EUROPEAN CHEMICALS AGENCY

Helsinki, 21 July 2017

Addressee: [redacted]

Decision number: CCH-D-2114363912-46-01/F
Substance name: 2,4,6-triisopropyl-m-phenylene diisocyanate
EC number: 218-485-4
CAS number: 2162-73-4
Registration number: [redacted]
Submission number: [redacted]
Submission date: 06.08.2014
Registered tonnage band: 100-1000T

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. **Vapour pressure (Annex VII, Section 7.5; test method: EU A.4/OECD TG 104) with the registered substance;**

2. ***In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. /OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102 with the registered substance;**

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

4. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3; test method: OECD TG 476 or TG 490) with the registered substance), provided that both studies requested under 2. and 3. have negative results;**

5. **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;**

6. **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;**

7. **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;**

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

9. **Identification of degradation products (Annex IX, 9.2.3.) using an appropriate test method;**

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

11. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: revise the environmental exposure estimation - use default release factors and other recommendations of ECHA Guidance R.16 and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA Guidance R.16 for estimation of environmental exposure;**

12. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health: provide a qualitative (semi-quantitative, if data are available) exposure assessment demonstrating the likelihood that effects are avoided for acute toxicity (inhalation), skin irritation, skin sensitisation, respiratory sensitisation and carcinogenicity for relevant exposure scenarios and detail the operational conditions and risk management measures ensuring that, and revise the risk characterisation accordingly.**

13. **Exposure assessment and risk characterisation (Article 14(6), Annex I, Section 5.1.1., in conjunction with Annex II, 0.1.2. and 8.2.2.2. (b) and Annex I Section 6.) for human health for workers via dermal route:**
    - further specify the type of glove material, thickness and breakthrough times;
    - further specify the type and quality of protective clothing.

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to IX 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 **28 July 2020**. 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/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.

Appendix 1: Reasons

0. Grouping of substances and read-across approach

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

- Skin sensitisation (Annex VII, Section 8.3)
- *In vitro* cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- *In vitro* gene mutation study in mammalian cells, if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2)
- Long-term toxicity on aquatic invertebrates (Annex IX, Section 9.1.5)

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 a property-specific context.

0.1 Description of the proposed grouping and read-across approach

You propose read-across from the substance toluene diisocyanate (TDI, EC 204-317-7, CAS 26471-62-5) (hereafter the 'source substance') to the registered substance 2,4,6-triisopropyl-m-phenylene diisocyanate (TRIDI, EC 218-485-4, CAS 2162-73-4) (hereafter the 'target substance') for each of the above-mentioned information requirements.

You provided the following description of the read-across in your registration dossier: "*Comparing the chemical structures of TRIDI and TDI it is apparent that they are closely related to each other (see Table 2). Both substances belong to the class of aromatic diisocyanates (possessing two isocyanate functional groups –N=C=O), which are localized at the 1st and 3rd position of benzene ring in TRIDI and can be either at 2nd and at 4th or at 2nd and at 6th position in TDI. The two substances differ in number and position of the alkyl substituent at the benzene ring. In TRIDI, isopropyl- (methylethyl) rests are localized at the 2nd, 4th and 6th positions, while only one methyl group is present at the benzene ring in TDI.*"

ECHA considers this as the hypothesis under which you make predictions for the properties listed above. You conclude that the analogue substance can be used to close data-gaps in the health hazard assessment of the target substance as the target and source substances share the following properties:

- Two isocyanate functional groups;
- Aromatic backbone structure, to which the isocyanate groups are covalently bound;

- Vicinal aliphatic side chain/s.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant proposes to amend the hypothesis for read-across. The category approach is more appropriate to justify similarity in mechanism/mode of action for (di)isocyanates as a group.*"

Furthermore, in your comments you propose to extend the read-across to include other category members 1,3-bis(1-isocyanato-1-methylethyl)benzene (TMXDI, EC 220-474-4, CAS 2778-42-9) and 4,4'-methylenedicyclohexyl diisocyanate (H12MDI, EC 225-863-2, CAS 5124-30-1), e.g. for the information requirements for genotoxicity. You indicate that the target and source substances share the following properties:

- Two isocyanate functional groups.

You conclude that the analogue substances can be used to close data-gaps in the hazard assessment of the registered (target) substance, as you consider the read-across approach is scientifically acceptable with high confidence based on your examination of the adequacy and scientific robustness of the provided read-across justifications and corresponding information using assessment elements (AE) of the ECHA Read-across assessment framework (RAAF).

ECHA acknowledges your intention to amend the hypothesis for read-across. ECHA notes that supporting (experimental) evidence has not been provided yet. ECHA analyses your comment in section (0.3(), below.

0.2 Support of the grouping and read-across approach

You have provided a read-across justification as a separate attachment in the registration named "[redacted]".

You have performed a search for structurally similar chemicals and concluded "*In these data bases the most similar chemical 2,4 + 2,6-Toluenediisocyanate (CAS No. 26471-62-5) with a similarity level of [redacted]% to TRIDI was identified, based on chemical structure similarity only (fingerprints, Tanimoto distance).*" Hence, ECHA notes that you performed a read-across based on an analogue approach.

In your comment(s) in the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant proposes to amend the respective sections of the read-across statement adding an explanation why established OEL values for aromatic diisocyanates could play an important role for the assessment of safe exposure levels for health effects of the target substance. Additionally, the Registrant proposes to prepare a read-across by using a category approach including publically available experimental toxicity data on diisocyanate source substances which are deemed suitable for read-across.*"

ECHA acknowledges your intention to include OEL values and publicly available empirical data to strengthen the read-across. ECHA notes however, that this substantiating information mentioned in your comment according to Article 50(1) has not been provided yet.

With respect to toxicological behaviour you provided a comparison of the toxicity of TRIDI and TDI which is based on study summaries of studies performed with TRIDI for acute oral and inhalation toxicity, skin irritation and eye irritation, QSAR predictions for skin sensitisation, repeated dose toxicity, genetic toxicity and carcinogenicity. For TDI, you have

provided study summaries of studies on sensitisation, repeated dose toxicity, developmental and reproductive toxicity, genetic toxicity and carcinogenicity. Based on this information, you classified the registered substance for acute inhalation toxicity 1, skin irritation 2, respiratory sensitisation 1, skin sensitisation 1, carcinogenicity 2, and STOT SE 3 (respiratory tract irritation).

With respect to ecotoxicological behaviour you provided a comparison of the ecotoxicity of TRIDI and TDI which is based on study summaries of studies performed with TRIDI for acute toxicity to fish and toxicity to aquatic microorganisms, QSAR predictions for long-term toxicity to fish, long-term toxicity to aquatic invertebrates and toxicity to algae. For TDI, you have provided study summaries of studies on acute toxicity to fish, long-term toxicity to fish, acute toxicity to invertebrates, long-term toxicity to invertebrates, toxicity to algae and toxicity to aquatic microorganisms. ECHA notes that you conclude "not to use the TDI data for the ecotoxicological endpoints." You have concluded not to classify the registered substance for the environmental hazards for which TDI is classified.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant proposes to conduct a hydrolysis study to re-evaluate if read-across is appropriate for ecotoxicological endpoints. Decisions on the read-across approach (usage of read-across data for ecotoxicological endpoints) will be based on the outcome of this study.*" ECHA acknowledges your intention to investigate the possibility to use read-across for addressing standard ecotoxicological endpoints. However, for the time being, it is not clear whether or not you will indeed use a read-across approach for addressing ecotoxicological endpoints and how the hydrolysis study would support such a read-across.

The information provided in your comments is not sufficient at this point to allow your adaptation of the information requirements to be accepted, as further described in sections below.

0.3 ECHA analysis of the 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) Explanation on why and how the structural similarities allow predictions

In order to meet the provisions in Annex XI, Section 1.5. to predict human health and ecotoxicological effects from data for a reference substance within the group by interpolation to other substances in the group, ECHA considers that structural similarity alone is not sufficient. 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. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*As described above, the Registrant proposes to amend the read-across statement, following a category approach with a group of (di)isocyanates which are deemed suitable to support the read-across. The reactivity, possible metabolites or degradation products of the source substances ((di)isocyanates as a group) and the target substances as well as their toxicity profile will be linked to the differences and the similarities in their structures. Furthermore, a mechanistic explanation (supported by experimental data, if possible) for similar toxicity will be added for each endpoint under consideration.*"

ECHA acknowledges your intention to provide an updated read-across approach. ECHA notes that (experimental) data mentioned in your comment according to Article 50(1) to substantiate the amended read-across approach has not been provided yet.

ECHA notes that you did not yet justify how the differences between the newly proposed source substances H12MDI and TMXDI would not influence the predictions: H12MDI is a fully aliphatic compound and lacks (vicinal) side chains. In TMXDI, the influence of the aromatic backbone on the isocyanates is de-coupled by an aliphatic structure; furthermore, as there are no vicinal side chains, the steric environment in the molecule is different.

ECHA notes the following short-comings of your approach:

1. Different potency of irritating property

The source substance TDI exhibits a LOAEC for acute inhalation toxicity of 0.36 mg/m^3 whereas the LOAEC of the target (registered) substance is 20 mg/m^3. Furthermore, the source substance is classified as eye irritant, while the target substance is not classified.

You indicated that "*TRIDI produced only slight iris/conjunctivae reactions which were seen in animals after 1 hour after application of the test substance. Assuming eye irritating properties of diisocyanates depend on a corresponding amine (which are known to be corrosive) which evolve through hydrolization in lachrymatory fluid, it can be speculated that isocyanate groups by TRIDI do not hydrolyse so rapidly as by TDI exerting their irritation effect*".

