~~Confidential~~

Helsinki, 11 March 2022

Addressees
Registrant(s) of PMHP_2479876 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
08/12/2016

Registered substance subject to this decision ("the Substance")
Substance name: Menthane, monohydroperoxy derivative
EC number: 247-987-6

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***17 June 2024***.

Requested information must be generated using the Substance unless otherwise specified.

A. Information required from all the Registrants subject to Annex VII of REACH

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471)

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

B. Information required from all the Registrants subject to Annex VIII of REACH

1. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells

2. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

3. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

C. Information required from all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendix/Appendices entitled "Reasons to request information required under Annexes VII to IX of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

[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 on Reasons common to several requests

1. **Assessment of your read-across approach under Annex XI, Section 1.5.**

In your registration dossier, you seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. 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. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[2,3].

A. Predictions for (eco)toxicological properties

You predict the properties of the Substance from the structurally similar substances:

- cumene hydroperoxide (EC No. 201-254-7) as 'source substance 1' - to predict both toxicological and ecotoxicological properties;
- diisopropylbenzene hydroperoxide (EC No. 247-988-1) as 'source substance 2' - to predict ecotoxicological properties.

You have provided a justification document "[redacted], in IUCLID, section 13. In this document you have addressed chemical and structural considerations, toxicokinetics and (eco)toxicological properties of the substances.

You have provided the following reasoning for the prediction of (eco)toxicological properties: *"The three hydroperoxides seem chemically sufficiently similar with either a cyclohexane or a benzene ring structure and a peroxide group attached either directly to the ring or via an alkyl group."* Further, you state that the effects of the Substance and the source substances *"will be due to the reactivity of the peroxide bond"* and because the aromatic ring in the structure of the source substances *"[…] is expected to have a stabilizing effect on the formed radical and thus increase reactivity of the peroxide group compared to the aliphatic ring structure in p-menthane hydroperoxide […]"* you conclude that *"this would render the chemical reactivity of diisopropylbenzene hydroperoxide and cumenehydroperoxide to be at least similar or even higher than that of p-menthane hydroperoxide. Both substances are therefore considered to represent a worst case for the reactivity (and concomitant toxicity) of p-menthane*

[2] Read-across assessment framework (RAAF, March 2017)
[3] RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)

hydroperoxide."

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted based on a worst-case approach.

i. Prediction of toxicological properties

ECHA notes the following shortcomings with regards to predictions of toxicological properties.

a. Missing supporting information to confirm your worst-case consideration for systemic toxicity (90-day toxicity study)

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include, among others, information to confirm your claimed worst-case prediction and bridging studies to compare properties of the Substance and source substance 1.

As indicated above, your read-across hypothesis is based on the assumption that the source substances constitute a worst-case for the prediction of the property under consideration of the Substance. In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm a conservative prediction of the properties of the Substance from the data on the source substance(s). Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and for the source substance(s).

In order to support your hypothesis you refer to the acute toxicity, corrosion, skin sensitisation properties of the Substance and of the source substance 1. You have provided repeated dose toxicity studies via inhalation and dermal administration on the source substance 1, as described in point b. below.

The acute toxicity, corrosion, skin sensitisation studies do not inform on the repeated dose toxicity properties of the Substance and of the source substance 1. Accordingly, this information is not considered as relevant to support your hypothesis. Further, ECHA notes that the data set reported in the technical dossier does not include any experimental data of comparable design and duration for the Substance to compare the systemic toxicity properties between the Substance and the source substance 1. In the absence of such information it is not possible to compare the sub-chronic toxicity properties of the Substance with those of the source substance 1.

In addition, the Substance is UVCB and one of its constituents, [redacted] which accounts for ca [redacted]% (w/w) of the composition, is not common for both the Substance and the source substance 1.
In this context, the impact of exposure to this compound on the prediction of properties of the Substance needs to be assessed to ensure that a reliable prediction can be made.

