EUROPEAN CHEMICALS AGENCY

Helsinki, 4 October 2017

Addressee: [redacted]

Decision number: CCH-D-2114370488-38-01/F
Substance name: 1-methyltrimethylene dimethacrylate
EC number: 214-711-0
CAS number: 1189-08-8
Registration number: [redacted]
Submission number: [redacted]
Submission date: 08.05.2014
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. **In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. / OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102 with the registered substance;**

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

3. **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 1. and 2. have negative results.**

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

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

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

7. **Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: Daphnia sp. Acute immobilisation test, EU C.2./OECD TG 202) with the registered substance;**

8. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Algae growth inhibition test, EU C. 3./OECD TG 201) with the registered substance;**

9. **Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: Fish, acute toxicity test, OECD TG 203) with the registered substance;**

10. **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;**

11. **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;**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. 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 adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **14 April 2020**. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

[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

You have applied a grouping and read-across approach according to Annex XI, Section 1.5. of the REACH Regulation for certain toxicological and ecotoxicological standard information requirements which are addressed in the current decision. ECHA has assessed first the scientific and regulatory validity of your grouping and read-across approach in general (Section 0 below) before the corresponding individual endpoints (sections 1-6, 8 and 10).

0. Grouping 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".

0.1. Information provided by the Registrant on the proposed grouping and read-across approach

In your registration dossier, you have reported a grouping and read-across approach to adapt the following standard information requirements for

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

Your dossier contains a category information section and you have provided a category justification document ("[redacted]"). Several endpoints also contain information which is justification of the read-across, and this is outlined below.

According to the information reported in the category information section of your technical dossier, the substance subject to this decision is a member of the "*the category of multifunctional methacrylates acid esters of glycols or aliphatic polyols which provide a consistent set of structure-property- and structure-activity relationship throughout all endpoints. Furthermore, they share common metabolic pathways. Where data gaps exist for one category member, they can be satisfied by read-across to data from other members of the category.*" You have identified the members of the category (8) and substances identified as supporting chemicals (3) – see table 1 below- in the Category justification document. You have grouped the members of the category in two subfamilies, the oxyethylene subfamily and the alkyldiol/triol subfamily and you have outlined two distinct trends between these two subfamilies, associating the variations of the partition coefficient to the molecular weight and volume of the members of the each subfamily. You concluded on this basis that "*This is a category with clear trends in the physicochemical properties of its members, related to molecular weight, molecular size and hydrophilicity*". You have also listed the category members in the category information section, listing only four (1,4-BDDMA, EGDMA, 1,3-BDDMA and TREGDMA) substances.

Table 1- Category membership

Name	EC No	CAS No	Role
Triethylenegycol dimethacrylate (TREGDMA)	203-652-6	109-16-0	Category member - oxyethylene subfamily
Ethylene glycol dimethacrylate (EGDMA)	202-617-2	97-90-5	Category member - oxyethylene subfamily
Diethyleneglycol dimethacrylate (DEGDMA)	219-099-9	2358-84-1	Category member - oxyethylene subfamily
1,4-Butanediol dimethacrylate (1,4-BDDMA	218-218-1	2082-81-7	Category member – alkyldiol/triol subfamily
1,3-Butanediol dimethacrylate (1,3-BDDMA)	214-711-0	1189-08-8	Category member – alkyldiol/triol subfamily
Glycerol 1,3-dimethacrylate (GDMA)	217-388-4	1830-78-0	Category member – alkyldiol/triol subfamily
1,6-Hexanediol dimethacrylate (1,6 HDDMA)	229-551-7	6606-59-3	Category member – alkyldiol/triol subfamily
Trimethylpropane trimethacrylate (TMPTMA)	221-950-4	3290-92-4	Category member – alkyldiol/triol subfamily
Methacrylic acid (MAA)	201-204-4	79-41-4	Supporting substance
Methyl methacrylate (MMA)	201-297-1	80-62-6	Supporting substance
Hydroxyethyl methacrylate (HEMA)	212-782-2	868-77-9	Supporting substance

You have provided a category justification document ("[redacted]") which contains a basis for read-across. You have also presented results of physico-chemical, environmental fate, human health and environmental studies conducted with some of these substances to support this basis. Separately, you have provided endpoint-specific comments within each endpoint which support the read-across.

In the category justification document, you use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group: on the basis of structural similarity/ similarity in physico-chemical/ ecotoxicological/ toxicological properties, and that they share common metabolic pathways, it is possible to predict the human health/ ecotoxicological properties of the registered substance. You propose that the source and registered substances have similar properties for the above-mentioned information requirements.

ECHA considers that this information is your read-across hypothesis.
ECHA considers the endpoint-specific justifications separately, after addressing the arguments in the category justification document.

0.2. ECHA's analysis of the grouping approach

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.

According to provisions of Annex XI, section 1.5., application of the group concept requires that physico-chemical properties, environmental fate and (eco)toxicologal properties may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group(read-across approach).

Based on the information provided in the category justification section included in your dossier, ECHA understands that your read-across hypothesis is based on structural similarities among the members of the category, the identification of common metabolic pathways for these substances and the observation of two distinct trends between the physicochemical properties of the members of the two subfamilies and their molecular weight or size.

ECHA has assessed your grouping approach against the requirements of Annex XI, section 1.5. and observes the following deficiencies.

ECHA notes that the grouping of substances does not define unambiguously the applicability domain of this category. You have provided one listing of category members (consisting of four substances) in the category information section, another listing of category members of eight substances in the justification document, and you have also indicated that there are two sub-families within the category (oxyethylene and alkyldiol/triol), without indicating the relevance for the category applicability domain. Information on applicability domain is necessary to outline possible differences among the category members and constitutes a set of inclusion and exclusion rules establishing the molecular structure(s) that a substance must have to be part of the category and describing the accepted structural differences within the category. You have not defined these inclusion and exclusion criteria, such as branching, whether mono and diesters can be part of the category and what is the minimum/maximum number of ethylene glycol moieties allowed in the alcohol carbon chain in the oxyethylene subfamily or the accepted range of alkyl chain length in the alkyldiol/triol subfamily. According to ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6, such criteria should be described in order to identify the range of values within which reliable estimations can be made for the members of the category and to define the borders of the category. ECHA considers that the general statement included in the category information section of your technical dossier does not characterise boundaries of the category in general and of the two subfamilies that you identified within the category.

