~~Confidential~~

Helsinki, 11 March 2022

Addressees
Registrant(s) of [redacted] as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
01/03/2016

Registered substance subject to this decision ("the Substance")
Substance name: α,α-dimethylbenzyl hydroperoxide
EC number: 201-254-7

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 VIII of REACH

1. 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)

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

1. In vivo genetic toxicity study

   In vivo genotoxicity study to be selected according to the following specifications:

   a. If the test results of request A.1 are negative:

   Transgenic rodent somatic and germ cell gene mutation assays (OECD TG 488 from 2020) in transgenic mice or rats, oral route on the following tissues: liver, glandular stomach; germ cells and duodenum must be harvested and stored for up to 5 years. The duodenum must be analysed if the results of the glandular stomach and of the liver are negative or inconclusive.

   OR

   In vivo mammalian alkaline comet assay (test method OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum.

   b. If the test results of request A.1 are positive:

   In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) combined with *in vivo* mammalian erythrocyte micronucleus test (test method: OECD TG 474) in rats, oral route. For the comet assay the following

tissues shall be analysed: liver, glandular stomach and duodenum.

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

3. 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:

- Appendices entitled "Reasons to request information required under Annexes VIII 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 A: Reasons to request information required under Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

You have provided the following studies on the Substance in your dossier:

i. In vitro DNA damage and/or repair study - induction and rejoining of DNA single strand breaks (no guideline, non-GLP, 1991), which gave a positive result.
ii. In vitro DNA damage and/or repair study - yeast cytogenetic assay (no guideline, non-GLP, 1994), which gave a positive result.
iii. In vitro cytogenicity / chromosome aberration study in mammalian cells (no guideline, non-GLP, 1997), which gave a positive result.

In addition, you have sought to adapt this information requirement according to Section 8.4.2., Column 2, Annex VIII by providing the following justification: "*Equivalent in vivo data available.*". In the IUCLID dossier (7.6.2. Genetic toxicity *in vivo*) you provided the following information with the Substance to support your adaptation:

iv. Micronucleus analysis in NTP toxicity studies (according to Standard NTP protocol, non-GLP, 2004), which gave a negative result.
v. DNA strand breaks in mouse skin study, (no guideline, non-GLP, 1994), which gave a negative result.
vi. Rodent dominant lethal assay (no guideline, non-GLP, 1972), which gave a negative result.

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

A. Studies i. to iii.

a) In vitro studies i. and ii.:

To fulfil the information requirement, a study must be an *in vitro* chromosomal aberration test or an *in vitro* micronucleus test, conducted in mammalian cells and comply with with the OECD TG 473 or OECD TG 487 (Article 13(3) of REACH and ECHA Guidance R.7, Table R.7.7-2).

Studies i. and ii. are not *in vitro* cytogenicity studies in mammalian cells nor an *in vitro* micronucleus studies. Therefore, the information provided in these studies (i. and ii. above) does not cover the key parameters required by the OECD TG 473/487.

b) In vitro study iii.:

To fulfil the information requirement, the study has to be an *in vitro* chromosomal aberration test or an *in vitro* micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively[2]. The key parameters of these test guidelines include:

a) Two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.
b) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.
c) The response for the concurrent negative control must be inside the historical control

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

range of the laboratory.

The reported data in study iii. did not include:
a) two separate test conditions: testing was conducted only in absence of metabolic activation;
b) a positive control; and
c) a negative control with a response inside the historical control range of the laboratory.

The information provided does not cover key parameters required by OECD TG 473/487, therefore, ECHA cannot conclude on the relevance and reliability of the positive effects detected in this study.

Conclusion

Studies i. to iii. do not fulfil the information requirement.

B. Adaptation according to Section 8.4.2, Column 2, Annex VIII to REACH

Under Section 8.4.2., Column 2, first indent, Annex VIII to REACH, the study may be omitted "if *adequate data from an in vivo cytogenicity test are available*". ECHA Guidance[3] clarifies that the *in vivo* study must be either a micronucleus test or a chromosomal aberration test, performed according to OECD TG 474 or 475, respectively[4].

a) In vivo study iv.:

For the data from an *in vivo* cytogenicity test to be considered adequate, the *in vivo* study you submitted has to meet the requirements of OECD TG 474, and the specifications/conditions of this test guideline include:
a) Animals must be exposed to the test chemical by an appropriate route. The route should be chosen to ensure adequate exposure of the target tissue(s).
b) In order to provide a clear negative outcome, the data available must show that "*bone marrow exposure to the test Substance occurred*".