You did not provide any information on the toxicological properties of this non-common

constituent. You also did not discuss what would be the impact of exposure to this constituent on the prediction of the systemic (target-organ) toxicity of the Substance.

In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

Therefore, based on the above, you have not established that the source substance 1 constitutes a worst-case for the prediction of the sub-chronic toxicity properties of the Substance.

b. Adequacy and reliability of source studies

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

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

For sub-chronic toxicity you have provided five repeated dose toxicity studies (one inhalation and 4 dermal) on source substance 1.

Specific reasons why the studies on the source substance 1 do not meet these criteria are explained further below under the applicable information requirement in Appendix C, section 1. Therefore, no reliable predictions can be made for these information requirements.

ii. Prediction of ecotoxicological properties

ECHA notes the following shortcomings with regards to predictions of ecotoxicological properties.

a. Missing supporting information to confirm your worst-case consideration

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include, among others, information to confirm your claimed worst-case prediction and bridging studies to compare properties of the Substance and source substances.

As indicated above, your read-across hypothesis is based on the assumption that the source substances constitute a worst-case for the prediction of the property under consideration of the Substance. In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm a conservative prediction of the properties of the Substance from the data on the source substance(s). Such information can be obtained, for example, from bridging studies

of comparable design and duration for the Substance and for the source substance(s).

In order to support your hypothesis you refer to the short-term toxicity to aquatic invertebrates properties of the Substance and of the source substances. You have provided in the dossier short-term toxicity to *Daphnia* studies (OECD TG 202) on the Substance and on the source substances with the following results:

- 48h-EC50 = 4.1 (3.63 – 4.57) mg/L for the Substance
- 48h-EC50 = 18.84 mg/L for source substance 1
- 48h-EC50 = 8.2 mg/L for source substance 2

In your comments to the draft decision, you indicate that the 48h-EC50 for the source substance 2 should be corrected from 8.2 mg/L to 3.6 mg/L, because the test material used in the study "*contained no more than 45% of the source substance diisopropylbenzene hydroperoxide*".

However, while you refer to daphnia immobilisation studies, you have provided no justification nor evidence on how information on reactivity and on immobilisation of daphnids is relevant for the prediction of toxicity to fish (mortality) and algae growth inhibition as investigated in the requested studies according to the OECD TGs 203 and 201, respectively. In the absence of adequate information allowing to compare the properties of the Substance and of the source substances, it cannot be confirmed that both substances cause the same type of effects.

Therefore, based on the above, you have not established that the source substances constitute a worst-case for the prediction of the aquatic toxicity properties of the Substance.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

Appendix A: Reasons to request information required under Annex VII of REACH

1. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

You have provided a key study in your dossier:

i. In vitro gene mutation study in bacteria (equivalent to OECD TG 471, non-GLP, 1988), which gave ambiguous results.

We have assessed this information and identified the following issue(s):

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[4] (1997). Some of the key parameters of this test guideline include:

a) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)
b) The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate or 5 ml/plate.
c) Triplicate plating must be used at each dose level.
d) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
e) The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.
f) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

The reported data for the study you have provided did not include:

a) results for the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).
b) a maximum dose of 5 mg/plate or 5 ml/plate or that induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance.
c) triplicate plating at each dose level – only 1 dose level was tested in the experimental conditions without S9 and 1-3 dose levels were tested in the experimental conditions with S9.
d) a positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
e) a negative control with a number of revertant colonies per plate inside the historical control range of the laboratory.
f) data on the number of revertant colonies per plate for the treated doses and the controls.

The information provided does not cover multiple of the key parameters required by OECD TG 471.

Therefore, the information requirement is not fulfilled.

In the comments to the draft decision you agree to perform the requested study.