Given that the category definition is not clear, ECHA is unable to verify that the substances in the category can be used so that human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach).

Nevertheless, the determination that the grouping is insufficiently defined, and thereby fails to provide a basis for prediction in accordance with Annex XI, 1.5. does not affect the possibility for you to invoke a read-across approach in order to predict human health or environmental effects of these substances individually on the basis of a one-to-one analogue approach.

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0.3 ECHA's analysis of the read-across approach for human health endpoints

ECHA has summarised your read-across hypothesis from the category justification document in section 0.1. The individual arguments supporting this read-across hypothesis are analysed below.

Consistent structure-property and -activity relationships throughout all endpoints
Your proposed adaptation argument is that the similarity in structures, similarity/trends in physico-chemical properties and toxicological properties between the source and target substance is a sufficient basis for predicting the properties of the substance. This argument is limited and in principle not sufficient. Similarity in structures, similarity/trends in physico-chemical properties and toxicological properties is a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or this specific case that similarity in structures, similarity/trends in physico-chemical and toxicological properties per se is sufficient to enable the prediction of human health properties of a substance. This is because similarity in structures, similarity/trends in physico-chemical and toxicological properties does not always lead to predictable or similar human health properties, and consequently cannot on its own constitute sufficient evidence of predictable or similar human health properties. Further elements are needed[2], as pointed out below, such as a well-founded hypothesis of (bio)transformation to a common compound(s), or that different compounds have the same type of effect(s), to allow a prediction of human health properties that does not underestimate risks.

The description of the members of the category included in the category justification document suggests elements of structural similarity among these substances. However, in Category information section (0.2 Related information) you have not provided a detailed demonstration of this structure-property and structure-activity relationship regarding human health and environmental properties of the substances. In the read-across justification document attached you have provided a structure-property explanation regarding physico-chemical properties of the category members.

ECHA understands that you have identified subfamilies in the category based on different physico-chemical properties/trends in the category:

- oxyethylene subfamily (EGDMA, DEGDMA, TREGDMA and GDMA) with similar logP values and a trend to increasing water solubility with increasing length of the oxyethylene chain length, and

- alkyldiol/triol subfamily (1,3-BDDMA, 1,4-BDDMA, HDDMA and TMPTMA) with increasing logP values and decreasing water solubility with increasing molecular weight/volume.

[2] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals and ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

ECHA acknowledges that you have linked structural differences with water solubility and log Kow. However, you have not explained how the structural differences and trends in physicochemical properties are linked with the predicted environmental and human health hazard properties, neither within a subfamily nor between the subfamilies which are currently part of the same claimed category.

More specifically, you have not explained how the structural differences such as different chain lengths of the parent compounds between the category members (within and between the subfamilies) relate to their toxicokinetic, especially metabolism, and toxicological properties. Furthermore, the subfamily of alkyldiol/triol includes also other structural differences than alkyl chain length, e.g. branching, and it has not been explained how such differences may influence the predicted properties. Consequently, there is not a robust basis for predicting the properties of the registered substance.

Shared common metabolic pathways
ECHA understands that regarding human health your read-across hypothesis is based also on the identification of common metabolic pathways for these substances. You have provided evidence in your category justification document demonstrating a rapid hydrolysis of the esters. ECHA considers that this is adequate to establish that the systemic exposure to the category members in their native form, i.e. as diesters, and the impact of such exposure on the properties of the substances may be low. However ECHA stresses that similarities in metabolic pathways may constitute a reason for grouping of substances together but this does not constitute a sufficient basis for predicting that the properties of these substances will be similar or follow a regular pattern. Additional information characterising the metabolic reactions involved and addressing the toxicodynamic properties of the different metabolites are required to establish a basis for making such predictions. Further, ECHA notes that no further information on the toxicological properties of the ultimate common metabolite of the category members, i.e. methacrylic acid, and on the properties of the non-common alcohols formed has been provided in the dossier. ECHA considers that in the absence of supporting information on the toxicity of the alcohol metabolites, it is not possible to predict the properties of the target substance from the data obtained with the source substance(s).

Evidence contradicting your hypothesis of similar properties
Based on the available data on Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD 422) conducted with the source substances TREGDMA and 1,4-BDDMA (alkyltriol/diol subfamily), the toxicological profile of these substances is different. In the Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD 422) conducted with the source substance TREGDMA no adverse repeated dose or reproductive toxicity effects were observed up to the highest dose (1000 mg/kg bw/day). However, in the OECD 422 study with the source substance 1,4-BDDMA effects on e.g. kidney (increased weight), thymus (decreased weight), stomach (mild diffused hyperplasia) and liver (minimal degree of multifocal perilobular hepatocytic vacuolation) were observed. In addition, fertility index was markedly reduced and litter and mean pup weights were reduced in the high dose group (1000 mg/kg bw/day).

This information contradicts your hypothesis of consistent structure-activity relationships, and is therefore an additional reason why your read-across hypothesis is not an adequate basis for predicting the properties of the registered substance.

You have made arguments to justify the read-across for specific endpoints, and ECHA additionally addresses these endpoint-specific arguments below.

Genotoxicity:

In the endpoint summary of genetic toxicity in IUCLID you conclude the following: "*it is unlikely that 1,3 -BDDMA or one of the other multifunctional methacrylates induces gene mutations. Thus, based on the available information, 1,3-BDDMA is considered to be non-mutagenic*". Based on the tests conducted with EGDMA, 1,4-BDDMA and TMPTMA you further conclude in the category justification document that "*The corresponding in vivo tests, three micronucleus tests in mouse bone marrow and the two UDS tests are all negative, which indicates the absence of mutagenicity in vivo. This likely reflects that it is the parent ester that is responsible for the clastogenicity in vitro and that these chemicals are rapidly metabolised in vivo to the corresponding acid and alcohol, which are not mutagenic".*

ECHA considers that this is an assertion of toxicological similarity, and as explained in section 0.2 and 0.3 above, this justification is not considered acceptable for predicting the properties of the registered substance.

In your comments to the draft decision you propose to fulfil data requirements 1-3 of this decision by using data from 1,4-BDDMA and justify the read-across approach based on a mode of action approach according to which "the same mode of action (the electrophilic reaction of the methacrylate double bond with DNA)" would apply to the source substance 1,4-BDDMA and the target substance 1,3-BDDMA. On that basis you conclude on a high level of confidence in this revised read-across approach.

