EUROPEAN CHEMICALS AGENCY

Helsinki, 7 March 2017

Addressee: [redacted]

Decision number: CCH-D-2114355391-52-01/F
Substance name: Cyclohexyl methacrylate
EC number: 202-943-5
CAS number: 101-43-9
Registration number: [redacted]
Submission number: [redacted]
Submission date: 29.10.2013
Registered tonnage band: [redacted]

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

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

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

4. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56./OECD TG 443) in rats, oral route with the registered substance specified as follows:**
   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce some toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;**

5. **Identification of DNEL(s) and risk characterisation (Annex I, Section 1.4. and 6.): revise long-term DNEL(s) for workers inhalation route systemic and local effects using the assessment factors recommended by ECHA and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation;**

6. **Identification of PNEC and risk characterisation (Annex I, Section 3.3.1. and 6.): revise PNECs for freshwater, marine water, intermittent releases, freshwater sediment, marine sediment and soil:**
   - using the study giving rise to the highest concern according to Annex I, Section 3.1.5 and revise the risk characterisation accordingly *or* provide a full justification for not using the study giving rise to the highest concern;
   - using the default assessment factors and other recommendations of ECHA Guidance R.10 and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA Guidance R.10 for PNEC derivation

7. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: generate an exposure assessment for the manufacture and industrial uses and generate the risk characterisation accordingly.**

8. **Exposure assessment (Annex I, Section 5.1.1.) for human health:**
   - provide documentation for the recommended personal protective equipment, i.e. Hand protection;
   - specify the type of glove material, thickness and breakthrough times;

You are required to submit the requested information in an updated registration dossier by **14 September 2020** except for the information requested under point 1 for a sub-chronic toxicity study (90-day) which shall be submitted in an updated registration dossier by **14 March 2018**. You may only commence the extended one-generation reproductive toxicity study as requested under point 4 after **14 June 2018**, unless an indication to the contrary is communicated to you by ECHA before that date. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

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.

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

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Appeal

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

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

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

Appendix 1: Reasons

0. Grouping of substances and read-across approach

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

In the registration, you have adapted the standard information requirements – *inter alia* - for

- Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species
- Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species
- Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

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

Annex XI, Section 1.5. requires a structural similarity among the substances within a group or category such that relevant properties of a substance within the group can be predicted from the data on reference substance(s) within the group by interpolation.

The following analysis presents your justification for the proposed grouping approach and read-across hypothesis within your weight of evidence analysis, together with ECHA's analysis concerning the justification in both a generic and a property-specific context.

0.1 Description of the grouping and read-across approach proposed by you

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you indicate that, based on ECHA's draft decision, you revised your dossier to meet more recent ECHA Guidance. ECHA has taken into account the information provided with the comments on the draft decision according to Article 50(1). ECHA points out that, as explained in the notification letter sent to you with the draft decision, ECHA does not take into account dossier updates during the current decision making process. ECHA notes that one of the documents attached to the comments, the WoE justification document, was inaccessible and could not be considered. Therefore, ECHA has exceptionally assessed the WoE justification document, which you had provided in parallel through the dossier update.

In your comments, you indicate that in addition to the existing read-across adaptation, you choose a weight of evidence adaptation because "*grouping is based on a very limited number of chemicals and trends are not apparent*". The weight of evidence is based on the hypothesis of common (bio)transformation products and includes an expansion of the category with new source substances. You specify that "*source and target substances have the same type of toxicological effects based on common underlying mechanisms. Besides that, two of the source substances are the hydrolysis products of the target substance.*"

ECHA has assessed the available information. In the CSR, section 5.1.3 (toxicokinetics), you quote that "Cyclohexyl methacrylate belongs to the lower methacrylate esters" (OECD SIAR) (1), and that "*Other short chain alkyl-methacrylate esters, like MMA, are initially hydrolysed by non-specific carboxylesterases to methacrylic acid and the structurally corresponding alcohol in several tissues (ECETOC 1995, 1996b)*" (2)

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

In the registration dossier with submission number [redacted] you have provided the following arguments to justify the read-across approach:

