Helsinki, 21 August 2018

Substance name: Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine (FC-770)
EC number: 473-390-7
CAS number: not available
Date of Latest submission(s) considered[1]: 24 February 2016
Decision/annotation number: Please refer to the REACH-IT message which delivered this communication (in format SEV-D-XXXXXXXXXX-XX-XX/F)
Addressees: Registrant(s)[2] of Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine

DECISION ON SUBSTANCE EVALUATION

Based on Article 46(1) of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), you are requested to submit the following information on the registered substance:

- Bioaccumulation in aquatic species; test method: Bioaccumulation in fish: aqueous and dietary exposure EU C.13/OECD 305 (aqueous or dietary exposure) as specified in Appendix 1.

You have to provide an update of the registration dossier(s) containing the requested information, including robust study summaries and, where relevant, an update of the Chemical Safety Report by **28 November 2019**. The deadline takes into account the time that you, the Registrant(s), may need to agree on who is to perform any required tests.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Further information, observations and technical guidance as appropriate are provided in Appendix 3. Appendix 4 contains a list of registration numbers for the addressees of this decision. This appendix is confidential and not included in the public version of this decision.

[1] This decision is based on the registration dossier(s) at the end of the 12 month evaluation period

[2] The terms Registrant(s), dossier(s) or registration(s) are used throughout the decision, irrespective of the number of registrants addressed by the decision.

1. Who performs the testing

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the study/ies on behalf of all Registrant(s) within 90 days. Instructions on how to do this are provided in Appendix 3.

2. Appeal

You can appeal this decision 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[3] by Leena Ylä-Mononen, Director of Evaluation

[3] 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

Based on the evaluation of all relevant information submitted on Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine and other relevant available information, ECHA explains in the following why further information is required in order to enable the evaluating Member State Competent Authority (MSCA) to complete the evaluation of whether the substance constitutes a risk to the environment.

The evaluating MSCA will subsequently review the information submitted by you and evaluate if further information should be requested in order to clarify the PBT/vPvB concern for the environment.

In order to enhance the readability of this statement of reasons, the evaluated substance will be systematically denominated with its trade name FC-770.

The concern identified

FC-770 is a multi-constituent substance comprising two main constituents that are both perfluorinated substituted morpholine compounds. FC-770 is screened to be a potential PBT/vPvB substance.

You state in the registration dossier(s) that FC-770 is not persistent in the aquatic and terrestrial compartments, because it is rapidly removed by volatilization from these compartments. This argument refers to a transfer process from one environmental compartment to another and not to a (bio)degradation process. Consequently, ECHA considers this argument not relevant for the determination of the P-character of FC-770.

Moreover, application of different environmental distribution models provides quite diverging results. If the Simple Treat model for water sewage treatment plants from EUSES is applied, the following relative mass distribution (assuming a log Koc = 4.72) is provided: air = 33 %; water = 4 %; soil = 63 %.

The predictions provided by the level III fugacity model from EpiSuite also indicate that substantial amounts of FC-770 are distributed to other compartments than air:
- release only to air ➔ air/water/soil/sediment = 90.3 % - 0.2 % - 8.9 % - 0.6 %
- release only to water ➔ air/water/soil/sediment = 6.1 % - 25.8 % - 0.6 % - 67.5%
- equal releases ➔ air/water/soil/sediment = 3.3 % - 4.2 % - 81.6 % - 10.9%

Therefore, it is concluded that model predictions depend on the way the compartments are modelled and also on the time and spatial scales for which an assessment is made and that according to environmental distribution modelling mass distribution of the substance may occur to all environmental compartments.

Overall conclusion: it is expected that FC-770 will occur in the condensed state and that the distribution seems to be highly dependent of the environmental release pattern. Hence, considerations concerning the (v)P-, (v)B- and T- properties, including bioaccumulative properties in fish and other species, are relevant.