ECHA notes that no further information accounting for the potential impact of the structural differences on this presumed similar mode of action has been presented. Therefore, ECHA cannot assess the reliability and adequacy of these scientific arguments in the context of this revised read-across approach.

Sub-chronic (90-day) toxicity:

For the sub-chronic (90-day) toxicity you have provided a Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD 422) conducted with 1,4-BDDMA, a 2-year feeding study conducted with 1,3-butanediol and a 78-week dermal study conducted with TREGDMA. You have provided the following justification:
...."In terms of repeat dose systemic toxicity the members of the category of multifunctional methacrylates demonstrate non-specific toxicity, i. e. effects on body weight gain, organ weight changes and slight histopathological changes. Severe target organ effects have not been observed. Within the concentration range of NOAELs reported here, there is also an absence of specific alerts from the primary metabolites (Methacrylic acid and the specific alcohol/diol – 300 mg/kg 1,3-BDDMA correspond to approx. 75 mg/kg 1,3-butanediol) even in studies of longer duration"...
ECHA considers that this is an assertion of toxicological similarity, and as explained in section 0.2 and 0.3 above, this justification is not considered acceptable for predicting the properties of the registered substance. ECHA notes that no studies on methacrylic acid, which is a common metabolite, have been provided in the registration dossier.

Regarding the supporting studies ECHA notes that

- based on the reporting in the IUCLID, the 2-year feeding study with 1,3-butanediol (claimed metabolite of the registered substance) is not considered adequate and reliable because e.g. the following parameters were not examined: clinical examinations, ophthalmology, body weight, clinical biochemistry, urianalysis, gross necropsy, analytical verification of doses and food consumption. Further, based on the reporting, it is not clear for which organs histopathology was done,

- the 78-day dermal study with the source substance TREGDMA is not considered adequate and reliable as sufficient dermal absorption of the test substance has not been demonstrated.

Therefore, contrary to the requirements of Annex XI, section 1.5. the results do not have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3) (OECD 408) and hence are not an adequate basis for supporting a claim of similar toxicological properties.

In your comments to the draft decision you indicated your intentions to update the read-across/category justification document by providing information on hydrolysis of the parent substance to methacrylic acid and 1,3-butanediol and to support the use of data from an OECD 422 study conducted with the analogue substance 1,4-BDDMA by using information on methyl methacrylate, and the metabolites 1,3-butanediol and methacrylic acid. On that basis you conclude on a high level of confidence in this revised read-across approach.

It is ECHA's understanding that you intend to use the existing OECD 422 study performed with 1,4-BDDMA as the source study to fulfil the information requirement of Annex IX, 8.6.2 and to support this read-across approach using data on the metabolites.

ECHA highlights that the exposure period in a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test conducted in accordance with the OECD 422 test guideline is shorter than the exposure period expected from a sub-chronic (90-day) repeated dose toxicity study performed according to the OECD 408 test guideline. Therefore, independently of the set of supporting evidence provided to justify the revised read-across approach, ECHA considers that this source study does not fulfil the requirement of Annex XI, Section 1.5 of the REACH Regulation for an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) and cannot be used as the sole source study to fulfil the information requirement of Annex IX, 8.6.2.

Pre-natal developmental toxicity

You have provided the following justification:
"According to REACH regulation, Annex XI, 1, a prenatal developmental toxicity study is scientifically not necessary. The available data for the members of the multifunctional methacrylates category are sufficient for classification, labelling and risk assessment. Thus, no further testing is proposed. A prenatal developmental toxicity study (similar to OECD guideline 414) is available for EGDMA. No developmental toxicity was observed in this study up to the highest tested dose of 500 mg/kg bw/d. For the members of the category of lower alkyl methacrylates, based on studies in experimental animals, there is no evidence of selective toxicity to the reproductive system. This is corroborated by the fact that the esters are rapidly metabolised in vivo and the primary metabolites, methacrylic acid, as well as the corresponding alcohol (1,3-butanediol), demonstrates an absence of concern for specific reproductive toxicity".

ECHA considers that this is an assertion of toxicological similarity, and as explained in section 0.2 and 0.3 above, this justification is not considered acceptable for predicting the properties of the registered substance. ECHA further notes that you have not provided any data or justification to demonstrate how the properties of lower alkyl methacrylates can be used to predict the properties of multifunctional methacrylates. Further, you have not provided data on the metabolism of the registered substance to substantiate your assertion of rapid metabolism, and in addition, no data on the proposed metabolites, methacrylic acid and 1,3-butanediol, has been provided to demonstrate *"an absence of concern for specific reproductive toxicity"*.

In your comments to the draft decision you explained your intention to update the read-across/category justification document and to support the use of information from the existing screening study conducted with the analogue substance 1,4-BDDMA by using information on the metabolites 1,3-butane diol and methacrylic acid. On that basis you conclude on a high level of confidence in this revised read-across approach.

It is ECHA's understanding that you intend to use the existing OECD 422 study performed with 1,4-BDDMA as the source study to fulfil the information requirement of Annex IX, 8.7.2 and to support this read-across approach using data on the metabolites.

ECHA notes that this source study corresponds to a screening study for reproductive and developmental toxicity performed according to the OECD test guideline 422. According to the provisions of Annex IX 8.7.2, information on pre-natal developmental toxicity as specified in the OECD test guideline 414 shall be provided. ECHA points out that the OECD test guideline 422 study does not provide an adequate coverage of some key parameters expected to be investigated in a study performed according to the OECD test guideline 414 such as examinations of foetuses for skeletal and visceral alterations. Therefore, ECHA considers that this source study does not fulfil the requirement of Annex XI, Section 1.5 of the REACH Regulation for an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3) and cannot be used as the sole source study to fulfil the information requirement of Annex IX, 8.7.2.

You have also provided comments on screening for reproductive/developmental toxicity study. In the comments you explained your intention to update the read-across/category justification document and to support the use of information from the existing screening study conducted with the analogue substance 1,4-BDDMA by providing information on 1,3-butanediol and methyl methacrylate. On that basis you conclude on a high level of confidence in this revised read-across approach.

ECHA outlines that reliable information characterising the claimed "short half-life and rapid ultimate metabolism to CO2 and water" is required to support the claim of limited potential of 1,3-butane diol to cause direct reproductive toxicity.