1. *"Cyclohexyl methacrylate belongs to the lower methacrylate esters, of which there are extensive data available for the methyl ester (MMA) and this has been reviewed in the EU Risk Assessment (2002). Sufficient data is available to confirm applicability of this data across all members of the category and this has been reviewed in the OECD SIAR (2009)."*
2. *"Studies completed after the MMA RA [risk assessment] have confirmed that all short chain alkyl-methacrylate esters are rapidly hydrolysed by ubiquitous carboxylesterases (see table below, adapted from [redacted]; 2002). First pass (local) hydrolysis of the parent ester has been shown to be significant for all routes of exposure. For example, no parent ester can be measured systemically following skin exposure to EMA and larger esters (including n-BMA), as the lower rate of absorption for these esters is within the metabolic capacity of the skin ([redacted] 2002). Parent ester will also be effectively hydrolysed within the G. I. tract and within the tissues of the upper respiratory tract (particularly the olfactory tissue). Systemically absorbed parent ester will be effectively removed during the first pass through the liver resulting in their relatively rapid elimination from the body."*

In the comments you submitted on the draft decision according to Article 50(1) you further justify:

3. The target substance cyclohexyl methacrylate and the source substances of the "alkyl methacrylates" share structural similarities and physicochemical and toxicological properties.
4. The further source substance methacrylic acid is the common hydrolysis product of the target and source substances. Cyclohexanol is the hydrolysis product of the target substance and is also taken into account as source substance.

Furthermore, in the comments you submitted on the draft decision according to Article 50(1) of the REACH Regulation, you further expand the category by including studies for further source substances. ECHA will assess the compliance of the updated dossier including these studies after the date set out in the above decision has passed.

0.2 Support of the grouping and read-across approach

In the registration dossier with submission number [redacted] you have provided fragmented information in the CSR and in individual endpoint summaries of the registration. In summary you provide the following arguments to support the read-across approach:

1. Structural similarity to source substances methyl-methacrylate and n-butyl-methacrylate
2. Common metabolite (methacrylic acid) for all category members/source- and target substance

In the comments you submitted on the draft decision according to Article 50(1) you provided a weight of evidence- and grouping and read across approach. You argue that the expanded category therein, in support of argument 1. (above), also includes substances n-butyl-methacrylic acid, isobutyl-methacrylic acid, 2-ethyl-butyl-methacrylic acid, methacrylic acid, and cyclohexanole/cyclohexanone, which are structurally analogous to the target substance and/or its metabolites and thus, also fall under argument 2., above. ECHA will assess newly provided studies for source substances when evaluating the compliance of the updated dossier after the date set out in the above decision has passed.

ECHA observes that in the dossier with submission number [redacted] you have provided the following study summaries from analogous substances. For the endpoint "sub-chronic toxicity study (90-day), oral route" there is:

a) Chronic toxicity study (2-year; non-guideline) by the oral route with the analogous substance methyl-methacrylate (EC 201-297-1) (Borzelleca 1964)

And for the endpoint "sub-chronic toxicity study (90-day), inhalation route":

b) Sub-acute toxicity study (28-day; OECD TG 412) by inhalation with the analogous substance butyl-methacrylate (EC 202-615-1)

For the endpoint "fertility" you have provided the following study summary:

c) Two-generation reproductive toxicity study (OECD TG 416) by the oral route with the analogous substance methyl-methacrylate (EC 201-297-1) ([redacted])

For the endpoint "developmental toxicity" you have provided the following study summaries:

d) pre-natal developmental toxicity study (OECD TG 414) by inhalation in rats with the analogous substance methyl-methacrylate (EC 201-297-1) ([redacted] 1991)
e) pre-natal developmental toxicity study (OECD TG 414) by the oral route in rabbits with the analogous substance methyl-methacrylate (EC 201-297-1) ([redacted])
f) teratogenicity study (non-guideline) by the inhalation route in mice with the analogous substance methyl-methacrylate (EC 201-297-1) (Tansy 1976)

In section 5.1.3 of the CSR (toxicokinetics) you have provided a summary of toxicokinetic information based on the analogous substances methyl- and n-butyl-methacrylate to support your read-across, but have not provided any toxicokinetic information on the registered substance to support and justify your prediction.

You have provided a sub-acute repeated dose toxicity study (28 days) by the oral route with the registered substance ([redacted]).