More specifically for the air compartment, it is noted that in a photolysis study in air with FC-770 no degradation was observed and also the analogous substance perfluoro-N-methylmorpholine (as indicated in the registration dossier(s)) is resistant to direct photolysis under mercury lamp irradiation as well as to indirect photolysis by hydroxyl radicals and singlet oxygen atoms. These experimental results lead to the conclusion that the minimum atmospheric lifetime for FC-770 is extremely long, probably 1000 years or longer. In publicly available literature (Prather *et al.,* 2001) atmospheric lifetimes of 3200 to 4100 years are reported for perfluorohexane and perfluoropentane. These data confirm that in general perfluorinated compounds are extremely stable in the atmosphere and there is no reason to assume that FC-770 behaves differently.

With regard to the water compartment, one experimental test was performed in aqueous medium with FC-770, i.e. a ready biodegradation test according to OECD TG 310 (headspace test) that showed 0 % degradation after 28 days. Although a biodegradation simulation study in water is lacking, the evaluating MSCA concludes that this experiment allows to state that FC-770 does not biodegrade to a relevant extent. As described by Siegemund *et al.* (2000), the polarizability and the high bond energies of carbon-fluorine bonds cause these compounds to be the most stable and less reactive organic compounds known and there are no indications that FC-770 behaves differently.

The evaluating MSCA considers that the available information is sufficient to assess the persistency for this substance at this step of the evaluation and that it is then appropriate to focus the information request on bioaccumulation at this stage. Thus, further testing on the degradation of the substance, e.g. via a simulation test, is currently not considered necessary to clarify the concern of PBT/vPvB properties.

Bioaccumulation in fish (aqueous or dietary exposure)

The concern(s) identified

As stated above, FC-770 is screened to be a potential PBT/vPvB substance. and it is appropriate to focus this evaluation step on the potential B/vB-character, as indicated in the ECHA REACH Guidance R11, 2017. No experimental data with regard to the bioaccumulation potential of FC-770 are available but the Log Kow value of 5.7 shows that the screening criterion for B (log K_{ow} > 4.5) is met.

Why new information is needed

At the moment no experimental studies on FC-770 with aquatic or terrestrial species regarding the bioaccumulation potential are available.

In the registration dossier(s) it is stated that because of the absence of toxic effects at the highest dose in an oral 28 day rat study and in a screening study for developmental/reproductive toxicity study with FC-770 the substance does not bioaccumulate in mammals. This argument is not considered to show sufficient proof of lack of bioaccumulation potential because the lack of toxic effects may as well be triggered by the low intrinsic toxicity of the substance in this type of study. Further, you also refer to the result of a preliminary pharmacokinetic study with rat. In this non GLP-

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experiment single doses of FC-770 up to 1000 mg/kgbw/d were administered. Monitoring of serum, liver, urine and faeces took place up to 48 hours after administration. In serum, liver and urine no quantifiable levels of test item were found. The test item was quantifiable in faecal samples but only up to 27 % of the administered dose. As the concentration in fat tissue was not measured and because most of the applied test item was not retrieved analytically, this experiment does not allow to come to a definitive conclusion on the bioaccumulation potential of FC-770 in mammals.

Based on measured values for the solubility of FC-770 in water and in octanol, a log K_{ow}-value of 5.7 is calculated in the registration dossier. Therefore, FC-770 screens as a potential B/vB substance. Moreover, no indications of metabolisation were seen in any of the available tests.

The BCF estimation with EpiSuite is considered to be inconclusive for FC-770. Based on a log K_{ow}-value obtained via KOWWIN (i.e. 4.55) and taking into consideration the model suggested biotransformation half-life of 2.001 days, BCFBAF model estimates the BCF-values in the range of 466.5 to 788.4 L/kg. On the contrary, based on a log K_{ow}-value of 5.7 and assuming that no biotransformation takes place, BCFBAF model estimates a BCF-value of 18370 L/kg. In view of these diverging QSAR predictions, the concern for substantial bioaccumulation potential remains and in order to be able to come to a robust conclusion, further testing is considered necessary.

