[If applicable: MSC identifiers]

Helsinki, 13 December 2018

Addressee: [redacted]

Decision number: CCH-D-2114453640-54-01/F
Substance name: Reaction mass of 4-(2,6,6-trimethylcyclohex-2-ene-1-yl)-but-3-ene-2-one and 4-(2,6,6-trimethylcyclohex-1-ene-1-yl)-but-3-ene-2-one
List number: 907-706-6
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 12 November 2014
Registered tonnage band: 100-1000

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. **High-pressure liquid chromatogram, gas chromatogram (Annex VI, Section 2.3.6.);**

   - **Identification and quantification of the constituents**

2. **Surface tension (Annex VII, Section 7.6.; test method: EU A.5./OECD TG 115) with the registered substance;**

3. **Partition coefficient n-octanol/water (Annex VII, Section 7.8.; using an appropriate test method) with the registered substance;**

4. **In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. / OECD TG 471) with the registered substance;**

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

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

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

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

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

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

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

12. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**

13. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

14. **Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: DOC die-away test, OECD TG 301A) or**

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Modified OECD screening test, OECD TG 301E) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F) or

    Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310)

    with the registered substance;

15. **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;**

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

17. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method:**

Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305) with the registered substance; The bioaccumulation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.

You have to submit the requested information in an updated registration dossier by ***20 December 2021***. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

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

Appeal

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

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

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

Appendix 1: Reasons

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation.

0. General considerations for toxicological and ecotoxicological information

Your registration dossier contains for the endpoints addressed in this Decision (points 4-17), adaptation arguments either in the form of a weight-of-evidence approach according to Annex XI, Section 1.2., predictions generated with the use of QSAR models under Annex XI, Section 1.3. and/or grouping and read-across approach under Annex XI, Section 1.5. of the REACH Regulation. ECHA has assessed your adaptation arguments in line with the conditions specified in Annex XI of the REACH Regulation:

(i) For the use of existing data on human health and environmental properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3), according to Annex XI, Section 1.1.2., the following conditions need to be met:

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

(ii) For the use of adaptations using Weight of Evidence (WoE) according to Annex XI, Section 1.2., it is required that there is sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion. Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to the specific standard information requirement.

Adequate and reliable documentation of the evidence based approach needs to be provided. This documentation describes how the assessment of the relative weights of different pieces of the available information has been retrieved and gathered, how the individual components have been integrated with their relative weights and how the conclusion is drawn. The weight given to the available evidence will be influenced by factors such as the quality of the data, consistency of results/data, nature and severity of effects, relevance of the information for

the given regulatory endpoint.

(iii) For the use of QSAR models under Annex XI, Section 1.3., the following conditions shall be necessarily fulfilled: results are derived from a (Q)SAR model whose scientific validity has been established; the substance falls within the applicability domain of the model; results are adequate for the purpose of classification and labelling and/or risk assessment; adequate and reliable documentation of the applied method is provided.

(iv) For the use of read-across approach according to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Unambiguous substance identity for both the source substance and the target substance is therefore a prerequisite for a read-across assessment. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data on reference substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[2]. This hypothesis explains why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case. Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

In your comments on the draft decision, regarding your read-across approach you indicate that > [redacted]% of the registered substance consists of [redacted], and therefore, the data generated with the registered substance or the individual constituent are relevant for assessing the toxicological properties of the registered substance.

ECHA notes that in your comments to the draft decision, you do not bring any new arguments and/or respond to the deficiencies identified by ECHA in your read-across justification. Your adaptation arguments in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation are rejected.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest

[2] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.

dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

1. High-pressure liquid chromatogram, gas chromatogram (Annex VI, Section 2.3.6.)

"High-pressure liquid chromatogram (HPLC) or gas chromatogram (GC)" is an information requirement as laid down in Annex VI, Section 2.3.6. of the REACH Regulation. Adequate information needs to be present in the technical dossier to meet this requirement.

The HPLC (file name "[redacted]") attached in IUCLID section 1.4 includes a chromatogram on pag. 2 which shows two peaks identified with CAS numbers 127-41-3 and 14901-07-6, which are the same CAS used for the identification of the main constituents in IUCLID section 1.2 for the multi-constituent substance. However, the chromatogram shows also a large peak (retention time 150-250 min.) which has not been identified, nor quantified.

The presence of such unidentified peak, and the lack of explanation on why this peak is present in the chromatogram, does not allow the verification of the composition of the registered substance as provided in IUCLID section 1.2.

In your comments to the draft decision you agreed to provide the requested information.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

Therefore, you are requested to explain how the results of the HPLC have been used to determine the composition of the registered substance as reported in IUCLID 1.2. In particular you will need to identify the peak, and explain why it was not taken into consideration for deriving the composition of the substance.

You shall provide this information in IUCLID section 1.4.

2. Surface tension (Annex VII, Section 7.6.)

"Surface tension" is a standard information requirement as laid down in Annex VII, Section 7.6 of the REACH Regulation.

You have provided a calculated value using the [redacted] PhysChem Suite for one of the constituents of the registered substance. ECHA has evaluated the information as a QSAR prediction under a read-across approach. While ECHA acknowledges that the structure used for the prediction is one of the constituents of the registered substance, and the structural difference between the two constituents of the registered substance is only the position of the double bond, you have not explained why the model used for the calculation fulfils the criteria in Annex XI, Section 1.3. In particular, you have not established the scientific validity of the model, you have not shown that the substance falls within the applicability domain of the model, and you have not provided adequate and reliable documentation of the applied method.

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 to the draft decision you agreed to provide the requested information.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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: Surface tension (test method EU A.5) or surface tension of aqueous solutions (test method: OECD TG 115).

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

"Partition coefficient n-octanol/water" is a standard information requirement as laid down in Annex VII, Section 7.8 of the REACH Regulation.

