ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 12 April 2017

Addressee: [redacted]

Decision number: CCH-D-2114355354-50-01/F
Substance name: (1-methyl-1,2-ethanediyl)bis[oxy(methyl-2,1-ethanediyl)] diacrylate
EC number: 256-032-2
CAS number: 42978-66-5
Registration number: [redacted]
Submission number: [redacted]
Submission date: 06.10.2010
Registered tonnage band: 1000 tonnes or more per year

DECISION ON A COMPLIANCE CHECK

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

1. **Name or other identifier of the registered substance (Annex VI, Section 2.1)**
   - **Chemical name;**
2. **Composition of the registered substance (Annex VI, Section 2.3)**
   - **Concentration values;**
3. **Partition coefficient n-octanol/water (Annex VII, Section 7.8; test method: OECD TG 117) with the registered substance;**
4. **In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum, with the registered substance; OR; Transgenic rodent somatic and germ cell gene mutation assay (Annex IX, Section 8.4, column 2; test method: EU B.58/OECD TG 488) in transgenic mice or rats, oral route on the following tissues: liver, glandular stomach with the registered substance.**
5. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2; test method: EU B.31/OECD TG 414) in a first species (rats or rabbits), oral route with the registered substance;**
6. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2; test method: EU B.31/OECD TG 414) in a second species (rats or rabbits), oral route with the registered substance;**
7. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3; test method: EU B.56/OECD TG 443) in rats, oral route with the registered substance specified as follows:**

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

- **Dose level setting shall aim to induce some toxicity at the highest dose level;**
- **Cohort 1A (Reproductive toxicity);**
- **Cohort 1B (Reproductive toxicity);**
- **with extension to mate the Cohort 1B animals to produce the F2 generation if the substance displays genotoxic effects in any of the somatic cell mutagenicity tests *in vivo*, required under point 4, which could lead to classification as Mutagen Category 2;**
- **without extension to mate the Cohort 1B animals to produce the F2 generation in case the above condition is not met.**

8. **Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25/OECD TG 309) at a temperature of 12 °C with the registered substance; including assessment of biodegradation of each constituent and relevant impurity present in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable; this can be done simultaneously during the same study;**

9. **Identification of degradation products (Annex IX, 9.2.3) using an appropriate test method with the registered substance, including each constituent and relevant impurities present in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable;**

10. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305, [aqueous exposure/dietary exposure]) with the registered substance; including assessment of bioaccumulation or bioconcentration of each constituent and impurity present in concentrations at or above 0.1% (w/w); this can be done simultaneously during the same study; for the PBT/vPvB assessment, you shall also investigate the bioaccumulation or bioconcentration potential of degradation products.**

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

You are required to submit the requested information in an updated registration dossier by **20 April 2020**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow time for addressing the substance identification deficiencies and for sequential testing. The *in vivo* mammalian alkaline comet assay or transgenic rodent somatic and the germ cell gene mutation assay, requested under point 4 above, shall be conducted prior to the conduct of extended one-generation reproductive toxicity study, requested under point 7 above, as the results of the *former* may inform on the design of the latter study.

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

Appeal

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

Authorised[1] by 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.

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Appendix 1: Reasons

IDENTIFICATION OF THE SUBSTANCE

In order to ensure that potential hazardous properties of substances are not underestimated, the substance identification deficiencies must be resolved before identifying the test sample to be used for the testing requested in the present decision.

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

1. **Name or other identifier of the registered substance (Annex VI, Section 2.1)**

ECHA notes that the Registrant identified the registered substance as of Unknown or Variable composition, Complex reaction products or Biological materials (UVCB). Information required to be provided according to Annex VI, Section 2.1 of the REACH Regulation on the naming of UVCB substances such as the registered substance shall consist of two parts: (1) the chemical name and (2) a more detailed description of the manufacturing process, as indicated in section 4.3 of the Guidance for identification and naming of substances under REACH and CLP (Version: 1.3, February 2014) – referred to as "the Guidance" hereinafter. More explicitly, the chemical name provided needs to be representative for the registered UVCB substance and the respective identified have to be consistent with that name.

You assigned the chemical name "[redacted]" to the registered substance in the IUPAC field.

Whilst this chemical name "[redacted]" refers to a well-defined substance, the provided CAS (number: 42978-66-5, CAS name: "[redacted]") and EC (number: 256-032-2, EC name: "([redacted])") entries are generic and refer to a UVCB substance. Because of these differences in providing information on the identity of the substance, ECHA considers that the provided chemical name is inappropriate for the registered substance.

Accordingly, you are requested to provide the chemical name in the "IUPAC name" field which is representative for the registered UVCB substance. The chemical name shall define unambiguously the manufactured substance covered by the registration.

You shall ensure that the chemical name of the registered substance is representative of the UVCB substance as described by the manufacturing process. In particular, the naming of the starting materials used in the process and to be quoted in the name of the registered substance shall also follow the naming conventions specified in the Guidance.

Regarding how to report the chemical name and description of the UVCB substance, this information shall be included in the "IUPAC name" and Description field in IUCLID section 1.1, respectively. Further technical details on how to report the chemical name and manufacturing process description of UVCB substances in IUCLID are available in the Data Submission Manual – Part 18: How to report the substance identity in IUCLID 5 for registration under REACH (version: 2.0, July 2012) on the ECHA website.

In the comments to the draft decision you agreed with the information requirement and you intend to address the information requirement in an update of the registration dossier.

You clarified that the substance subject to the present decision is a UVCB substance and that indeed the current IUPAC name in section 1.1 of the dossier refers to a specific substance constituent and thus needs to be changed. Furthermore, you suggested to use the same name as CAS name.

The information you provided in the comments appears to adress the non compliance identified and will be assessed on the basis of the updated dossier following the decision making process.

Irrespective of whether the newly provided information in your dossier update on 11 April 2016 (submission number [redacted]) may be sufficient to meet the information requirement addressed in the decision, ECHA can already point out the following:
You have provided in the IUPAC name field of IUCLID section 1.1 a chemical name, "(1-methyl-1,2-ethanediyl)bis[oxy(methyl-2,1-ethanediyl)] diacrylate". The SMILES notation was not removed and structural formula was not changed. .

2. Composition of the registered substance (Annex VI, Section 2.3)

The substance composition corresponds to the chemical representation of what the substance consists of and is therefore an essential part of substance identification and the corner stone of all the REACH obligations.

In that respect, according to chapter 4.3 of the Guidance for identification and naming of substances under REACH and CLP (Version: 1.3, February 2014), you need to specify for each constituent the typical, minimum and maximum concentration levels regardless of the substance type.

ECHA notes that the registration does not contain sufficient and appropriate information for establishing the composition of the registered substance and therefore its identity, as required under Annex VI, section 2.3. of the REACH Regulation.

More specifically, ECHA notes that you have only provided the typical concentration for all constituents specified in section 1.2 of the IUCLID dossier. The information on the concentration ranges (minimum and maximum) for each constituent that is important in order to understand the variability of the composition of the registered substance, have not been provided.