Considerations on the test method and testing strategy

A Bioaccumulation test in Fish (Aqueous or Dietary Exposure according to OECD TG 305) on the whole substance is considered appropriate. A bioaccumulation study on the whole substance (and not on one of the two main constituents) is requested because:

1. FC -770 is synthesised in large-scale specialised equipment and synthesis of the individual constituents in smaller non-specialised equipment is deemed to be impractical.
2. Taking into account their respective chemical structures, it is expected that the two main constituents (isopropyl and n-propyl) will show a similar behaviour with regard to their bioaccumulation potential. In case one of the two constituents would be found to be more bioaccumulative than the other, this approach will allow to determine which constituent constitutes the worst case.
3. From an analytical point of view, difficulties are not expected as chromatographic techniques are able to differentiate the two constituents.

It is noted that a dietary bioaccumulation study yields a dietary biomagnification factor (BMF) and not directly a bioconcentration factor (BCF). Unlike BCF-values, BMF-values are not directly comparable to REACH Annex XIII B/vB criteria. Calculation methods are available to estimate a kinetic BCF-value from data generated in the dietary study, but these estimations are accompanied with uncertainty and therefore a study with aqueous exposure is preferred in this case, if technically feasible. In your comments on the draft decision, you do not support conducting a dietary exposure study. In addition to the uncertainty due to the estimation methods to convert the BMF value to a kinetic BCF value, you indicate that FC-770 is a volatile, fluorinated inert, which makes estimation

methods even more uncertain. In your view it would not be possible to accurately and consistently dose the fish food due to the extremely high Henry's Law Constant of FC-770 and the residual water content of the feed. ECHA considers the substance to be slightly volatile (Vapour pressure = 6750 Pa at 20°C) and therefore mixing the liquid with food seems feasible. ECHA agrees that aqueous exposure is the first choice in this case and that a study with dietary exposure should only be conducted if it proves to be technically impossible to maintain a stable and quantifiable test item concentration in the aqueous solution.

It is recognized that testing via aqueous exposure may provide misleading results if the applied test item concentration is close to or higher than the water solubility, while low test item concentrations may pose analytical difficulties if the available substance specific analytical technique is not sensitive enough to determine test item concentrations in a reliable way (i.e. Limit of Quantification is close to the applied test item concentration). Further, it is noted that FC-770 shows a high density (1.80 g/cm³) and a poor water solubility (66.2 µg/L). As a result it is possible that in this experiment layer formation occurs and that the aqueous phase is not fully homogeneous. Therefore, you must monitor and report the truly dissolved test item concentrations during the whole uptake phase of the study.

In your comments on the draft decision, you state that you have discussed the possibility of performing an aqueous-exposure, non-labelled BCF study with a testing laboratory and provide their explanation of how the study could be performed. The laboratory has confirmed that they should be able to perform the requested study.

You also state that FC-770 is not expected to form a layer in the water column during exposure as you have never seen this behaviour in your laboratories. You suggest demonstrating the homogeneity and stability of the exposure concentrations as a preliminary study before the BCF study by analysing samples at different time periods from different locations and depths. However, ECHA requires that the homogenity and stability of the exposure concentrations will also be quantitatively monitored in the definitive study and not only in the preliminary study. This is to ensure that the aqueous phase is fully homogeneous and that the fish are exposed to stable concentrations of the test substance, as required by OECD TG 305 (see paragraphs 7 and 10 of OECD TG 305). Any test substance which is not truly dissolved is considered to be less bioavailable to the fish.

The use of test item radiolabelled with a ^{14}C atom was proposed in the initial draft decision in order to facilitate the monitoring of the test item. In your comments you pointed out that for various reasons the synthesis of ^{14}C labelled FC-770 is impractical and expensive. Furthermore, you indicated in your comments that you have found a suitable laboratory with the analytical capability to reach a detection limit in water well below 20 µg/L without the use of radiolabelled test material. Taking into account this information, the bioaccumulation study may be carried out with non-radiolabelled test material on the condition that a systematic and reliable monitoring of the truly dissolved test item is performed and reported during the whole uptake phase of the study, as

discussed above. A flow-through apparatus shall be used that allows to stabilize the dissolved test item concentration.