You have provided a weight-of-evidence (WoE) approach according to Annex XI, Section 1.2. The experimental studies provided as part of the WoE approach for the registered substance and for one of the constituents of the registered substance have not been performed according to any accepted test guideline and the reporting is inadequate for ECHA to perform an independent assessment of the results. The third part of the WoE approach is a value taken from a publication and a database and report a much higher value for this endpoint. In addition, the category justification document attached to the dossier reports also much higher values for the proposed category members. ECHA has evaluated the provided sources of information individually and together with respect to relevance and reliability and concludes that the value used for Chemical Safety Assessment (1.620 at 25 °C and pH 5.29) is not consistent. Therefore, the WoE adaptation is rejected.

In your comments to the draft decision you refer to an existing study (logKow reported as 4.1) and that you have updated the dossier with this study. You request ECHA to remove this request from the decision.

ECHA cannot evaluate the relevance or the results of this study based on the information submitted in your comments to the draft decision, i.e. a single value.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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.

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. Guidance for determining appropriate test methods for the partition coefficient n-octanol/water is available in the ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.1.8 (version 6.0, July 2017).

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

An "In vitro gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. of the REACH Regulation.

According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA.

In your registration dossier you have provided the following:

i. One experimental study report, based on publication (J. Lalko, et al., Food and Chemical Toxicology 45 (2007) S251–S257). The test material used is the registered substance. The study uses S. *typhimurium* strains TA100, TA1535, TA1538, TA98 and TA1537. Results: negative with and without metabolic activation. You flagged the study as "WoE".
ii. Weight of evidence QSAR prediction with *S. typhimurium* TA 102 without S9 for the registered substance. In the technical dossier you provided an automated report generated with the OECD QSAR Toolbox indicating negative results.
iii. One experimental study report based on publication (Mortelmans, K, et al., Environ. Mutagen. Vol. 8 (Suppl 7) (1986) 1-119). The test material used is a read-across substance bete ionone (4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one EC no. 238-969-9). The study uses S. *typhimurium* strains TA100, TA1535, TA1538, TA98 and TA1537. Results: negative with and without metabolic activation. You flagged the study as "WoE".

Based on this information, ECHA understands that you have sought to adapt this information requirement according to Annex XI, Sections 1.2 and 1.5. of the REACH Regulation. However, ECHA notes that the experimental study (i) does not meet the information requirements, covered by OECD TG 471 (updated 1997). According to paragraph 13 of the test guideline, at least five strains of bacteria should be used: S. *typhimurium* TA1535; TA1537 or TA97a or TA97; TA98; TA100; S. *typhimurium* TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101). This includes four strains of S. *typhimurium* (TA1535; TA1537 or TA97a or TA97; TA98; and TA100) that have been shown to be reliable and reproducibly responsive between laboratories. These four S. *typhimurium* strains have GC base pairs at the primary reversion site and it is known that they may not detect certain oxidising mutagens, cross-linking agents and hydrazines. Such substances may be detected by *E.coli* WP2 strains or *S. typhimurium* TA102 which have an AT base pair at the primary reversion site. The experimental study (i) does not include information obtained from testing in strains capable of detecting certain oxidising mutagens, cross-linking agents and hydrazines.

Similarly, the source study (iii) (Mortelmans et al., 1986) used in your read-across approach also does not include information obtained from testing in strains capable of detecting certain oxidising mutagens, cross-linking agents and hydrazines.

Furthermore, you have indicated "(Q)SAR" in the administrative section of the endpoint study record in the technical dossier for the above-mentioned study (ii). You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict gene mutation in bacteria for the registered substance based on read-across.

ECHA has hence assessed your adaptation in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation and notes that:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence it is not possible to conclude whether properties could be read across.

You have further indicated within the Endpoint Study Summary for "Genetic Toxicity in vitro" that you consider the information you provided in the Endpoint Study Records for Genetic Toxicity *in vitro* to be a Weight of Evidence Approach.

ECHA notes that, for the reasons explained above, the information provided does not constitute relevant and reliable information in the context of a weight of evidence approach.

ECHA therefore concludes that:

- The proposed adaptation is not in line neither with the conditions specified in Annex XI, Section 1.5., nor with those specified in Annex XI, Section 1.2. and is therefore rejected.
- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

In your comments to the draft decision you refer to existing studies and a publication performed with "target substance" or "read-across substances". You indicate that the substance is "not likely to classify as a gene mutant in vitro". You further state that "the study has been updated in the dossier", therefore you request ECHA to remove this request from the decision.

ECHA notes that in your comments you have provided two study records. ECHA points out that one of the studies you refer to, based on a publication (Food and Chemical Toxicology, 2007) has already been assessed and rejected in the draft decision sent to you. Moreover, ECHA notes that you have disregarded the study, by assigning a reliability score of 4 (not

assignable) in your IUCLID dossier. Further, ECHA notes that for the second study you refer to in your comments, you have not specified the test material and why you consider it representative for the registered substance. Therefore, ECHA cannot evaluate the relevance or the results of the study presented in the comments.

In addition, ECHA notes that you have not improved your read-across justification, which was rejected by ECHA in Section 0 of this decision.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit following information derived with the registered substance subject to the present decision: Bacterial reverse mutation test (test method: EUB.13/14. / OECD TG 471).

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

An "In vitro cytogenicity study in mammalian cells or an in vitro micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. of the REACH Regulation.
In your registration dossier you have provided the following:

i. Weight of evidence QSAR prediction with Chinese hamster lung cells. You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict chromosome aberration for the registered substance based on read-across. The report indicates negative results.
ii. Weight of evidence QSAR prediction for the analogue substance 4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one (EC no 204-841-6) using the Danish EPA Model predicting negative results.

Based on this information, ECHA understands that you have sought to adapt this information requirement according to Annex XI, Sections 1.2 and 1.5. of the REACH Regulation.

Furthermore, you have indicated "(Q)SAR" in the administrative section of the endpoint study record in the technical dossier for the above-mentioned study (ii). You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this

report that it is used to predict chromosome aberration for the registered substance based on read-across.

ECHA has hence assessed your adaptation in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation and notes that:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence it is not possible to conclude whether properties could be read across.

