EUROPEAN CHEMICALS AGENCY

Helsinki, 19 July 2017

Addressee: [redacted]

Decision number: CCH-D-2114363808-37-01/F
Substance name: perfluamine
EC number: 206-420-2
CAS number: 338-83-0
Registration number: [redacted]
Submission number: [redacted]
Submission date: 24.06.2013
Registered tonnage band: 100-1000T

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information on

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

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

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

4. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) with the registered substance if 2 and 3 have negative results;**

5. **Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD [421/422]) in rats, oral route with the registered substance;**

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

7. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the FZ-7941 (cell crude of FC-3283) composition of the registered substance;**

8. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the FZ-7941 (cell crude of FC-3283) composition of the registered substance;**

9. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the FZ-7941**

(cell crude of FC-3283) composition of the registered substance;

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

ECHA observes that in your comments on proposals for amendments submitted by Member State Competent Authorities you note that you "*have not submitted separate dossiers for FZ-7941 and FC-3283 because as per the REACH guidance on substance identification and naming of substances [you] had concluded that both FZ-7941 and FC-3283 could be included in the same dossier*". ECHA understands that you have considered that FZ-7941 and FC-3283 refer to the same substance. The properties of both FZ-7941 and FC-3283 should then be addressed in the registration dossier according to the requirements specified in Title II of the REACH Regulation.

You may still adapt the standard information required (for the whole substance, or for one of its compositions) according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. Please note however that, in order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **27 January 2020**. You shall also update the chemical safety report, where relevant.

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

Appeal

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

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

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

Appendix 1: Reasons

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

0. Grouping of substances and read-across approach

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests. Such other means include the use of information from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met". In the registration, you have adapted the standard information requirements, relevant to
the current decision (Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.), In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.), In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.), In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.), Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) and Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) by applying a read-across adaptation following REACH Annex XI, Section 1.5. with the following substances:

Sub-chronic toxicity study oral:

Perfluorohexanes, CAS# 1064697-81-9
Perfluoroheptanes, CAS# 1064698-16-3
Perfluorotributylamines, CAS# 1064698-37-8
Perfluoro-N-methylmorpholine, CAS# 382-28-5
Perfluoro-N-C1,3-alkyl morpholines, CAS# 1093615-61-2
Perfluoro-C6,8-furans, pyrans and acyclic ethers , CAS# 1064698-52-7)

Sub-chronic toxicity study inhalation:

Perfluorotributylamines, CAS# 1064698-37-8)

Perfluorohexanes, CAS# 1064697-81-9

In vitro gene mutation study in bacteria:

Perfluorohexanes, CAS# 1064697-81-9
Perfluoroheptanes, CAS# 1064698-16-3
Perfluorotributylamines, CAS# 1064698-37-8
Perfluoro-N-methylmorpholine, CAS# 382-28-5
Perfluoro-N-C1,3-alkyl morpholines, CAS# 1093615-61-2
Perfluoro-C6,8-furans, pyrans and acyclic ethers , CAS# 1064698-52-7

***In vitro* cytogenicity study in mammalian cells and *In vitro* gene mutation study in mammalian cells:**

Perfluoro-N-C1,3-alkyl morpholines, CAS# 1093615-61-2

Screening for reproductive/developmental toxicity and Pre-natal developmental toxicity studies:

Perfluoro-N-C1,3-alkyl morpholines, CAS# 1093615-61-2

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

You have provided the following arguments to justify the read-across approaches in general terms. You consider the Perfluorinated Organic Chemicals, C5-C18 as a category, defined as a chemically related group of substances including:

Perfluorohexanes, CAS# 1064697-81-9
Perfluoroheptanes, CAS# 1064698-16-3
Perfluorotributyl amines, CAS# 1064698-37-8
Perfluorotripropylamine, CAS# 338-83-0
Perfluoro-N-methylmorpholine, CAS# 382-28-5
Perfluoro-N-C1,3-alkyl morpholines, CAS# 1093615-61-2
Perfluoro-C6,8-furans, pyrans and acyclic ethers , CAS# 1064698-52-7

You further explain that:

"Members of this category are fully fluorinated, meaning that fluorine, rather than hydrogen, is bonded to all carbon atoms in the molecule. Fluorine is the most electronegative of the elements (fluorine has an electronegativity of 3.98 on the Pauling scale, as compared to 2.2 for hydrogen). This electronegativity is expected to dominate over all other aspects of substance chemistry and is the underlying basis for similarity of substances in this category. The members of this category have previously been described in the EU under the generic CAS# 86508-42-1, and are listed in chemical inventories of other jurisdictions under this generic number. All of these chemicals stem from the same manufacturing process ([redacted]*), have similar physicochemical properties including high vapor pressure and low water solubility. The category hypothesis is that the similarity in chemical makeup and physicochemical characteristics lead to similar toxicokinetics and lack of metabolism in vivo, and that environmental fate, toxicity and ecotoxicity data can be read across between category members or filled in via trend analysis, and also lack any chemically reactive groups, which forms the technical basis for the category*.