The concentration range values must be representative for the registered substance as manufactured and it shall be clarified how the minimum and maximum values for each individual constituent was obtained (i.e. information on the batch selection, sampling procedure, the measured values, calculations used etc.). Without this information ECHA is not able to conclude on the representativeness of these values and the identity of the substance covered by the registration shall not be considered unambiguously clear.

Therefore you are required to specify a concentration range (minimum and maximum values) for each detected individual constituent.

Regarding how to report the composition in IUCLID section 1.2, the following applies: Details of the protocol followed to determine the different concentration values of each individual constituent shall be provided in the "Remarks" field of the corresponding repeatable block for that individual constituent.

Where you cover different grades of the same substance in a registration, you shall report separately the compositional information of each grade. This means that if the substance covered by the registration has two (or more) different compositions, then these must be presented separately. Information on how to report several compositions in IUCLID is specified in paragraph 2.3, Q&A8 of the "Data Submission Manual – Part 18: How to report the substance identity in IUCLID 5 for registration under REACH" (version: 2.0, July 2012), available on the ECHA website.

ECHA highlights that failure to report separately the compositional information of each grade of a substance may result in one or more grades not being covered by this registration.

You should also note that multiple compositions may indicate multiple substances and consequently the requirement for multiple registrations.

In the comments to the draft decision you agreed that the typical, minimum and maximum concentration levels for each constituent should be included in the section 1.2 of the IUCLID dossier.

Irrespective of whether the newly provided information in your dossier update on 11 April 2016 (submission number [redacted]) may be sufficient to meet the information requirement addressed in the decision, ECHA can already point out the following:
You have provided some concentration ranges.

INFORMATION RELATING TO INTRINSIC PROPERTIES

3. Partition coefficient n-octanol/water (Annex VII, Section 7.8)

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

"Partition coefficient n-octanol/water" is a standard information requirement as laid down in Annex VII, Section 7.8 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 your registration dossier you have provided three studies:

> Key study, EU method A.8 shake-flask method, non-GLP, 1995, CAS 42978-66-5, test material (as cited in study report): Laromer TPGDA (Tripropylenglykoldiacrylat), analytical purity: 90.4 %. Result Log Pow 2.0 25°C (used for the material safety data sheet - MSDS).

Supporting study 1, OECD 107, shake-flask method, non-GLP, 1998, CAS 42978-66-5, test material (as cited in study report): Tripropylenglykoldiacrylat, analytical purity: 85.3 %. Result log Pow 2.1 25°C.

Supporting study 2, EU A.8, HPLC method, non-GLP, CAS 42978-66-5, test material (as cited in study report): Laromer TPGDA (Tripropylenglykoldiacrylat), analytical purity: 90.4 %. Result Log Pow 2.77 25°C.

According to you, all tests have been performed with the registered substance subject to the present decision. ECHA notes that according to the composition reported in the technical dossier, main components represent ca. [redacted]% of the substance and that the composition also contains <7% of non-specified impurities. In the substance composition section of the technical dossier, you have not provided concentration ranges for the components. The purity for the substance that has been used in the key study and supporting study 2 has been reported to be 90.4%. Because of the discrepancy between the information on the composition and the used test material for the partition coefficient n-octanol/water endpoint the results cannot be considered representative for the registered substance without a proper justification and information on the ranges of the constituents. With the information provided at this stage, it is not possible to verify that the result is representative for the whole registered UVCB substance. In addition, ECHA notes that the key study and the supporting study 2), originate from the same study report (94P08921) and they were performed with the same test substance; however, their reported Log Kow values differ significantly: 2 versus 2.77. A higher Log Kow value indicates a higher potential for adsorption and bioaccumulation for a substance. In addition, you have not provided a justification why the value Log Kow 2 has been selected as the key study and used in the risk assessment and MSDS.

Generally, the HPLC test method is recommended to establish the partition coefficient n-octanol/water endpoint for UVCB substances. Nevertheless, the robust study summary of the HPLC method in the supportive study 2 does not provide enough information to verify that the result covers the whole registered UVCB substance, for example, an elution profile chromatogram with indicated cut offs and the Log Kow values relative to area % of the Log Kow peak are missing.

ECHA notes that the supporting study 1 has been performed with yet another test material sample (purity 85.3%) and its value Log Kow 2.1 is slightly higher, but close to the value obtained with the selected key study.

For risk assessment purposes it is important to have information on the range of Log Kow value(s) for such a UVCB substance. This may affect the assessment of various other properties of the substance such as environmental fate and other PBT properties. You have used the value Log Kow 2.0 to adapt the information requirement for bioaccumulation and value Log Kow 2.1 in your distribution modelling. ECHA considers that a single Log Kow value is not representative for the whole composition of the registered UVCB substance. Therefore this value is not sufficient for Log Kow based adaptations, classification and labelling and risk assessment purposes; as it cannot be assessed if this value is representative for the whole composition of the substance.

You have not provided an adequate and reliable documentation of the applied methods and the test samples. ECHA notes that you have not justified why the value provided for a suggested representative test material is applicable to the whole UVCB substance. ECHA considers that for UVCB substances the HPLC method is suitable for determination of Log Kow, and a defined range of values should be presented, with an indication of the proportion of substance within a given range (e.g. > 90% w/w of constituents have log Kow in the range 4-5), to allow the significance of these results to be reflected in the risk assessment.

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

In your comments you have indicated that the shake flask method was chosen as key value because it is a direct method and reflects the actual behaviour of the substance. ECHA understands that with shake flask method an average value for a UVCB substance can be obtained. However, for UVCB substances it is necessary to deliver information on Log Kow values or ranges for the whole composition and not only an average value. Therefore HPLC based test with detailed reporting is required.

According to you, the test guideline states that suitable reference substances should be used which are structurally related to the test substance and that such reference substances were not available. ECHA considers that the composition of the substance allows the use of recommended reference substances according to the instructions in the OECD Test No. 117: Partition Coefficient (n-octanol/water), HPLC Method test guideline. According to guideline; "it is preferable that these reference substances should be structurally related to the test substance." This is a recommendation, however not an explicit requirement.

You also commented that unexpected interaction of the test substance with the solvent and/or stationary phase can also lead to higher/lower values compared to the shake-flask method. ECHA considers HPLC method as a reliable and suitable method for a UVCB substance governing organic molecules, such as within the composition of the registered substance. It is your responsability to find suitable test conditions and to report possible issues which could be caused by unexpected interaction of the test substance with the solvent and/or stationary phase.

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: Partition coefficient n-octanol/water according to OECD Test No. 117: Partition Coefficient (n-octanol/water), HPLC Method.

4. ***In vivo mammalian alkaline comet assay (Annex IX/X, Section 8.4, column 2)* or Transgenic rodent somatic and germ cell gene mutation assays (Annex IX/X, Section 8.4., column 2)**

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

"Mutagenicity" is an information requirement as laid down in Annex VIII, Section 8.4. of the REACH Regulation. Column 2 of Annex IX, Section 8.4. provides that "If there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and there are no results available from an *in vivo* study already, an appropriate *in vivo* somatic cell genotoxicity study shall be proposed by the Registrant."