In the general comments to the draft decision (which ECHA understands are applicable to all the data requirements 1 – 6), you acknowledged that "the current category document submitted in 2014 does not fully meet" the current expectations regarding adaptations based on grouping of substances and read-across. You reported that based on the available information on the hydrolysis of the methacrylate esters and taking into account the information available on the metabolites formed, you have a high confidence in this read-across approach. You noted though that the reporting of the data on the metabolites currently included in the dossier is insufficient.

You expressed your intentions to revise the overall category approach and the endpoint specific sections in compliance with the RAAF. Specifically, information on the hydrolysis of the parent ester 1,3-BDDMA, on the further metabolism of 1,3-butane diol would be provided including QSAR data and the use of information on analogous substances on the alcohol metabolite further discussed in this revision.

You also pointed out in your comments to the draft decision that "if the situation arises that new studies are required for both BDDMA isomers, we suggest to test only 1,4-BDDMA (Tetramethylene dimethacrylate), due to higher production amounts and thus potentially higher exposure of the population, and to use read-across for 1,3-BDDMA".

ECHA acknowledges your intentions to revise and strengthen the adaptation in accordance with ECHA's RAAF by providing further information characterising the fast hydrolysis of 1,3-BDDMA, clarifying the further metabolism of the metabolite 1,3-butane diol and by elaborating on the possibility to use information on analogue substances to 1,3-butane diol in order to predict the properties of the registered substance.

As a general rule, ECHA stresses that for a read-across approach based on metabolism (RAAF Scenario 1), reliable data establishing rapid and complete hydrolysis of the parent substance is essential to support the read-across hypothesis. Furthermore, adequate and reliable information on the toxicological properties of the metabolites needs to be provided.

Should information from other source substances such as methyl methacrylate, ethylene glycol and propylene glycol be used in an adaptation, adequate and reliable documentation establishing the relevance of this information needs to be provided. In case multiple source substances are used to predict the properties of the target substance, details on the use and integration of the multiple source data needs to be unambiguously and transparently reported.

ECHA further stresses that reliability and adequacy of the source or supporting studies, and particularly in case of old non-guideline studies, need to be accounted for, e.g. duration of the studies and the parameters examined in the studies need to be compared to current OECD/EU guidelines. The impact of possible deficiencies is to be addressed and the relevance and reliability of the studies evaluated accordingly.

ECHA stresses that the selection of the source substance needs to be scientifically justified and in particular the read-across should not lead to an underestimation of the effect(s) as per RAAF Scenario 1.

ECHA notes that your comments to the draft decision, do not address the deficiencies indicated above regarding read-across approach provided for toxicological endpoints. For the reasons presented above, ECHA cannot conclude at this stage whether the revised read-across approach referred in your comments to the draft decision will comply with the requirements of Annex XI, section 1.5 of the REACH Regulation.

Summary for toxicological endpoints

In the light of the deficiencies as described above, both for the general read-across hypothesis and the endpoint-specific justifications, ECHA considers that this grouping and read-across approach does not comply with the general rules of adaptation as set out in Annex XI, 1.5. of the REACH Regulation. Therefore, this adaptation cannot be accepted and there is a data gap for the endpoints covered by this read-across approach.

0.4 ECHA's analysis of the read-across approach for environmental endpoints

ECHA has summarised your read-across hypothesis from the category justification document in section 0.1. The individual arguments supporting this read-across hypothesis for environmental endpoints are analysed below.

Lack of evidence supporting your hypothesis of similar properties
ECHA notes that both the source substance and the registered substance belong to the alkydiol/triol subfamily. The description of the members of the category included in the category justification document suggests elements of structural similarity between these substances. However, ECHA notes some deficiencies in your read-across justification.

In your read-across justification document you provide data matrices listing toxicity values in several environmental hazard endpoints (Short-term toxicity to fish, Long-term toxicity to fish, Short-term toxicity to aquatic invertebrates, Long-term toxicity to aquatic invertebrates, Effects on algae and aquatic plants) for the eight category members. However, ECHA notes that you do not provide toxicity data for both the source substance 1,4-BDDMA and the registered substance 1,3-BDDMA in any of the endpoints which would allow anchoring the toxicity levels.

Therefore, ECHA concludes that based on the presented information it is not possible to confirm that the source and target substances would have similar properties regarding toxicity to aquatic invertebrates and algae. In the absence of such information there is not an adequate basis for predicting the properties of the target substance from the data obtained with the source substance.

Considerations of impurities

Furthermore, the substance characterisation of the source substance(s) need to be sufficiently detailed in order to assess whether the attempted prediction is not compromised by the composition and/or impurities. In the ECHA practical guide 6 "How to report on Read-Across" it is recommended to follow the ECHA Guidance for identification and naming of substances under REACH and CLP (version 2.1, June 2017) also for the source substances. This ensures that the identity of the source substance and its impurity profile allows an assessment of the suitability of the substances for read-across purposes.

ECHA acknowledges that you have characterised the tested substance in the endpoint study records provided in sections 6.1.4 Long-term toxicity to aquatic invertebrates and 6.1.5 Toxicity to algae of the technical dossier by the following information: EC name tetramethylene dimethacrylate; EC number 218-218-1; CAS number 2082-81-7; *"Analytical purity: 99.67 %"*; *"Impurities (identity and concentrations): 107 ppm MEHQ (stabiliser)"*.

ECHA observes that the reported purity of the tested material is [redacted] including impurity [redacted]. ECHA notes that the registered (target) substance includes a number of impurities that the tested material (source substance) does not contain, such as reaction mass of butane-1,3-diyl bis(2-methylacrylate) and methanol (typical concentration [redacted] %; range [redacted] %) and reaction mass of butane-1,3-diyl bis(2-methylacrylate) and 3-hydroxybutyl methacrylate (typical concentration [redacted] %; range [redacted] %). You have not addressed the impact of such impurities on the proposed prediction. Hence ECHA cannot reach a conclusion that the source substance can be used to predict and will not underestimate properties of the registered substance.

In the absence of unambiguous information on the composition and impurity profile of the test sample used to generate the source data, ECHA cannot verify the adequacy of this information for the purpose of classification and/or risk assessment of the registered substance, as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation.