The reported data for the *in vivo* study (iv.) you submitted did not report any systemic or target organ (bone marrow) effects, therefore you did not demonstrate that the Substance is absorbed after dermal administration. Moreover there are no toxicokinetic studies provided with the Substance showing evidence of absorption after dermal exposure.
The information provided does not cover specifications/conditions required by OECD TG 474.

b) In vivo study v.:

According to the information reported in the technical dossier, the study (v.) is a non-guideline, non-standard test measuring the induction of DNA single strand breaks in epidermal cells by topically applied cumene hydroperoxide. According to the ECHA Guidance R.4[5], a set of key elements needs to be considered when evaluating the reliability of data. These elements includes that "*there must be an adequate description of the study e.g. a complete test report, or a sufficiently detailed description of the test procedure, which must be in accordance with generally accepted scientific standards*". The ECHA Guidance R.4 specifies that "*Where critical supporting information is not reported (e.g. species tested, substance identity and dosing procedure) the test data should be considered to be unreliable for the*

[3] ECHA Guidance R.7a, R.7.7.6.3, p.568
[4] ECHA Guidance R.7a, Table R.7.7–3, p.558
[5] ECHA Guidance R.4.2

purposes of REACH". The information on study v. that you have reported in your dossier does not provide details on the test procedure applied and to compare it with recognised test methods or generally accepted scientific standard. In the absence of this information, the data from study v. is considered unreliable.

c) *In vivo study vi.:*

Study vi. is a rodent dominant lethal test. The dominant lethal mutations detected by the OECD TG 478 are generally the result of structural and/or numerical chromosomal aberrations. This study is an *in vivo* cytogenicity test, however it is performed on germ cells. Therefore, the results of such test cannot be used for the first level of classification as germ cell mutagen, i.e. category 2. Indeed *in vivo* data obtained on somatic cells is necessary for this purpose.

Moreover, for the data to be considered adequate, the *in vivo* cytogenicity test you submitted has to meet the requirements of OECD TG 478, and the specifications/conditions of this test guideline include:

a) The study must include a minimum of three doses/groups of treated animals, as well as a negative control group and a positive control group.
b) Intraperitoneal injection is not normally recommended since it is not an intended route of human exposure, and should only be used with specific justification.

The reported data for the *in vivo* study you submitted did not include:
a) the appropriate number of doses and no reference to positive or negative control groups;

b) no justification for the administration of the test item via intraperitoneal injection has been provided.

The information provided does not cover specifications/conditions required by OECD TG 478.

Conclusion

For the reasons presented above, the studies iv. to vi. do not constitute adequate in vivo cytogenicity studies. Therefore, the requirements of Section 8.4.2., Column 2, first indent, Annex VIII to REACH are not met.

Study design

To fulfil the information requirement for the Substance, either *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) are considered suitable.

In your comments on the draft decision you agree with the data gaps identified by ECHA. You also refer to the RAC opinion on cumene dated 17 September 2020 recommending a classification as Carc. 1B (reference CLH-O-0000006849-56-01/F). Since cumene is present as an impurity in the composition of the Substance in concentrations of at least 0.1% and up to 10-20%, you propose to self-classify the Substance as Carc. 1B. Such a classification would constitute a waiver for the information requirement of Annex VIII Section 8.4.2 according to the provisions of Annex VIII, Section 8.4.2 column 2. You indicate that "*This could be applied rapidly after the finalization of the present CCH decision, and updated afterward if necessary following the publication of the updated classification of cumene in the future ATP to CLP*

regulation".

ECHA has assessed the information provided in your comments against the provisions of Annex VIII, Section 8.4.2 column 2. The information you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as the self-classification is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

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

1. **In vivo genotoxicity study to be selected according to the following scenarios**

   a. If the test results of request A.1 are negative:

   Transgenic rodent somatic and germ cell gene mutation assay OR In vivo mammalian alkaline comet assay

   b. If the test results of request A.1 are positive:

   In vivo mammalian alkaline comet assay combined with the in vivo mammalian erythrocyte micronucleus test

Under Annex IX, Section 8.4, column 2 of REACH, the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an *in vivo* somatic cell genotoxicity study.