ECHA understands that your hypothesis is based on the structural similarity of the registered substance and analogue substances within the "The Perfluorinated Organic Chemicals, C5-C18" category (all substances are fully fluorinated, having between five and eighteen carbons, at most one oxygen atom, at most two nitrogen atoms, and no hydrogen or olefin bonds), the similar chemical and physicochemical properties of the substances, toxicological similarity, and as a consequence of these properties, similarity in toxicokinetics and lack of metabolism of the substances in vivo, and that this hypothesis is the basis on which you predict the properties of the registered substance from data for reference substance(s) within the group/category.

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

Grouping of substances

You have proposed a grouping of substances, and the structural similarity which defines that grouping, as set out above. You have further explained your read-across hypothesis on the basis of the structural similarity which defines the grouping, the specific relevant part being "Members of this category are fully fluorinated ...".

However, the registered substance is present in two different compositions/grades, with the second one containing a significant number and amount of impurities of concern. For example, one particular impurity, hydride isomers of 1,1,2,2,3,3,3-heptafluoro-N,N´-bis(heptafluoropropyl)-1-propanamine, covers a significant proportion of the substance (7-28%, typically 14%), and has hydride groups instead of fluorine atoms. You claimed that also the impurities and minor constituents are included within the category definition.

However, these chemical components are not covered by the category definition of chemical structures (i.e. the requirement for fully fluorinated carbon atoms), and you have not justified that these hydride isomers in the cell crude grade would have a similar chemistry to fluorine-substituted substances. Therefore, ECHA considers that these substances cannot be assumed to be chemically inert like per-fluorinated substances, and that the category justification excludes these components, both on the basis of their structure and their different chemical properties.

ECHA accordingly considers that you have not provided a read-across justification that allows for prediction of the properties of the registered substance for the composition/ grade of substance which includes a significant proportion of hydride isomers. For this reason the requirements of read-across set out in Annex XI, 1.5. are not met.

ECHA additionally notes that in the toxicology data, it is not specified which grade of the registered substance has been used, and ECHA is unable to determine the effects of the two different compositions as a result of your incomplete documentation of the grade of the substance used; ECHA notes that pursuant to Annex XI, section 1.5 adequate and reliable documentation of your read-across is required.

Read-across hypothesis

You proposed a read-across hypothesis based on structural similarity, similar chemical and physicochemical properties of the substances, toxicological similarity, and similarity in toxicokinetics and lack of metabolism of the substances in vivo.

The read-across hypothesis was assessed by ECHA against the requirements of Annex XI, 1.5, as set out further below. Specifically, Annex XI, 1.5 requires that "Application of the group concept requires that physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach)." ECHA considers that there must be a well-founded basis for predicting the human health properties of the registered substance, such as a well-founded hypothesis of (bio)transformation to (a) common compound(s), and/or that different compounds have the same type of effect(s), to allow a prediction of human health properties that does not underestimate risks. ECHA has examined your read-across hypothesis for the registered substance, and considers that you have not provided a well-founded basis for prediction of the properties of the registered substance for the reasons set out below.

i) Structural similarity

You have proposed that structural similarity is a basis for predicting the properties of the registered substance. Structural similarity is a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or this specific case that structural similarity per se is sufficient to enable the prediction of human health properties of a substance, since structural similarity does not always lead to predictable or similar human health properties.

ii) Similar chemical and physicochemical properties

You have proposed that the chemical and physicochemical properties of the substances are similar and follow a regular pattern, and that this is a basis for predicting the properties of the registered substance. While the physicochemical properties of the proposed category members shows some similarity and the similarity or a regular pattern of chemical and physicochemical properties are a prerequisite for applying the grouping and read-across approach, ECHA does not accept in general or this specific case that chemical and physicochemical similarity or regular properties per se are sufficient to enable the prediction of human health properties of a substance, since physicochemical similarity or regular properties does not always lead to predictable or similar human health properties.

iii) Toxicological similarity

You have proposed that the toxicological properties of the substances are similar and follow a regular pattern, and that this is a basis for predicting the properties of the registered substance. The toxicological information available in the data matrix shows results in the same range and indicating a general low toxicity.