Consistent structure-property and -activity relationships throughout all endpoints

Your proposed adaptation argument is also that the similarity in structures, similarity/trends in physico-chemical properties and ecotoxicological properties between the source and target substance is a sufficient basis for predicting the properties of the substance. This argument is limited and is in principle not capable of being sufficient. Similarity in structures, similarity/trends in physico-chemical properties and ecotoxicological properties properties is a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or this specific case that similarity in structures, similarity/trends in physico-chemical properties and ecotoxicological properties per se is sufficient to enable the prediction of environmental properties of a substance. This is because similarity in structures and similarity/trends in physico-chemical properties does not always lead to predictable or similar environmental properties, and consequently cannot on its own constitute sufficient evidence of predictable or similar environmental properties. Further elements are needed[3], as pointed out above, such as supporting evidence to show similarity in ecotoxicological effects, or that the impurities would not contribute to the prediction, to allow a prediction of environmental properties that does not underestimate risks.

The description of the members of the category included in the category justification document suggests elements of structural similarity among these substances. However, in Category information section (0.2 Related information) you have not provided a detailed demonstration of this structure-property and structure-activity relationship regarding human health and environmental properties of the substances. In the read-across justification document attached you have provided a structure-property explanation regarding physico-chemical properties of the category members.

ECHA understands that you have identified subfamilies in the category based on different physico-chemical properties/trends in the category:

- oxyethylene subfamily (EGDMA, DEGDMA, TREGDMA and GDMA) with similar logP values and a trend to increasing water solubility with increasing length of the oxyethylene chain length, and

- alkyldiol/triol subfamily (1,3-BDDMA, 1,4-BDDMA, HDDMA and TMPTMA) with increasing logP values and decreasing water solubility with increasing molecular weight/volume.

ECHA acknowledges that you have linked structural differences with water solubility and log Kow. However, you have not explained how the structural differences and trends in physicochemical properties are linked with the predicted environmental and human health hazard properties, neither within a subfamily nor between the subfamilies which are currently part of the same claimed category.

[3] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals and ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

More specifically, you have not explained how the structural differences such as different chain lengths of the parent compounds between the category members (within and between the subfamilies) relate to their ecotoxicological properties. Furthermore, the subfamily of alkyldiol/triol includes also other structural differences than alkyl chain length, e.g. branching, and it has not been explained how such differences may influence the predicted properties. Consequently, there is not a robust basis for predicting the properties of the registered substance.

Long-term toxicity aquatic invertebrates

For the long-term toxicity on aquatic invertebrates you have provided a 21-d toxicity study on the structural analogue 1,4-BDDMA (CAS No 2082-81-7, EC No 218-218-1).

You have provided the following justification for *Long-term toxicity to aquatic invertebrates* in the category justification document:
"*There are data available for three of seven substances in the category (TREGDMA, EGDMA, 1,4-BDDMA). The available studies include both ends of the glycol ester subcategory as well as two members of the aliphatic multifunctional subcategory.*"

ECHA considers that this is an assertion of ecotoxicological similarity, and as explained in section 0.2 and 0.4 above, this justification is not considered acceptable for predicting the properties of the registered substance.

In your comments to the draft decision you explained your intention to update the read-across/category justification document. You indicated an intention to provide data on metabolic pathways and toxicological data for the metabolites to improve the read-across adaptation. ECHA considers that these intentions do not address the deficiencies indicated above regarding read-across approach provided for ecotoxicological endpoints i.e. Lack of evidence supporting your hypothesis of similar properties, consistent structure-property and -activity relationships throughout all endpoints, and considerations of impurities. Therefore, it is ECHA's understanding of your comments to the draft decision that you intend to improve read-across and grouping only to predict Human Health properties.

Toxicity to aquatic algae

For the toxicity on aquatic algae you have provided a 72-h toxicity study on the structural analogue 1,4-BDDMA (CAS No 2082-81-7, EC No 218-218-1).

You have provided the following justification for *Algae and aquatic plants* in the category justification document:
"*All tests were performed with the test species Pseudokirchneriella subcapitata or Desmodesmus subspicatus (1,4-BDDMA) and complied with the OECD 201 test protocol. All data presented are 72h exposure data. For acute toxicity to algae there is a trend of increasing toxicity (72 h EC50 and 72 h EC10) with increasing logP, while the glycol dimethacrylate subfamily with similar logP also shows similar or even decreasing ecotoxicity with increasing size.*"

ECHA considers that this is an assertion of ecotoxicological similarity, and as explained in section 0.2 and 0.4 above, this justification is not considered acceptable for predicting the properties of the registered substance.

In your comments to the draft decision you explained your intention to update the read-across/category justification document. You indicated an intention to provide data on metabolic pathways and toxicological data for the metabolites to improve the read-across adaptation. ECHA considers that these intentions do not address the deficiencies indicated above regarding read-across approach provided for ecotoxicological endpoints i.e. Lack of evidence supporting your hypothesis of similar properties, consistent structure-property and -activity relationships throughout all endpoints, and considerations of impurities. Therefore, it is ECHA's understanding of your comments on the draft decision that you intend to improve read-across and grouping only to predict Human Health properties.

Summary for (eco)toxicological endpoints

In the light of the deficiencies as described above, both for the general read-across hypothesis and the endpoint-specific justifications, ECHA considers that this grouping and read-across approach does not comply with the general rules of adaptation as set out in Annex XI, 1.5. of the REACH Regulation. Therefore, this adaptation cannot be accepted and there is a data gap for the endpoints covered by this read-across approach.

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

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for an Ames test (OECD TG 471, GLP) with the analogue substance 1,4-BDDMA (CAS no 2082-81-7, EC no 218-218-1). You have provided the following justification for the adaptation: "*In the Ames test S. typhimurium TA 102 or E. coli WP2 are missing. However, data sets including S. typhimurium TA 102 are available for other methacrylates from the category. Throughout the entire category of multifunctional methacrylates there is no indication of bacterial mutagenity*".

However, as explained above in section 0 "Grouping and read-across approach" above, your adaptation of the information requirement is rejected.

Additionally, the provided study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in Annex XI, 1.5 of the REACH Regulation, and in particular the requirement to have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3). Specifically, the test you refer to used four different strains of *S. typhimurium* TA 1535, TA 1537, TA 98, TA 100 and TA1538 and it did not include tests with strains S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101). However, since the test was conducted, significant changes have been made to OECD TG guideline 471 so that additionally testing with S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101) is now required.

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.

In your comments to this draft decision you explained your intention to update the read-across/category justification document and provide further information to improve the read across approach. Your comments to the draft decision are addressed in section 0 "Grouping and read-across approach".