In relation to the first condition, your dossier contains positive results for the *in vitro* gene mutation study in bacteria which raise the concerns for gene mutation.

In relation to the second condition, your dossier contains the following *in vivo* studies with the Substance:

i. Micronucleus analysis in NTP toxicity studies (according to Standard NTP protocol, non-GLP, 2004), which gave a negative result.
ii. DNA strand breaks in mouse skin study, (no guideline, non-GLP, 1994), which gave a negative result.
iii. Rodent dominant lethal assay (no guideline, non-GLP, 1972), which gave a negative result.

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

ECHA Guidance R.7a clarifies that in order to justify that an *in vivo* somatic cell genotoxicity study does not need to be performed in accordance with Annex IX, Section 8.4, column 2, the results of the available *in vivo* studies must address the specific concern raised by the *in vitro* positive result.

The provided *in vivo* tests are not appropriate to address the gene mutation concern identified by the *in vitro* gene mutation study in bacteria (OECD TG 471), since they can only detect chromosomal aberrations. Therefore, the conditions set out in Annex IX, Section 8.4, column 2 are met and the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered.

i. Test selection

According to the ECHA Guidance Chapter R.7a, Section R.7.7.6.3, the transgenic rodent somatic and germ cell gene mutation assay ("TGR assay", OECD TG 488) or the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) are suitable to follow up a positive *in vitro* result on gene mutation.

This decision, however, also requests an *in vitro* cytogenicity test (see above Appendix A, section 1), which may raise a concern for chromosomal aberration in case of positive results.

In case there is also a concern for chromosomal aberration, the *in vivo* mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) and the comet assay can be combined in a single study (see OECD TG 474 para. 37c; OECD TG 489 para. 33; ECHA Guidance R.7a, Section R.7.7.6.3). While the MN test can detect both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the comet assay can detect primary DNA damage that may lead to gene mutations and/or structural chromosomal aberrations. A combined study will thus address both the identified concerns for chromosomal aberration as well as gene mutation.

The combined study, together with the results of the *in vitro* mutagenicity studies, can be used to make definitive conclusions about the mechanism(s) inducing *in vivo* mutagenicity and lack thereof. Furthermore, the combined study can help reduce the number of tests performed and the number of animals used while addressing (structural and numerical) chromosomal aberrations as well as gene mutations.

Therefore it is appropriate to wait for the results of the *in vitro* test requested under A.1. and, depending on these results, to conduct either 1)the TGR assay or the comet assay if the test results of request A.1 are negative; or 2) the comet assay in combination with the MN test if the test results of request A.1 are positive. The deadline set in this decision allows for sequential testing.

In your comments on the draft decision you agree with the data gaps identified by ECHA. You also refer to the RAC opinion on cumene dated 17 September 2020 recommending a classification as Carc. 1B (reference CLH-O-0000006849-56-01/F). Since cumene is present as an impurity in the composition of the Substance in concentrations of at least 0.1% and up to 10-20%, you propose to self-classify the Substance as Carc. 1B. You consider that such a classification would constitute a justification for waiving for the information requirement of Annex IX Section 8.4. You indicate that "*This could be applied rapidly after the finalization of the present CCH decision, and updated afterward if necessary following the publication of the updated classification of cumene in the future ATP to CLP regulation*".

ECHA has assessed the information that you provided in your comments.

As indicated above, under Annex IX, Section 8.4, column 2 of REACH, the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an *in vivo* somatic cell genotoxicity study. The classification of the Substance as Carc. 1B is not a valid waiver for the information requirement for an *in vivo* somatic cell genotoxicity. Therefore, the data gap persists. You remain responsible for complying with the request for an *in vivo* test in this decision by the set deadline.

ii. Test design

In case you do self-classify the Substance as Carc. 1B. instead of conducting the *in vitro* cytogenicity study (request A.1) as you suggest in your comments, the concern on gene mutation arising from the positive results obtained in the *in vitro* gene mutation study in bacteria must be followed up as specified in a) below.

In case you decide to conduct the *in vitro* cytogenicity study requested in this decision, you must take into account the results from that *in vitro* cytogenicity study in the selection of the appropriate in vivo study as specified in a) and b) below.