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

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

(i) Substance characterisation of source and target substances

The substance characterisation of the source substance(s) need to be sufficiently detailed in order to assess whether the attempted prediction is not compromised by the composition and/or impurities. In the ECHA practical guide 6 "*How to report on Read-Across"* it is recommended to follow the ECHA *Guidance for identification and naming of substances under REACH and CLP* (version 1.3, February 2014) also for the source substances. This ensures that the identity of the source substance and its impurity profile allows an assessment of the suitability of the substances for read-across purposes.

ECHA notes the following observations: Purity of the analogous source substances has not been reported in studies (a) and (h), above.

(ii) Explanation on why and how the structural similarities allow predictions

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

ECHA notes the following observations:

a. Regarding argument 2. in section 0.1 above, ECHA notes that there is one study cited for risk assessment, not several, as implied by the use of plural. There is no information on gastro-intestinal uptake ratios and systemic availability provided, and neither the "*table below, adapted from* [redacted] *2002.*"
b. The qualitative nature of the argument "short chain alkyl-methacrylate esters [...] are initially hydrolysed by non-specific carboxylesterases to methacrylic acid and the structurally corresponding alcohol in several tissues" does not allow quantitative assessment. There is no specification of "several tissues".
c. Your hypothesis of structural similarity is focussed on the common metabolite methacrylic acid, and fails to include cyclohexanol as the second hydrolysis product.
d. There is no data presented to substantiate the claim that hydrolysis by ubiquitously present carboxylases happens and is quantitative. You concede that "*activities of local tissue esterases of the nasal epithelial cells appear to be lower in man than in rodents (*[redacted]*, 1996)*"
e. There is no evidence presented to substantiate the claim "toxicokinetics seem to be similar in man and experimental animal". (see section 0.3.c. below)

In the comments submitted on the draft decision according to Article 50(1) of the REACH Regulation, you provide information to address, or partly address, the shortcomings of a, b, c, d, and e.

ECHA cautions that, for the cited reference [redacted] 2002, ECHA is unable to conclude on whether or not the metabolic capacity of local tissues is indeed sufficient to support quantitative hydrolysis.

ECHA concludes that, while the information provided in your comments address some of ECHAs previous concerns, you have not addressed all differences between the source substances and the target substance. The provided explanation is not yet considered as fully valid to establish a scientific credible link between the structural similarity and the prediction.

(iii) Support of a similar or regular pattern as a result of structural similarity

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances.*" One prerequisite for a prediction based on read-across therefore is that the substances involved are structural similar and are likely to have similar properties. One important aspect in this regard is the analysis of the data matrix to compare the properties of source and target substances and to establish whether indeed they are similar or follow a regular pattern.

For the registration dossier with submission number [redacted], ECHA notes the following observations:

a. There is no data matrix available which demonstrates differences and similarities in the toxicological characteristics of the target substances and different source substances.
b. Arguments for read-across are based on studies conducted with only one analogous substance methyl-methacrylate, for all except one endpoint.
c. Available data on repeated dose toxicity (human health) of the registered substance is limited to one sub-acute (28-day) repeated dose toxicity study. There is no similarly reliable study for the analogous substance methyl-methacrylate available for comparison of effects.
d. There is no data to demonstrate any absence of effects for the hydrolysis product cyclohexanol, which constitutes [redacted]% of the molar mass balance of the registered substance.

In the comments submitted on the draft decision according to Article 50(1) of the REACH Regulation, you provide information to address, or partly address, the shortcomings of a, b, and d, which involve assessment of newly available studies. You specify that apart from experimental data on new source substances, you intend to conduct experimental studies to investigate repeated dose-, reproductive-, and developmental toxicity of the target substance, for future inclusion in a reliable data matrix. ECHA welcomes the approach as going into the right direction.

ECHA concludes that the data matrix submitted as part of the comments according to article 50(1) could indicate a similar or regular pattern of toxicity as a result of structural similarity. However, ECHA will assess newly provided studies for source substances, and newly available information for the target substance as part of a data matrix, when evaluating the compliance of the updated dossier after the date set out in the above decision has passed. Until then ECHA cannot verify the proposed category, and the proposed analogue substances. ECHA concludes that the currently available information is currently insufficient to predict properties of the registered substance.