Considering that the measured water solubility amounts to 66.2 µg/L and in order to avoid that a fraction of the test item is not bioavailable, the applied test item concentration in the water phase shall not be close to the water solubility limit. A test item concentration of around 20 µg/L is recommended for one of the test concentrations. As indicated in paragraph 17 of the OECD Guideline 305, the uptake phase usually takes 28 days and this period shall not be shortened. In your comments on the draft decision, you indicated that you would perform a study with an uptake phase of at least 28 days and the depuration phase will be shortened as a way to require fewer fish and a kinetic BCF will be calculated. ECHA notes that it is not possible to predict whether a shortened depuration phase will allow to calculate a reliable kinetic BCF value. Moreover, paragraph 39 of OECD TG 305 states that: "For substances following first order kinetics, a period of half the duration of the uptake phase is usually sufficient for an appropriate (e.g. 95%) reduction in the body burden of the substance to occur (cf. Annex 5 for explanation of the estimation). If the time required to reach 95% loss is impractically long, exceeding for example twice the normal duration of the uptake phase (i.e. more than 56 days) a shorter period may be used (e.g. until the concentration of test substance is less than 10% of steady-state concentration). However, longer depuration periods may be necessary for substances having more complex patterns of uptake and depuration than are represented by a one-compartment fish model that yields first order kinetics".

Furthermore, as proposed by a MSCA in its proposal for amendment, according to OECD TG 305 two concentrations (below water solubility) should be employed if the BCF could be dependent of the test concentration. Indeed, as the substance might bind to protein it is possible that the accumulation in fish might be concentration dependent. Hence, you are required to test two concentrations unless you justify, in accordance with OECD TG 305, that one concentration is sufficient to fully address the bioconcentration potential of the substance.

As described in the OECD Guideline 305, the results shall be corrected for fish growth and normalized to 5 % lipid content and excessive fish growth should be avoided in order to enhance the reliability of the obtained results. This normalisation might however not be appropriate if FC-770 binds to proteins rather than it solubilises in the lipids of the fish (which is known for some perfluorinated substances).

Due to this particular concern for perfluorinated compounds, further examination of the bioaccumulation potential might be necessary depending on the results obtained from this requested bioaccumulation study.

ECHA points out that the goal of the study is to establish an overall BCF-value for FC-770. If bioaccumulation is proven to be substantial and if technically possible to collect information with regard to the distribution of FC-770 in various fish tissues, it is recommended that such information should be reported as it contributes to the understanding of the bioaccumulation process of FC-770 in the fish organisms.

Paragraph 21 of OECD TG 305 states that: "… for special purposes, specified tissues or organs (e.g. muscle, liver), may be used if the fish are sufficiently large or the fish may be divided into edible (fillet) and non-edible (viscera) fractions''.

If it is technically not possible to perform the test as described above applying aqueous exposure, the bioaccumulation test shall be carried out applying dietary exposure.

What is the possible regulatory outcome

If it is concluded that the registered substance meets the vPvB criteria according to REACH Annex XIII, the substance may become a candidate for identification as substance of very high concern or other regulatory measures that will be determined afterwards.

Consideration of alternative approaches

This test will allow to conclude on the bioaccumulation potential of FC-770. The request for bioaccumulation testing is suitable and necessary to obtain information that will allow to clarify the PBT/vPvB concern. ECHA notes that no equally suitable alternative way is available to obtain this information.

Conclusion

Therefore, based on the substance evaluation and pursuant to Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study using the registered substance subject to this decision: Bioaccumulation in Fish: Aqueous or Dietary Exposure test according to EU C.13 (OECD TG 305).