You have further indicated within the Endpoint Study Summary for "Genetic Toxicity in vitro" that you consider the information you provided in the Endpoint Study Records for Genetic Toxicity *in vitro* to be a Weight of Evidence Approach.

ECHA notes that, for the reasons explained above, the information provided does not constitute relevant and reliable information in the context of a weight of evidence approach.

ECHA therefore concludes that:

- The proposed adaptation is not in line neither with the conditions specified in Annex XI, Section 1.5., nor with those specified in Annex XI, Section 1.2. and is therefore rejected.

- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

In your comments to the draft decision you refer to data from publication and study report for the "target substance" and "read-across substances". You indicate that the substance is "not mutagenic in the bacteria" and you request ECHA to remove this request from the decision. Further you state that "the study has been updated in the dossier".

Firstly, ECHA notes that in the studies you have provided in your comments, you refer to the tested substance as "test chemical", without specifying if the studies have been performed with the registered substance or with a read-across substance. Moreover, you did not explain why you consider the "test material" representative for the registered substance. Therefore, ECHA cannot evaluate the relevance or the results of the study presented in the comments.

In addition, ECHA notes that you have not improved your read-across justification, which was rejected by ECHA in Section 0 of this decision.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained. Currently your dossier does not have acceptable information on the two information requirements mentioned above under points 4 and 5. Adequate information on *in vitro* gene mutation in mammalian cells will however need to be present in the technical dossier for the registered substance to meet this information requirement provided that both studies requested under 4 and 5 have negative results.

In your comments to the draft decision you state that data has been already generated as per OECD TG 476. You further state that "the study has been updated in recent dossier update", therefore, you request ECHA to remove this request from the decision.

ECHA notes that you have not specified the test material used in the study and why you consider it representative for the registered substance. Therefore, ECHA cannot evaluate the relevance or the results of the study presented in the comments.

In addition, ECHA notes that you have not improved your read-across justification, which was rejected by ECHA in Section 0 of this decision.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that both studies requested under 4 and 5 have negative results.

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

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.

In the technical dossier you have provided the following study records as weight of evidence:

(i) Published study (E. C. Hagan et al., 1967; Fd Cosmet. Toxicol. Vol 5, pp. 141-157). Chronic oral toxicity study in rats with the registered substance. The LOAEL was considered to be 50 mg/kg/day.

(ii) Weight of evidence QSAR prediction for a 28-day repeated dose toxicity study with the registered substance. You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict the chronic/sub-chronic properties of the registered substance based on read-across. A dose descriptor of 180 mg/kg/d is predicted.

(iii) One experimental study report based on publication (Oser et al., 1965; Fd Chem. Toxicology: Vol . 3, page 563-569). The test material used is the analogue substance 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one (EC no. 238-969-9). The study is an oral 90-day repeated dose toxicity study conducted in rats using a single test dose and identifying a NOAEL of 11.6 mg/kgbw/d. You flagged the study as "WoE".

(iv) One experimental study report based on publication (Oser et al., 1965; Fd Chem. Toxicology: Vol . 3, page 563-569). The test material used is the analogue substance 4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one (EC no. 204-841-6). The study is an oral 90-day repeated dose toxicity study conducted in rats using a single test dose and identifying a NOAEL of 11.1 mg/kgbw/d. You flagged the study as "WoE".

(v) Published study (Fukuyama et al., 1999; Toxicology Letters 111 (1999) 175–187). 6-week inhalation toxicity study in female rats with the registered substance. The NOAEC was established at 5 mg/m^3. You flagged the study as "WoE".

(vi) Weight of evidence QSAR prediction for a 28-day repeated dose toxicity study with the registered substance. You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict the chronic/sub-chronic properties of the registered substance based on read-across. A dose descriptor of 672 mg/m^3 is predicted.

(vii) Published study (Baker et al., 2004; Food and Chemical Toxicology 42S (2004) S53–S83). 90-day inhalation toxicity study in rats with the analogue substance 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one (EC no 238-969-9). The NOAEC was established at 7.5 mg/L. You flagged the study as "WoE".

(viii) Published study (Baker et al., 2004; Food and Chemical Toxicology 42S (2004) S53–S83). 90-day inhalation toxicity study in rats with the analogue substance

4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one (EC no 204-841-6). The NOAEC was established at 10 mg/L. You flagged the study as "WoE".

(ix) Weight of evidence QSAR prediction for a 28-day repeated dose toxicity study with the registered substance. You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict the sub-acute toxicity properties of the registered substance based on read-across. A dose descriptor of 262.5 mg/kg bw/d is predicted.

(x) Information from a 90-day dermal study conducted by the US EPA in rabbits with the analogue substance 4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one (EC no 204-841-6) (HPV141 U.S. Environmental Protection Agency - (http://www.epa.gov/HPV/pubs/summaries/viewsrch.htm)). The lowest toxic dose established at 180 ml/kg. You flagged the study as "WoE".

Based on this information, ECHA understands that you have sought to adapt this information requirement according to Annex XI, Sections 1.2 and 1.5. of the REACH Regulation.

ECHA points out that the limited reporting of the study (i) (Hagan et al, 1967) reveals shortcomings in the study design when compared to the recommendations of the OECD test guideline 408. Specifically, the number of animals used insufficient, no dose selection rationale not provided, in-life observations insufficient, blood chemistry parameters not provided, limited pathology and histopathology performed. Furthermore, ECHA highlights that the study (v) (Fukuyama et al, 1999) was conducted in female rats only over a period of 6 weeks. These are significant deviations from the recommendations of the OECD TG 413 requiring testing over 13 weeks in both sexes.

Therefore ECHA concludes that the information obtained from these studies is not adequate on their own to fulfil the information requirement of Annex IX, Section 8.6.2 for a sub-chronic (90-day) repeated dose toxicity study.

ECHA has further assessed your adaptation in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation and notes that for the information provided as study (ii), study (vi) and study (ix) above:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence it is not possible to conclude whether properties could be read across.