(iv) Reliability and adequacy of the source studies

Annex XI, Section 1.5 provides, with regard to the reliability and adequacy of the source studies, that in all cases the results of the read-across should:

- *be adequate for the purpose of classification and labelling and/or risk assessment,*
- *have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3),*
- *cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter, and*
- *adequate and reliable documentation of the applied method shall be provided.*

ECHA notes the following observations:

a. The chronic toxicity study you provided (0.2.a.) is not described in sufficient detail in the dossier to allow for adequate assessment, and hence fails reliability criteria in its current state of documentation.

For the registration dossier with the submission number [redacted], ECHA concludes that the reliability of the source study 0.2.a., which investigates the properties to be read-across to the registered substance, cannot be assessed. It can therefore not be verified whether the study design is adequate and reliable for the purpose of the prediction, whether the test material used represents the source substance as described in the justification documents, and whether the results are adequate for the purpose of classification and labelling and risk assessment.

ECHA concludes that the source study 0.2.a. does not provide the information required by Annex IX, Section 8.6.2., because based on the available information it does not meet the requirements of Annex XI, Section 1.1.2. and Annex XI 1.5.

(v) Toxicokinetics

One important aspect in establishing that substances have similar effects, or follow a regular pattern, is the comparison of absorption, distribution, metabolism and elimination of source and target substances. This allows assessing the qualitative and quantitative internal systemic exposure of the test organism when exposed to source and target, respectively.

For the registration dossier with the submission number [redacted], ECHA notes the following observations:

a. There is no data presented to substantiate the claim that hydrolysis by ubiquitously present carboxylases is quantitative. You concede that "activities of local tissue esterases of the nasal epithelial cells appear to be lower in man than in rodents ([redacted], 1996)".
b. There is no reliable evidence presented to substantiate the claim "toxicokinetics seem to be similar in man and experimental animal". Data presented for the analogous substance methyl-methacrylate is limited to a high-level summary. There is no toxicokinetic data available for the registered substance. There is no toxicokinetic data available for the second source substance n-butyl-methacrylate, nor for any other potential category members with higher chain lengths.

In the comments submitted on the draft decision according to Article 50(1) of the REACH Regulation, you provide information to address, or partly address, the shortcomings of a. and b. ECHA notes that for b., information with supporting evidence is limited to comparisons after dermal uptake, and does not detail systemic effects in both experimental animals and humans. A first pass clearing effect by the liver relates to the oral route, not systemic availability in general. Furthermore, the comparison of rodent and human metabolism with supporting evidence covers only the dermal route of administration. ECHA further notes that the supporting evidence is presented for source substances, including hexyl-methacrylate, but not for the target substance.

ECHA observes that in the technical dossier you have provided a toxicokinetic assessment of source substances. ECHA notes that no toxicokinetic data has been provided on the registered substance. Consequently, it is currently not possible to conclude whether there are differences in the toxicokinetic behaviour, in particular in metabolic fate / (bio)transformation of the substances and how these differences may influence the toxicity profile of the target and source substances. ECHA considers that also due to the lack of toxicokinetic data, there is not an adequate basis for predicting the properties of cyclohexyl-methacrylate from the data of the source substances.

(vi) Bias in the selection of source substances and source study

Annex I section 1.1.4 requires "*...that the study or studies giving rise to the highest concern shall be used to establish the DNELs.;"* In the context of a read-across approach this has two aspects: the selection of the source substance and the selection of the source study.

For the registration dossier with the submission number [redacted], ECHA notes the following observations:

a. You chose the oral chronic toxicity study 0.2.a, but did not evaluate any of the repeated dose toxicity studies by the inhalation route of the source substance methyl-methacrylate, which showed signs of general systemic toxicity, including histopathological changes in several organs, at concentrations of 2000 ppm.
b. You did not provide any other studies on source substances with a wider range of side chains to demonstrate their similarities with the toxicodynamic and toxicokinetic profile of methyl-methacrylate, in order to adequately predict for similarities to cyclohexyl-methacrylate.

In the comments submitted on the draft decision according to Article 50(1) of the REACH Regulation, you provide information to address the shortcomings of a. and b. You further indicate that you will conduct experimental studies to investigate repeated dose-, reproductive-, and developmental toxicity of the target substance. ECHA welcomes your willingness to generate factual evidence from experimental studies to test your hypothesis. ECHA will assess such newly provided studies for source substances, and newly available information for the target substance, when evaluating the compliance of the updated dossier after the date set out in the above decision has passed.