The significant difference in local toxicity demonstrates differences in reactivity of the isocyanate groups, which might be attributable to other functional groups/side chains in their vicinity and resulting sterical influences, as well as direct electronic effects from the aromatic backbone.

This difference in reactivity may also be important when assessing the (systemic) toxicity of the registered substance, and you did not address how this would influence the (systemic) toxicity.

Furthermore, compared with TDI, the lower irritating/corrosive properties for TRIDI will allow higher concentrations/doses, which can be administered in studies designed to detect (systemic) effects, without exerting local effects or cytotoxicty.

To ECHA's understanding, you assume that TDI presents a worst case for systemic toxicity and consequently you use the TDI data for the prediction of systemic effects. However, as the above arguments demonstrate, systemic effects by the target substance TRIDI cannot be ruled out or may even be higher than for the source substance, since its (local) reactivity is different from that of the source substance TDI. Thus, ECHA does not regard TDI as a worst case concerning systemic availability.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that

- "*The Registrant proposes to revise the read-across statement. Differences in the reactivity of the target and the source substances with regard to their influence on systemic toxicity will be discussed. This applies for all substances the Registrant proposes to include in the read-across approach as mentioned in section 0.1 above.*"

- "*The Registrant proposes read-across to other (di)isocyanates, following the category*

approach. The Registrant will show that TRIDI as the most lipophilic substance of the group possesses lower reactivity towards mucous membranes, displaying in lower reactivity of the isocyanate groups probably due to the vicinity of isopropyl groups which represent a sterical hindrance for the isocyanate groups. The lower reactivity towards mucous membranes could mean a lower reactivity per se to the biomolecules, probably leading though to similar effects but with the lower strength."

- *"The Registrant proposes to amend corresponding sections in the read-across statement, improving the explanation also by comparing and evaluating systemic toxicity effects of further (di)isocyanate substances which the Registrant proposes to include in the read-across as mentioned in section 0.1 of this document."*

ECHA acknowledges your intention to improve the read-across. ECHA notes that substantiating information mentioned in your comments according to Article 50(1) with respect to "*Different potency of irritating property*" has not been provided yet. ECHA can therefore not analyse the proposed read-across yet.

2. Structural differences

While you substantiated the structural analogy by several models, the differences in aliphatic side-chains neighboring the isocyanate functional groups and their location on the aromatic ring are not addressed in detail for systemic toxicity of the substance, and the consequences, especially for systemic toxicity, are indicated to be negligible, while no data has been presented to substantiate this. Therefore you have not demonstrated that TRIDI has no systemic toxicity.

In your comments according to Article 50(1) of the REACH Regulation you stated that "*The Registrant proposes to follow a category approach and will amend corresponding sections in the read-across statement, improving the explanation by addressing details in the structural differences of dissimilar (di)isocyanates. Since the underlying effect is the high reactivity of isocyanates groups toward biomolecules resulting in severe adverse effects (respiratory tract is the target organ of very structurally dissimilar isocyanates), structural differences between (di)isocyanates do not play a significant role for the validity of the prediction by read-across.*" Furthermore, you specified that "*Since a high reactivity of isocyanate groups to biomolecules (i.e. proteins and DNA, affecting their structure and function) resulting in a variety of adverse effects is the underlying mode of action of (di)isocyanates as a group, structural differences do not influence the read-across validity because the functional isocyanate with its effect on functionality of biomolecules is thought to be of greater importance in this case than the structural differences (a detailed read-across justification will be provided via update of the registration dossier).*"

ECHA agrees that the isocyanate group could be highly reactive. However, ECHA disagrees that structural differences would not influence the reactivity of the isocyanate group, and hence, the validity of the read-across. With regard to your comment(s) on the draft decision, ECHA notes that no substantiating information (*e.g.* in form of experimental studies) has been included in the amended read-across approach with additional category members that would support your hypothesis. ECHA notes that you did not analyse potential differences in reactivity at all.

ECHA notes that differences in reactivity of diisocyanates are the result of their structural differences. More specifically, aromatic diisocyanates (e.g., TDI) appear to be of higher reactivity compared to diisocyanates in which the isocyanate group is bound by an aliphatic structure (e.g., H12MDI, TMXDI). Furthermore, TDI appears more reactive than TRIDI probably due to electronic effects, with less de-activating inductive effects than in the case

of TRIDI. Furthermore, aliphatic side-chains, which in TRIDI are vicinal to the reactive isocyanate groups, might lead to 'sterical shielding' with reduced reactivity of the isocyanate group. The differences in (local) reactivity are demonstrated by the differences in pulmonary irritation and chromosomal aberrations in the technical dossier and comments to this decision.

With regard to systemic availability, the high local reactivity of the aromatic di-isocyanate source substance limits both dosing and systemic availability. ECHA notes that you did not provide information on systemic availability of the target substance. However, due to the lower reactivity of the target substance, it can be dosed higher than the source substance without exerting dose-limiting local effects. Hence, the registered substance might become systemically available to a significant extent.

Therefore, ECHA concludes that the use of aliphatic isocyanate source substance (e.g., H12MDI) does not allow predictions for the target substance for local and systemic toxicity because of lower reactivity of the isocyanate group of the source substances. The use of sterically uninhibited aromatic diisocyanates as source substances (e.g. TDI) does not allow predictions for systemic effects due to dose-limiting effects of the more reactive uninhibited aromatic source substance.

3. Missing information on repeated dose toxicity and reproduction toxicity with the registered substance

In the registration dossier, no information is provided on repeated dose toxicity or reproductive toxicity studies of any duration with the registered substance, which longer-term studies from source substances could be referenced and compared to. Furthermore, you fail to explain why reproductive organs would be less sensitive than other organs receptive through systemic availability.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant proposes to amend the read-across statement, improving the explanation. The proposed category approach of read-across (please refer to section 0.1 above) will enable to assess toxicity to reproductive organs, reproductive and developmental function of (di)isocyanates as a group and to conclude whether read-across to TRIDI is plausible.*"

ECHA notes that no substantiating (experimental) evidence mentioned in your comment according to Article 50(1) has been provided yet.
ECHA notes that all allegations and claims of the read-across justification need to be supported with reliable (experimental) evidence confirming such claims. In the absence of such, *e.g.* studies with repeated dosing investigating specific parameters of certain endpoints (OECD TG 422,), it may be difficult to prove that the proposed read-across adaptation is adequate to predict certain related properties of the registered substance.

4. Different toxicity for toxicity to algae and aquatic invertebrates based on QSAR estimations

ECHA notes that you conclude yourself "*not to use the TDI data for the ecotoxicological endpoints.*"

ECHA agrees to above mentioned statement and concludes further that you have not addressed the structural differences between the source substances and the target substance, and did not explain why those differences would not lead to differences in the (eco)toxicity profile of target and source substances. The provided explanation is not

considered as valid to establish a scientifically credible link between the structural similarity and the prediction.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that no link could be established between the structural similarity and the prediction by QSAR estimation. Based on physico-chemical properties, TRIDI and TDI seemed to behave differently in the aquatic environment.* [...] *As already pointed out in section 0.2, the Registrant proposes to conduct a study on hydrolysis at first. Based on the outcome of the study (behaviour at different pH values and occurrence of hydrolysis products) the applicability of read-across for ecotoxicological endpoints will be re-evaluated.*"

As indicated above, ECHA acknowledges your intention to investigate the possibility to use read-across for addressing standard ecotoxicological endpoints. However, for the time being it is not clear whether or not you will use the read-across approach for addressing ecotoxicological endpoints and how the hydrolysis study would support such read-across. Without any factual evidence, ECHA cannot assess whether such hypothetical read-across would be acceptable or not. Thus, the information provided in your comments is not sufficient to allow a prediction of the relevant environmental properties of the target substance at this stage.

0.4 Conclusion on the read-across approach

ECHA considers that structural similarity alone is not sufficient for predicting (eco)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 notes that in view of the issues listed above it has not been demonstrated that the source and read-across substances have the same properties or follow a similar pattern with regard to studies on sensitisation, repeated dose toxicity, developmental and reproductive toxicity, genetic toxicity, growth inhibition study on aquatic plants and long-term toxicity to aquatic invertebrates. ECHA concludes that you have failed to meet the requirement of Annex XI, Section 1.5. that human health and ecotoxicological effects may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach).

Pursuant to Article 41(1) of the REACH Regulation, ECHA concludes that the adaptation of the standard information requirements for the endpoints sensitisation, repeated dose toxicity, genetic toxicity, toxicity to reproduction, growth inhibition study on aquatic plants and long-term toxicity to aquatic invertebrates 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 those adaptations in the technical dossier that are based on Annex XI, 1.5.

Detailed endpoint-specific reasons to support rejecting the adaptations of in vitro gene mutations in bacteria, in vitro cytogenicity in mammalian cells and in vitro gene mutations in mammalian cells are documented in the endpoint-specific sections below.

ECHA decided that, for the time being, the endpoints of sensitisation, repeated dose toxicity, developmental toxicity and reproductive toxicity are not within the scope of this compliance check.

1. Vapour pressure (Annex VII, Section 7.5.)

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.

"Vapour pressure" is a standard information requirement as laid down in Annex VII, Section 7.5 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.

