~~Confidential~~

Helsinki, 20 May 2021

Addressees
Registrant(s) of 1,1-difluoroethane-CAS_75-37-6 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
20/11/2019

Registered substance subject to this decision ("the Substance")
Substance name: 1,1-difluoroethane
EC number: 200-866-1
CAS number: 75-37-6

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 ***25 August 2023***.

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) with the Substance

B. 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) with the Substance

2. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method OECD TG 476 or TG 490) with the Substance.

3. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method OECD 421/422) in rats, inhalation route with the Substance

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 413) by inhalation route, in rats, with the Substance

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

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";
- 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". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations 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 Christel Schilliger-Musset, 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.

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.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

ECHA has considered the scientific and regulatory validity of your read-across approach 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 substances within the group. Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3].

You have provided a read-across justification document in IUCLID.

You read-across between the structurally similar substances, 1,1,1-trifluoroethane, EC No. 206-996-5 (CAS No. 420-46-2) and 1,1,1,2-tetrafluoroethane, EC No. 212-377-0 (CAS No. 811-97-2) as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties:
"The basic structures of the target and source substances are similar. Majority of the simulated metabolites (according to QSAR Toolbox v. 4.3) are the same too. Also, the physicochemical data shows that the physicochemical profiles of the target and source substances are similar [...]".

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 to be quantitatively equal to those of the source substance.

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

Read-across hypothesis

A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the source substance(s) and your Substance[4]. It should explain why the differences in the chemical structures should

[2] ECHA Guidance R.6
[3] ECHA Read-across assessment framework
[4] Guidance on information requirements and chemical safety assessment, Chapter R.6: QSARs and grouping of chemicals.

not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

Your read-across hypothesis is that the structural similarity between the source substances and your Substance is a sufficient basis for predicting the properties of your Substance.

You have provided endpoint-specific hypotheses. The hypotheses are included in QSAR Toolbox reports and consist of automatically generated descriptions of target and source substances, including considerations on predicted metabolites.

However, no justification is provided in order to discuss the impact of similarities and differences between target and source substances.

While structural similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar human health properties. You have not provided a well-founded hypothesis to establish a reliable prediction for a toxicological property, based on recognition of the structural similarities and differences between the source substances and your Substance. In particular, you have not transparently reported your consideration on the impact of the structural differences such as the number of fluorines on the properties of the substances.

Supporting information
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*"[5]. The set of supporting information should allow to verify the crucial aspects of the read-across prediction and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include supporting information/bridging studies to compare properties of the Substance and source substances.

The data set reported in the technical dossier does not include relevant, reliable and adequate information on the properties under consideration for your Substance and the source substances to support your read-across predictions, e.g. bridging studies of comparable design and duration.

In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

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.

Further specific considerations are addressed under the individual endpoints.

[5] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

2. Assessment of your weight of evidence adaptations under Annex XI, Section 1.2

You seek to adapt the following standard information requirements by applying weight of evidence approaches in accordance with Annex XI, Section 1.2:

- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- *In vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

ECHA has considered the scientific and regulatory validity of your weight of evidence approach in general before assessing the specific standard information requirements in the following appendices.

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 not included a justification for your weight of evidence adaptations, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Irrespective of this principle deficiency on the documentation, which in itself could lead to the rejection of the adaptations, ECHA has assessed the provided sources of information with a view to their relevance and reliability for the endpoints in question

In the following, ECHA gives the reasons why it considers in general a deficiency with regard to the reliability of information provided on analogue substances, while the specific deficiencies of the weight of evidence are set out in the reasons given for the individual information requirements in the Appendices below.

Reliability of the provided information with analogue substances

ECHA understands that you intend to predict the toxicological properties of the Substance for the listed above endpoints, from data obtained with analogue substances in a read-across approach as part of your weight-of-evidence approach.

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.

You have provided a read-across justification document in IUCLID.

You read-across between the structurally similar substances, 1,1,1-trifluoroethane, EC No. 206-996-5 (CAS No. 420-46-2) and 1,1,1,2-tetrafluoroethane, EC No. 212-377-0 (CAS No. 811-97-2) as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: "The analogue substances 1,1,1-trifluoroethane and 1,1,1,2-tetrafluoroethane share the same functional groups with the substance 1,1-difluoroethane and also have comparable values for the relevant molecular properties".

For the same reasons given in section 1 above (sub-sections about read across hypothesis and supporting information), the information as currently submitted cannot provide any weight for the assessment of the Substance. More specifically, you have not provided a well-founded hypothesis to establish a reliable prediction for a toxicological property, based on recognition of the structural similarities and differences between the source substances and your Substance. In particular, you have not transparently reported your consideration on the impact of the structural differences such as the number of fluorines on the properties of the substances.