The technical dossier contains two *in vitro* studies providing information on the potential for the registered substance to induce gene mutations:

- one bacterial reverse mutation test performed according to the OECD test guideline 471 using the registered substance (*Salmonella typhimurium/Escherichia coli* reverse mutation assay with Tripropylenglykoldiacrylat, study report no. 40M0410/034087). You concluded on the basis of the information obtained from this test that the registered substance was weakly mutagenic in *Salmolella typhimurium* strain TA 1535 under the conditions of this test.
- One Mouse Lymphoma Forward Mutation Assay performed in 1980 according to Clive D, Spector JFS *(1975): (Mutat. Res. 31, 17-29)* with the registered substance. Positive results were obtained in this study and you concluded that "*the test material was therefore considered to be weakly active in the Mouse Lymphoma Forward Mutation Assay*".

The positive results in these tests indicate that the substance is inducing gene mutations under the conditions of the tests.

The technical dossier contains several *in vivo* studies performed with the registered substance that show negative results.

- Two micronucleus studies performed in mice ([redacted]., 2007 and [redacted], 2004) via the oral and intraperitoneal route suggest that the registered substance does not exhibit clastogenic properties. Whilst ECHA recognises that these studies provide adequate and reliable information on the potential of the registered substance to induce cytogenic/clastogenic effects, ECHA points out that these tests do not constitute adequate investigations to follow-up on positive *in vitro* findings for gene mutation.
- A combined single cell gel assay and micronucleus assay (Tice RR *et al.*, 1997) performed in mice via the dermal route and using the registered substance. ECHA points out that limited information on the composition of the test material has been reported: a purity of 80% has been reported in IUCLID, but no further details on the composition of the remaining 20% of the test material is provided. According to the information provided in the IUCLID dossier, "*Peripheral blood leukocytes were evaluated for DNA damage (single-strand breaks, alkali labile sites, DNA crosslinking) at weeks 4, 8, 12, 16, and 20 by using the alkaline (pH > 13) single cell gel (SCG) assay*". The substance 12-O-tetra-decanoylphorbol-13-acetate has been used as positive control in this study. The following justification for the selection of this substance has been provided in the IUCLID dossier: "*positive control for tumor induction in this transgenic mouse model*". ECHA also notes that you report that "*There is no data in the publication, that this substance is a known mutagen*". ECHA observes that an absence of positive response has been observed with the positive control in this test, as reported in the results section of the endpoint study record in IUCLID: "*TPA (0.002 µmol per mouse), the positive control for the tumorigenicity studies, also failed to significantly alter the extent of DNA migration or its intercellular dispersion in leukocytes of mice treated by dermal application*".

- You have assigned a Klimisch score of 2 to this study and conclude on the basis of the information obtained in this study that *"the dermal application of TPGDA, a multifunctional acrylate to female Tg.AC mice over a 20-week period, failed to induce a significant increase in DNA damage in circulating leukocytes at multiple sample times or chromosomal damage in proliferating bone marrow cells. The absence of genotoxic damage in these two cell populations suggests that this acrylate is not genotoxic or that it is genotoxic but not readily absorbed across the skin and systemically distributed throughout the body".*
  Taking into account the absence of positive response with the substance used as positive control, the limited information on the composition of the test material used and the uncertainty on the systemic availability of the test material after dermal exposure ECHA considers that this study does not provide adequate and reliable information to follow-up on the concern for gene mutations.

ECHA further notes that you have included an adaptation justification to omit the further studies on genetic toxicity *in vivo*. This adaptation is based on a review of existing *in vitro* and *in vivo* mutagenicity studies by [redacted] (2008) concluding that *"Despite differences in acrylate or methacrylate functionality or in the number of functional groups, a consistent pattern of test response was seen in a typical regulatory battery of mutagenicity tests".*

According to the information you reported in your adaptation this pattern can be described as follows: acrylic acid or over 60 acrylates and methacrylates did not cause point mutations *in vitro* and no effects were observed in *in vivo* clastogenicity/aneuploidy studies. You also highlight that no evidence of carcinogenicity was observed in chronic rodent cancer bioassays performed with acrylic acid. Eventually, you report that *"acrylic acid and the entire acrylate and methacrylate chemical class produced a consistently positive response when tested in the mouse lymphoma assay and/or other in vitro mammalian cell assays designed to detect clastogenicity, especially at concentrations causing considerable cytotoxicity. The biological relevance of this in vitro response is questioned based on the non-concordance of in vitro results with those of in vivo studies addressing the same mutagenic endpoint (clastogenicity)".* You conclude on that basis that *"the acrylates and methacrylates behave as a single chemical category, and genotoxicity behaviour of a similar chemical, i.e. TPGDA, can be predicted with confidence by inclusion within this chemical class, thus avoiding unnecessary testing"* and that *"in view of the vast data set concerning in vivo micronucleus and chromosome aberration assays for this chemical class and the lack of a tumorigenic response of acrylic acid and several acrylate esters in chronic bioassays, further testing of TPGDA in genetic toxicity assays in vivo is not deemed necessary".*

While you have not explicitly claimed an adaptation in your waiving argument, you have provided information that ECHA understands to be an attempt to adapt the information requirement according to Annex XI, Section 1.5 of the REACH Regulation. You indicate in your adaptation argument that acrylates and methacrylates behave as a category of chemicals and you consider that the properties of the registered substance can be predicted within this category. ECHA observes that you have not provided any documentation supporting and justifying the formation of this category of chemicals, and that you have not established and demonstrated a basis according to which the properties of the registered substance can be predicted within this category from data on other category members as required by the provisions of Annex XI, section 1.5 of the REACH Regulation.

ECHA further notes that none of the studies on other acrylate compounds referred to in your adaptation argument have been provided. In particular, none of the chronic or carcinogenicity studies performed with the registered substance or any other member of the proposed category referred to in your adaptation argument has been reported in the technical dossier. Therefore, ECHA considers that your conclusions that "*in view of the vast data set concerning in vivo micronucleus and chromosome aberration assays for this chemical class and the lack of a tumorigenic response of acrylic acid and several acrylate esters in chronic bioassays, further testing of TPGDA in genetic toxicity assays in vivo is not deemed necessary*" are not supported by scientific evidence and cannot be verified. As a consequence, ECHA considers that you have not provided any scientific evidence to support and demonstrate your read-across hypothesis according to which the properties of the registered substance can be predicted within this category from data on other category members, as required by the provisions of Annex XI, section 1.5 of the REACH Regulation. Therefore, your adaptation of the information requirement cannot be accepted.

Since no appropriate *in vivo* genotoxicity study to follow up the concern on gene mutations is provided for the registered substance, there is an information gap and it is necessary to provide information for this endpoint.

