SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Amphoteric Fluorinated Surfactant

EC No. Confidential
CAS RN Confidential

Evaluating Member State: **Belgium**

Dated: 27 July 2023

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2018

Member State concluded the evaluation without any further need to ask more information from the registrants under Article 46(1) decision.

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B, the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

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Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Amphoteric Fluorinated Surfactant (further in the document referred to as "AFS") was originally selected for substance evaluation to clarify concerns about:

- Suspected PBT/vPvB.
- Wide dispersive use.
- Exposure of environment.

During the evaluation, the following additional concern was identified:

- Potential endocrine disruptor.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

An additional concern as potential endocrine disruptor (ED) was identified during Substance Evaluation for one of the degradation products of AFS, more specifically for 6:2 fluorotelomer sulfonate (6:2 FTS). To address the ED concern for this degradation product, a Draft Decision was drawn up and submitted to the Member State Committee (MSC) on 12 May 2020. In December 2019, the German Competent Authority (CA) has submitted an Annex XV dossier proposing restrictions on "Undecafluorohexanoic acid (PFHxA), its salts and related substances" (EC No: -; CAS No: -)[2]. In this restriction (proposal), AFS was identified as a related substance to PFHxA and included in the scope of the restriction.

Consequently, the Draft Decision on the ED properties of 6:2 FTS was withdrawn after the MSC-70 meeting on 8 July 2020. While the eMSCA has a concern regarding the ED properties of 6:2 FTS, the eMSCA does not consider it proportionate to follow up on these with further information requirements or potential SVHC identification according to Art. 57 as it is expected that the two substances (AFS and 6:2 FTS) fall under the scope of the restriction of PFHxA and precursors, thereby ultimately limiting their further impact on the environment.

Furthermore, in April 2023, in the conclusion document for EC No. 241-527-8[3] and EC No. 218-407-9[4], the German CA concluded that the available data clarify that PFHxA acts as an endocrine disruptor (ED) for the environment in accordance with the ED definition of the World Health Organisation (WHO). However, there is no official identification of PFHxA as ED by RAC (Committee for Risk Assessment) or MSC.

As a result of its evaluation, the eMSCA has concluded that after release into the environment, AFS will degrade to a whole series of poly- and perfluorinated compounds, of which perfluoroheptanoic acid (PFHpA) and perfluorohexanoic acid (PFHxA) appear to be the most recalcitrant. For that reason, the eMSCA has concluded that release of AFS

[2] Registry of restriction intentions until outcome. Undecafluorohexanoic acid (PFHxA), its salts and related substances (EC No: -; CAS No: -). https://echa.europa.eu/en/registry-of-restriction-intentions/-/dislist/details/0b0236e18323a25d (latest update on 18 May 2022)

[3] Substance Evaluation Conclusion Document on EC No 241-527-8. 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl acrylate. April 2023. Evaluating Member State: Germany. https://echa.europa.eu/documents/10162/5c201ae4-8b10-ca18-df24-7ae5a7f83e37

[4] Substance Evaluation Conclusion Document on EC No 218-407-9. 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl methacrylate. April 2023. Evaluating Member State: Germany. https://echa.europa.eu/documents/10162/15a5aaeb-0159-d730-c4f7-66c8dd85a8b4

will cause continuously increasing levels of PFHpA and PFHxA in various environmental compartments.

"Perfluoroheptanoic acid and its salts" (EC No: -; CAS No: -) have been identified as a substance of very high concern (SVHC), meeting the criteria set out in Article 57 c, d, e, and f[5]. On 17 January 2023, "Perfluoroheptanoic acid and its salts" was included as an SVHC in the Candidate List for eventual inclusion in Annex XIV (ECHA Decision, 2022).