Besides, the data set reported in the technical dossier does not include relevant, reliable and adequate information on the properties under consideration for your Substance and the source substances to support your read-across predictions, e.g. bridging studies of comparable design and duration. In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

In your comments on the draft decision, you noted your intention to improve the weight of evidence and the read-across approach, but you have not provided any further information. You remain responsible for complying with this decision by the set deadline.

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

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

1. In vitro gene mutation study in bacteria

An *In vitro* gene mutation study in bacteria is a standard information requirement in Annex VII to REACH.

You have adapted this information requirement by using a weight of evidence approach under Annex XI, Section 1.2. In support of your adaptation, you have provided the following study records with analogue substances:

With the Substance:

(i) Longstaff E, et al (1984), *in vitro* gene mutation study in bacteria, equivalent or similar to OECD Guideline 471 (Key Study).

With 1,1,1-trifluoroethane:

(ii) [redacted] (1996), *in vitro* gene mutation study in bacteria, equivalent or similar to OECD Guideline 471.

With 1,1,1,2-tetrafluoroethane:

(iii) [redacted] (1995), *in vitro* gene mutation study in bacteria, equivalent or similar to OECD Guideline 471.

(iv) Longstaff E, et al (1984), *in vitro* gene mutation study in bacteria, equivalent or similar to OECD Guideline 471.

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

As explained under *Appendix on Reasons common to several requests* (section 2, weight of evidence), 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 a weight of evidence adaptation for the information requirement of Section 8.4.1 at Annex VII must include similar information as obtained in a study in accordance with OECD TG 471: Detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies; and data provided on 5 bacterial 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).

The sources of information (i) to (iv) provide relevant information on detection and quantification of gene mutation in 5 bacterial strains (TA1535, TA1537, TA 100, TA 98 and *E. coli* WP2 uvrA).

However, these sources of information have the following deficiencies affecting their reliability.

In general, the reliability of sources of information (ii), (iii) and (iv) is significantly affected by the deficiencies identified and explained in the above *Appendix on Reasons common to several requests (*section 2, weight of evidence).

Regarding the study (i) with the Substance, ECHA identified the following issue(s):

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471 (1997). 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) At least 5 doses must be evaluated, in each test condition.
d) Triplicate plating must be used at each dose level.
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 however does not include:

a) the appropriate 5 strains, as the information provided does not include results in TA1537 or TA97a or TA97 and 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) the evaluation of at least 5 doses in each test condition.
d) triplicate plating at each dose level.
e) a positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
f) a negative control with a number of revertant colonies per plate inside the historical control range of the laboratory and data on the number of revertant colonies per plate for the treated doses and the controls..

In sum, the sources of information (i) to (iv) have significant reliability issues and cannot contribute to the conclusion on the potential of the Substance to cause genotoxicity in bacteria.

In your comments on the draft decision, you noted your intention to improve the weight of evidence and the read-across approach, but you have not provided any further information. You remain responsible for complying with this decision by the set deadline.

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 *in vitro* gene mutation study in bacteria. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

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

To fulfil the information requirement for the Substance, an *in vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471) is considered suitable.

Possibility for data sharing

The jointly submitted registration for the Substance contains data which is relevant for this endpoint. In accordance with Title III of the REACH Regulation, you may request it from the other registrant(s) and then make every effort to reach an agreement on the sharing of data and costs.

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

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 10 to 100 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII and VIII to 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 a standard information requirement in Annex VIII to REACH (Section 8.4.2.).

You have adapted this information requirement by using a weight of evidence approach under Annex XI, Section 1.2. In support of your adaptation, you have provided the following study records with analogue substances:

With 1,1,1-trifluoroethane:

(i) [redacted] (1996), *in vitro* cytogenicity/ chromosome aberration study in mammalian cells, equivalent or similar to OECD Guideline 473.

With 1,1,1,2-tetrafluoroethane:

(ii) [redacted] (1995), *in vitro* cytogenicity/ chromosome aberration study in mammalian cells (Chinese hamster lung cell line), equivalent or similar to OECD Guideline 473.

(iii) [redacted] (1995), *in vitro* cytogenicity/ chromosome aberration study in mammalian cells (human lymphocytes), equivalent or similar to OECD Guideline 473.

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

As explained under *Appendix on Reasons common to several requests* (section 2, weight of evidence), 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 8.4.2. at Annex VIII must include: Detection and quantification of cytotoxicity and the frequency of cells with structural chromosomal aberration(s) or the frequency of micronuclei in cultured mammalian cells *(in vitro)* or in mammals (*in vivo*). A level of information on these aspects similar to that obtained from in vitro/in vivo chromosomal aberration tests (OECD TG 473/OECD TG 474) or in vitro/in vivo micronucleus tests (OECD TG 487/OECD TG 475) is required.