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 submit the following information derived with the registered substance subject to the present decision: Bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

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

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing two study records for *in vitro* cytogenicity study in mammalian cells (OECD TG 473, GLP, 1955 and 2000) and Mammalian erythrocyte micronucleus test (OECD 474, GLP, 1998) with the analogue substance 1,4-BDDMA (CAS no 2082-81-7, EC no 218-218-1).

In your comments to this draft decision you explained your intention to update the read-across/category justification document and provide further information to improve the read across approach. Your comments to the draft decision are addressed in section 0 "Grouping and read-across approach".

However, as explained above in section 0 "Grouping and read-across approach" above, 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* mammalian cell micronucleus test (OECD TG 487) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

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

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

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

An "*In vitro* gene mutation study in 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.

In the technical dossier you have provided a study record for an *in vitro* gene mutation in mammalian cells (equivalent or similar to OECD 476, GLP, RI 2) with the registered substance from 1985.

ECHA considers that this is not a study carried out according to the test methods referred to in Article 13(3), i.e. the current OECD test guideline for in vitro mammalian cell mutagenicity. ECHA notes that this test does not provide equivalent data according to the criteria in Annex XI, 1.1.2. of the REACH Regulation, specifically the requirement for adequate and reliable documentation of the study. There is no information about the number of treated cells and replicates, there is no reporting of historical control data, no colony sizing is reported and no statistics are provided. In view of these deficiencies, ECHA is not able to independently verify that this study fulfils the information requirement.

Therefore, for the reasons presented above this study does not provide the information required by Annex VIII, Section 8.4.3.

In addition you have provided a study record for an *in vitro* gene mutation in mammalian cells (equivalent or similar to OECD 476, GLP, RI 1) with the analogue substance 1,4-BDDMA (CAS no 2082-81-7, EC no 218-218-1), and an Unscheduled DNA synthesis study (according to Butterworth et al., Mutat. Res. 189: 123-133 (1987) described as an ASTM guideline, GLP) with an analogue substance EGDMA (CAS no 97-90-5, EC no 202-617-2).

You have provided the following justification:

"1,4 -BDDMA did not induce gene mutations in bacteria, consistent with findings with other methacrylates including the members of the multifunctional methacrylate category. Of the two mammalian gene mutation tests, an HPRT test with 1,4 -BDDMA was negative while a mouse lymphoma assay with 1,3 -BDDMA was slightly positive with metabolic activation.

This finding is consistent with the fact that it is well established that the mouse lymphoma assay also detects clastogenic chemicals (deletions of the distal part of the chromosome with the TK gene) - and 1,4 -BDDMA was positive in one of the in vitro chromosome aberration tests - also at the limit of cytotoxicity. With the negative UDS test with EGDMA (with an otherwise similar pattern of test data) and the also negative HPRT test with 1,4 -BDDMA it is unlikely that 1,3 -BDDMA or one of the other multifunctional methacrylates induces gene mutations. Thus, based on the available information, 1,3-BDDMA is considered to be non-mutagenic".

ECHA considers that your suggestion that the registered substance is clastogenic in vitro represents speculation, and that you do not provide additional justification for the read-across. In your comments to this draft decision you explained your intention to update the read-across/category justification document and provide further information to improve the read across approach. Your comments to the draft decision are addressed in section 0 "Grouping and read-across approach". However, as explained above in section 0 "Grouping and read-across approach" above, 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 cell gene mutation tests using the *Hprt* and *xprt* genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.3.

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

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

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a Combined Repeated Dose Toxicity Study with the Reproduction Developmental Toxicity Screening Test (OECD 422) conducted with the analogue substance 1,4-BDDMA (CAS no 2082-81-7, EC no 218-218-1).

In your comments to this draft decision you explained your intention to update the read-across/category justification document and provide further information to improve the read across approach. Your comments to the draft decision are addressed in section 0 "Grouping and read-across approach". However, as explained above in section 0 "Grouping and read-across approach" above, your adaptation of the information requirement is rejected.

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

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

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Reproductive/developmental toxicity screening test (test method: OECD TG 421) in rats by the oral route.

Notes for your considerations:

You should also carefully consider the order of testing especially the requested screening (OECD TG 421) and the developmental toxicity studies (OECD TG 414) to ensure unnecessary animal testing is avoided, paying particular attention to ECHA's end point specific guidance document[4].

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

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422, key study) with the analogue substance 1,4-BDDMA (CAS no 2082-81-7, EC no 218-218-1), 2-year feeding study with an analogue substance 1,3-butanediol (CAS no 107-88-0, EC no 203-529-7; Publication, year 1967), and 78-wk dermal study in mice with an analogue substance TREGDMA (CAS no 109-16-0, EC no 203-652-6; US EPA guideline, GLP) .

In your comments to this draft decision you explained your intention to update the read-across/category justification document and provide further information to improve the read across approach. Your comments to the draft decision are addressed in section 0 "Grouping and read-across approach". However, as explained above in section 0 "Grouping and read-across approach" above, your adaptation of the information requirement is rejected.

In addition, ECHA notes that a combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (test method: OECD TG 422) does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days.

You claim that "*slight effects*" such as body and organ weight and histopathological changes "*do not justify the conduct of studies of longer duration*". ECHA notes that the duration of the screening study is in general 6 weeks for males and 54 days for females. ECHA further notes that according to ECHA Guidance of *on information requirements and chemical safety assessment*, Chapter R.7a, section R.7.5 (version 6.0, July 2017) "the 28-day study provides toxicological information "*during a relatively limited period of the animal's life span*" and the 90-day study "*from sub-chronic exposure (a prolonged period of the animal's life span) covering post-weaning maturation and growth well into adulthood, on target organs and on potential accumulation of the substance*", and "

[4] ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance Version 6.0, July 2017, (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf).

It should be noted that potential effects in certain target organs (e.g., the thyroid) following repeated exposure may not be observed within the span of the 28-day study", and "*In addition, interpretation of the results* [screening studies] *may be complicated due to differences in sensitivity between pregnant and non-pregnant animals, and an assessment of the general toxicity may be more difficult especially when serum and histopathological parameters are not evaluated at the same time in the study. Consequently, where the combined study is used for the assessment of repeated dose toxicity, the use of data obtained from such a study should be clearly indicated".* ECHA considers that based on the above and effects observed in the OECD 422 study, a sub-chronic (90-day) study is justified.