Considering the implication of the identification of "Perfluoroheptanoic acid and its salts" as an SVHC, for substances which transform and/or degrade to PFHpA, this is reported in Chapter R.11 (ECHA, 2017: ECHA Guidance on PBT/vPvB assessment, p. 25):

'If a registered substance contains a constituent, impurity or additive or transforms/degrades to a substance which is in the Candidate List because of meeting the PBT and/or vPvB criteria, the registrant must conclude his substance to meet the PBT or vPvB criteria accordingly.'

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the eMSCA to the following conclusions, as summarised in the table below.

Table 1: Conclusion of substance evaluation

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	X
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	
Restrictions	X (Within the scope of restriction of PFHxA)
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

[5] Registry of SVHC intentions until outcome. Perfluoroheptanoic acid and its salts (EC No: -; CAS No: -). https://echa.europa.eu/en/registry-of-SVHC-intentions/-/dislist/details/0b0236e187714636

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

Not applicable.

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

4.1.3. Restriction

An Annex XV dossier proposing restrictions on "Undecafluorohexanoic acid (PFHxA), its salts and related substances" (EC No: -; CAS No: -) is currently being processed.[6] The RAC and SEAC final opinion is available, however the Adopted Restriction / Commission Communication is not available yet at the time this conclusion document was published.

In the compiled RAC and SEAC final opinion (RAC and SEAC, 2021), it is clearly defined which substances qualify as a related substance to PFHxA, and which substances are therefore included in the restriction for "Undecafluorohexanoic acid (PFHxA), its salts and related substances". The restriction will include the following substances, according to the RAC and SEAC final opinion (RAC and SEAC, 2021):

"1. Undecafluorohexanoic acid (PFHxA), its salts and related substances
(a) having a linear or branched perfluoropentyl group with the formula C_5F_{11}- directly attached to another carbon atom as one of the structural elements.
(b) having a linear or branched perfluorohexyl group with the formula C_6F_{13}-.

2. The following substances shall be derogated:
(a) C_6F_{14}.
(b) C_6F_{13}-C(=O)OH, C_6F_{13}-C(=O)O-X' or C_6F_{13}-CF_2-X' (where X' = any group, including salts).
(c) Any substance having a perfluoroalkyl group C_6F_{13}- directly attached to a sulphur atom.
(d) Any substance having a perfluoroalkyl group C_6F_{13} -directly attached to an oxygen atom at one of the non-terminal carbons."

The structural formula of AFS is confidential. AFS is defined as a related substance to PFHxA and is therefore included in the scope of the restriction for "Undecafluorohexanoic acid (PFHxA), its salts and related substances."

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

[6] Registry of restriction intentions until outcome. Undecafluorohexanoic acid (PFHxA), its salts and related substances (EC No: -; CAS No: -). https://echa.europa.eu/en/registry-of-restriction-intentions/-/dislist/details/0b0236e18323a25d (latest update on 18 May 2022)

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Not applicable.

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

AFS is defined as a related substance to PFHxA and is therefore included in the scope of the restriction for "Undecafluorohexanoic acid (PFHxA), its salts and related substances." As explained in section 4.1.3., the Annex XV dossier proposing restrictions for "Undecafluorohexanoic acid (PFHxA), its salts and related substances" is currently being processed.[7]

[7] Registry of restriction intentions until outcome. Undecafluorohexanoic acid (PFHxA), its salts and related substances (EC No: -; CAS No: -). https://echa.europa.eu/en/registry-of-restriction-intentions/-/dislist/details/0b0236e18323a25d (latest update on 18 May 2022)

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

AFS was originally selected for substance evaluation to clarify concerns about:

- Suspected PBT/vPvB.
- Wide dispersive use.
- Exposure of environment.

During the evaluation, the following additional concern was identified:

- Potential endocrine disruptor.