ECHA concludes that it is currently not possible to verify that the source studies selected are giving rise to the highest concern and furthermore that you have selected the studies from source substances which are most appropriate, as required in Annex I, section 1.1.4.

0.4 Conclusion on the read-across approach

ECHA considers that structural similarity alone is not sufficient for predicting toxicological properties. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. ECHA notes that in view of the issues listed above it has not been reliably demonstrated that the source and read-across substances have the same properties or follow a similar pattern with regard to studies on sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.), pre-natal developmental toxicity study (Annex IX and Annex X, Section 8.7.2.) in a first and in a second species, and extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.). ECHA concludes that you have failed to meet the requirement of Annex XI, Section 1.5. that human health and ecotoxicological effects may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach).

Thus, the adaptation does not comply with the general rules of adaptation as set out in Annex XI, 1.5. Therefore, ECHA rejects all adaptations in the technical dossier that are based on Annex XI, 1.5.

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

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

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

You have not provided any study record of a sub-chronic toxicity study (90 day) in the dossier that would meet the information requirement of Annex IX, Section 8.6.2.

The technical dossier does not contain an adaptation in accordance with column 2 of Annex IX, Section 8.6.2. or with the general rules of Annex XI for this standard information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a chronic toxicity study (two year duration, possibly similar to OECD TG 452 with the analogue substance methyl-methacrylate (EC no 201-297-1). ECHA acknowledges the information you provided with your comments on the draft decision according to Article 50(1) of the REACH Regulation. However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is currently rejected.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you concluded that "*Studies available with the source substances are considered to be most relevant and suitable to cover the endpoint repeated dose toxicity and to fulfil the REACH information requirements of Annex IX, Section 8.6.2.*

Based on the WoE approach in principle the subchronic toxicity can be determined based on read-across to the lower methacrylates as well as to the metabolic cleavage products. The toxicity pattern of those products is very much in line with the low toxicity seen in the 28-day study with cyclohexyl methacrylate. Nevertheless to make the WoE approach more robust we propose a Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening (OECD 422/408). Within this extended OECD 422 study, with a 10 weeks pre-mating phase, animals will be exposed for 90 days and in addition reproduction parameter will be assessed."

ECHA acknowledges your comment and the reference to sub-chronic studies, for analogous substances with molecular weight closer to the target substance, and for the second hydrolysis product cyclohexanole. However, since your read-across approach is currently rejected and the weight of evidence approach is mainly based on the currently rejected read-across, your adaptation based on Annex XI, Section 1.2., weight of evidence, is also currently rejected.
ECHA acknowledges your agreement to perform a sub-chronic toxicity study (OECD TG 408) combined with a reproduction/developmental toxicity screening test (OECD TG 422) to make the WoE approach more robust. ECHA reminds you that the performed study needs to adequately and reliable cover the key parameters foreseen to be investigated in a sub-chronic toxicity study according to OECD TG 408.

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

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, the exposure concentrations reported in the chemical safety report for the inhalation route is low (maximum 70 mg/m^3). Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

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

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

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

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for a pre-natal developmental toxicity study (OECD TG 414) with the analogue substance methyl-methacrylate (EC no 201-297-1). However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is currently rejected.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agreed to perform a pre-natal developmental toxicity study (OECD TG 414) in a first species with the registered substance, to make the WoE approach more robust..

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

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

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

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

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

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

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

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for a pre-natal developmental toxicity study (OECD TG 414) with the analogue substance methyl-methacrylate (EC no 201-297-1).

ECHA acknowledges the information you provided with your comments on the draft decision according to Article 50(1) of the REACH Regulation. However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is currently rejected.

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

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you agreed to perform a pre-natal developmental toxicity study (OECD TG 414) in a first species with the registered substance to fulfil the standard information requirement of Annex IX, Section 8.7.2. You further indicate that "*If the results of the target and source substance are in compliance for the first species, the study for the second species is covered by using the study performed with the analogue substance MMA*". ECHA acknowledges your strategy and reminds that 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.

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.

