considers that you have not demonstrated that soil exposure is unlikely.

Furthermore, ECHA notes that the registered substance has low water solubility (0.032 µg/L) and high partition coefficient (log Kow 9.3), indicating adsorptive properties. Consequently, soil simulation testing appears to be necessary.

ECHA notes that with the current information gaps, the Chemical safety Assessment (CSA) cannot be used to justify why there is no need to investigate further the degradation of the substance and its degradation products. Furthermore, ECHA considers that the information is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment as the PBT/vPvB status of the registered substance is unclear.

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

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) Aerobic and anaerobic transformation in soil (test method EU C.23. / OECD TG 307) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.3.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 3.0, February 2016) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-9 (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. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 307. Therefore, the test should be performed at the temperature of 12°C.

Simulation tests performed in sediment or in soil possibly imply the formation of non-extractable residues (NER). These residues (of the parent substance and/or transformation products) are bound to the soil or to the sediment particles. NERs may potentially be re-mobilised as parent substance or transformation product unless they are irreversibly bound 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 NERs as irreversibly bound residues. You are therefore requested to justify scientifically that the extraction method you will apply is appropriate to identify NERs as residues irreversibility bound to the soil.

In your comments according to Article 50(1) you stated that "[...] *Testing should therefore be limited to an aerobic sediment test. The Registrant is aware that an aerobic transformation test in aquatic sediment systems (OECD TG 308) is underway on TEHTM and is due to be reported later in the year. The outcome of this study can be expected to provide a valuable insight into the degradation behaviour of the alcohol esters of l,2,4-benzenetricarboxylic acid and the Registrant will await the outcome of this study prior to determining whether adaptation by a read-across approach would be justified in the case of the registered substance.".*

ECHA notes that the information mentioned in the comment according to Article 50(1) has not been provided yet. Hence, the compliance of your updated registration dossier with the information requirements for this endpoint will be examined by ECHA after the deadline set in the adopted decision has passed. ECHA reminds you that the assessment of the proposed read-across adaptation will be according to the rules set out in Annex XI, Section 1.5., and as further specified in the read-across assessment framework.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Aerobic and anaerobic transformation in soil (test method: EU C.23./OECD TG 307).

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

"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 according to Annex IX, Section 9.2.1.4., column 2. You provided the following justification for the adaptation: "*In accordance with REACH Regulation 1907/2006/EC (Annex IX - 9.2.1.2 & 9.2.1.4 - column 2) simulation tests of biodegradation in water and sediment do not need to be conducted as the substance can be regarded as biodegradable via common microbial pathways although the rate of degradation is likely to be limited due to limited bioavailability as a result of low water solubility.*"

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.2.1.4., column 2 because ECHA observes that in the registration dossier you have concluded that the substance is not readily biodegradable. In addition, based on how the uses have been reported in the technical dossier, ECHA considers that sediment exposure cannot be excluded, e.g. Environmental Release Category (ERC) 8c, 8f, 9a and 9b. ECHA therefore considers that you have not demonstrated that sediment exposure is unlikely.

Furthermore, ECHA notes that the registered substance has low water solubility (0.032 µg/L) and high partition coefficient (log Kow 9.3), indicating adsorptive properties. Consequently, sediment simulation testing appears to be necessary.

ECHA notes that with the current information gaps, the Chemical safety Assessment (CSA) cannot be used to justify why there is no need to investigate further the degradation of the substance and its degradation products. Furthermore, ECHA considers that the information is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment as the PBT/vPvB status of the registered substance is unclear.

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

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) Aerobic and anaerobic transformation in aquatic sediment systems (test method EU C.24. / OECD TG 308) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.4.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 3.0, February 2016) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-9 (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. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 308. Therefore, the test should be performed at the temperature of 12°C.