Deadline to submit the requested Information

In the draft decision communicated to you, the time indicated to provide the requested information was 12 months from the date of adoption of the decision. With your comments on the draft decision, you provided an estimate from the testing laboratory which indicated that 8-12 months are required to complete the OECD TG 305 test. In view of the specific character of the test item, ECHA has set the deadline to 15 months to allow for conduct of the study and updating of the registration dossier and chemical safety assessment.

References

Prather, M., D. Ehhalt, Dentener F, Derwent R, Dlugokencky E, Holland E, Isaksen I, Katima J, Kirchhoff V, Matson P, Midgley P, Wang M (2001), Chapter 4 Atmospheric Chemistry and Greenhouse gases in Climate Change; The Scientific Basis, J.T. Houghton et al., eds., Cambridge U. Press, pp. 239-287.

Siegemund G, Schwertfeger W, Feiring A, Smart B, Behr F, Vogel H, McKusick B (2000), Fluorine compounds, organic., Ullmann's Encyclopedia of Industrial Chemistry.

Appendix 2: Procedural history

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to suspected PBT/vPvB, wide dispersive use and exposure to environment, Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine, CAS No n.a. (EC No 473-390-7) was included in the Community rolling action plan (CoRAP) for substance evaluation to be evaluated in 2016. The updated CoRAP was published on the ECHA website on 22 March 2016. The Competent Authority of Belgium (hereafter called the evaluating MSCA) was appointed to carry out the evaluation.

Pursuant to Article 45(4) of the REACH Regulation the evaluating MSCA carried out the evaluation of the above substance based on the information in your registration(s) and other relevant and available information.

The evaluating MSCA considered that further information was required to clarify the following concern: suspected PBT/vPvB. Therefore, it prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. It submitted the draft decision to ECHA on 17 March 2017.

The decision making followed the procedure of Articles 50 and 52 of the REACH Regulation as described below.

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

ECHA received comments from you and forwarded them to the evaluating MSCA without delay.

The evaluating MSCA took the comments from you, which were sent within the commenting period, into account and they are reflected in the Reasons (Appendix 1). The request(s) or the deadline were amended.

Proposals for amendment by other MSCAs and referral to Member State Committee

The evaluating MSCA notified the draft decision to the Competent Authorities of the other Member States and ECHA for proposal(s) for amendment.

Subsequently, the evaluating MSCA received proposals for amendment to the draft decision. They are reflected in the Reasons (Appendix 1).

ECHA referred the draft decision, together with your comments, to the Member State Committee.

ECHA invited you to comment on the proposed amendments. You did not provide any comments on the proposed amendments.

MSC agreement seeking stage

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-60 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided by you in the registration(s) is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on your dossier(s) at a later stage, nor does it prevent a subsequent decision under the current substance evaluation or a new substance evaluation process once the present substance evaluation has been completed.

2. 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.

3. In relation to the required experimental study/ies, the sample of the substance to be used shall have a composition that is within the specifications of the substance composition that are given by all Registrant(s). It is the responsibility of all the Registrant(s) to agree on the tested material to be subjected to the test(s) subject to this decision and to document the necessary information on composition of the test material. The substance identity information of the registered substance and of the sample tested must enable the evaluating MSCA and ECHA to confirm the relevance of the testing for the substance subject to substance evaluation.

4. In relation to the experimental stud(y/ies) the legal text foresees the sharing of information and costs between Registrant(s) (Article 53 of the REACH Regulation). You are therefore required to make every effort to reach an agreement regarding each experimental study for every endpoint as to who is to carry out the study on behalf of the other Registrant(s) and to inform ECHA accordingly within 90 days from the date of this decision under Article 53(1) of the REACH Regulation. This information should be submitted to ECHA using the following form stating the decision number above at:
https://comments.echa.europa.eu/comments_cms/SEDraftDecisionComments.aspx

   Further advice can be found at
http://echa.europa.eu/regulations/reach/registration/data-sharing. If ECHA is not informed of such agreement within 90 days, it will designate one of the Registrants to perform the stud(y/ies) on behalf of all of them.