ECHA observes that you first determined the vapour pressure of the registered substance by means of Differential Scanning Calorimetry (DSC) according to the EU test method A.4. "Dynamic Method". However, the experimentally determined vapour pressure value at 20 °C was 7.9×10^{-4} mbar, which is outside the range of applicability for DSC measurements recommended in the above mentioned test method. Consequently, you reported in IUCLID section 4.6 an estimation of the vapour pressure according to the Grain Watson correlation which is described in the Appendix 1 of the EU test method A.4 as well as in the Annex of the OECD Guideline 104. The method is applicable over the pressure range from 10^5 Pa to 10^{-5} Pa and provided as a result a value of the vapour pressure of 1.8×10^{-6} atm at 20 °C, corresponding to 0.19 Pa.

Furthermore, ECHA notes that you reported as supporting study a (Q)SAR calculation with the US-EPA software EPIWIN/MPBPWIN (v 1.43) where the Antoine Method gave a result of 0.0118 Pa, the Mackay Method of 0.0351 Pa and the Modified Grain Method of 0.019 Pa.

ECHA notes that calculated values by use of the Grain Watson correlation, as described in Appendix 1 of EU test method A.4 and in the Annex of the OECD guideline 104, can be used either for deciding which of the experimental methods is appropriate or for providing an estimate or limit value in cases where the experimental method cannot be applied due to technical reasons. However, ECHA observes that you have not followed the estimation with an experimental measurement while several measurement methods are available and might be appropriate, as recommended in the two above mentioned test methods/guidelines. Furthermore, as indicated in ECHA's Guidance on information requirements and chemical safety assessment, Chapter R.7a, section R.7.1.5, (Q)SAR approaches may be used only if determination by experiment is not possible. ECHA also observes that the estimations differ by one order of magnitude (i.e. 0.19 Pa and 0.019 Pa). Therefore, ECHA concludes that the information you have provided does not fulfil the information requirements for this endpoint since greatly differing estimated values have been provided while a measured value could have been determined. Therefore the requirements of Annex XI, Section 1.3 have not been met as results are not adequate for the purpose of risk assessment. Thus, it is necessary to obtain a reliable measurement of the vapour pressure of the registered substance considering the relevance of the vapour pressure as a key physicochemical parameter for hazard and exposure assessment.

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.

You shall have particular regard for the recommended range of applicability of each measuring method.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that the information provided on this*

endpoint for the registered substance in the technical dossier does not meet the information requirement. Conclusion: The Registrant proposes to conduct the test according to the test method EU A.4/OECD TG 104".

ECHA acknowledges your agreement to the request set out in this decision.
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: Vapour pressure (test method: EU A.4./OECD TG 104).

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

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.

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement. According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA.

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

You have provided a test according to OECD TG 471 and GLP from the year 1990 with an assigned reliability score of 2. The test used four different strains of S. typhimurium TA 1535, TA 1537, TA 98 and TA 100 and it did not include tests with strains S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101). In assessing whether equivalent data according to the criteria in Annex XI, 1.1.2. of the REACH Regulation was provided in this case, it is important to note, that this substance's suspected modes of action based on the structure of the substance, crosslinking, is not covered by the choice of strains in the above mentioned test. Hence, there is a concern which is not covered by the test provided in the registration.However, since the test was conducted, significant changes have been made to OECD TG guideline 471 so that additionally testing with S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101) is now required. Therefore, the provided study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in point 2 of Annex XI, Section 1.1.2. of the REACH Regulation.

The registered substance's potential to induce gene-mutations by crosslinking should be investigated by using the 5th strain in the Ames test. Furthermore, reliable test results for bacterial gene mutation and mammalian cytogenicity are the basis to conclude whether a test on mammalian gene mutation is required.

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

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant proposes to amend the technical dossier and the read-across justification for this endpoint. The Registrant agrees that a test in a fifth strain is missing and proposes to conduct a study with one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.*" You further commented that ECHA should have considered a QSAR prediction, which had been assigned as key study under a different endpoint, and a supporting study with the analogous substance TDI.

ECHA acknowledges your agreement to the request set out in this decision. ECHA notes that your conclusion from the QSAR prediction "*All chemicals in the category possessed the same DNA binding mechanism and the same structural alerts (isocyanate group) which can be trigger of genotoxicity events*" supports the concern for bacterial gene mutation in a fifth strain, which is not covered by existing data. The lower reactivity of the registered substance as compared to TDI remains to be investigated further. Furthermore, the supporting study with the analogous substance TDI does not include a fifth bacterial strain E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

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 bacterial reverse mutation test (test method EU B.13/14. / OECD TG 471) is appropriate to address the standard information requirement of Annex VII, Section 8.4.1. of the REACH Regulation.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to complete the following information derived with the registered substance subject to the present decision: Bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

3. *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 according to Annex XI, Section 1.5. of the REACH Regulation by providing the following information:

1. (Q)SAR Toolbox prediction based on read-across: Negative prediction of chromosomal aberration for 2,4-diisocyanato-1,3,5-tri(propan-2-yl)benzene;
2. Study summary of a publication on chromosome aberrations in cultured human lymphocytes performed with the analogues substance toluene diisocyanante (CAS

number [redacted]
3. Document: [redacted]
4. Estimation of toxic hazard for 2,4,6-triisopropyl-m-phenylene diisocyanate using Software Tool TOXTREE (v2.1.0).

QSAR Toolbox prediction on read-across

ECHA notes that you have provided as key information a "OECD QSAR toolbox prediction based on read-across" to fulfil the standard information requirements for *in vitro* cytogenicity study in mammalian cells. You have further indicated in IUCLID under "study result type" that the provided information is "read-across based on grouping of substances" (category approach). Hence, ECHA is evaluating your approach according to the criteria of Annex XI, Section 1.5.

ECHA observes that, in the QSAR Toolbox prediction report, you did not clearly establish why structural similarity among the category members could constitute an element according to which properties of the registered substance could be predicted from the category members. Further, ECHA notes that no information on the allowed structural differences among the category members is included in the prediction report. According to information provided in the appendix 1 of the report, significant structural differences are observed among the analogue substances. The impact of these considerable differences in the chemical structures of the category members on the possibility to predict properties of the registered substance has not been discussed or addressed in the justification.

ECHA notes that your prediction is based on the result with 4 analogue substances[2] with 3 positive and 4 negative results for "chromosome aberration" and the confidence for the prediction is 57%. You concluded that the prediction for the registered substance is "negative". However, you did not discuss the validity of this conclusion. Furthermore, you did not provide information on the tests (e.g., type of test method, type of cells used), the test conditions (e.g., substance concentrations, metabolic activation) and details of the results.

Hence, the information you provided does not allow concluding that human health effects (*in vitro* chromosomal aberration) for the registered substance can be predicted from the data of the reference substances as required in Annex XI, Section 1.5 of the REACH Regulation.

In your comments on the draft decision according to Article 50(1) you agree "*that such a prediction cannot be accepted.*"

Read-across to toluene diisocyanate

You have provided as supporting information a study summary for a test on chromosome aberrations in cultured human lymphocytes (according to OECD TG 473) performed with the analogue substance TDI (CAS number [redacted]) with ambiguous results with and without metabolic activation. You have further provided a document to justify your read-across.

[2] Two of which are almost identical:
- toluene diisocyanate, commercial grade (2,4 (80%)- and 2,6 (20%)-) (CAS 26471-62-5)
- 2,4-toluene diisocyanate (CAS 584-84-9)

However, as explained above in Appendix 1, section 0 of this decision, this read-across adaptation of the information requirement is rejected.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you "*propose(s) to follow the category approach also for this endpoint, so that it will be possible to assess chromosome aberration potential in vitro of (di)isocyanates as a group*", giving two examples of further category members, which are negative in the chromosomal aberration test. You further stated that "*The registrant proposes to cover the endpoint using read-across data from other diisocyanates. Since the majority of (di)isocyanates induce chromosome aberrations, a certain chromosome aberration potential in vitro may also be concluded for TRIDI. The positive results demonstrate clearly, that structurally dissimilar diisocyanates are almost all positive in the chromosome aberration test. Therefore, also TRIDI should be considered as a substance possessing chromosome aberration potential in vitro, too. However, since the results of all in vivo tests for all proposed source substances are negative, it can be concluded that (di)isocyanates are not genetically toxic substances in vivo and, therefore, the results of in vitro studies do not correlate with the results of the in vivo studies, the latter being of higher value. Thus, an additional in vitro test, i.e., the requested cytogenicity study in mammalian cells or in vitro micronucleus study with the registered substance, will not provide additional result that would change this conclusion (disregarding of a potential positive or negative result).*"

ECHA notes that due to the structural differences of the source substances and the registered substance, a relevant difference in local reactivity can be observed between aromatic isocyanates, aliphatic isocyanates, and isocyanates with vicinal side chains (see section 0.3(2)). ECHA notes further that substantiating information is missing on why predictions are possible between structurally highly differeing di-isocyanates, *i.e.* from sterically unshielded di-isocyanates to the sterically shielded and inductively de-activated aromatic di-isocyanate target substance.

ECHA notes that, in the two newly proposed category members, the isocyanate functional group is linked to an aliphatic side-chain or backbone, whereas the registered substance is an aromatic di-isocyanate. You explain that "*the cyclic structures of hexyl moieties probably induce the electron-releasing inductive effect on the isocyanate moiety so that the reactivity of isocyanate group is strongly affected leading also to the negative response in the chromosome aberration test.*" ECHA agrees that the reactivity of aromatic di-isocyanates is different from aliphatic di-isocyanates, which exhibit a lower reactivity even in the absence of any sterical shielding (H12MDI). Therefore, a negative *in vitro* test result from an aliphatic source substance is insufficient to predict negative results *in vitro* for the aromatic target substance. ECHA notes further that substantiating information is missing on why predictions are possible from (sterically partially) shielded aliphatic di-isocyanates, to the sterically shielded aromatic di-isocyanate target substance. Thus, ECHA concludes that for this endpoint, there is no basis to predict effects, or their absence, for aromatic di-isocyanates from di-isocyanates covalently bound to an aliphatic structure.