[4] ECHA Guidance R.7a, Table R.7.7–2, p.557

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

2. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5 and provided the following information:

i. EU Method C.3 study ([redacted] 1992) with the 'source substance 2' diisopropylbezene hydroperoxide (EC No. 247-988-1)

As explained in the Appendix on general considerations your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

In the comments to the draft decision you agree to perform the requested study.

Appendix B: Reasons to request information required under Annex VIII of REACH

1. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

i. Triggering of the study

Your dossier contains (i) a negative result for *in vitro* cytogenicity study in mammalian cells and (ii) no data or inadequate data for the other study (*in vitro* gene mutation study in bacteria).

The *in vitro* gene mutation study in bacteria, provided in the dossier is rejected for the reasons provided in Appendix A, section 1.

The result of the request for information in Appendix A, section 1 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

ii. Assessment of information provided

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence) and provided the following study records to support your adaptation:

With the Substance:

i. *In vitro* gene mutation study in bacteria (OECD TG 471, non-GLP, 1988), which gave ambiguous results.
ii. *In vitro* cytogenicity / chromosome aberration study in mammalian cells (equivalent to OECD TG 473, GLP, 2012), which gave negative results.

With 'source substance 1' cumene hydroperoxide (EC No. 201-254-7):

iii. *In vitro* gene mutation study in bacteria (equivalent to OECD TG 471, non-GLP, 1998), which gave positive results.
iv. *In vitro* gene mutation study in bacteria (equivalent to EU Method B.13/14, GLP, 1989), which gave negative results with metabolic activation.
v. *In vitro* gene mutation study in bacteria (NTP protocol, non-GLP, 1986), which gave positive results
vi. *In vitro* DNA damage and/or repair study (no guideline, non-GLP, 1994), which gave positive results.
vii. *In vivo* mutagenicity – DNA damage and repair (equivalent to OECD TG 474, non-GLP, 2004), which gave negative results.

With diisopropylbenzene hydroperoxide; EC: 247-988-1
viii. *In vitro* gene mutation study in bacteria (equivalent to EU Method B.13/14, GLP, 1989), which gave negative results

Based on the presented lines of evidence you argue that the Substance is "*non-mutagenic*"

ECHA has evaluated the provided information and identified the following deficiencie(s):

A. Lack of adequate and reliable documentation

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

You have provided summaries of the studies, provided as separate endpoint study records for in vitro and in vivo genotoxicity, and briefly present each of the sources of information and describe the results. You conclude that based on a weight of evidence approach "*the available data indicate that there is no evidence for any mutagenic or clastogenic effects of p-menthane hydroperoxide*".

Whilst these reports can be regarded as integrated summaries of the data sets, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information under point B, below.

B. No or no adequate information for genotoxicity in mammalian cells

As explained above, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.3 at Annex VIII includes:

- Detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells (*in vitro*) or mutant frequency for each tissue in mammals (*in vivo*).

- A level of information on these aspects similar to that obtained from *in vitro* tests: mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) as well as from in vivo Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays (OECD TG 488) must be provided.

None of the reported sources of information provide relevant information on detection and quantification of gene mutation in cultured mammalian cells, due to the following reasons:

- The sources of information i, iii, iv, v., and viii. are conducted in bacteria and the source of information vi. – in yeast, therefore, they do not inform on the properties of gene mutation in mammalian cells.
- The sources of information ii. and vii. are, respectively, *in vitro* chromosomal aberration test and *in vivo* mammalian erythrocyte micronucleus test which provide information on cytotoxicity and the frequency of cells with structural chromosomal aberrations (source ii.) or frequency of micronuclei in mammals (source vii) but do not inform on gene mutations.

Conclusion

It is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an *in vitro* gene mutation study in mammalian cells. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

Consequently, you are required to provide information for this endpoint, if the *in vitro* gene mutation study in bacteria provides a negative result.

Study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

In the comments to the draft decision you agree to perform the requested study.

2. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You did not provide any experimental data for this endpoint. Instead, you have provided the following reasoning for not conducting the study:
1)As the substance is used in industrial settings only, no oral exposure is expected. The dermal route is considered the most relevant route of exposure.
2) The critical effect found in repeated dose studies with structurally related organic peroxides is related to the corrosiveness of these substances. The test substance is corrosive as well and expected to exhibit local corrosive effects in the dose range of interest for the reproduction study. For reasons of animal welfare such studies should be avoided (Annex XI Section 2).
3)In addition the test substance is known to hydrolyse under acid conditions. These conditions will be fulfilled after oral application, but not after dermal or inhalation exposure, which will hamper the extrapolation from oral to other routes of exposure .
4) For local effects no route to route extrapolation can be applied. Therefore the performance of a test with the oral route is considered not adequate to fulfil the requirements, while the test via dermal or inhalation exposure is not possible based on animal welfare/ethical reasons. It is expected that the DNEL for local effects after single and repeated exposure will be sufficient to protect for any systemic effects including effects on the reproduction.

You may adapt the standard information requirement according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation.

You did not specify which legal basis you refer to, however, based on the provided information in point 2) ECHA understands that you sought to adapt the standard information requirement according Annex XI, section 2.
In addition, based on the information in points 1) and 3) ECHA understands your claim that the oral route is not the most appropriate route of administration, due to the known hydrolysis properties of the Substance under acidic conditions, its local (corrosive) effects and lack of oral exposure.

ECHA has evaluated the provided information and identified the following issues:

A. Adaptation according Annex XI, section 2

According to the Annex XI, section 2, the study may be omitted, if it is technically not possible to conduct the study as a consequence of the substance properties. The guidance given in the test methods referred to in Article 13(3), more specifically on the technical limitations of a specific method, shall always be respected. According to the OECD TG 422 (paragraph 25) "*When the oral route is selected, the test chemical is usually administered by gavage; however, alternatively, test chemicals may also be administered via the diet or drinking water".*

You claim that the Substance is corrosive and it is "*expected to exhibit local corrosive effects in the dose range of interest for the reproduction study".* In addition, you claim that the Substance is "*known to hydrolyse under acid conditions"* which would "*hamper the extrapolation from oral to other routes"*. Based on this you conclude that oral studies should be avoided "*for reasons of animal welfare*".

ECHA points out that Annex XI, Section 2 makes no reference to corrosivity as a reason for why it is technically not possible to conduct the study as a consequence of the properties of the substance. Regarding corrosivity, ECHA would like to point out that non-corrosive concentration(s) can be tested, a corrosive substance can be diluted and the concentration decreased. Consequently, corrosion of the tissue of the test animals would not take place. The ECHA Guidance R.7.6.2.3.2, Stage 4 -"(iv) Route of administration for reproductive toxicity studies" provides further recommendations for testing of corrosive substances.

Therefore, you have not demonstrated that it would not be technically possible to conduct the oral study via intubation as well as via dietary administration.

Based on above, your adaptation under the Annex XI, section 2 is rejected.

B. Most appropriate route of exposure

With regar to your statements 1) and 3), the ECHA Guidance R.7a states in its introductory section on *Selection of the appropriate route of administration for toxicity testing* that "*The overall objective of such testing is to determine the potential hazard of the test substance to human beings*". Under section R.7.6.2.3.2, Stage 4 -"(iv) Route of administration for reproductive toxicity studies", the Guidance indicates that "*the selection of the "most appropriate route of administration" focuses on identification of hazards (…) and depends on the most appropriate route for identification of the intrinsic properties of the substance for reproductive hazard*". The oral route is the default route of administration for reproductive toxicity studies, except for gases. The ECHA guidance also specifies that "*corrosive or highly*

irritating substances should be tested preferentially via the oral route" and provides recommendations on how to ensure that doses/concentrations causing corrosivity can be avoided.

Regarding the provided statement 4), extrapolation from systemic toxicity obtained via the oral route can be extrapolated to exposure via the dermal and inhalation route. The ECHA Guidance R.8 provides information on how such extrapolation can be conducted.