Similarity or a regular pattern of toxicological properties are a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or this specific case that toxicological similarity or regular properties per se are sufficient to enable the prediction of human health properties of a substance, since toxicological similarity or regular properties in one toxicological endpoint does not always lead to predictable or similar human health properties in other toxicological endpoints.

iv) Similarity in toxicokinetics and lack of metabolism of the substances in vivo

With regard to toxicokinetics you state in your category justification document that "*Based on physical properties, all members of this category are not expected to be internally absorbed and any absorbed amount is expected to be rapidly excreted due to the physical properties and the inability to be metabolized.*" You also provide reasoning based on the chemistry of the substances. However, since no toxicokinetic (including metabolism) data on the registered substance are available to substantiate the hypothesis of similarity of toxicokinetics and lack of metabolism in vivo, ECHA considers that the similarity of toxicokinetics and lack of metabolism in vivo of the registered substance has not been established. For this reason, ECHA considers that your hypothesis is not an adequate basis for predicting the properties of the substance.

ECHA further notes that similarity regarding the toxicokinetics and lack of metabolism in vivo alone is not sufficient for concluding that the substances have similar toxicological properties. Specifically, even assuming that the registered substance is not chemically changed, ECHA considers that there is not an adequate basis for considering that the registered substance is incapable of interacting with biological systems. ECHA notes that in a 30-day inhalation study ([redacted] 1977, key study) with a structurally-analogous member of the category, perfluorotributylamine, effects on hematology parameters were

observed. This means that a systemic effect from another category member has been observed, which would also have (according to your proposed basis) poor absorption, rapid clearance and lack of metabolism. Therefore, it is also possible that there could be toxicological effects from other category members. ECHA considers that it is additionally necessary to provide a basis for understanding the toxicodynamic properties of the registered substance, in order to be able to predict the properties of the registered substance. In this regard, ECHA notes that for the registered substance, there are no higher-tier toxicological studies, and so the basis for understanding the toxicodynamic properties of the registered substance is inadequate. For this reason also, ECHA considers that your hypothesis is not an adequate basis for predicting the properties of the substance.

Following the receiving of the draft decision you submitted comments with information from additional studies provided on structurally-related substances, including repeated-dose toxicity studies and toxicokinetic studies. ECHA acknowledges your explanation on the haematological finding in the study of [redacted] (1977) and notes you have provided some chemically-based reasoning to explain the properties of the registered substance. You have also provided some comments about the second composition of the registered substance.

Additional studies on structurally-related substances

You have provided several additional studies, including on repeated dose toxicity and toxicokinetics. However, since there is not a valid reasoning for why the read-across can be accepted, these studies cannot be read-across to predict the properties of the registered substance. You have made reference to multiple studies on PMM and FC-770. Insufficient information is provided in this comment for ECHA to be able to evaluate these studies, as only very brief summaries are provided which do not comply with the requirements for (robust) study summaries. ECHA can only evaluate these studies when they are provided in a dossier update.

Chemically-based reasoning to explain the properties of the registered substance
On page 4 of your "Specific comments..." you have included new reasoning to explain the human health properties of the registered substance. You argue that "Based upon the physical and chemical properties, all three chemicals are not expected to be internally absorbed." However, ECHA notes that you have alluded to toxicokinetic data on a specific substance (FC-770), but that does not substantially change ECHA's response to this general argument that has been given in the draft decision. ECHA therefore considers that you have not provided reasoning to justify read-across, given the reasons already set out in the draft decision, according to Annex XI, 1.5.

Haematological findings in the study of [redacted] (1977)
ECHA notes your hypothesis that the effects in this study are a statistical artefact and without biological consequence. Irrespective of whether this is the case or not, ECHA notes that for the registered substance, there are no higher-tier toxicological studies, and so the basis for understanding the toxicodynamic properties of the registered substance is inadequate. These important aspects of the read-across were not addressed by your comments. Due to the arguments above the read-across cannot be accepted.