In the case of aromatic isocyanates, the source substances are di-isocyanates with reactive isocyanate functional groups. The vicinal isocyanate functional groups in the registered substance are sterically shielded by the isopropyl groups. ECHA agrees with you that, in an *in vitro* test, a positive result for the registered substance cannot be ruled out. For the conditions *in vivo*, the high local reactivity of aromatic source substances limit the dosing and consequently, the bone marrow might not have been reached. ECHA notes that you did not provide information if the bone marrow was reached by the source substance. However, and in any case, due to the lower reactivity of the target substance, the latter can be dosed higher than the source substances without exerting dose-limiting local effects. Therefore,

the target substance may become systemically available reaching the bone marrow. Hence, the negative information on *in vivo* clastogenicity of the source substance cannot be considered appropriate to predict the absence of effects of the target substance.

Therefore, the clastogenicity of the target substance should be clarified through an *in vitro* study with the target substance as requested below. In the event of a positive result from such an *in vitro* study, performance of an *in vivo* cytogenicity study has to be considered, to clarify the concern.

TOXTREE

You attached a document named "Estimation of toxic hazard for 2,4,6-triisopropyl-m-phenylene diisocyanate using Software Tool TOXTREE (v2.1.0)" to Section 13 of IUCLID. In this document you conclude that: "*According to the modelling results of Toxtree, at least one structural alert was identified for 2,4,6-triisopropyl-m-phenylene diisocyanate, which might induce positive response in in-vivo micronucleus assay.*"

ECHA notes that the provided information indicates a concern for cytogenic effects based on one structural alert identified in the registered substance.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that provided TOXTREE prediction indicates a concern for cytogenic effects based on one structural alert identified in the registered substance and therefore cannot be accepted.*" and "*The Registrant is intended to use the prediction by TOXTREE only as supporting piece of evidence that (di)isocyanates as a group induce chromosome aberrations in mammalian cells in vitro.*"

ECHA acknowledges your comment according to Article 50(1).

Conclusion

For the reasons listed above, ECHA considers that your adaptation does not allow concluding that human health effects (*in vitro* chromosomal aberration) for the target substance can be predicted from the data of the source substances. As a consequence, ECHA is of the opinion that this information, as currently provided, does not constitute relevant information in the context of a read-across approach intended to indicate the presence or absence of the dangerous property addressed by the endpoint under consideration. As a consequence, ECHA is of the opinion that this information, as currently provided, does not meet the requirements according to Annex XI of the REACH Regulation. 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 *in vitro* mammalian chromosome aberration test (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).

Notes for your consideration:

In case of a positive outcome of the *in vitro* clastogenicity study, you should submit a testing proposal in accordance with Annex IX, Section 8.4.

4. *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 so far contains negative results for the first of these information requirements. ECHA notes further that the registration dossier does not contain appropriate study records for the second information requirement. 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 provided that both studies requested under 2. and 3. have negative results

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing the following information:

1. (Q)SAR Toolbox prediction (negative) based on read-across: Prediction of Gene mutation for 2,4-diisocyanato-1,3,5-tri(propan-2-yl)benzene
2. Study summary of a publication on a L5178Y Mouse Lymphoma Cell Forward mutation assay (according to OECD TG 476) performed with the analogue substances 2,4-toluene diisocyanate and 2,6- toluene diisocyanate (CAS numbers 584-84-9 and 91-08-7).
3. Document: [redacted]

QSAR Toolbox prediction on read-across

ECHA notes that you have provided as key information a "OECD QSAR toolbox prediction based on read-across" to fulfil the standard information requirements for *in vitro* gene mutation study in mammalian cells. You have further indicated in IUCLID under "study result type" that the provided information is "read-across based on grouping of substances (category approach). Hence, ECHA is evaluating your approach according to the criteria of Annex XI, Section 1.5.

ECHA observes that the provided QSAR prediction is for *in vitro* gene mutation in bacteria and not for *in vitro* gene mutation in mammalian cells. Hence, the prediction does not address the endpoint of Annex VIII, Section 8.4.3. of the REACH Regulation and the adaptation is rejected.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*This study (prediction) does not belong to this endpoint but it*

belongs to the mutagenicity in bacterial strains (see above section 2.). The study is flagged as "key" by mistake. It should be "supporting" for the endpoint Annex VIII, Section 8.4.1.: mutagenicity in bacterial strains."

ECHA notes that the information mentioned in your comment has been considered under request 2. above, *bacterial gene mutation* (REACH Annex VII, Section 8.4.1.).

Read-across to 2,4-toluene diisocyanate and 2,6- toluene diisocyanate

You have provided as supporting information a study summary for a gene mutation test in mouse lymphoma cells (according to OECD TG 476) performed with the analogue substances 2,4- and 2,6-toluene diisocyanante (CAS number [redacted]) with positive results with and without metabolic activation. You have further provided a document to justify your read-across.

As explained above in Appendix 1, section 0 of this decision, this read-across adaptation of the information requirement is rejected.

Furthermore, in the document "[redacted]" which you provided as attachment to IUCLID Section 13 it is concluded that "*Based on available data on genetic toxicity potential for TDI and for TRIDI it can be concluded that TRIDI is very likely to be "genotoxic" because of isocyanate groups which are known to react with DNA and form covalent adducts leading to mutation ([redacted], 2001)."*

ECHA notes that the provided information indicates a concern based on functional groups known to form DNA-adducts and, subsequently, mutations. In contrast, you conclude that the registered substance is not mutagenic. Therefore, ECHA rejects the read-across hypothesis as insufficient to conclude on TRIDI's mutagenic properties.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The registrant proposes to cover the endpoint using read-across data from other diisocyanates. Since a lot of (di)isocyanates induce mutations in in vitro test systems, a certain mutagenicity potential in vitro can also be concluded for TRIDI. However, since all the results of in vivo tests with the proposed source substances are negative (please refer to table 1 of Annex I), it can be concluded that (di)isocyanates are not genetically toxic substances in vivo and, therefore, the results of in vitro studies do not correlate with the results of in vivo studies, the latter being of higher value. Thus, an additional in vitro test, i.e., the requested in vitro gene mutation study in mammalian cells with the registered substance, will not provide additional result that would change this conclusion (disregarding of a potential positive or negative result).*"
ECHA notes that you have provided the same (in essence) comment with respect to request 3, above. Therefore, ECHA refers to its response to your read-across comment on request 3., above. ECHA considers that those considerations and conclusion why the prediction cannot be made are valid also for the current endpoint addressed in this section. Therefore, in analogy to section 3, the mammalian mutagenicity of the registered substance should be clarified through an *in vitro* study with the registered substance as requested below.

As explained above and under section 3, 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 test – *hprt* test (OECD TG 476) and the *in vitro* mammalian cell gene mutation test – Mouse lymphoma assay (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) provided that both studies requested under 2. and 3. have negative results.

Notes for your consideration:

In case of a positive outcome of the *in vitro* mammalian gene mutation study, you should submit a testing proposal in accordance with Annex IX, Section 8.4.

5. 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 VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for toxicity to aquatic algae (OECD TG 201) with the analogue substance(s) 2,4-/2,6-Toluene diisocyanate (80:20) (EC no 247-722-4).

However, ECHA notes that in the provided read-across justification named "[redacted]" you have concluded on following: "*the toxicity level of TRIDI and TDI differ so strong from each other that it is concluded not to use the TDI data for the ecotoxicological endpoints*". As you have concluded yourself that the provided studies cannot be used for adaptation of the information requirement, ECHA has not assessed this read-across justification further.

Furthermore, you generated the information on growth inhibition of aquatic plants by the application of quantitative structure activity relationship models ((Q)SARs). However, ECHA observes that you have disregarded these results in the dossier. Nevertheless, ECHA underlines that according to Annex XI, Section 1.3. of the REACH Regulation the results of (Q)SARs may be used instead of testing when the following conditions are met:

- results are derived from a (Q)SAR model whose scientific validity has been established,
- the substance falls within the applicability domain of the (Q)SAR model,
- results are adequate for the purpose of classification and labelling and/or risk assessment, and
- adequate and reliable documentation of the applied model is provided.

You did not provide the adequate and reliable documentation of the applied models referred to under the fourth bullet point above. Without such documentation ECHA is not in a

position to assess whether the other conditions outlined in the first three bullet points are fulfilled. As you have not demonstrated that the conditions of the adaptation of Annex XI, Section 1.3. of the REACH Regulation are fulfilled, the adaptation cannot be accepted.

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that there is a discrepancy between the read-across statement and the technical dossier.* [...] *The Registrant proposes a tiered approach investigating hydrolysis first of all. Based on the outcome of the study, further decisions on the (ecotoxicological) testing strategy will be taken. The outcome of the hydrolysis study will identify relevant hydrolysis (degradation) products and their kinetics. Furthermore, results of the study will allow proper analytical verification of tested concentrations in the requested aquatic toxicity studies.* [...] *Moreover, necessity and feasibility of further ecotoxicological testing needs to be re-evaluated after the outcome of the study on hydrolysis is known. [...] However, the Registrant indicates herewith its potential willingness to conduct the requested study on growth inhibition of aquatic plants if the corresponding results will lead to additional information referring to the ecotoxicological behaviour of the substance.*"

ECHA acknowledges your willingness to conduct the requested study on growth inhibition of aquatic plants.