Simulation tests performed in sediment or in soil possibly imply the formation of non-extractable residues (NER). These residues (of the parent substance and/or transformation products) are bound to the soil or to the sediment particles. NERs may potentially be re-mobilised as parent substance or transformation product unless they are irreversibly bound by covalent bonds or incorporated into the biomass. The amount and kind of NERs 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 NERs as irreversibly bound residues. You are therefore requested to justify scientifically that the extraction method you will apply is appropriate to identify NERs as residues irreversibility bound to the sediment.

In your comments according to Article 50(1) you stated that "[...] *Testing should therefore be limited to an aerobic sediment test. The Registrant is aware that an aerobic transformation test in aquatic sediment systems (OECD TG 308) is underway on TEHTM and is due to be reported later in the year. The outcome of this study can be expected to provide a valuable insight into the degradation behaviour of the alcohol esters of l,2,4-benzenetricarboxylic acid and the Registrant will await the outcome of this study prior to determining whether adaptation by a read-across approach would be justified in the case of the registered substance.*".

ECHA notes that the information mentioned in the comment according to Article 50(1) has not been provided yet. Hence, the compliance of your updated registration dossier with the information requirements for this endpoint will be examined by ECHA after the deadline set in the adopted decision has passed. ECHA reminds you that the assessment of the proposed read-across adaptation will be according to the general rules of adaptation as set out in Annex XI, Section 1.5.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Aerobic and anaerobic transformation in aquatic sediment systems (test method: EU C.24./OECD TG 308).

Notes for your consideration

Before conducting the tests requested under sections 6 and 7 above you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4 and R.7.9.6 (version 3.0, February 2016) and Chapter R.11, Section R.11.4.1.1 (version 2.0, November 2014) on PBT assessment to determine the sequence in which the simulation tests are to be conducted and the necessity to conduct all of them. The order in which the simulation biodegradation tests are performed needs to take into account the intrinsic properties of the registered substance and the identified use and release patterns which could significantly influence the environmental fate of the registered substance.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when results of the tests detailed above is available. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

Once results of the requested simulation tests and Extended one generation reproductive toxicity study are available, you should consider whether there is a need to investigate further the bioaccumulation in aquatic organisms in order to fulfil the information requirements of section 9.3.2 of Annex IX, and if necessary, submit testing proposal for aquatic bioaccumulation. If it is concluded that the substance (or any of its degradation products) meets P ant T or vP properties further investigation on bioaccumulation would be necessary to conclude if the substance would meet PBT or vPvB properties or not.

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

The identification of the degradation products is a standard information requirement according to column 1, Section 9.2.3. of Annex IX of the REACH Regulation. Column 2 of Section 9.2.3. of Annex IX further states that the information does not need to be provided if the substance is readily biodegradable.

You have not provided any study record identifying the degradation products of the substance and, in addition, the technical dossier does not contain an adaptation which could meet the criteria of either the specific adaptation rules of Column 2 of Annex IX, section 9.2, or the general adaptation rules of Annex XI.

Furthermore, as concluded by you in the registration dossier, the substance is not readily biodegradable and consequently the identification of degradation products is required.
As explained fully in sections (6) and (7) above, ECHA considers that with the current information the CSA cannot be used to justify that there is no need to investigate further the degradation of the substance and its degradation products. ECHA notes further that the information requested here may be needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment.
As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

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

In your comments according to Article 50(1) you stated that "[...] *Testing should therefore be limited to an aerobic sediment test. The Registrant is aware that an aerobic transformation test in aquatic sediment systems (OECD TG 308) is underway on TEHTM and is due to be reported later in the year. The outcome of this study can be expected to provide a valuable insight into the degradation behaviour of the alcohol esters of l,2,4-benzenetricarboxylic acid and the Registrant will await the outcome of this study prior to determining whether adaptation by a read-across approach would be justified in the case of the registered substance.".*

ECHA notes that the information mentioned in the comment according to Article 50(1) has not been provided yet. Hence, the compliance of your updated registration dossier with the information requirements for this endpoint will be examined by ECHA after the deadline set in the adopted decision has passed. ECHA reminds you that the assessment of the proposed read-across adaptation will be according to the general rules of adaptation as set out in Annex XI, Section 1.5.