Conclusion on the read-across approach

ECHA considers that the individual arguments that you have proposed to justify the read-across are insufficient for the reasons as set out above. Additionally, ECHA has taken into account the weight of all of your arguments together. ECHA considers that the arguments

when taken all together do not provide a suitable basis for predicting the properties of the registered substance.

ECHA considers that this grouping and read-across approach does not provide a robust basis whereby the human health effects may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach), and hence does not comply with the general rules of adaptation as set out in Annex XI, 1.5. of the REACH Regulation. ECHA notes that there are specific considerations for the individual endpoints which also result in a failure to meet the requirement of Annex XI, 1.5, and these are set out under the endpoint concerned.

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

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

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

For the repeated dose toxicity endpointyou have sought instead to adapt this information requirement according to Annex XI, Sections 1.2. and 1.5. of the REACH Regulation. You state that "*Trend analysis from category members show that members are practically nontoxic by oral exposure. Slope of trend line equals zero.*" You make reference to the category members:

Perfluorohexanes (PFHx), CAS# 1064697-81-9
Perfluoroheptanes (PFHp), CAS# 1064698-16-3
Perfluorotributylamines (PTPA), CAS# 1064698-37-8
Perfluorotripropylamines, CAS# 338-83-0
Perfluoro-N-methylmorpholine (PMM), CAS# 382-28-5
Perfluoro-N-C1,3-alkyl morpholines (FC-770), CAS# 1093615-61-2
Perfluoro-C6,8-furans, pyrans and acyclic ethers (FC-77), CAS# 1064698-52-7.

Although you have mentioned weight of evidence, ECHA considers that this is essentially a grouping and read-across approach. Hence, ECHA has evaluated your adaptation with respect to the provisions stipulated in Annex XI, Section 1.5. However, as concluded in Appendix, section 0, of this decision your read-across adaptation according to REACH Annex XI, section 1.5 cannot be accepted.

For the repeated dose oral toxicity endpoint, you have provided one endpoint study record for 'repeated dose toxicity; oral', entitled "Repeated dose toxicity: [redacted]". This endpoint study record makes reference to multiple repeat-dose toxicity studies.

However, ECHA notes that a robust study summary is required under Article 10(a)(vii), and ECHA considers that the information provided in the endpoint study record does not meet the requirements of a robust study summary, as defined in Article 3(28). ECHA considers

that it is necessary to provide a separate endpoint study record for each study used in the trend analysis. Specifically, the endpoint study record does not provide data on doses, number of animals, substance purity, methods, results, etc. ECHA has provided a practical guide for "*How to report robust study summaries*", available at: http://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf. ECHA considers there is not sufficient information to make an independent assessment of these studies minimising the need to consult the full study report, and accordingly considers that for repeated dose toxicity; oral', you have failed to meet the requirement of Annex XI, 1.5 that adequate and reliable documentation of the applied method shall be provided.

Additionally, ECHA notes that it appears that these studies are of 28-day duration (although ECHA cannot be definitive as a result of the inadequate documentation), and that source studies of 28-day duration do not fulfil the requirement of Annex XI, Section 1.5 of the REACH Regulation for an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3).

For the repeated dose inhalation you provided the following studies using read-across to other members of the proposed category:

- A 28 day study ([redacted], 1977, no guideline, no GLP) with perfluorotributylamines, (CAS 1064698-37-8). A NOAEL > 7.28 mL test article/cubic meter was obtained. In this study thickened alveolar septa and focal fatty degeneration of liver were observed. However, you claim that these outcomes were seen in both control and test animals. The reporting of this study is not very clear.
- A 90 day GLP study performed equivalent or similar to OECD Guideline 413 (Subchronic Inhalation Toxicity: 90-Day Study) with Perfluorohexanes, CAS# 1064697-81-9. In this study a NOAEL of ca. 77070 ppm taking into account the molecular weight of PTPA was calculated.
- A disregarded study ([redacted], 1992), similar to OECD 412 (Sub-acute inhalation toxicity: 28-Day Study) with Perfluorohexanes, CAS# 1064697-81-9. This study established a NOAEL of more than 50129 ppm (analytical) and found no treatment-related mortality, clinical signs, body weight changes, food or water consumption, macroscopic pathology, or organ weight changes.

The 90 day study fulfils the requirement of Annex XI, Section 1.5 of the REACH Regulation for an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3). However, as concluded in Appendix, section 0, of this decision your read-across adaptation accoring to REACH Annex XI, section 1.5 cannot be accepted.