ECHA notes your intention to undertake a hydrolysis study and investigate hydrolysis rates and degradation products of the registered substance. ECHA notes further you intention to use the outcome of the study to design the ecotoxicological testing strategy. However, at this stage impact and potential suitability of this approach cannot be assessed.

ECHA reminds that guidance on how degradation/transformation products should be considered for various standard information requirements and steps of chemical safety assessment (CSA) is given in different sections of ECHA's Guidance on Information Requirements and Chemical Safety assessment (e.g. Chapter R.7bversion 4.0, June 207; Chapter R.11 version 3.0, June 2017; Chapter R.16, Version 3.0, February 2016).

At the same time ECHA notes, in response to the assumption in your comments, that the hydrolysis study may be undertaken at different concentrations than an aquatic toxicity tests – so results of the hydrolysis study itself may not represent and confirm tested concentrations in the requested aquatic toxicity studies. Thus, analytical verification of exposure concentrations within algae growth inhibition test, as described in the requested EU C.3./OECD TG 201, is deemed necessary.

The information provided in your comments is not sufficient to allow at this moment any adaptation of the information requirement to be accepted. Therefore, the information provided on this endpoint for the registered substance in the technical dossier does not

meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

6. 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.

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 long-term toxicity to aquatic invertebrates (OECD TG 211) with the analogue substance(s) 2,4-/2,6-Toluene diisocyanate (80:20) (EC no 247-722-4).

However, ECHA notes that in the provided read-across justification named "[redacted]" you have concluded on following: "*the toxicity level of TRIDI and TDI differ so strong from each other that it is concluded not to use the TDI data for the ecotoxicological endpoints*". As you have concluded yourself that the provided studies cannot be used for adaptation of the information requirement, ECHA has not assessed this read-across justification further. Furthermore, you generated the information on long-term toxicity testing on aquatic invertebrates by the application of quantitative structure activity relationship models (QSARs). According to Annex XI, Section 1.3. of the REACH Regulation the results of (QSAR) predictions may be used instead of testing when the following conditions are met:

- results are derived from a (Q)SAR model whose scientific validity has been established,
- the substance falls within the applicability domain of the (Q)SAR model,
- results are adequate for the purpose of classification and labelling and/or risk assessment, and
- adequate and reliable documentation of the applied model is provided.

You did not provide the adequate and reliable documentation of the applied models referred to under the fourth bullet point above. Without such documentation ECHA is not in a position to assess whether the other conditions outlined in the first three bullet points are fulfilled. As you have not demonstrated that the conditions of the adaptation of Annex XI, Section 1.3. of the REACH Regulation are fulfilled, ECHA cannot accept the adaptation.

For the adaptation to be acceptable, you would have to provide the above mentioned documentation and you would have to demonstrate that the first three conditions for applying the proposed adaptation are fulfilled. The general form of the (Q)SAR Model Reporting Format (QMRF) and (Q)SAR Prediction Reporting Format (QPRF), are described in the ECHA Guidance on information requirements and chemical safety assessment Chapter R.6: (Q)SARs and grouping of chemicals (ECHA, May 2008). Under REACH, reporting formats can be submitted to ECHA as attached files in an IUCLID dossier.
As the conditions for adapting the information requirement in accordance with Annex XI, Section 1.3. of the REACH Regulation have not been fulfilled and no other scientifically valid

information is available in the dossier for the endpoint in question, ECHA concludes that there is information gap and that it is necessary to provide information for the endpoint in order to bring the registration dossier into compliance with relevant information requirement.

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

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

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that there is a discrepancy between the read-across statement and the technical dossier. As outlined under section 5 (Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)), the Registrant proposes a tiered approach investigating hydrolysis first of all. Additional information on the necessity and feasibility of further ecotoxicological testing can be found in section 5 above.* [...] *Based on the above reasoning, the hydrolysis study needs to be conducted first of all. Furthermore, the risk assessment (see section 11 – 13) should be revised taking the outcome of the hydrolysis study into account. This will lead to an extensive revision of the chemical safety assessment. After the outcome of the chemical safety assessment is known, further conclusions on long-term toxicity can be drawn. This includes the evaluation of the potential applicability for a waiving argument according to column 2 of Annex IX (Section 9.1) as outlined above.*"

For the time being it is not clear whether or not you will use a read-across approach for addressing ecotoxicological endpoints, including the long-term toxicity testing on aquatic invertebrates, and how the outcome of the hydrolysis study would support such read-across.

The information provided in your comments is not sufficient to allow at this moment any adaptation of the information requirement to be accepted. Therefore, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In regard of the long-term toxicity testing, ECHA reminds that the "Long-term toxicity testing on aquatic invertebrates" is a standard information requirement. Furthermore, ECHA notes that ECHA *Guidance on information requirements and chemical safety assessment,* Chapter R7b (version 4.0, June 2017) specifies that long-term aquatic toxicity testing might be triggered by the outcome of risk characterisation (e.g. refinement is needed when PEC/PNEC ratio for fresh or marine waters is above 1) or by the needs of the PBT assessment (tiered approach to be applied before starting T-testing) or by physico-chemical properties of the substance (e.g. long-term aquatic toxicity testing to be applied to substances poorly soluble in water, when the short term toxicity test do not reveal any toxicity up to the water solubility limit). ECHA observes that based on the information provided in the registration dossier the substance should be considered as poorly water soluble (water solubility is below 1 mg/l) and the short-term aquatic toxicity studies did not indicate toxic effect concentrations at the water solubility limit. Furthermore, degradation simulation and bioaccumulation studies are requested to be conducted, which might have

an impact on the outcome of the PBT/vPvB assessment. Thus, ECHA considers that the long-term aquatic toxicity testing is triggered for the substance.

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

Notes for your consideration

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

7. 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.

You have not provided any study record of long-term toxicity on fish in the dossier that would meet the information requirement of Annex IX, Section 9.1.6.1.

You sought to adapt the information requirement on long-term toxicity testing on fish by providing results obtained from the application of quantitative structure activity relationship models ((Q)SARs). According to Annex XI, Section 1.3. of the REACH Regulation the results of (Q)SARs may be used instead of testing when the following conditions are met:

- results are derived from a (Q)SAR model whose scientific validity has been established,
- the substance falls within the applicability domain of the (Q)SAR model,
- results are adequate for the purpose of classification and labelling and/or risk assessment, and
- adequate and reliable documentation of the applied model is provided.

You did not provide the adequate and reliable documentation of the applied models referred to under the fourth bullet point above. Without such documentation ECHA is not in a position to assess whether the other conditions outlined in the first three bullet points are fulfilled. As you have not demonstrated that the conditions of the adaptation of Annex XI, Section 1.3. of the REACH Regulation are fulfilled, ECHA cannot accept the adaptation.

For the adaptation to be acceptable, you would have to provide the above mentioned documentation and you would have to demonstrate that the first three conditions for applying the proposed adaptation are fulfilled. The general form of the (Q)SAR Model

Reporting Format (QMRF) and (Q)SAR Prediction Reporting Format (QPRF), are described in the ECHA Guidance on information requirements and chemical safety assessment Chapter R.6: (Q)SARs and grouping of chemicals (ECHA, May 2008). Under REACH, reporting formats can be submitted to ECHA as attached files in an IUCLID dossier.

As the conditions for adapting the information requirement in accordance with Annex XI, Section 1.3. of the REACH Regulation have not been fulfilled and no other information is available in the dossier for the endpoint in question, ECHA concludes that there is information gap and that it is necessary to provide information for the endpoint in order to bring the registration dossier into compliance with relevant information requirements.
As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish early-life stage toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

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 4.0, June 2017), 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 4.0, June 2017)). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as most appropriate and suitable.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that the QPRF/QMRF are lacking (also in case of the endpoints mentioned above: 5 and 6). Nevertheless, the same approach as outlined under section 6 (Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)) is suggested here. Thus, the Registrant proposes a tiered approach investigating hydrolysis followed by revision of the risk assessment and identifying the impact of the chemical safety assessment. For the long-term toxicity testing on fish, it should also be mentioned that no acute toxicity effects have been observed in the acute toxicity test towards fish ([redacted], 2002).* [...]".

For the time being it is not clear whether or not you will use a read-across approach for addressing ecotoxicological endpoints, including the long-term toxicity testing on fish, and how the outcome of the hydrolysis study would support such read-across.

The information provided in your comments is not sufficient to allow at this moment any adaptation of the information requirement to be accepted. Therefore, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In regard of the long-term toxicity testing, ECHA reminds that the "Long-term toxicity testing on fish" is a standard information requirement. Furthermore, ECHA notes that ECHA *Guidance on information requirements and chemical safety assessment,* Chapter R7b

(version 4.0, June 2017) specifies that long-term aquatic toxicity testing might be trigerred by the outcome of risk characterisation (e.g. refinement is needed when PEC/PNEC ratio for fresh or marine waters is above 1) or by the needs of the PBT assessment (tiered approach to be applied before starting T-testing) or by physico-chemical properties of the substance (e.g. long-term aquatic toxicity testing to be applied to substances poorly soluble in water, when the short term toxicity test do not reveal any toxicity up to the water solubility limit). ECHA observes that based on the information provided in the registration dossier the substance should be considered as poorly water soluble (water solubility is below 1 mg/l) and short-term aquatic toxicity studies did not indicate toxic effect concentrations at the water solubility limit. Furthermore, degradation simulation and bioaccumulation studies are requested to be conducted, which might have an impact on the outcome of the PBT/vPvB assessment. Thus, ECHA considers that the long-term aquatic toxicity testing is triggered for the substance.