With regard to the information reported from studies (iii), (iv), (vii) and (viii) above conducted with analogue substances, ECHA points out that you have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s). You have also not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance. Furthermore, ECHA observes only one test dose was used in these studies. This shortcoming impacts the adequacy of these studies for hazard identification and risk assessment purposes.

ECHA observes that the limited reporting of the study (x) (US EPA, 2001) does not allow for an independent assessment of the adequacy and reliability of this information. ECHA also stresses that you have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s). You have also not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.

You have flagged all the information presented above as weight of evidence. ECHA notes that, for the reasons explained above, the information provided does not constitute relevant and reliable information in the context of a weight of evidence approach.

ECHA therefore concludes that:

- The proposed adaptation is not in line neither with the conditions specified in Annex XI, Section 1.5., nor with those specified in Annex XI, Section 1.2. and is therefore rejected.
- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

In your comments to the draft decision, you refer to several studies available to assess chronic toxicity of the registered substance. You further refer to Annex VIII, Column 2 to waive the requested study and you request ECHA to remove the request in the decision.

ECHA notes that all of the studies you referred to in your comments to the draft decision have already been assessed and rejected by ECHA and the reasons for that are provided above in this draft decision. Further, ECHA points out that Annex VIII, Section 8.6.1., Column 2 describes the conditions under which a 28-day repeated dose toxicity study can be omitted for substances registered for 10-100 tonnes per year (Annex VIII). However, your registration is for 100 -1000 tonnes per year and an adaptation according to Annex VIII, Column 2 is not relevant for this endpoint.

In addition, ECHA notes that you have not improved your read-across justification, which was rejected by ECHA in Section 0 of this decision.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration.

Hence, the test shall be performed by the oral route using the test method OECD TG 408.

According to the test method 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: OECD TG 408) in rats.

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

A "reproductive/developmental toxicity screening test " (OECD TG 421) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation.

In the technical dossier under this endpoint you have provided the following information:

i. Weight of evidence QSAR prediction for a reproductive/developmental toxicity screening test with the registered substance. You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict the reproductive toxicity properties of the registered substance based on read-across. A dose descriptor of 409 mg/kg/d is predicted.

ii. Weight of evidence QSAR prediction for an estrogen receptor binding assay with the registered substance. You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict the affinity of the registered substance to bind the estrogen receptor based on read-across. A prediction of 2.75E-03 % is reported.

iii. Published study (Willhite, 1986; Toxicology and Applied Pharmacology 83, 563–575.S53–S83) investigating "The teratogenic potency of b-ionone was evaluated in timed pregnant LHK:LVG (SYR) hamsters". This study was conducted with the analogue substance 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one (EC 238-969-9) via the oral route. The NOAEL was established at 240 mg/kg bw/d. You flagged the study as "WoE".

iv. Published study (Gomes-Carneiro et al., 2003; Toxicology Letters 138, 205–213) investigating "the reproductive and embryotoxic effect of β-ionone was evaluated

in pregnant Wistar rats treated by gavage with BI.Effect of BI on embryolethal effects of cyclophosphamide(CP)". This study was conducted with the analogue substance 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one (EC 201-224-3) via the oral route. The NOAEL was established at 750 mg/kg bw/d. You flagged the study as "WoE".

v. Published study (Politano et al., 2007; International Journal of Toxicology, 26:271–276, 2007) on the "Evaluation of the Developmental Toxicity of Alpha-iso-methylionone in Rats". This study was conducted with the analogue substance 3-methyl-4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one (EC 204-846-3) in rats via the oral route. The NOAEL was established at 30 mg/kg bw/d. You flagged the study as "WoE".

Based on this information, ECHA understands that you have sought to adapt this information requirement according to Annex XI, Sections 1.2 and 1.5. of the REACH Regulation.

ECHA has assessed your adaptation in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation and notes that for the information provided as study (i) and study (ii) above:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence it is not possible to conclude whether properties could be read across.

With regard to the information reported from studies (iii), (iv) and (v) above conducted with analogue substances, ECHA points out that you have not provided any documentation or any assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s). You have also not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance. Furthermore, ECHA points out that the investigations reported in these publications have not been conducted according to internationally recognised test guidelines. No critical assessment of the design of hese studies against the recommendations of the OECD test guideline 421 identifying the deviations and limitations of each of these studies has been included in the technical dossier. Therefore ECHA considers that you have not established how and why these lines of information, when taken together, can be used to conclude on the reproductive toxicity of the registered substance.

You have flagged all the information presented above as weight of evidence. ECHA notes that, for the reasons explained above, the information provided does not constitute relevant and reliable information in the context of a weight of evidence approach.

ECHA therefore concludes that:

- The proposed adaptation is not in line neither with the conditions specified in Annex XI, Section 1.5., nor with those specified in Annex XI, Section 1.2. and is therefore rejected.
- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

In your comments to the draft decision you refer to reproductive toxicity studies performed with "Reaction mass the test chemical". You conclude that "no adverse effects on reproductive function were observed" for the "target substance", and "no adverse effects on sexual function and fertility" were observed for "the test chemical" and "its read-across substance". You request ECHA to remove the request from the decision.

ECHA notes that most of the studies you referred to in your comments have already been evaluated and rejected by ECHA and the reasons for that are provided above in this decision. Moreover, ECHA notes that you have not improved your read-across justification, which was rejected by ECHA in Section 0 of this decision.

In addition you refer to a reproductive toxicity study by Belisto et al. (publication in Food and Chemical Toxicology, 2007), performed with a "test chemical" in rats. You have not specified the test material used in the study and why you consider it representative for the registered substance. You did not specify the guidelines followed or the GLP compliance of the study. Therefore, ECHA cannot evaluate the relevance or the results of the studies presented in the comments.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

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

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

by the oral route.

Notes for your considerations

You should also carefully consider the order of testing of the requested screening (OECD TG 421/422) and the developmental toxicity studies (OECD TG 414) to ensure that unnecessary animal testing is avoided, paying particular attention to the endpoint specific guidance Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)

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

A "pre-natal developmental toxicity study" (test method 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.