According to the ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) Chapter R.7a, section R.7.7.6.3, the transgenic rodent somatic and germ cell gene mutation assays ("TGR assay", OECD TG 488) and the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) are suitable to follow up a positive *in vitro* result on gene mutation. Hence, ECHA considers that the TGR and the comet assay are suitable tests to follow up the concern on gene mutation for the substance subject to the decision.

In case you decide to perform the TGR assay according to the test method EU B.58/OECD TG 488, the test shall be performed in transgenic mice or rats and the substance is usually administered orally. In case you decide to perform the comet assay according to the test method OECD TG 489, the test shall be performed in rats. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

According to the test method OECD TG 489, the test shall be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the substance, and probable different local absorption rates of the substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to sample both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract."

You indicated in your comments to the draft decision that new data relevant for the endpoint under consideration has been generated and that an updated dossier was ready for submission when the compliance check was received. You have also further elaborated on the positive results observed in the Ames test mentioned in the draft decision, and have provided clarifications on the positive response observed in the mouse lymphoma assay. The new data has been included in the dossier update submitted on 11 April 2016 with the submission number [redacted].

ECHA has assessed the information presented in your comments. ECHA also screened the new information in the updated dossier. The information provided could be adequate to address the concerns on this endpoint raised in the draft decision. However, 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. All the new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: In vivo mammalian alkaline comet assay (test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum; or Transgenic rodent somatic and germ cell gene mutation assays (test method: EU B.58/OECD TG 488) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach.

The *in vivo* mammalian alkaline comet assay or transgenic rodent somatic and the germ cell gene mutation assay, requested under point 4 above, shall be conducted prior to the conduct of extended one-generation reproductive toxicity study, requested under point 7 above, as the results of the *former* may inform on the design of the latter study.

Notes for your consideration

You are reminded that according to Annex X, Section 8.4., column 2 of the REACH Regulation, if positive results from an *in vivo* somatic cell study are available, "the potential for germ cell mutagenicity should be considered on the basis of all available data, including toxicokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered".

In case you decide to perform the TGR assay, you may consider collecting (see OECD TG 488, paragraph 33) and storing male germ cells for potential further analysis of germ cell mutagenicity in case positive result(s) are obtained from the somatic cells.

In case you decide to perform the comet assay, you may consider examining gonadal cells when conducting the comet assay (OECD TG 489), as it would optimise the use of animals. ECHA notes that a positive result in whole gonads is not necessarily reflective of germ cell damage since gonads contain a mixture of somatic and germ cells. However, such positive result would indicate that the substance and/or its metabolite(s) have reached the gonads and caused genotoxic effects. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

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

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

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.

In the technical dossier you have provided a study record for a "*Teratology Screen in rats using C-180, C-181, C-182, C-236, C-253, C-255, C-256, C-257, C-258 and C-259 (Revised Final Report) with cover letter*" (TSCATS/OTS0000544-0, EPA, 1987). However, this study does not provide the information required by Annex IX, Section 8.7.2, for the following reasons:

- The identity and composition of the test material are not unambiguously established. No information on the analytical purity is available, therefore the authors "*assume*" that it is 100% pure.
- Only one test dose was used in this study. This test dose of 250 mg/kg/day is lower than the limit test dose of 1000mg/kg/d recommended in the OECD test guideline 414;
- No maternal toxicity was observed at the dose of 250 mg/kg/day. According to the OECD test guideline 414, "*the highest dose should be chosen with the aim to induce some developmental and/or maternal toxicity (clinical signs or a decrease in body weight)*", however, no maternal and no developmental toxicity was observed in this study.

In the light of the deficiencies listed above, ECHA considers that the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement.

ECHA notes that you have also provided information from a screening study for reproductive and developmental toxicity performed with the analogue substance 1,6-Hexamethylene Diacrylate (HDDA) (EC No. 235-921-9, CAS No. 13048-33-4). You have provided the following read-across justification in section 5.9.3 of the Chemical Safety report: "*HDDA (CAS # 13048-33-4), DPGDA (CAS#57472-68-1) and TPGDA (CAS # 42978-66-5) are suitable for read across among each other as they are all structurally similar Difunctional Acrylates with comparable toxicological properties (all are sensitizing and have irritating effects on skin and eyes)*".

ECHA notes that the claim that these substances are "*structurally similar difunctional acrylates with comparable toxicological properties (all are sensitizing and have irritating effects on skin and eyes)*" is not sufficient to justify this read-across approach for the following reasons:

The differences in structure and composition between the registered and analogue substances have not been established and no justification on why these similarities and differences constitute an adequate basis for prediction has been provided. More generally, ECHA notes that there is no documentation establishing a basis whereby relevant human health and environmental properties of the registered substance may be predicted from data for the analogue substance 1,6-Hexamethylene Diacrylate (HDDA) (EC No. 235-921-9, CAS No. 13048-33-4). Similarities in skin sensitization and irritation properties cannot be considered as evidence of similarities in properties for the endpoint under consideration.

Furthermore, ECHA points out that the OECD Guideline 422 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. In the light of the above deficiencies, ECHA considers that you have not established and demonstrated a basis according to which the properties of the registered substance can be predicted from data on the analogue substance 1,6-Hexamethylene Diacrylate (HDDA) (EC No. 235-921-9, CAS No. 13048-33-4) as required by the provisions of Annex XI, section 1.5 of the REACH Regulation. ECHA further points out that the source study does not cover the key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations, as required by the provisions of Annex XI, section 1.5 of the REACH Regulation, and can therefore not be used as stand-alone line of information to fulfil this information requirement.

For all the reasons listed above, there is an information gap and it is necessary to provide information for this endpoint.

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

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

You have indicated in your comments to the draft decision that a dose-range finding study had been conducted prior to the pre-natal developmental toxicity study conducted in rats and included in the registration dossier as *Key.TSCATS. OTS0000544-0.variousOTS-No.Developmental toxicity/teratogenicity to rat,* and indicated that the results from this range-finding study have been used to set the test dose used in the pre-natal developmental toxicity study. You have claimed that this information had been submitted to ECHA in a previous submission. You have also introduced new supporting information in your comments consisting in data from a dose-range finding study and from a definitive pre-natal developmental toxicity study conducted with the analogue substance 1,6-hexanediol diacrylate (HDDA, CAS No. 13048-33-4). You have considered that both studies provided are reliable to evaluate the developmental toxicity of the substance subject to this decision and you have highlighted that these studies would be included in the coming dossier update along with a read-across justification.

ECHA points out that no information on the dose-range finding study conducted with the substance subject to this decision was included in the dossier submission [redacted] which has been subject to this compliance check. You have indicated in your comments that "*The results of this study were provided for the registration in 2010 in a separate robust study summary in IUCLID*". One previous dossier submission has been recorded for this registration dossier in REACH-IT: submission number [redacted], submission date: 07/09/2010. No endpoint study record reporting the results from the dose-range finding study could be found in the technical dossier associated with this submission. The selection of the dose used in the *TSCATS. OTS0000544-0* study is justified in both submissions with the statement "

Dose selection rationale: the selected dose was specific for that material, no further information" in the endpoint study record for this study in IUCLID and with the statement "*This dose level was determined in a previous maternal tolerance study*" in section 5.9.3. Summary and discussion of reproductive toxicity of the Chemical Safety Report.