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.

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

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

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

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

a) The information requirement

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a two-generation reproductive toxicity study (OECD TG 416) with the analogue substance methyl-methacrylate (EC no 201-297-1). ECHA acknowledges the information you provided with your comments on the draft decision according to Article 50(1) of the REACH Regulation. However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is currently rejected.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation, you concluded that "*Based on the WoE approach in principle the subchronic toxicity can be determined based on read-across to the lower methacrylates as well as to the metabolic cleavage products. The toxicological pattern of those products is very much in line with the low toxicity seen in the 28d-study with cyclohexyl methacrylate. Nevertheless to make the WoE approach more robust we propose a Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening (OECD 422/408). Within this extended OECD 422 study, with a 10 weeks pre-mating phase, animals will be exposed for 90 days and in addition reproduction parameter will be assessed.*"

ECHA acknowledges your intention to conduct a combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (OECD TG 422) in rats by the oral route with the registered substance including a pre-mating period of ten weeks to fulfil the information requirement of Annex VIII, Section 8.7.1. ECHA notes that such a study on its own does not fulfil the standard information requirement of Annex X, Section 8.7.3. for an extended one-generation reproductive toxicity study. However, such a study might support potential adaptations according to REACH Annex XI, Section 1.2. and/or 1.5. 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.

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

b) The specifications for the study design

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

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

Premating exposure duration and dose-level setting

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

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015).

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

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

Species and route selection

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

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

c) Outcome

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

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

Currently, the extension of Cohort 1B and the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) are not requested. However, the sub-chronic toxicity study (90-day) requested in this decision (request 1) and/or any other relevant information may trigger changes in the study design. Therefore, the sub-chronic toxicity study (90-day) is to be conducted first and the study results submitted to ECHA in a dossier update by **14 March 2018**. If, on the basis of this update and/or other relevant information, a need for changes to the study design is identified, ECHA will inform you by **14 June 2018** (i.e. within three months after expiry of the 12-month deadline to provide the sub-chronic toxicity study (90-day)) of its intention to initiate a new decision making procedure under Articles 41, 50 and 51 of the REACH Regulation to address the design of the extended one-generation reproductive toxicity study.

If you do not receive a communication from ECHA by **14 June 2018**, the request of the present decision for the extended one-generation reproductive toxicity study remains effective and you may commence the conduct of the study and the results will need to be submitted by the deadline given in this decision **14 September 2020**.

Notes for your consideration

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

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

5. Identification of DNEL(s) and risk characterisation (Annex I, Sections 1.4. and 6.)

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

Annex I, Section 1.4.1 of the REACH Regulation requires that the following factors shall, among others, be taken into account when deriving DNELs:

a) the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
b) the nature and severity of the effect;
c) the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
d) and that the DNELs reflect the likely route(s), duration and frequency of exposure.

The ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.8 provides further details and specifically provides default factors which should be applied to derive DNELs in the absence of substance specific information to fulfil the REACH obligations.

DNELs and assessment factors should be derived according to provisions of Annex I section 1.4.1 of the REACH Regulation or a substance specific justification is required.

ECHA notes that the assessment factors (AF) applied were not derived in accordance to the default assessment factors recommended in the ECHA Guidance R.8 for DNEL derivation and you have not provided a full justification for the derivation of DNELs in line with Annex I, 1.4.1. In particular, ECHA notes that for estimation of DNELs for long-term exposure (inhalation) - local and systemic effects - an intraspecies default AF of 3 has been used, based on ECETOC 2010, which is not in accordance with the ECHA Guidance R.8. As no adequate substance-specific justifications were provided, either the default ECHA assessment factors should be used, or substance-specific justifications for using another AF is required. According to ECHA Guidance R.8, deviations from default assessment factors should be justified with substance-specific arguments. More specifically, the introductory part of paragraph R.8.4.3, page 22 reports: "However, when the available data do not allow the derivation of substance-specific or analogue-specific assessment factors, default assessment factors should be applied."

ECHA further notes that the reference to the ECETOC guidance cannot replace the ECHA Guidance which has been agreed between all stakeholders, including industry representatives. The guidance document R.8 was developed in order to define further the derivation of DNELs according to the provisions of Annex I section 1.4.1 of the REACH Regulation. ECHA notes that in the updated dossier there are no substance specific assessment factors which would be justified by any substance specific information. As no adequate substance-specific justifications were provided to deviate from default assessment factors, ECHA concludes that default assessment factors from ECHA Guidance should be used in DNEL derivation.