In the technical dossier under this endpoint you have provided the following information:

i. Weight of evidence QSAR prediction for a pre-natal developmental toxicity study with the registered substance. You provided an automated report generated with the OECD QSAR Toolbox and it is indicated within this report that it is used to predict the pre-natal developmental toxicity properties of the registered substance based on read-across. A NOAEL of 194 mg/kg bw/d is predicted

ii. Published study (Politano et al., 2007; International Journal of Toxicology, 26:271–276, 2007) on the "Evaluation of the Developmental Toxicity of Alpha-iso-methylionone in Rats". This study was conducted with the analogue substance 3-methyl-4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one (EC 204-846-3) in rats via the oral route. The NOAEL was established at 30 mg/kg bw/d. You flagged the study as "WoE".

iii. Published study (Willhite, 1986; Toxicology and Applied Pharmacology 83, 563–575.S53–S83) investigating "The teratogenic potency of b-ionone was evaluated in timed pregnant LHK:LVG (SYR) hamsters". This study was conducted with the analogue substance 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one (EC 238-969-9) via the oral route. The NOAEL was established at 480 mg/kg bw/d and 240 mg/kg bw/d for the F1 generation. You flagged the study as "WoE".

iv. Published study (Gomes-Carneiro et al., 2003; Toxicology Letters 138, 205–213) investigating "the reproductive and embryotoxic effect of β-ionone was evaluated in pregnant Wistar rats treated by gavage with BI.Effect of BI on embryolethal effects of cyclophosphamide(CP)". This study was conducted with the analogue substance 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one (EC 201-224-3) via the oral route. The NOAEL was established at 750 mg/kg bw/d for maternal toxicity and at 1000 mg/kg bw/d for developmental toxicity. You flagged the study as "WoE".

Based on this information, ECHA understands that you have sought to adapt this information requirement according to Annex XI, Sections 1.2 and 1.5. of the REACH Regulation.

ECHA has assessed your adaptation in line with the conditions specified in Annex XI, Section 1.5. of the REACH Regulation and notes that for the information provided as study (i) and study (ii) above:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence it is not possible to conclude whether properties could be read across.

With regard to the information reported from studies (iii), (iv) and (v) above conducted with analogue substances, ECHA points out that you have not provided any documentation or any assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s). You have also not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance. Furthermore, ECHA points out that the investigations reported in these publications have not been conducted according to internationally recognised test guidelines. No critical assessment of the design of hese studies against the recommendations of the OECD test guideline 414 identifying the deviations and limitations of each of these studies has been included in the technical dossier. Therefore ECHA considers that you have not established how and why these lines of information, when taken together, can be used to conclude on the pre-natal developmental toxicity of the registered substance.

You have flagged all the information presented above as weight of evidence. ECHA notes that, for the reasons explained above, the information provided does not constitute relevant and reliable information in the context of a weight of evidence approach.

ECHA therefore concludes that:

- The proposed adaptation is not in line neither with the conditions specified in Annex XI, Section 1.5., nor with those specified in Annex XI, Section 1.2. and is therefore rejected.
- Contrary to Article 3(28) of the REACH Regulation, the documentation of the endpoint study records is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment.

In your comments to the draft decision you refer to "different studies" performed with "Reaction mass the test chemical". You further state in your comments that "the study has been recently updated within the dossier".

Firstly, ECHA points out that one of the studies you refer to in your comments (Gomes-Carneiro et al., 2003; Toxicology Letters 138, 205–213), performed with the analogue substance (EC 201-224-3) has already been analysed and rejected by ECHA and the reasons for that are provided above in this draft decision.

Secondly, ECHA notes that in the comments to your draft decision you refer to two studies, reported in a publication in *Regulatory Toxicology and Pharmacology* 97, 2018; 110-119. In the first study you refer to the test material as "test chemical" and in the second study the test substance is described as "alpha-iso-methylionone". You did not explain why you consider the test material in both studies to be representative for the registered substance. Therefore, ECHA cannot evaluate the relevance or the results of the studies presented in the comments.

Moreover, ECHA notes that you have not improved your read-across justification, which was rejected by ECHA in Section 0 of this decision.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section 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: OECD TG 414) in a first species (rat or rabbit) by the oral route.

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

"Short-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex VII, Section 9.1.1. of the REACH Regulation.

In the technical dossier under this endpoint you have provided the following information:

- Weight of evidence ("(Q)SAR", reliability 2): an automated report generated with the OECD QSAR Toolbox, 48-h EC50 6.87 mg/L;
- Weight of evidence ("(Q)SAR", reliability 2): an automated report generated with the OECD QSAR Toolbox, 48-h EC50 5.6 mg/L; and
- Weight of evidence ("read-across based on grouping of substances", reliability 2): publication Gutiérrez et al. 2009, Daphnia magna, test material Alpha iso methyl ionone (CAS 127-51-5, EC 204-846-3), LC50 0.02 mg/L.

ECHA has evaluated the information you have provided and notes the following:

The two first study records you provided include automated reports generated with the OECD QSAR Toolbox and it is indicated in these reports that it is used to predict the 48-h EC50 on *Daphnia magna* for the registered substance based on read-across.

ECHA has hence assessed your adaptation in line with the conditions specified in *General considerations for toxicological and ecotoxicological information* (section iv for read-across approach) and notes that:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence concluding whether properties could be read across.

The third study record is not a guideline study and it is based on a publication by Gutiérrez et al. (2009). You report that the study is conducted with effluent but you also report Alpha iso methyl ionone (CAS 127-51-5, EC 204-846-3) as the test substance. ECHA has assessed your adaptation in line with the conditions specified in *General considerations for toxicological and ecotoxicological information* and firstly notes that, while there is a read-across justification document provided in Section 13 of the IUCLID dossier, the source substance Alpha iso methyl ionone (CAS 127-51-5, EC 204-846-3) is not listed as a source substance in that justification document. There is no other documentation in the IUCLID dossier to justify the read-across prediction from this source substance. Therefore, your dossier is lacking a basis for predicting relevant ecotoxicological properties of the registered substance from data for the source substance. Secondly, you have not provided adequate and reliable documentation of the non-guideline study which would enable assessment of the study and its adequacy for the purpose of classification and labelling and/or risk assessment. For example, it is unclear how the effect value of 0.02 mg/L has been derived from the data on the effluent.