Furthermore, ECHA notes that the exposure duration of two of the source studies that you have used in your read-across approach, ([redacted], 1977 and [redacted], 1992) 28-day exposure period, is shorter than the exposure period expected from a sub-chronic (90-day) repeated dose toxicity study performed according to the OECD 408 test guideline.

Therefore, ECHA considers that, in addition to the basis for rejection of the read-across set out in Section 0, these source studies do not fulfil the requirement of Annex XI, Section 1.5 of the REACH Regulation for an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) and the requirement of Annex XI, Section 1.2. of the test method "*as being equivalent*".

As explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement on the basis on Annex XI, 1.5. is rejected.

Therefore, your adaptation of the information requirement is rejected.

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

ECHA has evaluated the most appropriate route of administration for the study. The substance is a liquid with low water solubility (about 0.381 ug/L at 23C). It has a low vapour pressure (516 Pa) and an estimated Log Kow between 5.3 - 6.1 (based on read across). The substance has no skin corrosive/irritant properties and there are no indications of different effects between the oral and inhalation route. Moreover, there are no spray applications with the registered substance. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration.

Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

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

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

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

For gene mutation in bacterial cells, you have sought instead to adapt this information requirement according to Annex XI, Section 1.2. and 1.5. of the REACH Regulation. You state that "*Trend analysis from category members show that members are practically nontoxic by oral exposure. Slope of trend line equals zero.*" You make reference to the category members:

Perfluorohexanes, CAS# 1064697-81-9
Perfluoroheptanes, CAS# 1064698-16-3
Perfluorotributylamines, CAS# 1064698-37-8
Perfluorotripropylamines, CAS# 338-83-0
Perfluoro-N-methylmorpholine, CAS# 382-28-5
Perfluoro-N-C1,3-alkyl morpholines, CAS# 1093615-61-2
Perfluoro-C6,8-furans, pyrans and acyclic ethers , CAS# 1064698-52-7

Although you have mentioned weight of evidence, ECHA considers that this is essentially a grouping and read-across approach. Hence, ECHA has evaluated your adaptation with respect to the provisions stipulated in Annex XI, Section 1.5. However, as concluded in Appendix, section 0, of this decision your read-across adaptation according to REACH Annex XI, section 1.5 cannot be accepted.

It is a requirement of Annex XI, 1.5 that adequate and reliable documentation of the applied method shall be provided. You have provided one endpoint study record for 'gene mutation in bacterial cells', entitled "[redacted]" with a trend analysis of the Ames assays performed on the proposed category members. This endpoint study record makes reference to multiple Ames studies. However, ECHA notes that a robust study summary is required under Article 10(a)(vii), and ECHA considers that the information provided in the endpoint study record does not meet the requirements of a robust study summary, as defined in Article 3(28). ECHA considers that it is necessary to provide a separate endpoint study record for each study used in the trend analysis. Specifically, the endpoint study record does not provide data on strains, substance purity, doses, methods, results, etc. ECHA has provided a practical guide for "*How to report robust study summaries*", available at: http://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf. ECHA considers there is not sufficient information to make an independent assessment of the studies used in the trend analysis minimising the need to consult the full study report, and accordingly considers that for gene mutation in bacterial cells endpoint, you have failed to provide adequate and reliable documentation.

Furthermore, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement on the basis on Annex XI, 1.5. is rejected.Therefore, your adaptation of the information requirement is rejected.

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

ECHA considers that the bacterial reverse mutation test (test method EU B.13/14. / OECD TG 471) is appropriate to address the standard information requirement of Annex VII, Section 8.4.1. of the REACH Regulation.
Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471).

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

An "*In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for an OECD Guideline 473 (In vitro Mammalian Chromosome Aberration Test), GLP with a member of the proposed category (CAS number 1093615-61-2) showing negative results with or without metabolic activation.

However, as explained above in Appendix 1, section 0 of this decision, your read-across justification is insufficient.

Therefore, your adaptation of the information requirement is rejected.

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

ECHA considers that the *in vitro* mammalian chromosome aberration test (test method OECD TG 473) and the *in vitro* mammalian cell micronucleus test (OECD TG 487) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

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

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.
An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing an OECD Guideline 476 (In vitro Mammalian Cell Gene Mutation Test), GLP with a member of the proposed category (CAS number 1093615-61-2) showing negative results with or without metabolic activation.

However, as explained above in Appendix 1, section 0 of this decision, your read-across justification is insufficient.