You have further indicated in your comments that "*because of the pronounced maternal toxicity including mortality at 500 mg/kg/d, half of this dose was selected for the main study*". According to the recommendation of the OECD 414 test guideline, "*at least three dose levels and a concurrent control should be used*". ECHA considers that the outcome of the dose-range finding does not justify the use of a single test dose of 250 mg/kg/d in the pre-natal developmental toxicity study, as pointed out in the draft decision issued to you.

ECHA also points out that, as outlined in the draft decision, the identity and the composition of the test material used in this *TSCATS. OTS0000544-0* study merits to be clarified. The information currently provided only allows you to "assume" that this study has been conducted with a 100% pure substance. You have not provided clarifications on this aspect in your comments. The uncertainty on the identity and composition of the test material persists and raises questions on the relevance of this data for hazard identification purposes for the substance subject to this decision.

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. All the new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

Irrespective of whether the newly provided information may be sufficient to meet the information requirement addressed in the decision, ECHA makes the following observations with regard to the new information:

- A read-across justification has been included in the dossier update to document the read-across approaches used to fulfil the information requirements for the endpoints toxicity to reproduction (fertility) and for repeated-dose toxicity after oral exposure by using data on the analogue substance HDDA. ECHA notes that the endpoint pre-natal developmental toxicity study is not included in the scope of this read-across approach.
ECHA also understands from the information provided in the comments and in this read-across justification document that the dose range finding study and the pre-natal developmental toxicity study conducted with HDDA are used as supporting information in these read-across approaches and are not meant to serve as source studies in order to predict properties of the substance subject to this decision. On that basis, ECHA considers that you have not submitted a read-across adaptation to predict the properties of the substance subject to this decision from data on the analogue substance HDDA.

- ECHA points out that according to the information provided in the updated dossier, the pre-natal developmental toxicity study conducted with the analogue substance HDDA *RA.HDDA.Hazleton299-534.Developmental toxicity/teratogenicity, rat* was conducted with a single dose of 750 mg/kg bw/day. For the reasons explained above referring to the pre-natal developmental toxicity study conducted with the substance subject to this decision ECHA highlights that this study is not compliant with the requirements of the OECD 414 test guideline whereby "*at least three dose levels and a concurrent control should be used*".
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ECHA notes that the toxicity of source and target substance appear to differ. The pre-natal developmental toxicity study using the source substance was successfully conducted at 750 mg/kg bw/day. In contrast, mortality was observed with what is claimed to be the source substance at 500 mg/kg bw/day.

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

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

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

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

In the technical dossier you have provided a study record for a "*Teratology Screen in rats using C-180, C-181, C-182, C-236, C-253, C-255, C-256, C-257, C-258 and C-259 (Revised Final Report) with cover letter*" (TSCATS/OTS0000544-0, EPA, 1987). However, this study does not provide the information required by Annex X, Section 8.7.2., for the reasons presented in section 5 above.

You have sought to adapt the information requirement of Annex X, Section 8.7.2 for a second pre-natal developmental toxicity study and you provided the following justification for the adaptation: "*Review of all available data for the so called "Multifunctional Acrylate" substances indicate, that they do not appear to represent a fetotoxic or teratogenic hazard from available data, because any effects noted (if at all) have been found at maternally toxic levels ([redacted], 1986). Testing for teratogenicity in a second species is therefore not warranted*".

While you have not explicitly claimed a specific adaptation rule in your adaptation argument, you have provided information that ECHA understands to be an attempt to adapt the information requirement according to Annex XI, Section 1.5 of the REACH Regulation. You indicate in your adaptation argument that based on the available data, the "*so called "Multifunctional Acrylate" substances indicate, that they do not appear to represent a fetotoxic or teratogenic hazard*". ECHA observes that you have not provided any information on the group of substances you refer to as ""*multifunctional acrylate" substances*" and on the identity of the members of the group. ECHA notes that the available data on the members of the groups for the endpoint under consideration that you mention in your adaptation argument has not been reported and considers that you have not demonstrated that this group of substances form a category of chemicals whose properties can be predicted from data on substances within the group as required by the provisions of Annex XI, section 1.5 of the REACH Regulation.

ECHA further highlights that you have not established and justified why the registered substance can be considered as a member of this category and that you have not provided a basis according to which the properties of the registered substance can be predicted within this category from data on other category members as required by the provisions of Annex XI, section 1.5 of the REACH Regulation.

Further, ECHA points out that you have not provided any documentation and scientific evidence to demonstrate your grouping and read-across hypothesis and to support your conclusions that *"testing for teratogenicity in a second species is therefore not warranted"* as required by the provisions of Annex XI, section 1.5 of the REACH Regulation.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information 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 consideration, ECHA considers testing should be performed with rabbits or rats as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

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

Notes for your consideration

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must consider the specific adaptation possibilities of Annex X, Section 8.7.2., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

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

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

The basic test design of an extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3, Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3.
Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) The information requirement

You have sought to adapt the information requirement of Annex X, Section 8.7.3 for an extended-one generation reproductive toxicity study and you provided the following justification for the adaptation: "*Several studies according to OECD 422 guideline have been conducted for the so called "Multifunctional Acrylate" substances. There was no indication that these type of substances do have an effect on fertility. In addition there was also no indication of an effect on reproductive organs in the available repeated dose toxicity studies conducted with "Multifunctional Acrylates". It was therefore concluded that a 2-Generation Study is not necessary as no further information gain is to be expected*".

While you have not explicitly claimed a specific adaptation rule in your adaptation argument, you have provided information that ECHA understands to be an attempt to adapt the information requirement according to Annex XI, Section 1.5. of the REACH Regulation. You indicate in your adaptation argument that based on the several studies performed with ""*so called "Multifunctional Acrylate*" substances, there are no indications that these substances do have an effect on fertility. ECHA observes that you have not provided any information on the group of substances you refer to as ""*multifunctional acrylate" substances*" and on the identity of the members of the group. ECHA further highlights that you have not established and justified why the registered substance can be considered as a member of this category and that you have not provided a basis according to which the properties of the registered substance can be predicted within this category from data on other category members as required by the provisions of Annex XI, section 1.5 of the REACH Regulation.

In your adaptation argument you refer to data generated from studies conducted according to the OECD test guideline 422. ECHA points out that the statistical power of screening studies performed according to the test guideline OECD 422 is lower than that extended from a study conducted according to the OECD test guideline 443. Further, screening studies conducted according to OECD test guideline 421/422 and repeated dose toxicity studies generate limited information on male and female reproductive performance such as gonadal function, mating behaviour, conception, development of the conceptus and parturition. In addition, due to limited exposure duration and examinations during various life stages critical information on reproductive toxicity, e.g. on sexual maturation and integrity of reproductive organs after in utero and postnatal exposure is lacking. Therefore, ECHA is of the opinion that the information obtained from screening studies performed according to the OECD test guidelines 421 and 422 and from repeated dose toxicity studies does not cover the information obtained from an extended-one generation reproductive toxicity study in regards to exposure duration, parameters, statistical power and life stages investigated.