You have further indicated in the Endpoint Study Summary for "Short-term toxicity to aquatic invertebrates" that you consider the information you provided for this endpoint in a Weight of Evidence Approach.

ECHA has assessed your adaptation in line with the conditions specified in *General considerations for toxicological and ecotoxicological information* (section ii for weight of evidence approach) and notes that: You have not provided sufficent documentation to describe the assigned weights of different pieces of evidence and subsequent integration and comparison of all information pieces with their relative weights in order to draw a conclusion on the hazard property. Therefore the information provided does not constitute relevant and reliable information in the context of a weight of evidence approach.

ECHA therefore concludes that the proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.2. and is therefore rejected.

In your comments to the draft decision you referred to studies performed according to OECD TG 202 and EU C.6. You concluded that the "test chemical is toxic to the aquatic environment" and can be considered to be classified as Aquatic Chronic 2. You requested ECHA to remove the request from the decision.

The studies referred to in your comments on the draft decision did not contain sufficient information, for example on the test material, test guideline or GLP status, for ECHA to evaluate the relevance or the results of the referred studies.

In addition, classification as Aquatic Chronic 2 is not an acceptable waiver for this endpoint.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

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

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

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation.

In the technical dossier under this endpoint you have provided the following information:

- Weight of evidence ("(Q)SAR", reliability 2): an automated report generated with the OECD QSAR Toolbox, 72-h EC50 1.93821 mg/L; and
- Weight of evidence ("read-across based on grouping of substances (category approach)", reliability 2): publication Shaoa et al 2011, test material: 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one (CAS 14901-07-6, EC 238-969-9), *Microcystis aeruginosa*, Strain: NIES-843, EC50 21.23 mg/L

ECHA has evaluated the information you have provided and notes the following:

The first study record you provided includes an automated report generated with the OECD QSAR Toolbox and it is indicated in this report that it is used to predict the 72-h EC50 on *Pseudokirchneriella subcapitata* for the registered substance based on read-across.

ECHA has hence assessed your adaptation in line with the conditions specified in *General considerations for toxicological and ecotoxicological information* (section iv for read-across approach) and notes that:

- You have not provided an assessment to address structural similarity/dissimilarity between the registered substance and the proposed analogue(s).
- You have not provided any read-across hypothesis establishing why the results generated with the source substance can be used to predict the results for the target substance.
- You have not provided any experimental studies neither with the registered substance nor with structurally similar analogue(s) which would substantiate the prediction. Absence of experimental data to substantiate the hypothesis for the prediction makes any adaptation based on read-across invalid as it does not allow a comparative assessment of properties of the source and target substance and hence concluding whether properties could be read across.

The second study record presents a publication Shaoa et al 2011 and is not a guideline study. It describes the toxicity of beta ionone (a constituent of the registered substance) in *Microcystis aeruginosa*. ECHA notes that the species is not suitable using the test procedures specified in the OECD TG 201 (Annex II) / EU C.3 (Appendix 1) and thus fulfilling this standard information requirement. You have not reported the growth rates of the controls during the study nor confirmed that exponential growth has been maintained throughout the test period under the prevailing conditions.

You have further indicated in the Endpoint Study Summary for "Toxicity to aquatic algae and cyanobacteria" that you consider the information you provided for this endpoint in a Weight of Evidence Approach.

ECHA has assessed your adaptation in line with the conditions specified in *General considerations for toxicological and ecotoxicological information* (section ii for weight of evidence approach) and notes that: You have not provided sufficent documentation to describe the assigned weights of different pieces of evidence and subsequent integration and comparison of all information pieces with their relative weights in order to draw a conclusion on the hazard property. Therefore the information provided does not constitute relevant and reliable information in the context of a weight of evidence approach.

ECHA therefore concludes that the proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.2. and is therefore rejected.

In your comments to the draft decision you referred to studies performed according to OECD TG 201, a publication and a third study without any bibliographical reference. You concluded that "the chemical" is toxic and can be considered to be classified as Aquatic Chronic 3. You requested ECHA to remove the request from the decision.

The studies referred to in your comments to the draft decision did not contain sufficient information, for example on the test material for ECHA to evaluate the relevance or the results of the referred studies.

In addition, classification as Aquatic Chronic 3 is not an acceptable waiver for this endpoint.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Algae growth inhibition test, EU C.3./OECD TG 201).

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

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.5., column 2. You provided the following justification for the adaptation: *"According to annex IX of column I ; Long-term toxicity testing on invertebrate (species : Daphnia magna) need not to be conducted as it is already provided as a part of Annex VII requirements.Therefore this end point was considered for waiver."*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2 because you have not provided a long-term toxicity study on invertebrates neither as a part of Annex VII nor Annex IX information requirements.

In your comments to the draft decision you referred to two new predictions to assess long-term toxicity to Daphnia. You conclude that the substance is toxic, readily biodegradable and should be classified as Aquatic Chronic 2. You requested ECHA to remove this request from the decision.

The predictions referred to by you in your comments to the draft decision did not fulfil the Annex XI, Section 1.3. requirements, for the same reasons as indicated in Section 0 above. Therefore, ECHA could not evaluate the relevance or the results of these predictions. Further, biodegradability of the registered substance could not be concluded, because the study referred to in your comments to the draft decision did not contain sufficient information for ECHA to evaluate the relevance or the results of the referred studies (see

Issue 14 below). Finally, classification as Aquatic Chronic 2 is not an acceptable waiver for this endpoint.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

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

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

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

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6.1. of the REACH Regulation.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2: *"According to column I of annex IX, long-term toxicity testing on fish need not to be conducted as it is already provided as part of Annex VIII requirements.Therefore this study was considered for waiver."*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2 because you have not provided a long-term toxicity study on fish neither as a part of Annex VIII nor Annex IX information requirements.