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 has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure. According to Chemical Safety Report no human inhalation exposure occurs. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

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

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

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

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study record for a pre-natal developmental toxicity (OECD 414, GLP) with an analogue substance EGDMA (CAS 97-90-5, EC no 202-617-2).

In your comments to this draft decision you explained your intention to update the read-across/category justification document and provide further information to improve the read across approach. Your comments to the draft decision are addressed in section 0 "Grouping and read-across approach". However, as explained above in section 0 "Grouping and read-across approach" above, your adaptation of the information requirement is rejected.
In addition, you have provided a study record for a Combined Repeated Dose Toxicity Study with the Reproduction Developmental Toxicity Screening Test (OECD 422) conducted with the analogue substance 1,4-BDDMA (CAS no 2082-81-7, EC no 218-218-1). However, this study does not provide the information required by Annex IX, Section 8.7.2. because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations.

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

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

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

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

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

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

"Short-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex VII, Section 9.1.1. of the REACH Regulation. 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 VII, Section 9.1.1., column 2. You provided the following justification for the adaptation: *"In accordance with REACH regulation Annex VII. 9.1.1., column 1, long term toxicity data are provided instead of a short-term toxicity study."*

As a long term toxicity data you have provided a study record for a *Daphnia magna* reproduction test (OECD TG 211) with the analogue substance tetramethylene dimethacrylate (EC no 218-218-1). However, as explained above in section 0 "Grouping and read-across approach" of this decision, your adaptation of the information requirement cannot be accepted.

As there is no reliable data for long-term toxicity on aquatic invertebrates currently available in the registration dossier your adaptation of the information requirement for short-term toxicity on aquatic invertebrates cannot be accepted.

In your comments to this draft decision you have stated the following to fulfil this information gap: "*Illustrate current knowledge of near-baseline toxicity as relevant MoA for methacrylates, including 1,4-BDDMA, based on QSAR*". Based on this statement, ECHA understands that you may refer to adapting the information requirement by (Q)SAR models. ECHA acknowledges that (Q)SAR models may be used instead of testing if conditions set out in Section 1.3 of Annex XI to the REACH Regulation are met. The use of QSARs to adapt information requirements is further specified in the ECHA Guidance on information requirements and chemical safety assessment (May 2008), Chapter R.6. ECHA will evaluate any new information/approach provided (in an updated dossier) in the Dossier Evaluation Follow-Up Process and will come to a conclusion on whether the information provided adequately fulfils the information requirements addressed in the decision.

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

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Daphnia sp. Acute immobilisation test, EU C.2./OECD TG 202).

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

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

"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. You provided a study record for an Algae growth inhibition test (OECD TG 201) with the analogue substance tetramethylene dimethacrylate (EC no 218-218-1).

However, as explained above in section 0 "Grouping and read-across approach" of this decision, your adaptation of the information requirement cannot be accepted.

In your comments to this draft decision you explained your intention to update the read-across/category justification document. However, as described above in section 0 "Grouping and read-across approach", it is ECHA's understanding that you intend to improve read-across and grouping only to predict Human Health properties.

In your comments to this draft decision you also provided the same statement as outlined and addressed in request 7 above, Short-term toxicity testing on aquatic invertebrates, which ECHA understand is your intended approach to fulfil this 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) 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.

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: Algae growth inhibition test, EU C.3./OECD TG 201).

9. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

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

"Short-term toxicity testing on fish" is a standard information requirement as laid down in Annex VIII, Section 9.1.3. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for a short term toxicity test on fish (key study, reliability 2, [redacted] 1987, *Idus melanotus* exposed for 48 hrs) in a static, freshwater system on registered substance according to guideline DIN 38 412 part 15. However, this study does not provide the information required by Annex VIII, Section 9.1.3., because you did not provide data generated by the corresponding test method referred to in Article 13(3) of the REACH Regulation, i.e. Fish, acute toxicity test (test method EU C.1./OECD TG 203). Therefore, ECHA considers that you sought to adapt the information requirement in accordance with Annex XI, Section 1.1.2.
In accordance with Annex XI, Section 1.1.2., data generated by another than the corresponding test methods referred to in Article 13(3) of the REACH Regulation shall be considered equivalent if the following conditions are met:

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

ECHA notes that the exposure duration was set at 48 hours. A standard test duration for a short-term toxicity test on fish according to OECD TG 203 (1992), Fish, acute toxicity test is 96 hours. Therefore, the exposure duration of the test provided is not comparable to or longer than the corresponding test methods referred to in Article 13(3). Furthermore, ECHA observes that there is no information provided in the technical dossier on the experimental conditions, such as the dissolved oxygen concentration of the test solutions.

Therefore, ECHA concludes that the toxicity study on fish provided in the registration dossier does not fulfil the conditions of Annex XI, 1.1.2. for being recognised as equivalent to data from the test method referred to in Article 13(3).

In your comments to this draft decision you provided the same statement as outlined and addressed in request 7 above, Short-term toxicity testing on aquatic invertebrates.

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 acute toxicity test (test method EU C.1. / OECD TG 203) is the preferred test to cover the standard information requirement of Annex VIII, Section 9.1.3.

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: Short-term toxicity testing on fish - Fish, acute toxicity test (test method: EU C.1./OECD TG 203).

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

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a *Daphnia magna* reproduction test (OECD TG 211) with the analogue substance tetramethylene dimethacrylate (EC no 218-218-1).

However, as explained above in section 0 "Grouping and read-across approach" of this decision, your adaptation of the information requirement cannot be accepted.

In your comments to this draft decision you explained your intention to update the read-across/category justification document. However, as described above in section 0 "Grouping and read-across approach", it is ECHA's understanding that you intend to improve read-across and grouping only to predict Human Health properties.

In addition, your comments to this draft decision which you provided and ECHA addressed in section 0 "Grouping and read-across approach" and in request 7 above, Short-term toxicity testing on aquatic invertebrates, you also indicated the following: "*modify the respective PNEC assessment factors*" and "*update also the respective exposure assessment and risk assessment*". As you also state that "*Initial PEC/PNEC calculations provide confidence that we can address your concerns without further testing of vertebrates animals*", ECHA understands that you intend to adapt the information requirement for long-term toxicity to fish by provisions set out in column 2 of section 9.1 of Annex IX. However, it is not clear in your comments to the draft decision what is your intended approach to fulfil the information requirement for long-term toxicity to aquatic invertebrates. Currently the information requirement for long-term toxicity testing on aquatic invertebrates is adapted and the adaptation is not accepted as described above.