Therefore, ECHA considers that your conclusions that "*a 2-Generation Study is not necessary as no further information gain is to be expected*" are not supported by scientific evidence and cannot be verified. As a consequence, ECHA considers that your adaptation does not meet the general rule for adaptation of Annex XI, Section 1.5. Therefore, your adaptation of the information requirement cannot be accepted.

Consequently there is an information gap and it is necessary to provide information for this endpoint. Thus, an extended one-generation reproductive toxicity study according Annex X, Section 8.7.3. is required. The following refers to the specifications of this required study.

b) The specifications for the study design

Premating exposure duration and dose-level setting

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

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.6 (version 4.0, July 2015). The highest dose level shall aim to induce some toxicity to allow comparison of effect levels and effects of reproductive toxicity with those of systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

It is recommended that results from a range-finding study (or range finding studies) for the extended one-generation reproductive toxicity study are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Extension of Cohort 1B

If the column 2 conditions of 8.7.3., Annex X are met, Cohort 1B must be extended, which means that the F2 generation is produced by mating the Cohort 1B animals. This extension provides information also on the sexual function and fertility of the F1 animals. The extension is inter alia required, if the use of the registered substance is leading to significant exposure of consumers and professionals (column 2, first paragraph, lit. (a) of section 8.7.3., Annex X) and if the substance displays genotoxic effects in somatic cell mutagenicity tests *in vivo* which could lead to classifying it as Mutagen Category 2, or there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure, or there are indications for endocrine-disrupting modes of action (column 2, first paragraph, lit. (b) of section 8.7.3., Annex X)".

The conditions to include the extension of Cohort 1B are currently not met.

In particular, whilst the condition of Annex X, column 2, section 8.7.3 (a), on exposure of consumers and professionals is met, no information from *in vivo* mutagenicity tests in somatic cell are currently available for this substance. In this specific case, this decision requires under point 4 above, an *in vivo* mammalian alkaline comet assay or a transgenic rodent somatic and germ cell gene mutation assay to be performed, which results will allow to conclude whether the second condition of section 8.7.3. (b) is met. The outcome of any of these *in vivo* mutagenicity tests shall be taken into account in establishing the design of the requested extended one-generation reproductive toxicity study. Therefore, should the substance display genotoxic effects in any of these *in vivo* somatic cell mutagenicity tests which could lead to classification as Mutagen Category 2, the conditions of Annex X, column 2, section 8.7.3 (a) and (b) would be fully met and the extension of the Cohort 1B animals to produce the F2 generation is required.

The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

Species and route selection

According to the test method EU B.56/ OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

In your comments to the draft decision, you agreed to conduct the requested study. You also suggested a tiered testing strategy according to which this extended-one generation reproductive toxicity study would be conducted before the second pre-natal developmental toxicity study and the need for conducting this second pre-natal developmental toxicity study would be re-assessed taking into account the outcome of the fertility study.

As indicated in the draft decision, the timeline is set to allow for sequential testing. You may therefore conduct the above tests in the order you find most appropriate.

Nevertheless, ECHA outlines that the provisions of Annex X, section 8.7 column 2 indicate that testing for effects on fertility must be considered even if the substance is subject to a harmonised classification or to a self-classification for developmental toxicity: *"If the substance is known to cause developmental toxicity, meeting the criteria for classification as toxic to reproduction category 1A or 1B: may damage the unborn child (H360D), and the available data are adequate to support robust risk assessment, then no further testing for developmental toxicity will be necessary. However, testing for effects on fertility must be considered."*

In this context, ECHA points out that the ECHA Guidance on information requirement and chemical safety assessment (Chapter R.7.a – endpoint specific guidance. Version 4.1 – October 2015) section R.7.6.1 define that "*fertility (as a REACH endpoint) covers functional fertility, morphological and histological changes related to reproductive organs in males and females as well as the ability to produce offspring and to nurse them*" and further specifies that "*Adverse effects on sexual function and fertility include any effect of a substance that has the potential to interfere with sexual function and fertility. This includes, but is not limited to, alterations to the female and male reproductive system, adverse effects on onset of puberty, gamete production and transport, reproductive (oestrus) cycle normality, sexual behaviour, fertility, gestation length, parturition, pregnancy outcomes, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive system".*

ECHA also screened the new information in the updated dossier. 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. All the new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

Irrespective of whether the newly provided information may be sufficient to meet the information requirement addressed in the decision, ECHA makes the following observations with regard to the new information:

A read-across justification has been included in the dossier update to document the read-across approaches used to fulfil the information requirements for the endpoints toxicity to reproduction (fertility) and for repeated-dose toxicity after oral exposure by using data on the analogue substance HDDA. The read-across approach is based on the biotransformation of the source and target substances into a common biotransformation product, i.e. acrylic acid, and two non-common alcohols.
ECHA observes that:

- No information characterising the rate and extent of the biotransformation of the source and target substances into the common and non-common compounds has been reported. A description of a common metabolic pathway – hydrolysis of the esters - does not provide quantitative information with regard to the biotransformation of the substances.

- No considerations on the impact of an exposure to the source and target substances in their native form have been included in the document.

- The extensive existing data referred to in the document to establish the toxicological properties of the non-common compounds tripproyleneglycol and hexanediol has not been included in the updated dossier.

- The source studies referred to in the read-across justification and included in the updated dossier - [redacted] - consists in a combined repeated dose toxicity with reproduction/developmental toxicity screening study performed according to the OECD 422 test guideline. Information from a screening study conducted according to the OECD test guideline 421 in rats via gavage with a single dose group of 750mg/kg/d of the analogue HDDA - *Supp.RA.HDDA.* [redacted] - has been added in the updated dossier as supporting information. As pointed out in the draft decision issued to the registrant, ECHA stresses that the information obtained from screening studies performed according to the OECD test guidelines 421 and 422 and from repeated dose toxicity studies does not cover the information obtained from an extended-one generation reproductive toxicity study in regards to exposure duration, parameters, statistical power and life stages investigated.

c) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce some toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity)
    - with extension to mate the Cohort 1B animals to produce the F2 generation if the substance displays genotoxic effects in any of the somatic cell mutagenicity tests *in vivo*, required under point 4, which could lead to classification as Mutagen Category 2;
    - without extension to mate the Cohort 1B animals to produce the F2 generation in case the above condition is not met.

Notes for your consideration

No triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if new information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the new information shows triggers which are described in column 2 of Section 8.7.3, Annex X and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.0, July 2015). You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented. The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented. The above recommendation is also relevant for extension of Cohort 1B, in case some new information other, than required under point 4 in vivo mutagenicity test, becomes available showing that the triggers for extension are met.