Therefore, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.
ECHA considers that the *in vitro* mammalian cell gene mutation tests using the *Hprt* and *xprt* genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.3.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that both studies requested under 2. and 3. have negative results.

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Screening for reproductive/developmental toxicity" (test method OECD TG 421 or 422) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from *in vitro* methods that the substance may be a developmental toxicant. No such evidence is presented in the dossier. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing an oral (gavage) GLP study accordinig to OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test) with the category member Perfluoro-N-C1,3-alkyl morpholines, CAS# 1093615-61-2. Mating performance, fertility, duration of gestation, litter size and survival, and litter and pup weights did not indicate any obvious effect of treatment at any of the dose levels tested (up to 1000 mg kg bw/d).

However, as explained above in Appendix 1, section 0 of this decision, your read-across justification is insufficient.

Therefore, your adaptation of the information requirement is rejected.

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

According to the test methods OECD TG 421/422, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

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

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

Reproductive/developmental toxicity screening test (test method: OECD TG 421) *or* Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route.

Notes for your considerations:

For the selection of the appropriate test, please consult ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7a, section R.7.5 and 7.6 (version 4.1, October 2015). You should also carefully consider the order of testing especially the requested screening (OECD TG 421/211) and the developmental toxicity studies (OECD TG 414) to ensure unnecessary animal testing is avoided, paying particular attention to ECHA's end point specific guidance document[2].

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

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

You have not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2.

In the technical dossier, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a Reproductive Developmental Screening Test that has been conducted with Perfluoroisopropylmorpholine (FC-770) and a 90-Day Inhalation study that was conducted with perfluorohexane. However, these studies do not provide the information required by Annex IX, Section 8.7.2., because they do not cover key parameters of a pre-natal developmental toxicity study, such as examinations of foetuses for skeletal and visceral alterations. Therefore, your adaptation of the information requirement is rejected.

Moreover, as explained above in Appendix 1, section 0 of this decision, your read-across justification is insufficient.

Therefore, your adaptation of the information requirement is rejected.

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

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

[2] ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance Version 5.0, December 2016, p 461-2 (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf).

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

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

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation as weight of evidence two study records:

- READ ACROSS: FC-3284: Growth Inhibition Test with the Unicellular Green Alga, Pseudokirchneriella subcapitata (OECD TG201) with the analogue substance) Perfluoro-N-methylmorpholine, CAS 382-28-5
- READ ACROSS: Fresh water algal growth inhibition test with MTDID 7145 (OECD TG 201) with the analogue substance Perfluoro-N-C1,3-alkyl morpholines FC-770, CAS 1093615-61-2

You provided the following read-across hypothesis for this endpoint: "*Perfluorotripropyl amines (PTPA) is a member of the Perfluorinated Organic Chemicals, C5-C18 category. Because these substances exhibit similarity in their physicochemical properties and toxicological properties in mammals, and because available data indicates that parent molecules are not reactive toward biological molecules and cannot undergo bioactivation by normal enzymatic processes, they can be considered members of a chemical category. Data gaps for ecological toxicity can therefore be addressed by read-across and/or trend analysis between category members. No studies of toxicity to algae and cyanobacteria are available for PTPA. Reliable OECD201 studies are available for algae toxicity of category members perfluoromethyl morpholine (PMM), and FC-770. In both cases, EC50s (72-h and 48-h, respectively) were in excess of the maximum achievable test substance concentrations. Analytically determined test substance concentrations are not reasonable to use for readacross since the solubilities of PMM and FC-770 are substantially higher than that of PTPA. Lack of toxicity at the limit of solubility is read across qualitatively to PTPA. The solubility of PTPA was determined to be 5.96 µg/L in organism-free Daphnia medium controls during the short-term toxicity test. This value is greater than the measured PTPA solubility in water (0.381 µg/L) but less than the analytically determined concentrations in medium containing live daphnids. The organism-free medium solubility value is understood to be better representative of PTPA solubility in natural waters, and avoids potential impacts*

on the analytical result by the action of living organisms. Therefore, 5.96 µg/L is accepted as the basis for estimating the highest possible exposure concentration of PTPA in order to define the EC50."

ECHA notes that there are two compositions/grades of the registered substance. The first (FC-3283) is of high purity (91.5%) and contain mainly perfluorinated impurities. The second grade (FZ-7941 (cell crude of FC-3283)), however, contains a significant proportion of hydride isomers ([redacted]%, typically [redacted]%).