Based on the above, ECHA concludes that the information you provided does not fulfil the information requirement.

Information on study design

A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats with oral[5] administration of the Substance. Recognising that the registered substance is classified as corrosive, the Registrant is advised to examine how the concentration of the test substance can be adjusted to avoid corrosion while at the same time allowing detection of potential systemic toxicity effects of the substance.

In the comments to the draft decision you agree to perform the requested study.

3. Short-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5 and provided the following information:

i. EU Method C.1/OECD TG 203 study ([redacted] 1995) with 'source substance 2' diisopropylbezene hydroperoxide (EC No. 247-988-1)
ii. OECD TG 203 study ([redacted] 1993) with 'source substance 1' cumene hydroperoxide (EC No. 201-254-7)

As explained in the Appendix on general considerations your adaptation is rejected.

In the comments to the draft decision, you reiterate your intention to adapt the information requirement according to Annex XI, Section 1.5.

You propose to update the read-across approach by using only 'source substance 2' to predict the (eco)toxicological properties of the Substance.

With your comments, you have attached an updated justification document [redacted]

You have provided the following reasoning for the prediction of short-term and long-term toxicity to fish: "*Based on chemical, toxicokinetic and toxicodynamic properties, paramenthane hydroperoxide* [the Substance] *is considered to be sufficiently similar to diisopropyl benzene hydroperoxide* ['source substance 2'] *to allow read-across to data generated for these substances. Effects related to paramenthane hydroperoxide and the source substance will be due to the reactivity of the peroxide bond.*"

ECHA understands that you intend to predict the properties of the Substance using a read-

[5] ECHA Guidance R.7a, Section R.7.6.2.3.2.

across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

ECHA acknowledges your intentions to refine your read-across approach. However, based on the intentions and justification provided in the comments to the draft decision, the following shortcomings of the approach are noted.

Missing supporting information to compare properties of the substances

As explained under Appendix on Reasons common to several requests, according to Annex XI, Section 1.5 of the REACH Regulation supporting information must be provided to establish that the properties of the Substance can be predicted from the data on the source substance(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm a conservative prediction of the properties of the Substance from the data on the source substance(s).

In order to support your hypothesis, in your comments you refer to the following information:

- You consider that fish is not the most sensitive of the aquatic species based on "*relevant toxicological literature as well as the ECHA Guidance*" and that this is demonstrated by the data for 'source substance 2'.
- The 'source substance 2' is not readily biodegradable and the Substance is readily biodegradable. Therefore, considering the environmental fate properties you expect that 'source substance 2' is present at higher concentrations in the aquatic enviroment than the Substance. On this basis, you consider that 'source substance 2' represents a worst-case for the read-across.
- You consider that the bridging short-term toxicity to *Daphnia* study with 'source substance 2' (48h-EC50 = 3.6 mg/L, value provided in the comments corrected based on test material purity) shows sufficient similarity with the outcome of the study with the Substance (48h-EC50 = 4.1 mg/L).

To further substantiate the read across approach, you indicate your intention to perform the algae growth inhibition study (request A.2) and the long-term toxicity to *Daphnia* study (request C.3) with the Substance to be used as bridging information. You also indicate that the long-term toxicity studies on fish and invertebrates on the 'source substance 2' have been requested by ECHA in a separate compliance check decision. You conclude that "*When the outcome of these studies confirms the validity of the read-across to diisopropylbenzene hydroxyperoxide* [source substance 2]*, a read-across to the acute and long-term fish study is proposed*".

You express your intention to provide the updated read-across approach in a future update of your registration dossier.