The sources of information (i), (ii) and (iii) provide relevant information on detection and quantification of cytotoxicity and the frequency of cells with structural chromosomal aberration(s).

However, the reliability of sources of information (i), (ii) and (iii) is significantly affected by the deficiencies identified and explained in the above *Appendix on Reasons common to several requests* (section 2, weight of evidence).

In your comments on the draft decision, you noted your intention to improve the weight of evidence and the read-across approach, but you have not provided any further information. You remain responsible for complying with this decision by the set deadline.

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* cytogenicity study in mammalian cells or an *In vitro* micronucleus study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

Therefore your adaptation is rejected and the information requirement is not fulfilled.

To fulfil the information requirement for the Substance, both an *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) and an *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

Possibility for data sharing

The jointly submitted registration for the Substance contains data which is relevant for this endpoint. In accordance with Title III of the REACH Regulation, you may request it from the other registrant(s) and then make every effort to reach an agreement on the sharing of data and costs.

2. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is a standard information requirement in 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.

Your dossier contains data for an *in vitro* gene mutation study in bacteria, and an adaptation for an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study.

Triggering of the information requirement
The information for the *in vitro* gene mutation study in bacteria and for the *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study provided in the dossier are rejected for the reasons provided in section 1 of Appendix A and section 1 of Appendix B.

Consequently, you are required to provide information for this endpoint, only if the *in vitro* gene mutation study in bacteria and the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provide a negative result. The deadline set in this decision for the provision of all information allows for sequential testing.

Rejection of the information provided
You have adapted this information requirement by using a weight of evidence approach under Annex XI, Section 1.2. In support of your adaptation, you have provided the following study records with analogue substances:

With 1,1,1,2-tetrafluoroethane:

(i) [redacted] (1995), *in vitro* gene mutation study in mammalian cells, equivalent or similar to OECD Guideline 476.

ECHA assessed this information and identified the following issues:

Firstly, Annex XI, Section 1.2 states that there may be sufficient weight of evidence "*from several independent sources of information*".

You have only provided one source of information.

Secondly, relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.3 at Annex VIII must include similar information that is produced by the OECD TG 476/490 and OECD TG 488. This 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*).

The source of information (i) provides relevant information on detection and quantification of gene mutation in cultured mammalian cells.

However, it has deficiencies affecting its reliability, as identified and explained under the above Appendix on Reasons common to several requests (section 2, weight of evidence).

For all these reasons your adaptation is rejected and the information requirement is not fulfilled.

In your comments on the draft decision, you noted your intention to improve the weight of evidence and the read-across approach, but you have not provided any further information. You remain responsible for complying with this decision by the set deadline.

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

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

3. 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 have adapted this information requirement according to Column 2 of Annex IX, Section 8.7 reporting that "*the study does not need to be conducted because a pre-natal developmental toxicity study is available*".

ECHA has assessed your adaptation according to Column 2 of Annex VIII, Section 8.7. and identified the following issue:

According to Annex VIII, Section 8.7., Column 2, first paragraph, fourth indent, the study does not need to be conducted if a pre-natal developmental toxicity study (OECD TG 414) is already available.

As explained in the Appendix on Reasons common to several requests (section 1, read across), your read across adaptation for a pre-natal developmental toxicity study (OECD TG 414) is rejected, therefore, an adequate pre-natal developmental toxicity study to waive the information requirement for Screening for reproductive/developmental toxicity is not available.

Based on the above, the information you provided do not fulfil the information requirement.

In your comments on the draft decision, you noted your intention to improve the read-across approach, but you have not provided any further information. You remain responsible for complying with this decision by the set deadline.

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 administration of the Substance by inhalation because the Substance is a gas.

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

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

1. Sub-chronic toxicity study (90-day), inhalation 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 adapted the standard information requirement in accordance with Annex XI, section 1.5. to REACH by providing the justification discussed in the Appendix on Reasons common to several requests above (section 1, read across) and the following study records with the source substances:

With 1,1,1-trifluoroethane:

(ii) [redacted] (1996). 90 days inhalation toxicity study in rats (OECD Guideline 413). NOAEC 137489.41 mg/m^3 (40000 ppm). Based on these results, the NOAEC for 1,1 -difluoroethane was determined to be 108057.26 mg/m3.

(iii) [redacted] (1996). 28 days inhalation toxicity study in rats (OECD Guideline 412). NOAEC 137489.41 mg/m^3 (40000 ppm). Based on these results, the NOAEC for 1,1 -difluoroethane was determined to be 108057.26 mg/m3.