Table 2: Evaluated endpoints

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Suspected PBT/vPvB	**Concern confirmed.** AFS itself is not PBT/vPvB. However, according to the PBT guidance (ECHA, 2017: ECHA Guidance on PBT/vPvB assessment, p. 25). '*If a registered substance contains a constituent, impurity or additive or transforms/degrades to a substance which is in the Candidate List because of meeting the PBT and/or vPvB criteria, the registrant must conclude his substance to meet the PBT or vPvB criteria accordingly*.' In the environment, AFS degrades to a whole series of poly- and perfluorinated compounds, of which perfluoroheptanoic acid (PFHpA) and perfluorohexanoic acid (PFHxA) appear to be the most recalcitrant. The eMSCA considers PFHpA the substance of relevance for the PBT assessment. PFHpA is identified as SVHC for its PBT/vPvB properties and is listed in the Candidate List (ECHA Decision, 2022). Therefore, AFS could be a PBT substance if proven that it degrades to PFHpA in relevant amounts. The eMSCA does not propose further action on this, as the substance is part of the restriction proposal on PFHxA and related substances.
Wide dispersive use	**Concern confirmed.** Because the use of the Substance is wide dispersive, exposure of the environment is expected to be substantial and difficult to mitigate.
Exposure of environment	**Concern confirmed.** Because the Substance is also used by consumers, exposure of the environment occurs via many point sources and is difficult to mitigate.
Potential endocrine disruptor	**Concern unresolved.** The concern is unresolved as the eMSCA has not requested information during its SEv to resolve the ED concern.

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
	In the conclusion document for EC No 241-527-8[8] and EC No 218-407-9[9], the German CA concluded that the available data clarifies that PFHxA acts as an ED for the environment in accordance with the Endocrine Disruptor (ED) definition of the World Health Organisation (WHO). However, there is no official identification of PFHxA as ED by RAC or MSC. While the eMSCA has a concern regarding the ED properties of 6:2 FTS, a degradation product of AFS, the eMSCA does not consider it proportionate to follow up on these with further information requirements or potential SVHC identification according to Art. 57 as it is expected that the two substances (AFS and 6:2 FTS) fall under the scope of the restriction proposal on PFHxA and related substances, thereby ultimately limiting their further impact on the environment.

7.2. Procedure

March 2018: The eMSCA started the Substance Evaluation process of AFS. During this Substance Evaluation, an additional concern as 'potential endocrine disruptor' was identified for a degradation product of AFS, more specifically 6:2 fluorotelomer sulfonate (6:2 FTS). A Draft Decision was prepared to clarify this concern.

March 2019: The Draft Decision (for AFS, regarding 6:2 FTS) was submitted to ECHA.

October 2019: Submission of the CLH report (proposal for harmonised classification and labelling) for "Perfluoroheptanoic acid" (EC No: 206-798-9; CAS No: 375-85-9) by BE CA.

November 2019: Start of CLH report consultation for "Perfluoroheptanoic acid".

December 2019: Submission of the Annex XV restriction report (proposal for a restriction) for "Undecafluorohexanoic acid (PFHxA), its salts and related substances" (EC No: -; CAS No: -) by DE CA.

March 2020: Start of Annex XV restriction report consultation for "Undecafluorohexanoic acid (PFHxA), its salts and related substances".

May 2020: The Draft Decision (for AFS, regarding 6:2 FTS) was referred to the Member State Committee (MSC).

July 2020: Withdrawal of the Draft Decision for AFS written by the eMSCA, after the MSC-70 meeting, due to the launched restriction (proposal) for "Undecafluorohexanoic acid (PFHxA), its salts and related substances", for which AFS is identified as a related substance.

December 2020: RAC Opinion in which the harmonised classification of PFHpA (Perfluoroheptanoic acid; EC No: 206-798-9; CAS No: 375-85-9) was adopted.