Regarding the information provided in the comments to support your proposed read-across approach, ECHA notes the following:

- Your general claim that fish is the most sensitive trophic level is not supported by any Substance-specific evidence on toxicity to fish. Furthermore, you have provided no justification nor evidence to explain how differences in toxicity within trophic levels (fish, algae and aquatic invertebrates) may be relevant to compare the toxicity to fish between the Substance and 'source substance 2'.
- Your claim that 'source substance 2' is not readily biodegradable and hence is expected to be present at higher concentrations in the environment does not inform on differences in the hazardous properties to be read across (i.e. short-term and long-

term toxicity to fish), which are determined from the results of experimental studies.

- ECHA agrees that, based on the corrected EC50 value provided for 'source substance 2' in your comments to the draft decision, there is no significant quantitative difference in short-term toxicity to aquatic invertebrates. ECHA also acknowledges your intention to provide more studies with the Substance (algae growth inhibition and long-term toxicity to *Daphnia*). However, these studies are yet to be generated and therefore their reliability cannot be assessed. Furthermore, in your comments you have provided no justification nor evidence on how information on algae growth inhibition and on daphnids (immobility and reproduction) is relevant for the prediction of toxicity to fish as investigated in the requested studies according to the OECD TGs 203 (i.e. lethal effects on juveniles) and 210 (lethal and sub-lethal effects early life stages).

Since the strategy you propose in your comments relies essentially on data which is yet to be generated, no conclusion on the compliance can currently be made. However, based on the information available in the dossier and in the comments to the draft decision, ECHA notes that there is currently no adequate information allowing to compare the properties of the Substance and of the source substance. In the absence of this information, it cannot be confirmed that both substances cause the same type of effects. Therefore you have currently not provided sufficient supporting information to strengthen the rationale for the read-across.

Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

On this basis, the information requirement is not fulfilled.

Appendix C: Reasons to request information required under Annex IX of REACH

1. 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 in Annex IX to REACH.

You have provided:

i. Sub-chronic toxicity study in rats, inhalation route (no guideline, non-GLP, 1979) with the 'source substance 1' cumene hydroperoxide (EC No. 201-254-7);
ii. Short-term repeated dose toxicity: dermal study in mice, (equivalent or similar to guideline OECD TG 410, non-GLP, 2003) with the source substance 1;
iii. Short-term repeated dose toxicity: dermal study in rats, equivalent or similar to guideline OECD TG 410, non-GLP, 2003) with the source substance 1;
iv. Sub-chronic toxicity toxicity: dermal study in mice, (equivalent or similar to guideline OECD TG 411 , non-GLP, 2004) with the source substance 1;
v. Sub-chronic toxicity toxicity: dermal study in rats, (equivalent or similar to guideline OECD TG 411, non-GLP, 2004) with the source substance 1.

ECHA has assessed this information and identified the following issue(s):

A. You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. As explained in the Appendix on Reasons common to several requests, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Moreover, ECHA has identified an endpoint specific issue with regards to your adaptation that is addressed under point B below.

B. According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should be adequate for the purpose of classification and labelling and/or risk assessment; and have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

The key parameters required by the OECD TG 408 include, among others:

1. testing of at least three dose levels and a concurrent control;
2. highest dose level should aim to induce some systemic toxicity, but not death or severe suffering;
3. dosing of the Substance daily for a period of 90 days until the scheduled termination of the study;
4. clinical biochemistry, ophthalmological examination, sensory reactivity to various stimuli and functional observations of the animals.

Adequacy/Reliability of studies on the source substance

As explained in the Appendix on Reasons common to several requests, the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 408.

The study (i.) you have provided was conducted with less than three dose levels, and therefore it does not fulfil the criterion set in OECD TG 408. The initial highest dose was too toxic and was terminated on day 5 while the new lowest dose was initiated on day 15. As doses were changed mid-experiment, for 10 days there were only 2 dose groups.

For the study (i.), the initial top dose was so toxic that it was terminated, while the new top dose did not cause any toxicity. No treatment related systemic effects were found for the

studies (ii. to v.). Therefore the studies do not fulfil the criterion set in OECD TG 408.