The read-across hypothesis is based on chemical similarity and inertness. You state that "*all of the isomers are fully fluorinated and have the same essential lack of reactivity*" and that "*The category consists of materials containing between five and eighteen carbon atoms. The chemical may also contain one nitrogen or oxygen atom, one nitrogen and one oxygen atom, or at most two nitrogen atoms. All heteroatoms are bonded only to carbon (i.e., no N-N, N-O, N-F or O-F bonds). The only bonds present are C-C, C-F, C-N, or, C-O. No unsaturated bonds are present. No hydrogen is present.*"

For the first composition (FC-3283), ECHA considers the read-across acceptable.

For the second composition (FZ-7941 (cell crude of FC-3283)), however, you have not justified why the hydride isomers in the cell crude grade would have a similar chemistry to fluorine-substituted substances. There is no consideration given to the presence of these hydride impurities in your read across argumentation, consequently the adaptation is not justified.

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

ECHA notes that in both your comments on the draft decision and to the MSCA PfA, on the two different grades, you have further explained that both FZ-7941 and FC-3283 could be included in the same dossier. You have outlined your intentions to provide documentation (for e.g. on uses, risk management measures) in an updated dossier, which will support this claim. ECHA understands that you have considered that FZ-7941 and FC-3283 refer to the same substance. The properties of both FZ-7941 and FC-3283 should then be addressed in the registration dossier according to the requirements specified in Title II of the REACH Regulation. As noted above, the standard information requirements can be also adapted according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation.

In summary, the information provided in your comments on the draft decision and to the MSCA PfA did not provide a sufficient reason for accepting the proposed read-across adaptation and consequently the draft decision was not amended.

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the with the FZ-7941 (cell crude of FC-3283) composition of the registered substance subject to the present decision: Algae growth inhibition test, EU C.3./OECD TG 201).

Notes for your consideration

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity tests and for calculation and expression of the result of the tests.

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a READ ACROSS: Data summary report on the test for acute and chronic toxicity of fluorochemicals to Daphnia magna (water flea) (OECD TG 211) with the analogue substance Perfluorotributylamines(PTBA), CAS# 1064698-37-8.

You provided the following read-across hypothesis for this endpoint: "Perfluorotripropyl amines (PTPA) is a member of the Perfluorinated Organic Chemicals, C5-C18 category. Because these substances exhibit similarity in their physicochemical properties and toxicological properties in mammals, and because available data indicates that parent molecules are not reactive toward biological molecules and cannot undergo bioactivation by normal enzymatic processes, they can be considered members of a chemical category. Data gaps for ecological toxicity can therefore be addressed by read-across and/or trend analysis between category members."

ECHA notes that there are two compositions/grades of the registered substance. The first (FC-3283) is of high purity (91.5%) and contain mainly perfluorinated impurities. The second grade (FZ-7941 (cell crude of FC-3283)), however, contains a significant proportion of hydride isomers ([redacted]%, typically [redacted]%).

The read across hypothesis is based on chemical similarity and inertness. You state that "all of the isomers are fully fluorinated and have the same essential lack of reactivity" and that "The category consists of materials containing between five and eighteen carbon atoms. The chemical may also contain one nitrogen or oxygen atom, one nitrogen and one oxygen atom, or at most two nitrogen atoms. All heteroatoms are bonded only to carbon (i.e., no N-N, N-O, N-F or O-F bonds). The only bonds present are C-C, C-F, C-N, or, C-O.

No unsaturated bonds are present. No hydrogen is present."

For the first composition (FC-3283), ECHA considers the read-across acceptable for environmental endpoints.

For the second composition (FZ-7941 (cell crude of FC-3283)), however, you have not justified why the hydride isomers in the cell crude grade would have a similar chemistry to fluorine-substituted substances. There is no consideration given to the presence of these hydride impurities in your read across argumentation, consequently the adaptation is not justified.
Therefore, your adaptation of the information requirement cannot be accepted.

As outlined in Section 7, Growth inhibition study aquatic plants, the information provided in your comments on the draft decision and to the MSCA PfA did not provide a sufficient reason for accepting the proposed read-across adaptation and consequently the draft decision was not amended.