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

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

"Simulation testing on ultimate degradation in water" is a standard information requirement as laid down in Annex IX, section 9.2.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of simulation testing on ultimate degradation in water in the dossier that would meet the information requirement of Annex IX, Section 9.2.1.2.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement of Annex IX, Section 9.2.1.2*: "Due to the hydrophilic character and the lacking of adsorptive properties a binding of TPGDA on the sediment is negligible. Hence, TPGDA will preferentially distribute into the compartment water (cf. 5.4.3). It could be shown that TPGDA is partly biodegradable in water (cf. 5.2.1). The structural related acrylate DPGDA, which differs only in a slightly shorter chain length is readily biodegradable (cf. 5.2.1). In Analogy to DPGDA it can be expected that TPGDA is ultimately biodegradable under environmental conditions. Therefore no simulation tests on biodegradation of TPGDA are provided."*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.2.1.2, column 2 because the respective adaptation conditions are not fulfilled. The registered substance is not shown to be readily biodegradable (Key study, R1, GLP, 1997, test material identity: registered substance, CAS 42978-66-5, EC 256-032-2, test done according to OECD TG 301 B; results 48 % CO2 evolution after 28 days) and the water solubility is reported to be 4.0 g/l at 20 °C pH 5.4 (OECD 105; name of test material Tripropylenglykoldiacrylat, analytical purity: 86,5 GC-area % for the main component, as a sum of two isomers, corrected with the content of water) which cannot be considered as highly insoluble. In addition, in the IUCLID section 5.1.2, hydrolysis, you state about the registered substance that "*the structure registered substance does not contain any hydrolysable functional groups*". Furthermore, while you have not explicitly claimed an adaptation in your waiving argument, you have provided information that ECHA understands to be an attempt to adapt the information requirement according to Annex XI, Section 1.5 of the REACH Regulation. In the IUCLID section 5.2.1, Biodegradation in water: screening tests, you have provided a supporting study (OECD 301A) on a structural analogue substance (CAS 574722-68-1; name of the test substance: Laromer DPGDA PV 086324, purity 84.3%), however your dossier does not contain any proper documentation, justification and evidence as required by Annex XI, 1.5 (for example detailed substance identification for the source substance or the identification of the degradation products of the source and the target substance) to prove that it would be likely that the (ultimate) degradation behaviour between these analogues would be similar under the environmentally relevant conditions, i.e. could be predicted for the registered substance subject to the present decision. ECHA considers that your adaptation does not meet the general rule for adaptation of Annex XI; Section 1.5. Therefore, your adaptation of the information requirement cannot be accepted.

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

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

According to ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 3.0, February 2016) Aerobic mineralisation in surface water – simulation biodegradation (test method EU C.25. / OECD TG 309) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.2.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 3.0, February 2016) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment".

The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-8 (version 3.0 February 2016) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 309. Therefore, the test should be performed at the temperature of 12°C.

According to Annex XIII of REACH, the identification of PBT/vPvB substances shall take account of the PBT/vPvB-properties of relevant constituents of the substance. Impurities present in concentrations at or above 0.1 % (w/w) are deemed to be relevant constituents of the substance. Indeed, Section R.11.4.1 (page 33) of REACH Guidance document R.11 on PBT/vPvB assessment (version 2.0, November 2014) indicates that "*constituents, impurities and additives are relevant for the PBT/vPvB assessment when they are present in concentration of ≥ 0.1% (w/w). This limit of 0.1% (w/w) is set based on a well-established practice rooted in a principle recognised in European Union legislation*". Therefore the biodegradation should be assessed for each constituent and relevant impurity present in the registered substance in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable.

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

In your comments, you indicated that you would like to use a grouping approach for fulfilling the standard information requirement of Annex IX, Section 9.2.1.2. ECHA points out that the information provided in the comments for the Multifunctional acrylates, their metabolism pathways, structures and chemical composition or the speed of their degradation is not included in the dossier submission [redacted] which has been subject to this compliance check. Furthermore, in your comments you stated: *"QSAR Prediction Reporting Formats (QPRF) are available for the estimations performed and are attached to this response in separate files."* ECHA notes that you did not substantiate the QSARs further in your comments, e.g. by attachments, and that seem not to be included in your dossier update (submission [redacted]).

In your comments you provided an overview of tested and/or estimated biodegradation properties for a group of nine Multifunctional acrylates. Furthermore, you stated that: *"Multifunctional acrylates are synthesized from alcohols and acrylic acid. Although – depending on the raw material chosen – a large variety of molecules is produced, they all have the same basic structure in common and are subject to the same metabolism pathways. Different lengths of the substances as well as branched structures do impact the speed of degradation. However, based on the chemical composition and structure of the multifunctional acrylates, the generation of persistent metabolites is not expected."* However, you did not create a linkage between the biodegradation results provided in your comments and the composition of the registered substance. ECHA notes that the group of nine multifunctional di- and try-acrylates can be considered to be structurally similar to the isomers covered by the main constituent of the registered substance. All are formed by acrylic acid and various polyalcohols resembling the starting material for the registered substance.

However, the degree of branching, carbon chain lengths and molecular weights differ. These parameters may influence the outcome of the biodegradation test. In addition, ECHA notes that in your comments you did not give any explanation on why the persistent metabolites or degradation products are not expected and no further information on the metabolites or the degradation products were provided.

The information requirement addressed in this draft decision is Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2). However, the experimental data points referenced in the table 4 of your comments seem to be related to ready or enhanced biodegradation tests and should be reported in the corresponding sector of the IUCLID dossier. Given that an acceptable experimental ready biodegradation study is already available for the registered substance, these additional experimental data do not alter the outcome of the readily biodegradability test. Furthermore, the predictions and experimental data provided by you in your comments do not cover all isomers of the main constituent and the minor constituents (and impurities and additives) above 0.1% w/w that are relevant for PBT assessment.

ECHA notes that the main constituent in the registration dossier includes several positional and stereoisomers, but the compositional data does not provide information on their % w/w concentration.

As stated above, no QSAR Prediction Reporting Formats (QPRF) were made available to ECHA with your comments and therefore it is not possible to understand which test protocol was used to measure the biodegradation properties of the substances in the training set and its relevance to the particular information requirement. ECHA notes that the predictions used should be shown to cover all aspects of the adapted experimental test, including for example the identification of the degradation products and/ or metabolites and the speed of biodegradation.

Furthermore, the data currently available in the technical dossier (submission [redacted]) indicates that the registered substance is not readily biodegradable and that you have not provided any study record of simulation testing on ultimate degradation in water in the dossier that would meet the information requirement of Annex IX, Section 9.2.1.2. Consequently, there is lack of information in the technical dossier for the standard information requirement for simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2); including assessment of biodegradation of each constituent and relevant impurity present in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable.

ECHA notes that in your comments you indicated that you will further support and confirm your conclusion that the registered substance or its metabolites are not persistent, by performing a biodegradation study according to OECD Guideline 301 B (Ready Biodegradability: CO2 Evolution Test) under enhanced conditions, e.g. prolonged exposure duration.