The studies you have provided do not have the required exposure duration of 90 days as required in OECD TG 408, because for study (i.) you indicated an exposure duration of 50 days for the lowest dose group; and for the studies (ii. to v.) the animals were exposed five times per week, weekdays only until the day prior to necropsy. The OECD TG 408 allows for such a dosing regimen but requires for a justification for this deviation from the standard dosing 7 days a week. No such justification was provided for any of these studies.

The studies you have provided were not performed according to the criteria of the OECD TG 408, since the following key parameters are missing: from all the studies (i. to v.) – ophthalmological examination, sensory reactivity to various stimuli and functional observations of the animals, and for the studies (ii. to v.) also clinical biochemistry.

Therefore, the studies submitted in your adaptation, as currently reported in your dossier, do not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG.

In the comments to the draft decision, you agree with ECHA's reasoning, related to the 90-day toxicity study, and you reiterate your adaptation of the information requirement according to Annex XI, Section 1.5. You intend to update the read-across approach by introducing a new source study with a new structurally similar analogue: diisopropylbenzene hydroperoxide (EC No. 247-988-1) referred in the draft decision as '*source substance 2'* and no longer to use cumene hydroperoxide "*as the most appropriate read-across source substance*". With your comments, you have attached an updated justification document "[redacted] where you provide the reasoning for predicting the properties of the Substance from the properties of the 'source substance 2', based on the structural and physical-chemical similarities between the substances, as well as on the newly generated data (OECD TG 408) for 'source substance 2' which was not available to you before. In addition, you intend to perform the screening for reproductive/developmental toxicity study (OECD TG 421) with the Substance requested in this decision (request B.2) and plan on using this study as a bridging study in your new read-across approach.

You also indicate your intention to provide the new source study and the bridging study with the Substance in a future update of your registration dossier.

ECHA acknowledges your intentions to improve the toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated and/or submitted to ECHA in your dossier. Therefore, no conclusion on the compliance can currently be made.

Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.
Based on the above, the information you provided does not fulfil the information requirement.

Information on the design of the study to be performed (route/ species/ strain)

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is a liquid of very low vapour pressure (418 Pa at 20°C) and no uses with spray application are reported that could potentially lead to aerosols of inhalable size. Recognising that the registered substance is classified as corrosive, the Registrant is advised to examine

how the concentration of the test substance can be adjusted to avoid corrosion while at the same time allowing detection of potential systemic toxicity effects of the substance.

Therefore the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

2. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You did not provide any experimental data for this endpoint. Instead, you have provided the following reasoning for not conducting the study:
1)As the substance is used in industrial settings only, no oral exposure is expected. The dermal route is considered the most relevant route of exposure.
2) The critical effect found in repeated dose studies with structurally related organic peroxides is related to the corrosiveness of these substances. The test substance is corrosive as well and expected to exhibit local corrosive effects in the dose range of interest for the reproduction study. For reasons of animal welfare such studies should be avoided (Annex XI Section 2).
3)In addition the test substance is known to hydrolyse under acid conditions. These conditions will be fulfilled after oral application, but not after dermal or inhalation exposure, which will hamper the extrapolation from oral to other routes of exposure .
4) For local effects no route to route extrapolation can be applied. Therefore the performance of a test with the oral route is considered not adequate to fulfil the requirements, while the test via dermal or inhalation exposure is not possible based on animal welfare/ethical reasons. It is expected that the DNEL for local effects after single and repeated exposure will be sufficient to protect for any systemic effects including effects on the reproduction.

ECHA has evaluated the provided information and identified the following issues:

Based on the provided information and for the reasons already explained under Appendix B, section 2 above, your adaptation is rejected.

In the comments to the draft decision, you agree with ECHA's reasoning, related to the developmental toxicity study. You indicate your intention to adapt this information requirement by means of grouping and read-across approach according to Annex XI, section 1.5 of the REACH Regulation.