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the with the FZ-7941 (cell crude of FC-3283) composition of the registered substance subject to the present decision: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

Notes for your consideration

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4) if it cannot be concluded based on acute aquatic toxicity data that neither fish nor invertebrates are substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), long-term fish toxicity testing may not be needed if such data is also not needed for concluding the PBT-assessment (c.f. ECHA Guidance on information requirements and chemical safety assessment (version 3.0, February 2016), Chapter 16). However, if in the CSA (including the PBT assessment) a risk to pelagic organisms is indicated, the long-term fish study needs to be conducted.

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity tests and for calculation and expression of the result of the tests.

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 3. Exposure considerations. You provided the following justification for the adaptation:

"PTPA is a liquid at room temperature with low water solubility (0.381 µg/L), vapor pressure (3.87 mm Hg at 20°C), and a high Henry's Law constant range (read across from analogous compounds of similar water solubility) of 3400 - 4020 atm·m³/mol. Releases are expected to be atmospheric emissions based upon its intended uses.
Fugitive emissions may occur at transfer points. During routine use, there is no anticipated release to aquatic systems. Based on its physicochemical qualities, PTPA will not partition to water or sediment but will remain in the atmosphere when released from industrial applications. A long-term presence of PTPA would not be maintained in the aquatic compartment and aquatic organisms would not be subject to a chronic exposure. The vapor pressure, low water solubility and the extremely high Henry's law constant combine to move PTPA from any aquatic compartment into the atmosphere. Therefore, this compound will remain in the atmosphere when released from industrial applications.

Exposure modeling was conducted using EUSES v.2.1.2 in order to generate environmental exposure data to evaluate the significance of exposure. Predicted environmental concentrations (PECs) in the freshwater and marine compartments were 4.18E-06 mg/L and 4.10E-07 mg/L, respectively. The predicted no-effect concentrations (PNECs) in freshwater and marine compartments are 1.192E-04 mg/L and 1.19E-05 mg/L. The resulting RCRs for the freshwater and marine water aquatic compartments, [redacted] and [redacted], are clearly < 1, indicating that exposures are always well below the derived PNEC. It should be noted that the PNECs are based on maximum attainable test substance concentration; no toxicity was observed in reliable tests. The PNECs are thus more conservative than is typical. There is no need for further information and testing."

ECHA notes that there are two compositions/grades of the registered substance. The first (FC-3283) is of high purity (91.5%) and contain mainly perfluorinated impurities. The second grade (FZ-7941 (cell crude of FC-3283)), however, contains a significant proportion of hydride isomers ([redacted]%, typically [redacted]%).

For the first composition (FC-3283), ECHA considers this waiving statement acceptable.

For the second composition (FZ-7941 (cell crude of FC-3283)), however, you have not justified why the hydride isomers in the cell crude grade would have a similar chemistry to fluorine-substituted substances. There is no consideration given to the presence of these hydride impurities in your read across argumentation, consequently the adaptation is not justified.

As ECHA rejects the read-across for the aquatic compartment as stated in the points X and Y above, consequently it is not possible to waive this endpoint based on the assumption that exposures are always well below the derived PNEC.

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

As outlined in Section 7, Growth inhibition study aquatic plants, the information provided in your comments on the draft decision and to the MSCA PfA did not provide a sufficient reason for accepting the proposed read-across adaptation and consequently the draft decision was not amended.

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

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) fish early-life stage toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

Regarding the long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6.1, ECHA considers that the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Figure R.7.8-4). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 3.0, February 2016). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as most appropriate and suitable.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the FZ-7941 (cell crude of FC-3283) composition of the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Notes for your consideration

Before conducting any of the tests mentioned above you shall consult the ECHA *Guidance on information requirements and chemical safety assessment (version 3.0, February 2016)*, Chapter R7b, Section R.7.8.5 to determine the sequence in which the aquatic long-term toxicity tests are to be conducted and the necessity to conduct long-term toxicity testing on fish.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), if it cannot be concluded based on acute aquatic toxicity data that neither fish nor invertebrates are substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), long-term fish

toxicity testing may not be needed if such data is also not needed for concluding the PBT-assessment (c.f. ECHA Guidance on information requirements and chemical safety assessment (version 3.0, February 2016), Chapter 16). However, if in the CSA (including the PBT assessment) a risk to pelagic organisms is indicated, the long-term fish study needs to be conducted.

Due to the low solubility of the substance in water you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity tests and for calculation and expression of the result of the tests.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 18 August 2016.

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

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

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

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

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

In addition, you provided comments on the draft decision. These comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-54 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for start of substance evaluation in 2018.

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

3. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

4. In carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.