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

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

Notes for your consideration

Before conducting the requested test you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4, R.7.9.5 and R.7.9.6 (version 3.0, February 2016). Furthermore, in accordance with Annex I, Section 4, of the REACH Regulation you shall revise the PBT assessment when results of the test detailed above is available. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

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

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

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

The results of the ready biodegradability test according to OECD TG 301 B, that you have submitted to ECHA, indicates that the registered substance is not readily biodegradable (48 % CO2 evolution after 28 days). Furthermore, you have not provided any information on the degradation products in your registration.

According to Annex XIII of REACH, the identification of PBT/vPvB substances shall take account of the PBT/vPvB-properties of relevant constituents of the substance. Impurities present in concentrations at or above 0.1 % (w/w) are deemed to be relevant constituents of the substance. Indeed, Section R.11.4.1 (page 33) of REACH Guidance document R.11 on PBT/vPvB assessment (version 2.0, November 2014) indicates that "*constituents, impurities and additives are relevant for the PBT/vPvB assessment when they are present in concentration of ≥ 0.1% (w/w). This limit of 0.1% (w/w) is set based on a well-established practice rooted in a principle recognised in European Union legislation*".

ECHA notes further that as explained fully in section (8) above, ECHA considers that with the current information gaps the CSA cannot be used to justify that there is no need to investigate further the degradation of the substance and its degradation products. ECHA notes further that the information requested here is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment.

Therefore degradation products should be identified for each constituent and relevant impurity present in the registered substance in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable. This should be done by using an appropriate analytical method. When analytically possible, the identification, stability, behaviour, molar quantity of the metabolites relative to the parent compound should be evaluated. In addition, the degradation half-life, log Kow and potential toxicity of the metabolites may also be investigated. You may obtain this information from the simulation study also requested in this decision, or by some other measure. You will need to provide a scientifically valid justification for the chosen method.
In your comments you state that the information you provided for the simulation testing on ultimate degradation in surface water (including the QSAR analyses that you aimed to separately attach to your response) demonstrates that multifunctional acrylates – including Tri(propylene glycol) diacrylate – do sufficiently degrade in the environment and do not form persistent metabolites. Furthermore, you conclude that an experimental study to identify degradation products of the registration item is therefore not deemed necessary.

ECHA points out that sufficient information on the substance identification, degradation and degradation products is currently not available in the dossier submission [redacted] which has been subject to this compliance check. Therefore, ECHA is not in the positon to verify your claim for no need to identify the degradation products for the registered substance.

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

Therefore, pursuant to Article 41(1)(a) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Identification of the degradation products by using an appropriate and suitable test method, as explained above in this section.

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016), Chapter R.7.9., Sections R.7.9.2.3 and R.7.9.4.

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

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

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2.of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

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

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex IX, Section 9.3.2, column 2 by stating that: "*Regarding the 1-octanol/water partition coefficient, accumulation of the test substance in organisms is not to be expected*".

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.3.2., column 2 because you have not demonstrated that the substance has a low potential for bioaccumulation. You, in fact refer to 1-octanol/water partition coefficient, without giving values that would cover the range for the registered substance, and have not submitted further adaptation arguments. Based on the information in the registration dossier, the direct and indirect exposure to the aquatic compartment cannot be excluded. Furthermore, the substance identification of the registered substance (UVCB) is not clear (see sections 1 and 2 of this decision), and the 1-octanol/water partition coefficient reported in the IUCLID dossier seems to be for one constituent only as explained chapter 3 above.

In addition, based on the information given in the technical dossier, there might be one or more relevant (> 0.1 % w/w) constituents which has a log Kow≥ 3 and thus is potentially bioaccumulative. Therefore, your adaptation of the information requirement cannot be accepted.

It should also be noted that according to Annex XIII of REACH, the identification of PBT/vPvB substances shall take account of the PBT/vPvB-properties of relevant constituents of the substance. Impurities present in concentrations at or above 0.1 % are deemed to be relevant constituents of the substance. Indeed, Section R.11.4.1 (page 33) of REACH Guidance document R.11 on PBT/vPvB assessment (version 2.0, November 2014) indicates that "*constituents, impurities and additives are relevant for the PBT/vPvB assessment when they are present in concentration of ≥ 0.1% (w/w). This limit of 0.1% (w/w) is set based on a well-established practice rooted in a principle recognised in European Union legislation*".

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7c* (version 2.0, November 2014) bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2.

ECHA Guidance defines further that results obtained from a test with aqueous exposure can be used directly for comparison with the B and vB criteria of Annex XIII of REACH Regulation and can be used for hazard classification and risk assessment. Comparing the results of a dietary study with the REACH Annex XIII B and vB criteria is more complex and has higher uncertainty. Therefore, the aqueous route of exposure is the preferred route and shall be used whenever technically feasible. If you decided to conduct the study using the dietary exposure route, you shall provide scientifically valid justification for your decision. You shall also attempt to estimate the corresponding BCF value from the dietary test data by using the approaches given in Annex 8 of the OECD 305 TG. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG. In your comments to the draft decision you provided a table with nine multifunctional di- and tryacrylates. For these substances you ran predictions for octanol/water partition coefficient and bioaccumulation by using EPISUITE, OASIS Catalogic and the Vega platform. ECHA notes that all the substances that these prediction were calculated are formed by acrylic acid and various polyalcohols resembling the starting material for the registered substance. However, the degree of branching, carbon chain lengths and molecular weights differ between these nine multifunctional di- and tryacrylates.

ECHA points out that the data provided by you in your comments to the draft decision is not sufficient to fulfil this information requirement. Providing predictions for structurally similar substances does not increase the confidence in the prediction of the registered UVCB substance. The confidence in the prediction can be enhanced if the predictions are accurate for structurally similar substances in the model's training/test set and if there is argumentation to demonstrate how any structural differences are likely to influence the prediction. This information is expected in the QPRFs that you did not provide to ECHA. For all QSAR predictions a QMRF describing the model is necessary to ECHA to assess the adaptation provided.

Furthermore, ECHA notes that the predictions and experimental data provided by you in your comments do not cover all isomers of the main constituent and the minor constituents of your registered substance (above 0.1% w/w) that are relevant for PBT assessment.

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision Bioaccumulation in fish: aqueous or dietary bioaccumulation fish test (test method: OECD TG 305). You shall also assess the bioaccumulation or bioconcentration of each constituent and impurity present in concentrations at or above 0.1% (w/w). This can be done simultaneously during the same study. For the PBT/vPvB assessment, the bioaccumulation or bioconcentration potential of degradation products shall also be investigated.

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R.11.4. and Figure R.11-4 on the PBT assessment for further information on the integrated testing strategy for the bioaccumulation assessment of the registered substance. You should revise the PBT assessment when information on bioaccumulation is available.

Appendix 2: Procedural history

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

The compliance check was initiated on 30 November 2015.

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

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

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

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

ECHA received proposals for amendment and modified the draft decision.
ECHA invited you to comment on the proposed amendments.

ECHA referred the draft decision to the Member State Committee.

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

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-52 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

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

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