In your comments to the draft decision you referred to two new predictions to assess long-term toxicity to fish. You conclude that the substance is toxic, readily biodegradable and should be classified as Aquatic Chronic 2. You requested ECHA to remove this request from the decision.

The predictions referred by you in your comments to the draft decision did not fulfil the Annex XI, Section 1.3. requirements, for the same reasons as indicated in Section 0 above. Therefore, ECHA could not evaluate the relevance or the results of these predictions. Further, biodegradability of the registered substance could not be concluded, because the study referred to in your comments to the draft decision did not contain sufficient information, for ECHA to evaluate the relevance or the results of the referred studies Finally, classification as Aquatic Chronic 2 is not an acceptable waiver for this endpoint.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), *Chapter R7b, Section R.7.8.4.1.*

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

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

Notes for your consideration for requests 10-13

Before conducting the tests requested above under points 12 and 13, you shall consult the ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b, Section R.7.8.5 to determine the necessity and sequence to conduct the long-term toxicity testing on aquatic invertebrates and on fish.

14. Ready biodegradability (Annex VII, Section 9.2.1.1.)

"Ready biodegradability" is a standard information requirement as laid down in Annex VII, section 9.2.1.1. of the REACH Regulation.

You have sought to adapt this information requirement according to Annex XI, Section 1.3. by providing the following information: QSAR prediction for the registered substance using the EPI Suite BIOWIN model, result: "*Ready Biodegradability Prediction: NO*".

ECHA has assessed your adaptation in line with the conditions specified in *General considerations for toxicological and ecotoxicological information* (section iii for QSARs) and notes that you have not provided adequate and reliable documentation of the method used, and therefore ECHA cannot assess the other criteria listed in Annex XI, Section 1.3.

ECHA therefore concludes that the proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.3. and is therefore rejected.

In your comments you referred to a newly performed Ready biodegradability test according to OECD 301F. You conclude that the substance is readily biodegradable and that the new data will be updated shortly.

Biodegradability of the registered substance could not be concluded, because the study referred to in your comments to the draft decision did not contain sufficient information, for ECHA to evaluate the relevance or the results of the referred studies.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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.

Regarding the test method, depending on the substance profile, you may conclude on ready biodegradability, by applying the most appropriate and suitable test guideline among those listed in the ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) and in the paragraph below. The test guidelines include the description of their applicability domain.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to perform one of the following tests with the registered substance subject to the present decision:

Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: DOC die-away test, OECD TG 301A)
or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: CO2 evolution test, OECD TG 301B)
or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: MITI test (I), OECD TG 301C)
or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Closed bottle test, OECD TG 301D)
or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Modified OECD screening test, OECD TG 301E)

or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Manometric respirometry test, OECD TG 301F)
or
Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: Ready biodegradability – CO2 in sealed vessels (headspace test), OECD TG 310) with the registered substance.

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

"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.

In the technical dossier under this endpoint you have provided the following information:
- Key study, calculation (if not (Q)SAR), reliability 2, PBT profiler version 1.301, Reaction mass of 4-(2,6,6-trimethylcyclohex-2-ene-1-yl)-but-3-ene-2-one and 4-(2,6,6-trimethylcyclo... / 907-706-6, Results: Half-Life 38 days (water), Half-Life 340 days (sediment);
- Supporting study, calculation (if not (Q)SAR), reliability 2, Fugacity Model by EPI Suite estimation database, Reaction mass of 4-(2,6,6-trimethylcyclohex-2-ene-1-yl)-but-3-ene-2-one and 4-(2,6,6-trimethylcyclo... / 907-706-6, Results: Half-Life 900 hr (water), Half-Life 8.1e+003 hr (sediment);
- Supporting study, read-across from supporting substance, reliability 2, PBT profiler database, 4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one / 127-41-3 / 204-841-6, Results: Half-Life 38 days (water), Half-Life 340 days (sediment);
- Supporting study, read-across from supporting substance, reliability 2, Fugacity Model by EPI Suite estimation database, 4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one / 127-41-3 / 204-841-6, Half-Life 900 hr (water), Half-Life 8.1e+003 hr (sediment).

ECHA has assessed the information in line with the conditions specified in *General considerations for toxicological and ecotoxicological information* (section iii for QSARs) and notes that you have not provided adequate and reliable documentation of the methods used, and therefore ECHA cannot assess the other criteria listed in Annex XI, Section 1.3. Furthermore, as decribed in ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.11* (version 3.0, June 2017) QSAR predictions can be used as part of a Weight-of-Evidence approach in persistency assessment - however, QSAR results alone are in most cases not sufficient to conclude on non-persistence but should be supported by additional information.

ECHA therefore concludes that the proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.3. and is therefore 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 you referred to a newly performed biodegradability study and concluded that the substance can be considered readily biodegradable. You requested ECHA to remove this request from the decision.

Biodegradability of the registered substance could not be concluded, because the study referred to in your comments to the draft decision did not contain sufficient information, for ECHA to evaluate the relevance or the results of the referred studies Further, biodegradability of the registered substance could not be concluded, because no results of an acceptable study have been provided (see Issue 14).

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) 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 the 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 4.0, June 2017) 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.

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

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).

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

The identification of the degradation products is a standard information requirement according to column 1, Section 9.2.3. of Annex IX of the REACH Regulation.

The biodegradation section in the technical dossier does not contain any information in relation to the identification of degradation products, nor an adaptation in accordance with column 2 of Annex IX, Sections 9.2 or 9.2.3. or with the general rules of Annex XI for this standard information requirement.

According to Annex IX, Section 9.2.3., column 2 of the REACH Regulation, identification of degradation products is not needed if the substance is readily biodegradable. ECHA notes that information compliant with Annex VII Section 9.2.1.1 on ready biodegradability is currently not present in the technical dossier, as discussed in request 14 above.