*a) Comet assay or TGR - if the test results of request A.1 are **negative**:*

In case the comet assay is appropriate and you decide to conduct this test, according to the test method OECD TG 489, the test must be performed in rats. Having considered the anticipated routes of human exposure and the need for adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

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

In case the TGR assay is appropriate and you decide to conduct this test, according to the test method OECD TG 488, the test must be performed in transgenic mice or rats and the test substance is usually administered orally.

Based on the recent update[6] of OECD TG 488, you are requested to follow the new 28+28d regimen, as it permits the testing of mutations in somatic tissues and as well as in tubule germ cells from the same animals.

According to the test method OECD TG 488, the test must be performed by analysing tissues from liver as slowly proliferating tissue and primary site of xenobiotic metabolism, glandular stomach and duodenum as rapidly proliferating tissue and site of direct contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for mutagenicity at the site of contact in the gastro-intestinal tract. However, duodenum must be stored (at or below −70 ºC) until the analysis of liver and glandular stomach is completed; the duodenum must then be analysed only if the results obtained for the glandular stomach and for the liver are negative or inconclusive.

*b) Comet assay combined with MN test - if the test results of request A.1 are **positive**:*

In case there is a concern for both gene mutation and chromosomal aberration, according to the test method OECD TG 489, the test must be performed in rats. Therefore, the combined test (OECD TG 489 and OECD TG 474) must be performed in rats. Having considered the anticipated routes of human exposure and the need for adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

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

[6] The updated OECD TG 488, adopted on 26 June 2020, is available on OECD website at https://www.oecd-ilibrary.org/docserver/9789264203907-en.pdf?expires=1596539942&id=id&accname=guest&checksum=D552783C4CB0FC8045D04C88EFFBFA66.

The combination of OECD TGs 489 and 474 should not impair the validity of and the results from each individual study. Careful consideration should be given to the dosing, and tissue sampling for comet analysis alongside the requirements of tissue sampling for the mammalian erythrocyte micronucleus test (see OECD TG 489, e.g. Bowen *et al*. 2011[7]).

iii. Germ cells

A subsequent germ cell genotoxicity study (TGR/OECD TG 488, or CA on spermatogonia/OECD TG 483, depending on the concern raised by the substance) may still be required under Annex IX of REACH, in case 1) an *in vivo* genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

Therefore, in case the comet assay is appropriate and you decide to conduct this test , you may consider to collect the male gonadal cells collected from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, in accordance to Annex IX, Section 8.4., column 2, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

In case the TGR is appropriate and you decide to perform this test, you must collect the male germ cells (from the seminiferous tubules) at the same time as the other tissues, in order to limit additional animal testing. According to the OECD 488, the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 ºC). This duration is sufficient to allow you or ECHA, in accordance to Annex IX, Section 8.4., column 2, to decide on the need for assessment of mutation frequency in the collected germ cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

2. 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: "*Cumene hydroperoxide is a strong oxidant. The O-O bond is unstable because of oxygen oxidation degree of -1. So the peroxide functional group is very reactive, particularly with reducing substances (for example organic matters), mineral acids.*".

We have assessed this information and identified the following issue:

A registrant may only adapt this information requirement based on the general rules set out in Annex XI.

Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH.

Therefore, you have not demonstrated that this information can be omitted.

[7] Bowen D.E. et al. 2011. Evaluation of a multi-endpoint assay in rats, combining the bone-marrow micronucleus test, the comet assay and the flow-cytometric peripheral blood micronucleus test. Mutation Research 722 7–19

On this basis, the information requirement is not fulfilled.

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

3. 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: "*Cumene hydroperoxide is a strong oxidant. The O-O bond is unstable because of oxygen oxidation degree of -1. So the peroxide functional group is very reactive, particularly with reducing substances (for example organic matters), mineral acids.*".

We have assessed this information and identified the following issue:

A registrant may only adapt this information requirement based on the general rules set out in Annex XI.

Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH.

Therefore, you have not demonstrated that this information can be omitted.

On this basis, the information requirement is not fulfilled.

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

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 C: 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[8].

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 all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

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[9].

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

Appendix D: 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 E: List of references - ECHA Guidance[10] 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)[11]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[12]

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[13]

[10] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[11] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[12] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[13] 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 F: 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]
[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.