As explained above, the information provided on DNEL for the registered substance in the chemical safety report does not meet the general provisions for preparing a chemical safety report as described in Annex I, 1.4.1.

Consequently, you are given two options: you shall revise the DNELs for workers by applying the assessment factors recommended by ECHA that are appropriate in this case as specified above. Subsequently, you shall re-assess related risks.

In the alternative, you shall, in accordance with Annex I, Section 1.4.1, provide a full justification for the DNELs derived for workers provided in the chemical safety report by specifying how the following has been taken into account:

a) the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
b) the nature and severity of the effect;
c) the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
d) and that the DNELs reflect the likely route(s), duration and frequency of exposure.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise long-term DNEL(s) for workers inhalation route for systemic and local effects using the default assessment factors and other recommendations of ECHA Guidance R.8 for DNEL derivation and revise the risk characterisation accordingly or provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation.

Notes for your consideration

The results of the studies requested with this decision shall be taken into account when revising the DNELs. ECHA notes that the assessment factor for intraspecies differences is not the only one deviating from those in ECHA Guidance R.8.

6. Identification of PNEC and risk characterisation (Annex I, Sections 3.3.1. and 6.)

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

Annex I, Section 3.1.5. of the REACH Regulation requires that the study or studies giving rise to the highest concern shall normally be used to draw a conclusion and a robust study summary shall be prepared for that study or studies and included in the technical dossier. In addition, Annex I, Section 3.1.5. requires that if a study giving rise to the highest concern is not used, then this shall be fully justified.

ECHA notes that you have provided PNECs that have been calculated considering that valid and reliable information for 3 short-term and 3 long-term aquatic toxicity studies were available in the dossier. However, as stated in section 0 of this Appendix, ECHA rejects the provided long-term toxicicty study results on Daphnia and fish adaptations in the technical dossier that are based on Annex XI, 1.5.. Therefore, the latter two tests cannot be used for PNEC derivation.

ECHA notes that PNECaquatic shall be calculated taking the results of the existing three short-term toxicity tests into account, using the study giving rise to the highest concern according to Annex I, Section 3.1.5 and an assessment factor of 1000 (ECHA *Guidance on information requirements and chemical safety assessment* (May 2008) R.10, Table R.10-4).

An updated derivation of the related PNECs (i.e. marine, freshwater sediment, marine sediment and soil) should also be done accordingly, following the ECHA *Guidance on information requirements and chemical safety assessment* (May 2008) R.10, chapter R.10.3.1., where information on the proper assessment factor can be found.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise PNECs for freshwater, marine water, intermittent releases, freshwater sediment, marine sediment and soil:
- using the study giving rise to the highest concern (i.e. toxicity study to aquatic algae and cyanobacteria) according to Annex I, Section 3.1.5 and revise the risk characterisation accordingly *or* provide a full justification for not using the study giving rise to the highest concern;
- using the default assessment factors and other recommendations of ECHA Guidance R.10 and revise the risk characterisation accordingly *or* provide a detailed justification on how the chosen approach meets the general requirements for PNEC derivation as described in Section 3.3. of Annex I, if not using the recommendations of ECHA Guidance R.10 for PNEC derivation.

In the comments submitted on the draft decision according to Article 50(1) of the REACH Regulation, you state that "*The dossier was revised accordingly.*" ECHA acknowledges your comment and will evaluate the updated dossier during the follow-up stage.

7. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.)

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

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

Annex I, Section 6 of the REACH Regulation requires registrants to characterise the risk for each exposure scenario and to consider the human population (exposed as workers, consumer or indirectly via the environment and if relevant a combination thereof) and the environmental spheres for which exposure to the substance is known or reasonable foreseeable, under the assumption that the risk management measures described under exposure scenario in Section 5 of the same Annex have been implemented. In addition, the overall environmental risk caused by the substance shall be reviewed by integrating the results for the overall releases, emissions and losses from all sources to all environmental compartments.