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

Notes for your consideration

Before conducting any of the tests mentioned above in points 6-7 you shall consult the ECHA *Guidance on information requirements and chemical safety assessment (version 4.0, June 2017),* Chapter R7b, Section R.7.8.5 to determine the sequence in which the aquatic long-term toxicity tests are to be conducted and the necessity to conduct long-term toxicity testing on fish. If the testing requested is adapted, as noted in the decision above, 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.

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

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

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.

"Simulation testing on ultimate degradation in water" is a standard information requirement as laid down in Annex IX, section 9.2.1.2. of the REACH Regulation. 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: '*No exposure to water and sediment is intended during the life cycle of the test substance. Indirect exposure to the environment is unlikely, which is also indicated by the manufacturing process. In accordance with REACH, Annex IX, Section 9.2.1.4, column 2, this endpoint can be waived.*'

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.2.1.2., column 2 because Annex IX, Section 9.2.1.2 does not foresee option to adopt the standard information requirement in column 1 based on lack of exposure. Furthermore, ECHA notes that, as summarised under section 14 below, there is uncertainty on the reliability and relevance of environmental exposure assessment provided in the CSR. Moreover, based on the information provided in the registration dossier, the substance is not readily biodegradable. Therefore, ECHA concludes that degradation simulation testing in water is relevant and necessary.

In response to a Member State Competent Authority (MSCAs) proposal for amendment (PfA), ECHA notes that further information on the degradation of the substance and its degradation products is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment. ECHA notes further that information on a relating endpoint, bioaccumulation, is missing and has been requested in this decision. ECHA hence considers that at this stage the information in the CSA is not complete due to the data gaps addressed in this decision. On this basis, the CSA cannot be used to justify that there is no need to investigate further the degradation of the substance and its degradation products.

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

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Aerobic mineralisation in surface water – simulation biodegradation (test method EU C.25. / OECD TG 309) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.2.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that the waiving arguments are not correct to meet this information requirement. The waiving argument will be revised accordingly.* [...] *It should, however, be noted that results of the hydrolysis study as well as the revision of the risk assessment (please see section 11 – 13) might lead to additional information used for the chemical safety assessment. Thus, even the output of the hazard and exposure assessment may be different. [...] The choice of the appropriate test(s) depends on the results of the chemical safety assessment and may include simulation testing in appropriate media (e.g. water, sediment or soil).* [...] *The Registrant proposes to revise the waiving arguments: "According to column 2 of section 9. 2. 1. 2 of Annex IX of REACH Regulation, a degradation simulation test in water does not need to be conducted because the target substance TRIDI is highly insoluble in water due to logPow of 7.56 (*[redacted]*2011a) and an estimated water solubility of 0.005141 mg/L (*[redacted]*2011b).*
Additional waiving arguments in accordance with column 2 of Annex IX (Section 9.2) may be applicable as well. However, this needs to be evaluated after the chemical safety assessment has been revised."

The information provided in your comments is not sufficient to allow your adaptation of the information requirement to be accepted. Therefore, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA notes that according to the OECD TG 309 low test concentrations (*e.g.* less than 1 µg/L to 100 µg/L) are preferrably be used: "*The lowest concentration should not exceed 10 µg/L, but lowest test concentrations of 1-2 µg/L or less than 1 µg/L are preferred.*" Furthermore, the test Guideline specifies that "*the method can be used for simulating biodegradation in surface water free of coarse particles ("pelagic test") or in turbid surface water which, for example, might exist near a water/sediment interface ("suspended sediment test").*" Therefore, ECHA considers that the low solubility and high adsorption potential of the substance does not prevent performance of the requested test.

In response to a MSCAs PfA, ECHA notes, in the OECD TG 309 Guideline two test options, the "pelagic test" and the "suspended sediment test", are described. ECHA considers that the pelagic test option should be followed as that is the recommended option for P assessment. The amount of suspended solids in the pelagic test should be representative of the level of suspended solids in EU surface water. The concentration of suspended solids in the surface water sample used should therefore be approximately 15 mg dw/L. Testing natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable. Furthermore, when reporting the non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

In your comments on the MSCAs PfA, in summary, you indicate that "*these additional requirements, apply to suspended particulate matter (SPM) and non-extractable residues (NER) should not affect registrant's proposal to conduct a hydrolysis study first and decide on next steps and potentially suitable follow-up test based on the outcome of the hydrolysis study*". Also you indicate that you *consider that the substance's hydrolytic properties should be in any case evaluated in advance of any additional biodegradation testing*.

ECHA notes that following a thorough analysis of these investigations of the substance's hydrolytic properties may allow you to conclude on the non-persistence of the registered substance. In the event that non-persistence of the substance in all relevant compartments can be shown and degradation products concluded not to be PBT/vPvBs the requested simulation testing might become unnecessary, as instructed by ECHA Guidance on information requirements and chemical safety assessment, Chapter R.11, Section R.11.4.1.1 (version 3.0, June 2017), "*Hydrolysis may proceed effectively in aquatic, sediment and soil compartments but it is however noted that there are substances reaching rapid hydrolysis rates which are well known to be persistent in soil and/or sediment, e.g. endosulfan. Therefore, rapid hydrolysis rates cannot alone lead to concluding that a substance is not persistent. Test results showing rapid hydrolysis rates always need to be evaluated carefully in context with other information on the substance, such as partitioning and ionogenic properties both of which may significantly influence the extent and strength of sorption to soil and sediment. Hydrolysis also needs to be consistently rapid across the range of environmentally relevant pH. To provide confidence in the hydrolysis results, analytical data identifying metabolites to provide a mass balance are also needed. These both demonstrate that primary degradation has occurred, and allow subsequent PBT assessment of the degradants*".

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Aerobic mineralisation in surface water – simulation biodegradation test (test method: EU C.25./OECD TG 309).

9. Identification of degradation products (Annex IX, 9.2.3.)

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.

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 study does not need to be conducted if the substance is readily biodegradable.

You have not provided any study record on identification of degradation products in the dossier that would meet the information requirement of Annex IX, Section 9.2.3. 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 K_{ow} and potential toxicity of the metabolite may be investigated. You may obtain this information from the simulation study also requested in this decision, or by some other measure.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that *"The Registrant agrees that there is a data gap.* [...]*[...] It should, however, be noted that results of the hydrolysis study as well as the revision of the risk assessment (please see section 11 – 13) might lead to additional information used for the chemical safety assessment. Thus, even the output of the hazard and exposure assessment may be different. In this case, the Registrant would like to re-evaluate the necessity of further biotic degradation studies based on column 2 of Annex IX (Section 9.2). [...] The Registrant proposes, therefore, to investigate hydrolysis of the substance in order to gain information about its degradation products. Furthermore, the risk assessment (see section 11 – 13) should be revised taking the outcome of the hydrolysis study into account. This will lead to an extensive revision of the chemical safety assessment. A waiving argument in accordance with column 2 of Annex IX (Section 9.2) may be applicable. However, this needs to be evaluated after the chemical safety assessment has been revised".*

ECHA notes that for the time being it is not clear how you will use the results of the hydrolysis study to decide on the further testing strategy, more specifically how you intend to use the information to be gained on the identity of degradation products. The information provided in your comments is not sufficient to allow at this moment any adaptation of the information requirement to be accepted.

In response to a MSCAs PfA, ECHA notes that the CSA with its current information gaps cannot be used to justify that there is no need to investigate further the degradation of the substance and its degradation products. ECHA considers that the requested information is needed in relation to the PBT/vPvB assessment and risk assessment.

In your comments on the MSCAs PfA, in summary, you indicate that *"these additional requirements should not affect registrant's proposal to conduct a hydrolysis study first and decide on next steps and potentially suitable follow-up test based on the outcome of the hydrolysis study"*. Also you indicate that you *consider that the substance's hydrolytic*

properties should be in any case evaluated in advance of any additional biodegradation testing.

As stated above in Section 8, a thorough analysis of these investigations of the substance's hydrolytic properties may allow you to conclude on the non-persistence of the registered substance. ECHA notes that identification of degradation products and their PBT/vPvB assessment are still required. Please refer to relevant, ECHA Guidance on information requirements and chemical safety assessment, Chapter R.11, Section R.11.4.1.1 (version 3.0, June, 2017) for support.

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

ECHA reminds that degradation/transformation products should be considered in the CSA of the substance and guidance on how degradation/transformation products should be considered for various standard information requirements and steps of CSA is given in different sections of ECHA's Guidance on Information Requirements and Chemical Safety assessment, Chapter R.7b, version 4.0, June 2017; Chapter R.11, version 3.0, June 2017; Chapter R.16, Version 3.0, February 2016. (e.g. PBT/vPvB assessment shall also take account of relevant transformation/degradation products.).

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 using an appropriate and suitable test method, as explained above in this section.
Notes for your consideration

Before conducting the above test you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment*(version 4.0, June 2017), Chapter R.7.9., 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. If the testing requested is adapted, as noted in the decision above, 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.

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

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.

"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 not provided any study record of bioaccumulation in aquatic species in the dossier that would meet the information requirement of Annex IX, Section 9.3.2.