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

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

Notes for your consideration

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

9. Long-term toxicity to sediment organisms (Annex X, Section 9.5.1.)

"Long-term toxicity to sediment organisms" is a standard information requirement as laid down in Annex X, Section 9.5.1. 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.

ECHA notes that you have sought to adapt the long-term toxicity testing on sediment organisms using the following justification: "*REACH Regulation 1907/2006 Annex X, Section 9.5.1 requires that toxicity to sediment organisms be investigated if there are concerns regarding exposure. Sediment toxicity testing is not needed due to the limited bioavailability of the substance as a result of its physico-chemical properties. This is supported by reference to the properties of the analogous phthalate esters (esters of 1,2-dicarboxylic acid rather than an ester of 1,2,4-tricarboxylic acid) for which data are available.*"

In your proposed adaptation you claim that there is no need to investigate the effects on sediment organisms further because of lack of exposure, the physical-chemical properties of the substance and data on analogue substance (esters of 1,2-dicarboxylic acid rather than an ester of 1,2,4-tricarboxylic acid).

ECHA notes that in order for an adaptation of Annex X, 9.5.1. Column 1 provisions to be justified, you would have to demonstrate by means of the exposure assessment in Chemical Safety Report (CSR) that the conditions of an adaptation possibility (Substance-tailored exposure-driven testing, Annex XI Section 3) are fulfilled. In establishing this, in some cases and as explained in ECHA *Guidance on information requirements and chemical safety assessment* (R.7b, version 3.0, February 2016, Section R.7.8.7.), you may use the EPM as part of a weight-of-evidence to adapt the standard information requirement. However, according to ECHA *Guidance on information requirements and chemical safety assessment* (R.7b, version 3.0, February 2016, Section R.7.8.7.) the EPM cannot be used in a weight of evidence approach for substances that are highly insoluble and for which no effects are observed in aquatic studies. For such substances at least one sediment study has to be performed. ECHA notes that as is shown in the aquatic studies in the technical dossier no effects were observed in any of the aquatic studies performed. In addition, as the substance has a reported water solubility of 0.032µg/l at 25°C ECHA considers that long-term sediment testing is indicated for the registered substance.

ECHA notes that you have not demonstrated that available data would lead to the conclusion that the substance is or is not toxic to sediment organisms based on the analogue approach mentioned in your waiving statement (Annex XI, 1.5.) as there is no sediment data available for the proposed analogue in your read-across justification document. In fact, the present substance has a high potential to adsorb to sediment (log Kow 9.3). Therefore, as the standard information requirements for long-term sediment testing have not been adapted in a justified manner, testing is required.

Therefore, in this specific case, ECHA notes that you have not justified an adaptation.

In your comments according to Article 50(1) you stated that "[...] *As mentioned above, the Registrant is aware that an aerobic transformation test in aquatic sediment systems (DECD TG 308) is underway on TEHTM and is due to be reported later in the year. The outcome of this study can be expected to provide a valuable insight into the degradation behaviour of the alcohol esters of l,2,4-benzenetricarboxylic acid, in particular the resultant metabolites, and the Registrant will await the outcome of this study prior to determining whether adaptation by a read-across approach would be justified in the case of the registered substance.".*

ECHA notes that the information mentioned in the comment according to Article 50(1) has not been provided yet. Hence, the compliance of your updated registration dossier with the information requirements for this endpoint will be examined by ECHA after the deadline set in the adopted decision has passed. ECHA reminds you that the assessment of the proposed read-across adaptation will be according to the general rules of adaptation as set out in Annex XI, Section 1.5.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Sediment-water Lumbriculus toxicity test using spiked sediment (Test method: OECD TG 225).

Notes for your consideration

ECHA considers that in this case the Lumbriculus toxicity test using spiked sediment would be the most appropriate test to be used because of the substance properties. The test organism would feed from sediment particles and would therefore have an internal exposure.

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 31 March 2016.

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

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

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

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

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments.

ECHA referred the draft decision to the Member State Committee.

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

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-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 request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new test(s) is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.