With 1,1,1,2-tetrafluoroethane:

(iv) [redacted] (1995). 90 days inhalation toxicity study in rats (OECD Guideline 413). NOAEC 208652.15 mg/m^3 (50000 ppm). Based on these results, the NOAEC for 1,1 -difluoroethane was determined to be 135071.57 mg/m3.

(v) [redacted] (1995). One-year dog inhalation toxicity study. NOAEC 500765.15 mg/m^3 (120000 ppm). Based on these results, the NOAEC for 1,1 -difluoroethane was determined to be 324171.78 mg/m3

As explained in the Appendix on Reasons common to several requests, your adaptation is rejected.

In your comments on the draft decision, you noted your intention to improve the read-across approach, but you have not provided any further information. You remain responsible for complying with this decision by the set deadline .

Information on the design of the study to be performed

Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the inhalation route is the most appropriate route of administration to investigate repeated dose toxicity because the Substance is a gas and human exposure by the inhalation route is likely. The sub-chronic toxicity study must be performed according to the OECD TG 413 in rats.

Possibility for data sharing

The other registrants of the joint submission relied on an adaptation to meet this information requirement. You may consider sharing this information.

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 have adapted the standard information requirement in accordance with Annex XI, section 1.5. to REACH by providing the justification discussed in the Appendix on Reasons common to several requests above and the following study records with the source substances:

With 1,1,1-trifluoroethane:

(i) [redacted] (1996). Pre-natal developmental toxicity (PNDT) inhalation study (OECD TG 414). Rats. NOAEC 40000 ppm. Based on these results, the NOAEC for 1,1 -difluoroethane was determined to be 108057.26 mg/m3.

(ii) [redacted] (1996). Pre-natal developmental toxicity (PNDT) inhalation study (OECD TG 414). New Zealand White Rabbits. NOAEC 40000 ppm. Based on these results, the NOAEC for 1,1 -difluoroethane was determined to be 108057.26 mg/m3.

With 1,1,1,2-tetrafluoroethane:

(iii) [redacted] (1995). Pre-natal developmental toxicity (PNDT) inhalation study (OECD TG 414). Rats. NOAEC 64379 ppm. . Based on these results, the NOAEC for 1,1 -difluoroethane was determined to be 173915.46 mg/m3.

With 1,1 –difluoroethane:

(iv) [redacted] (2009). Pre-natal developmental toxicity (PNDT) inhalation study (OECD TG 414). NOAEC 50000 ppm. Based on these results, the NOAEC for 1,1 -difluoroethane was determined to be 135071.57 mg/m3

We have assessed this information and identified the following issues:

Regarding the study (iv) with the Substance, ECHA identified the following issue:
In order to be considered compliant and enable assessing if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in one species.

According to Article 13(4) of REACH, toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). According to Article 141(2), Article 13 applies from entry into application of the REACH Regulation on 1 June 2008.

Based on the information provided in your dossier, the study you provided was conducted according to the OECD TG 414, but it is not GLP compliant.

Further, regarding all the information on the other source substances (i, ii, iii), your adaptation is rejected for the reasons set out in the Appendix on Reasons common to several requests (section 1, read across).

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

In your comments on the draft decision, you noted your intention to improve the read-across approach, but you have not provided any further information. You remain responsible for complying with this decision by the set deadline.

Information on the design of the study to be performed

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with administration of the Substance by inhalation because the Substance is a gas.

Possibility for data sharing

The other registrants of the joint submission relied on an adaptation to meet this information requirement. You may consider sharing this information.

3. Long-term toxicity testing on aquatic invertebrates

and

4. Long-term toxicity testing on fish

Long-term toxicity testing on aquatic invertebrates and long-term toxicity testing on fish are information requirements under Annex IX to REACH (Section 9.1.5. and Section 9.1.6.).

You have provided the following information in the dossier: a justification to omit the study, which you consider to be based on Annex IX, Section 9.1., Column 2. "*In accordance with column 2 of REACH Annex IX, the study does not need to be conducted since the chemical safety assessment indicates that there is no need to investigate further the effects on aquatic organisms. No emission to water is expected*".

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 and 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 your comments on the draft decision, you note that you interpreted Annex IX, Section 9.1., Column 2 adaptation as the long-term aquatic toxicity studies would not be needed in the absence of any concern derived from the Chemical Safety Assessment. You further indicate that you intend to "*revise all information available to assess these endpoints accordingly*" and that you will provide this information in an update of your registration dossier. The information in your comments is not sufficient for ECHA to make an assessment. Please note that this decision does not take into account 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).

On this basis, the information requirements are not fulfilled.

Study design

To fulfil the information requirement of long-term toxicity testing on fish 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[6].

B. Test material

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 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.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[7].

[6] https://echa.europa.eu/practical-guides
[7] 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 26 March 2020.

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[8] 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)[9]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[9]

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[10]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[8] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[9] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[10] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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]

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.