You proposed to adapt the information requirement on bioaccumulation in aquatic species by providing results obtained from the application of quantitative structure activity relationship models ((Q)SARs). According to Annex XI, Section 1.3. of the REACH Regulation the results of (Q)SARs may be used instead of testing when the following conditions are met:

- results are derived from a (Q)SAR model whose scientific validity has been established,
- the substance falls within the applicability domain of the (Q)SAR model,
- results are adequate for the purpose of classification and labelling and/or risk assessment, and
- adequate and reliable documentation of the applied model is provided.

You did not provide the adequate and reliable documentation of the applied models referred to under the fourth bullet point above. Without such documentation ECHA is not in a position to assess whether the other conditions outlined in the first three bullet points are fulfilled. As you have not demonstrated that the conditions of the adaptation of Annex XI, Section 1.3. of the REACH Regulation are fulfilled, ECHA cannot accept the adaptation.

For the adaptation to be acceptable, you would have to provide the above mentioned documentation and you would have to demonstrate that the first three conditions for applying the proposed adaptation are fulfilled. The general form of the (Q)SAR Model Reporting Format (QMRF) and (Q)SAR Prediction Reporting Format (QPRF), are described in the ECHA Guidance on information requirements and chemical safety assessment Chapter R.6: (Q)SARs and grouping of chemicals (ECHA, May 2008). Under REACH, reporting formats can be submitted to ECHA as attached files in an IUCLID dossier.

As the conditions for adapting the information requirement in accordance with Annex XI, Section 1.3. of the REACH Regulation have not been fulfilled and no other information is available in the dossier for the endpoint in question, ECHA concludes that there is information gap and that it is necessary to provide information for the endpoint in order to bring the registration dossier into compliance with relevant information requirement.

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7c* (version 3.0, June 2017)_bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2.

In response to MSCAs PfA, providing a preferred route of aqueous exposure, ECHA notes, ECHA Guidance defines further that results obtained from a test with aqueous exposure can be used directly for comparison with the B and vB criteria of Annex XIII of REACH Regulation and can be used for hazard classification and risk assessment. Comparing the results of a dietary study with the REACH Annex XIII B and vB criteria is more complex and has higher uncertainty. Therefore, the aqueous route of exposure is the preferred route and shall be used whenever technically feasible. If you decided to conduct the study using the dietary exposure route, you shall provide scientifically valid justification for your decision.

You shall also attempt to estimate the corresponding BCF value from the dietary test data by using the approaches given in Annex 8 of the OECD 305 TG. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG.
In your comments on the MSCAs PfA, in summary, you indicate that "*these additional requirements should not affect your testing strategy to conduct a hydrolysis study first and decide on next steps and potentially suitable follow-up test based on the outcome of the hydrolysis study*". Also you indicate you *consider that the substance's hydrolytic properties should be in any case evaluated in advance of any additional bioaccumulation testing*.

As stated above in Section 8 and 9, a thorough analysis of these investigations of the substance's hydrolytic properties may allow you to conclude on the non-persistence of the registered substance. Furthermore before conducting testing, you are advised to consult the ECHA Guidance on the information requirements and chemical safety assessment(version 3.0, June 2017), Chapter R.11. PBT/vPvB assessment, to consult the PBT assessment for Weight-of-Evidence determination and the integrated testing strategy for bioaccumulation assessment, in particular concerning relevant constituents, impurities, additives and degradation/transformation products. Also, you need to carefully consider the potential formation of stable degradation products with PBT/vPvB properties. Moreover, other than the PBT/vPvB assessment, other needs of the CSA (e.g. environmental hazard assessment, exposure assessment) for information on bioaccumulation of the substance has to be also considered by you.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that the QPRF/QMRF Reports are lacking. The Registrant proposes a waiver: "According to column 2 of section 9. 3. 2, a bioaccumulation test in fish (OECD 305) does not need to be conducted because the substance is expected to have a low bioaccumulation potential and a low potential to cross biological membranes. According to ECHA REACH Guidance R.11 (PBT AssessmentJune 2017), bioaccumulation in aquatic biota is expected for substances possessing a partition coefficient (logPow) in the range of 4.5 to 6. A higher logPow is probably more an effect of solubility than lipophilicity. The calculated logPow value for the substance TRIDI amounts to 7.56 ([redacted] 2011). This leads to the conclusion that no strong potential to bioaccumulation is expected. It should also be noted that the endpoint bioaccumulation was not sufficiently addressed in the technical dossier and the CSR since the QSAR results using BCFBAF v3.00 ([redacted] 2011c) were considered as valid. Thus, reevaluation of the bioaccumulation potential was necessary. Furthermore, the Registrant proposes to flag all ECOSAR predictions studies as "disregarded" because the substance does not fall into the applicability domain of the modelling tool and the predictions are based on the structurally similar "neutral organics" instead of "(di)isocyanates". This also accounts for the sections above (Section 5 – 7).".*

ECHA acknowledges your intention to disregard all ECOSAR prediction in the registration dossier, because the substance does not fall into the applicability domain of the modelling tool.

ECHA notes that the substance has high adsorption potential (log Kow = 7.56) and column 2 of Annex IX, Section 9.3.2. allows to adapt the requirement for an aquatic bioaccumulation study only if log K_{ow}< 3. ECHA notes that the REACH Guidance R.11 (version 3.0, June 2017) specifies that: "*If a Log Kow value indicates that the substance screens as B/vB* (*i.e.* log Kow > 4.5), *but a registrant concludes it is not B/vB based on other data, there should be specific reference to the REACH guidance indicating how such a conclusion was drawn. It should be noted that neither a high K_{oc} value nor low water solubility value can be used to argue that a substance lacks significant bioaccumulation*

potential. Instead these properties may influence the form of PBT testing required."

Moreover, the same guidance notes that: "*At Log Kow values between 4 and 5, Log BCF increases linearly with Log Kow. This linear relationship is the basis for the B screening criterion of Log Kow > 4.5. However, at very high Log Kow (>6), a decreasing relationship between the two parameters is observed.*" indicating further uncertainty about bioaccumulation potential for substances with log Kow>6.

Thus, ECHA considers that the information provided in your comment does not allow the adaptation of the information requirement, as neither a high K_{ow} value nor low water solubility value can be used to argue that a substance lacks significant bioaccumulation potential without further evidence of lack of significant bioaccumulation potential. Consequently, as summarised above, there is an information gap and it is necessary to provide information for this endpoint.

ECHA notes that for the PBT-assessment the bioaccumulation potential of degradation products (*here:* hydrolysis products) needs to be considered as well.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Bioaccumulation in fish: aqueous or dietary bioaccumulation fish test (test method: OECD TG 305).

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment (version 3.0, June 2017)*, Chapter R.7.10. This guidance document explains that if persistent metabolites are formed in substantial amounts (the results of the testing requested under sections 8 and 9 above should be considered) the bioaccumulation potential of these metabolites should also be assessed.

11. 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.

Pursuant to Annex I, Section 5.2.1 of the REACH Regulation the exposure estimation 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 a CSR.

In the present case, in the CSR you have provided 2 ESs: 1) Manufacture of 2,4-diisocyanato-1,3,5-triisopropylbenzene including packaging; 2) Industrial use resulting in manufacture of another substance).

ECHA notes that, in order to cover any exposures that may be related to the identified hazards, exposure estimation for both of the ESs (ESs 1-2) as stated by you in the CSR is

'/.../performed applying the approach by the European Diisocyanate and Polyol Producers Association (ISOPA) for toluol-2,4-diisocyanate'.

ECHA notes that there is no information available in the dossier neither reference to the publically available information on how the release factors used by you in the exposure assesment were derived by ISOPA (e.g. what are the conditions of use taken into account by ISOPA, what is underpining information for the values of release factors etc.). ECHA considers that an adequate and detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) of release factors used in exposure assessment, other than the default ERC release factors, is not provided in the CSR and therefore, it is not possible to conclude if emission estimations have been adequately estimated since you have not provided how these release factors you applied in the emission estimation of exposure scenarios 1 and 2 have been derived.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you stated that "*The Registrant agrees that the approach by the European Diisocyanate and Polyol Producers Association (ISOPA) is not sufficiently described and that the release factors applied for both exposure scenarios are not adequately justified. Conclusion: The Registrant proposes to provide a detailed justification (based on RMMs, OCs and substance properties) of using release factors other than ERC default values. Furthermore, the generation of measured data such as environmental release and/or occupational exposure data is currently discussed among the Registrants. If considered necessary, environmental exposures as well as the respective risk characterisation ratios will be recalculated.*".

ECHA acknowledges your commitment to update the dossier with the required information. The compliance of this information will be examined by ECHA in your updated registration after the deadline set in the adopted decision has passed.

In your comments on the MSCAs PfA, outlined in the Notes for consideration below, you indicate that you intend to investigate hydrolysis of the substance in order to gain information about its degradation products, a re-evaluation of the chemical safety assessment may be necessary.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested to use default release factors and other recommendations of ECHA Guidance R.16 for your environmental exposure assessment and revise the risk characterisation accordingly *or* provide a detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) for not using the default release factors as recommended in ECHA Guidance R.16 for estimation of environmental exposure.

Notes for your consideration

In response to MSCAs PfA, ECHA notes, as the information in the registration dossier indicates that the substance might undergo rapid transformation/degradation you are reminded to also consider the occurring transformation products for the environmental exposure and risk assessment to show that the identified uses will not lead to unacceptable effects in the environment.

12. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health

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 (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Pursuant to Article 14(4) of the REACH Regulation, 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 (Annex I, Section 5) and risk characterisation (Annex I, Section 6).

Annex I, Section 5. of the REACH Regulation indicates that the objective of the exposure assessment shall be to make a quantitative or qualitative estimate of the dose/concentration of the substance at which humans [...] are or may be exposed. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards.