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.

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:

Before conducting the requested test 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 necessity to conduct long-term toxicity testing on aquatic invertebrates.

Currently the long-term toxicity testing is needed in the absence of reliable short-term toxicity data (Requests 7-9 in this decision) and exposure assessment and risk characterisation. However, you may consider adapting long-term toxicity testing when reliable data on short-term toxicity become available, performing the exposure assessment and updating the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

If after the update of the chemical safety assessment you come to the conclusion that the long-term toxicity tests are still required to refine the risk assessment, you may further consider Integrated Testing Strategy (ITS) for aquatic toxicity. According to the ITS, as described in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially less sensitive than other trophic levels (i.e., fish, invertebrates, algae), long-term studies may be required on both fish and invertebrates. In such case, according to the ITS, the Daphnia study is to be conducted first. If based on the results of the long-term Daphnia study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

If you come to the conclusion that no further investigation of effects on aquatic organisms is required, you shall update your technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, 9.1.5 and 9.1.6. taking into account the new data generated by the short-term toxicity studies requested by the present decision and exposure assessment and risk characterisation.

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

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

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

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation: *"Long-term testing in fish is waived for 1,3-BDDMA since the substance is readily biodegradable. The risk characterization shows that the PEC/PNECaqua ratio for the aquatic environment is <1, indicating no need for further information or testing. According to REACH regulation Annex IX, 9.1. column 2, long-term testing shall only be considered when the chemical safety assessment indicates the need for further investigations. Because there is no indication of major differences in sensitivity between trophic levels and in the absence of any significant long-term bioaccumulation potential it is not necessary to perform further chronic fish test with the substance. The environmental risk assessment can be performed with sufficient reliability with the available long-term ecotoxicity data. Thus, no long-term toxicity testing is required for 1,3-BDDMA."*

ECHA notes that contrary to your claim, information present in your dossier indicates the need to investigate further the effects on aquatic organisms, as explained below. Firstly, although your statement pointing out that *"the substance is readily biodegradable"* may allow conclusion of PBT properties of the substance, it, however, does not allow to conclude risk assessment and thus the entire chemical safety assessment.

Ready biodegradability does not exclude the possibility that the substance would not induce toxic effects in aquatic organisms.

Secondly, you have argued that "*Because there is no indication of major differences in sensitivity between trophic levels and in the absence of any significant long-term bioaccumulation potential it is not necessary to perform further chronic fish tests with the substance*". ECHA understands that you refer to integrated testing strategy (ITS) described in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4).

ECHA notes that according to this ECHA Guidance, if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially less sensitive than other trophic levels (i.e., fish, invertebrates, algae), long-term studies may be required on both fish and invertebrates. In such case, according to the integrated testing strategy, the Daphnia study is to be conducted first. If based on the results of the long-term Daphnia study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, ECHA notes that this ITS approach cannot be applied in this case because you have not provided valid short-term toxicity data for aquatic invertebrates and fish (Requests 7-9) that would allow determination of relative species sensitivity. Therefore the standard information requirement of long-term toxicity to fish cannot be adapted based on ITS for aquatic pelagic toxicity.

Thirdly, you have not provided evidence to your justification that "*risk characterization shows that the PEC/PNECaqua ratio for the aquatic environment is <1*". ECHA notes that the registration dossier does not include a qualitative risk characterisation (RCR, PEC/PNECaqua ratio) that would allow you to adapt this information requirement. In the CSR you provided, the exposure assessment for the environment is missing. You claimed that no exposure assessment is necessary for the environment by stating for each exposure scenario that "*As no environmental hazard was identified no environmental-related exposure assessment and risk characterization was performed.*" Furthermore, in the absence of reliable short-term hazard data (Requests 7-9 in this decision), it is not possible to verify whether the substance induces toxic effects in short- or long-term exposure, neither is it possible to be used for a reliable risk characterisation. In the absence of quantitative risk characterisation your justification for adapting long-term toxicity to fish based on the assumed PEC/PNECaqua ratio for the aquatic environment of <1 is not substantiated.

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

In addition to your comments to this draft decision which ECHA addressed in request 7 above, you also indicated that you intend to "*modify the respective PNEC assessment factors*" and "*update also the respective exposure assessment and risk assessment*". As you also state that "*Initial PEC/PNEC calculations provide confidence that we can address your concerns without further testing of vertebrates animals*", ECHA understands that you intend to adapt the information requirement for long-term toxicity to fish by provisions set out in column 2 of section 9.1 of Annex IX. As described above, the column 2 adaptation currently provided in the technical dossier is rejected, therefore the reasoning of the rejection should be considered for any potential improvement of the adaptation.ECHA acknowledges that you have indicated in your comments to update the exposure assessment and risk characterisation but also to "*Discuss different sensitivies of the trophic levels*". ECHA points out that such comparison on sensitivity should be based on reliable short-term toxicity data (Requests 7-9 above) which are currently not present in the technical dossier.

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

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

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Figure R.7.8-4).

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA Guidance Chapter R7b, version 4.0, June 2017).

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

Notes for your consideration

Before conducting the test 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.

Currently the long-term toxicity testing is needed in the absence of reliable short-term toxicity data (Requests 7-9 in this decision) and exposure assessment and risk characterisation. However, you may consider adapting long-term toxicity testing when reliable data on short-term toxicity become available, you perform the exposure assessment and update the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

If after the update of the CSA you come to the conclusion, following the ECHA Guidance as mentioned above, that the long-term toxicity tests are still required to refine the risk assessment, you may further consider Integrated Testing Strategy (ITS) for aquatic toxicity. According to the ITS, as described in ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially less sensitive than other trophic levels (i.e., fish, invertebrates, algae), long-term studies may be required on both fish and invertebrates. In such case, according to the ITS, the Daphnia study is to be conducted first. If based on the results of the long-term Daphnia study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

If you come to the conclusion that no further investigation of effects on aquatic organisms is required, you shall update your technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, 9.1.5 and 9.1.6. taking into account the new data generated by the short-term toxicity studies requested by the present decision and exposure assessment and risk characterisation.

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 23 November 2016.

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

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

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

Note in request 1, In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. / OECD TG 471) with the registered substance, for clarity, the strains are included in the request and in Appendix 1 of the draft decision as follows: "using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102".

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

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

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

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

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

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