ECHA's Guidance on information requirements and chemical safety assessment, Part B: Hazard Assessment, Section B.8.4. (pages 47 to 48) (version 2.1, December 2011) states that "*if no adverse effects have been observed in studies at the highest recommended concentration/doses tested, this would normally indicate that no hazard has been identified and no DNEL or PNEC can be derived and hence exposure assessment for that route of exposure, type of effect or protection target would not be needed*".

In the CSR you provided, the exposure assessment for the environment is missing. You claimed that no exposure assessment is necessary for the environment by stating that "*In the chemical safety assessment performed according to Article 14(3) in connection with Annex I section 3 (Environmental Hazard Assessment) and section 4 (PBT/ vPvB Assessment) no hazard was identified. Therefore according to REACH Annex I (5.0) an exposure estimation is not necessary. Consequently all identified uses of the substance are assessed as safe for the environment.*"; e.g. no hazard was identified in the environmental assessment.

ECHA notes that adverse effects were observed in some environmental toxicity studies. In particular, in the algae toxicity study an EC50 of 12.5 mg/L and in the short-term toxicity study on aquatic invertebrates an EC50 of 33.9 mg/L were obtained.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to generate an exposure assessment for all the exposure scenarios, i.e. manufacture and distribution of the substance, use of substance as laboratory agent and Polymerization at production site of substance (on-site) and at downstream user sites (off-site), and revise the risk characterisation accordingly.

In the comments submitted on the draft decision according to Article 50(1) of the REACH Regulation, you state that "*The dossier was revised accordingly.*" ECHA acknowledges your comment and will evaluate the updated dossier during the follow-up stage.

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

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

According to Annex I, 0.3., 0.5. and 5.1.1. the applied Risk Management Measures (RMM) have to be described in the CSR. The CSR needs to contain sufficient information to allow ECHA to gain assurance that the risks are adequately controlled and that appropriate risk management measures can be prescribed by actors in the supply chain.

Accordingly, the supplier is required to describe the relevant RMM in detail in the Safety Data Sheet in order to minimise the exposure for workers handling the registered substance (e.g. the type of gloves to be worn, protection equipment for parts of the body other than the hand or respiratory protection shall be clearly specified based on the hazard of the substance or mixture and potential for contact and with regard to the amount and duration of exposure in accordance with Annex II, section 8.2.2.2.(b)(i), (ii) and 8.2.2.2.(c) respectively).

The information provided in the Safety Data Sheet (SDS) shall be consistent with information in the Chemical Safety Report (Annex II, section 0.1.2. of the REACH Regulation).

ECHA notes that specific detailed information on the recommended personal protective equipment is missing both from the CSR and from the information on safe use within the IUCLID dossier. In the CSR, you indicated the following for hand protection; use of suitable gloves; while in IUCLID Section 11 has reported no information on gloves.

To ensure the safe use of a substance, Annex I Section 5.1.1 requires a description of the risk management measures to reduce or avoid direct and indirect exposure of humans. Gloves need to be reported in the CSR and IUCLID Section 11 as required personal protective equipment to prevent dermal exposure to the substance. Generally, gloves that are capable of preventing exposure to the skin for a pre-determined duration shall be specified. Typically, this information, as a minimum, has to specify the glove material and, depending on the exposure scenarios, may also need to include the breakthrough time and thickness of the glove material.

Therefore, pursuant to Article 41(1)(c) you are required to provide in the CSR a description of the gloves to be used when handling the pure substance. The information provided by you shall be sufficiently detailed to allow suppliers to fulfil their obligations specified under Annex II for the compilation of the safety data sheets.

In the comments submitted on the draft decision according to Article 50(1) of the REACH Regulation, you state that "*The dossier was revised accordingly.*" ECHA acknowledges your comment and will evaluate the updated dossier during the follow-up stage.

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 12 April 2016.

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

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

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments.

ECHA referred the draft decision to the Member State Committee.

You did not provide comments on the proposed amendments.

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

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

4. In case the required test(s) is/are conducted with an analogue substance in the context of a read-across approach, the identity of the test material used to perform the test should be specified in line with ECHA's Practical Guide 6 "How to report on read-across". This is required to demonstrate that the test material is representative of the analogue substance identified in the read-across approach and used to predict the properties of the registered substance.