You propose to predict the properties of the Substance for pre-natal developmental toxicity from a source study with a structurally similar analogue substance: diisopropylbenzene hydroperoxide (EC No. 247-988-1) referred in the draft decision as '*source substance 2'*. With your comments, you have attached an updated justification document "[redacted] where you provide the reasoning for predicting the properties of the Substance from the properties of the 'source substance 2', based on the structural and physical-chemical similarities, as well as on the newly generated data (OECD TG 414) for 'source substance 2' which was not available to you before. In addition, you intend to perform the screening for reproductive/developmental toxicity study (OECD TG 421) with the Substance requested in this decision (request B.2) and plan on using this study as a bridging study in your new read-across approach.

You also indicate your intention to provide the new source study and the bridging study with the Substance in a future update of your registration dossier.

ECHA acknowledges your intentions to adapt this information using a read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated and/or submitted to ECHA in your dossier. Therefore, no conclusion on the compliance can currently be made.

Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

Therefore, the information requirement is not fulfilled.

Information on study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[6] administration of the Substance. Recognising that the registered substance is classified as corrosive, the Registrant is advised to examine how the concentration of the test substance can be adjusted to avoid corrosion while at the same time allowing detection of potential systemic toxicity effects of the substance.

3. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

You have omitted this information and you provided the following justification: "*A quantitative risk characterisation establishes control of risk and demonstrates that the risk characterisation ratio is well below 1 (see CSR in Chapter 13). Omission of a daphnia reproduction study does not result in increased uncertainty.*"

ECHA understands that you intend to adapt this information requirement under Annex IX, Section 9.1., Column 2.

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to aquatic invertebrates if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

On this basis, the information requirement is not fulfilled.

In the comments to the draft decision you agree to perform the requested study.

4. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

You have omitted this information and you provided the following justification: "*A quantitative risk characterisation establishes control of risk and demonstrates that the risk characterisation*

[6] ECHA Guidance R.7a, Section R.7.6.2.3.2.

ratio is well below 1 (see CSR in Chapter 13). Omission of a prolonged fish study does not result in increased uncertainty."

ECHA understands that you intend to adapt this information requirement under Annex IX, Section 9.1., Column 2.

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

In the comments to the draft decision, you indicate your intention to adapt the information requirement according to Annex XI, Section 1.5.

You propose to use 'source substance 2' to predict the (eco)toxicological properties of the Substance.

With your comments, you have attached an updated justification document "[redacted]

You have provided the following reasoning for the prediction of short-term and long-term toxicity to fish: "*Based on chemical, toxicokinetic and toxicodynamic properties, paramenthane hydroperoxide* [the Substance] *is considered to be sufficiently similar to diisopropyl benzene hydroperoxide* ['source substance 2'] *to allow read-across to data generated for these substances. Effects related to paramenthane hydroperoxide and the source substance will be due to the reactivity of the peroxide bond."*

ECHA understands that you intend to predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

You indicate that the long-term toxicity study on fish on the 'source substance 2' is not yet available and has been requested by ECHA in a separate compliance check decision. In the absence of the study on the source substance, the compliance of this study or the read-across prediction cannot yet be assessed. Therefore, the data gap remains and the information requirement is not fulfilled.

Furthermore, ECHA acknowledges your intentions to provide an updated read-across approach for the prediction of short-term and long-term toxicity to fish, as described in Appendix B.3 above (short-term toxicity to fish). However, based on the intentions and justification provided in the comments to the draft decision, ECHA has noted shortcomings of the approach as explained in Appendix B.3 above.

Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

Appendix D: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[7].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[8].

[7] https://echa.europa.eu/practical-guides
[8] https://echa.europa.eu/manuals

Appendix E: Procedure

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

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 01 February 2021.

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

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

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

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix F: List of references - ECHA Guidance[9] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[10]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[11]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[12]

[9] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[10] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[11] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[12] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix G: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.