Further, Annex I, Section 6.5. of the REACH Regulation states that for those human effects [...] for which it was not possible to determine a DNEL [...], a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out.

ECHA notes that the registered substance is self-classified for acute toxicity 1 (inhalation), skin irritation 2, respiratory sensitisation 1, skin sensitisation 1, carcinogenic 2. According to ECHA's Guidance on information requirements and chemical safety assessment, Chapter E, section E.3.4, pages 18 to 32, as well as ECHA Guidance R.8, Appendix R. 8-10 and 8-11, for endpoints such as irritation/corrosion, sensitisation, acute toxicity, carcinogenicity and mutagenicity where no dose descriptor is available, a more qualitative assessment has to be chosen. This qualitative approach shall define risk management measures (RMMs) and operational conditions (OCs) to prevent exposure and adequately protect against local effects.

Moreover, according to ECHA's Guidance on information requirements and chemical safety assessment, Part E, page 18: "It is to be stressed that when data are available that allow the derivation of a DNEL or DMEL for an endpoint (including irritation/corrosion, sensitisation, acute toxicity, carcinogenicity and mutagenicity), the quantitative or semi-quantitative approach (see Section E.3.3) should be followed [...]. The risk characterisation for such a substance in most cases needs to be both (semi-) quantitative (based on the lowest DN(M)EL for the endpoints for which a DNEL or DMEL could be derived) as well as qualitative, for the endpoints for which no DNEL or DMEL could be derived. Both assessments should demonstrate control of risks." ECHA notes additionally that for skin sensitisers the qualitative approach should be the first step while for respiratory sensitisers, there are currently no available standard methods to determine thresholds and DNELs, therefore such substances should normally results in a qualitative assessment for the hazard level of concern.

ECHA observes that you have conducted a quantitative exposure assessment/risk characterisation for the uses of the registered substance at industrial settings while under section 10 of the CSR you have indicated that "A qualitative risk assessment was performed as recommended by the REACH Guidance on Information Requirements and Chemical

Safety Assessment, Part E (Risk Characterisation) and Chapter R.13 (Risk Management Measures and Operational Conditions)". Nevertheless, ECHA observes that no qualitative assessment is undertaken for the endpoints where no dose descriptor is available.

According to the Guidance on information requirements and chemical safety assessment, Chapter E, table E.3-1, the risk management measures (RMMs) and operational conditions (OCs) to be considered in the exposure scenarios for a substance classified as acute toxicity 1 (inhalation), skin irritation 2, respiratory sensitisation 1, skin sensitisation 1, carcinogenicity 2 should be such as "any measure to eliminate exposure should be considered" and "very high level of containment required" and PPEs should entails the use of "substance/task appropriate gloves", "skin coverage with appropriate barrier material based on potential for contact with the chemical" and "substance/task appropriate respirator". Indeed, the primary approach to control exposure is to ensure, as far as possible, prevention of dermal contact and risk of inhalation.

A list of those measures is reported in Guidance Part E, table E.3.1 and the RMMs/OCs shall be aligned to a substance of such hazards (high hazard for dermal risk and moderate hazard for inhalation risk). The Practical Guide *How to undertake a qualitative human health assessment and document it in a chemical safety report* (Practical Guide 15, (version 1, November 2012)) provides further details on how to carry out a qualitative assessment.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you proposed to revise the risk assessment adequately and to integrate a qualitative approach in the future update. The compliance of this information will be examined by ECHA in your updated registration after the deadline set in the adopted decision has passed.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to provide a qualitative (semi-quantitative, if data are available) exposure assessment demonstrating the likelihood that effects for acute toxicity (inhalation), skin irritation, skin sensitisation, respiratory sensitisation and carcinogenicity for relevant exposure scenarios are avoided for all identified uses and to detail the operational conditions and risk management measures ensuring that, and revise the risk characterisation accordingly.

13. Exposure assessment and risk characterisation (Annex I, Section 5.1.1.) for human health

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.

Pursuant to Article 14(4) of the REACH Regulation, if the substance is 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 (Annex I, Section 5) and risk characterisation (Annex I, Section 6).

Regarding exposure assessment, Annex I, Section 5 of the REACH Regulation requires the Registrant to generate exposure scenarios and exposure estimations for the registered substance. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards.

Article 14(6) as well as Annex I, 0.1., 5.1.1., 5.2.4. and 6.2. of the REACH Regulation require registrants to identify and apply appropriate measures to adequately control the risks identified in a CSR. The exposure shall be estimated and risks shall be characterised in the CSR under the assumption that relevant risk management measures have been implemented.

According to Annex I, 0.3., 0.5. and 5.1.1. the applied Risk Management Measures (RMM) have to be described in the CSR. The CSR needs to contain sufficient information to allow ECHA to gain assurance that the risks are adequately controlled and that appropriate risk management measures can be prescribed by actors in the supply chain. Accordingly, the supplier is required to describe the relevant RMM in detail in the Safety Data Sheet (SDS) in order to minimise the exposure for workers handling the registered substance (e.g. the type of gloves to be worn, protection equipment for parts of the body other than the hand or respiratory protection shall be clearly specified based on the hazard of the substance or mixture and potential for contact and with regard to the amount and duration of exposure in accordance with Annex II, section 8.2.2.2.(b)(i), (ii) and 8.2.2.2.(c) respectively). The information provided in the Safety Data Sheet shall be consistent with information in the Chemical Safety Report (Annex II, section 0.1.2. of the REACH Regulation).

ECHA further notes that specific detailed information on the recommended personal protective equipment is missing both from the CSR and from the information on safe use within the IUCLID dossier.

ECHA notes that you have provided some information on the recommended personal protective equipment both in the CSR and in the information on safe use within the IUCLID dossier. In the CSR, you indicated the following for hand protection, protection of the parts of the body other than hand and respiratory protection: [PPE14] Use suitable eye protection and gloves, [PPE15] Wear suitable gloves tested to EN374, [PPE16] Wear chemically resistant gloves (tested to EN374) in combination with 'basic' employee training, [PPE17] Wear chemically resistant gloves (tested to EN374) in combination with specific activity training, [PPE29] Wear a respirator conforming to EN140 with Type A/P2 filter or better, [PPE32] Wear a full face respirator conforming to EN136 with Type A/P2 filter or Better, [E3] Avoid all skin contact with product, clean up contamination/spills as soon as they occur. Provide basic employee training to prevent / minimise exposures and to report any skin problems that may develop, [E19] Avoid all eye or skin contact with product, clean up contamination/spills as soon as they occur, while in IUCLID Section 11 has reported: Respiratory protection: protective mask with filter against organic vapour, in high concentration self-contained breathing apparatus, Hand protection: protective gloves, Eye/face protection: protective chemical goggles or face shield, Skin protection: antistatic protective clothing, boots with antistatic sole, cap.

To ensure the safe use of a substance, Annex I, Section 5.1.1. requires a description of the risk management measures to reduce or avoid direct and indirect exposure of humans. Gloves are reported in the CSR and IUCLID Section 11 as required personal protective equipment to prevent dermal exposure to the substance. Generally, gloves that are capable of preventing exposure to the skin for a pre-determined duration shall be specified. Typically, this information, as a minimum, has to specify the glove material and, depending on the exposure scenarios, may also need to include the breakthrough time and thickness of the glove material. Moreover, if it is necessary to protect a part of the body other than the hands, the type and quality of protection equipment required shall be specified, such as gauntlets, boots, bodysuit based on the hazards associated with the substance or mixture and the potential for contact. As a minimum, protective clothing to the standard EN 13034:2005 would be required (*Protective clothing against liquid chemicals. Performance*

requirements for chemical protective clothing offering limited protective performance against liquid chemicals (type 6 and type PB [6] equipment)).

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you proposed to revise in the future update the relevant sections in the technical dossier (CSR, Guidance on safe use) integrating sophisticated information about the PPEs to apply. The compliance of this information will be examined by ECHA in your updated registration after the deadline set in the adopted decision has passed.

Therefore, pursuant to Article 41(1) you are requested to provide documentation for the recommended personal protective equipment, i.e. Skin protection (Hand protection and protective clothing):
- further specify the type of glove material, thickness and breakthrough times;
- further specify the type and quality of protective clothing.

Deadline to submit the requested information in this decision

In the draft decision communicated to you the time indicated to provide the requested information was 24 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 36 months. You sought to justify this request stating: "*The scheduled period for conducting the studies requested by ECHA and the MSCA's is very tight and does not take into account the current limited laboratory capacity. Due to the upcoming last registration deadline for phase-in substances in 2018 and the dossier compliance checks as well as the substance evaluations, laboratories are fully booked for the next few months. The Lead Registrant has evaluated the possibility of conducting studies and received from some leading contract laboratories the following schedule:*" [...]. You were invited to provide adequate documentation as supporting evidence by 30 May 2017. On 29 May 2017 you provided supporting information to justify your request in the form of proof from the laboratory conducting the test. Therefore, bearing this in mind, ECHA has granted the request and set the deadline to 36 months as ECHA considers a deadline of 36 months is a reasonable time period for providing the required information in the form of an updated registration from the date of the adoption of the decision. The decision was therefore modified accordingly.

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 27 November 2015.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:
ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and did not amend the request(s).

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

ECHA received 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 included a request for extension of the deadline for providing the information required by this decision. On the basis of this request the deadline was amended. Appendix 1 was changed accordingly.

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-54 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 eventually result in a notification to the enforcement authorities of your Member State.

3. In carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, 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.