Furthermore, ECHA notes that you have not provided any justification in your chemical safety assessment (CSA) or in the technical dossier for why there is no need to provide information on the degradation products. ECHA considers that this information is needed in relation to the PBT/vPvB assessment and risk assessment.

In your comments you referred to a newly performed biodegradability study and concluded that the substance can be considered readily biodegradable. You requested ECHA to remove this request from the decision.

Biodegradability of the registered substance could not be concluded, because the study referred to in your comments to the draft decision did not contain sufficient information, for ECHA to evaluate the relevance or the results of the referred studies Further, biodegradability of the registered substance could not be concluded, because no results of an acceptable study have been provided (see Issue 14).

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

or by some other measure. You will need to provide a scientifically valid justification for the chosen method.

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:

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

Notes for your consideration for requests 15-16

Before conducting the tests requested under requests 15-16, you may conduct the ready biodegradability study requested under request 14 above. If the registered substance is shown to be readily biodegradable (with or without fulfilling the 10-d window) there is no need to provide the information requested in points 15-16. However, if the registered substance is shown not to be readily biodegradable, there is a need to conduct further testing on degradation as requested in points 15-16.

Additionally to the information requested in this decision, according to Annex IX, Sections 9.2.1.3 and 9.2.1.4, soil and sediment simulation testing are standard information requirements for substances with high potential to adsorb to soil / sediment. However ECHA considers that at this stage it is not possible to determine whether the substance is adsorptive since reliable information on physico-chemical properties needed to conclude on adsorption is missing and has been requested in this decision (requests 2 and 3 above). Once the results of the requested tests on surface activity (request 2) and partition coefficient (request 3) are available, you should determine whether your substance has high potential to adsorb to soil / sediment. In such a case, you should consider whether there is a need to investigate further the biodegradation potential in order to fulfil the information requirements of section 9.2.1.3 and 9.2.1.4 of Annex IX, as explained below, and if necessary, submit testing proposals for additional tests.

In case the simulation tests on soil and/or sediment are needed you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4 and R.7.9.6 (version 4.0, June 2017) and Chapter R.11, Section R.11.4.1.1 (version 3.0, June 2017) on PBT assessment to determine the sequence in which the simulation tests are to be conducted and the necessity to conduct all of them. The order in which the simulation biodegradation tests are performed needs to take into account the intrinsic properties of the registered substance and the identified use and release patterns which could significantly influence the environmental fate of the registered substance.

In addition, before providing the information on degradation products requested under point 16 you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R.7b., Sections R.7.9.2.3 and R.7.9.4. These guidance documents explain that the data on degradation products is only required if information on the degradation products following primary degradation is required in order to complete the chemical safety assessment. Section R.7.9.4. further states that when substance is not fully degraded or mineralised, degradation products may be determined by chemical analysis.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when results of the tests detailed above is available.

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

"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.

In the technical dossier under this endpoint you have provided the following information:

- Key study, calculation (if not (Q)SAR), reliability 2, PBT profiler database, Reaction mass of 4-(2,6,6-trimethylcyclohex-2-ene-1-yl)-but-3-ene-2-one and 4-(2,6,6-trimethylcyclo... / 907-706-6, BCF 160 (dimensioless);
- Supporting study, calculation (if not (Q)SAR), reliability 2, BCFBAF Program (v3.01) of EPI suit, Reaction mass of 4-(2,6,6-trimethylcyclohex-2-ene-1-yl)-but-3-ene-2-one and 4-(2,6,6-trimethylcyclo... / 907-706-6, BCF 158.7 L/kg;
- Supporting study, read-across from supporting substance, reliability 2, PBT profiler database, 4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one / 127-41-3 / 204-841-6 (alpha ionone), BCF 160;
- Supporting study, read-across from supporting substance, reliability 2, BCFBAF Program (v3.00), 4-(2,6,6-trimethylcyclohex-1-en-1-yl)but-3-en-2-one / 14901-07-6 / 238-969-9 (beta ionone), BCF 159 L/kg.

ECHA has assessed the information in line with the conditions specified in *General considerations for toxicological and ecotoxicological information* (section iii for QSARs) and notes that you have not provided adequate and reliable documentation of the methods used, and therefore ECHA cannot assess the other criteria listed in Annex XI, Section 1.3.

ECHA therefore concludes that the proposed adaptation is not in line with the conditions specified in Annex XI, Section 1.3. and is therefore 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 to the draft decision, you referred to new predictions performed to assess the bioaccumulation if the registered substance. You conclude that the substance is not bioaccumulative in food chain. You requested ECHA to remove this request from the decision.

The predictions referred to by you in your comments to the draft decision did not fulfil the Annex XI, Section 1.3. requirements, for the same reasons as indicated in Section 0 above. Therefore, ECHA could not evaluate the relevance or the results of these predictions.

In your comments to the draft decision, you also indicate your intentions to update your registration dossier. As indicated in the notification letter of the draft decision, ECHA does not take any dossier updates into account at this stage of the process. However, the latest dossier update will be taken into account in the follow-up evaluation according to Article 42 of REACH.

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

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7c* (version 3.0, June 2017) bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2. 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 and in OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation, ENV/JM/MONO (2017)16. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG.

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)

The bioaccumulation of each relevant constituent present in concentration at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed. This can be done simultaneously during the same study.

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.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. In particular, you are advised to first conclude whether the registered substance may fulfil the REACH Annex XIII criteria of being persistent or very persistent, and then to consult the PBT assessment for Weight-of-Evidence determination and integrated testing strategy for bioaccumulation assessment. You should revise the PBT assessment when information on bioaccumulation is available.

In addition, you are advised to consult the ECHA Guidance on the information requirements and chemical safety assessment (version 3.0, November 2017), Chapters R.4, 5, 6, R.7b and R.7c. Where you decide to adapt the testing requested 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, ECHA refers you to the advice provided in practical Guides 4, 5 and 6.

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 16 January 2018.

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

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

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

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

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

Appendix 3: Further information, observations and technical guidance

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

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

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

   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.