[8] Substance Evaluation Conclusion Document on EC No 241-527-8. 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl acrylate. April 2023. Evaluating Member State: Germany. https://echa.europa.eu/documents/10162/5c201ae4-8b10-ca18-df24-7ae5a7f83e37

[9] Substance Evaluation Conclusion Document on EC No 218-407-9. 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl methacrylate. April 2023. Evaluating Member State: Germany. https://echa.europa.eu/documents/10162/15a5aaeb-0159-d730-c4f7-66c8dd85a8b4

December 2021: Final RAC and SEAC opinion on the Annex XV dossier proposing restrictions on "Undecafluorohexanoic acid (PFHxA), its salts and related substances".

February 2022 (Official Journal of the European Union): Perfluoroheptanoic acid is included in Annex VI to Regulation (EC) No 1272/2008 (harmonised classification and labelling) with index number 607-761-00-3, it shall apply from 23 November 2023.

August 2022: Submission of the Annex XV report for identification of "Perfluoroheptanoic acid and its salts" (EC No: -; CAS No: -) as an SVHC by NL CA.

September 2022: Start of Annex XV SVHC report consultation for "Perfluoroheptanoic acid and its salts".

November 2022: Agreement in MSC regarding the identification of "Perfluoroheptanoic acid and its salts" as an SVHC, meeting the criteria of Article 57 (c), hazard class toxic for reproduction category 1B; (d), persistent, bioaccumulative and toxic (PBT); (e), very persistent and very bioaccumulative (vPvB); and (f), equivalent level of concern having probable serious effects to human health and to the environment.

January 2023: Inclusion of "Perfluoroheptanoic acid and its salts" as an SVHC in the Candidate List for eventual inclusion in Annex XIV.

7.3. Identity of the substance

Table 3: Substance identity

SUBSTANCE IDENTITY	
Public name:	Amphoteric Fluorinated Surfactant (AFS)
EC number:	Confidential
CAS number:	Confidential
Index number in Annex VI of the CLP Regulation:	Not listed in Annex VI of the CLP Regulation
Molecular formula:	Confidential
Molecular weight range:	Confidential
Synonyms:	Not applicable

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:

Confidential

7.4. Physico-chemical properties

Table 4: Summary of physico-chemical properties

OVERVIEW OF PHYSICO-CHEMICAL PROPERTIES[10]	
Property	**Value**
Physical state at 20 °C and 101.3 kPa	Yellow/red coloured, odourless solid According to EPA OPPTS 830.6303; EPA OPPTS 830.6302; EPA OPPTS 830.6304
Vapour pressure	$<10^{-6}$ Pa at 20 °C According to OECD TG 104; EU Method A.4 EPI Suite estimation (MPBPVP v1.43): 3.99 x 10^{-17} Pa at 25 °C and 3 x 10^{-19} mm Hg at 25 °C (Modified Grain Method)
Water solubility	107 mg/L No guideline mentioned. Estimation based on critical micelle concentration (CMC) EPI Suite estimation (WSKOW v1.42): 233 mg/L at 25 °C
Partition coefficient n-octanol/water (log K_{ow})	Log K_{ow} (P_{ow}): 1.35 at 25 °C According to OECD TG 123 (Slow-Stirring method) EPI Suite estimation (KOWWIN v1.68): Log K_{ow}: -2.12
Flammability	Non-flammable According to EU Method A.10
Explosive properties	Test waived. Substance considered non-explosive based on structural assessment.
Oxidising properties	Test waived. Substance considered non-oxidising due to its incapability of reacting exothermically with combustible materials.
Granulometry	Test waived. Study does not need to be conducted since the substance is marketed or used in a non-solid or non-granular form.
Melting point	No melting point observed. According to OECD TG 102. EU Method A.1; EPA OPPTS 830.7200 EPI Suite estimation (Joback; Gold, Ogle Methods): Mean: 312.16 °C
Boiling point	Test waived. Study does not need to be conducted since the substance is a solid which decomposes before boiling. EPI Suite estimation (Adapted Stein and Brown Method):

[10] REACH Registration dossier (https://echa.europa.eu/en/registration-dossier/-/registered-dossier/20210)

OVERVIEW OF PHYSICO-CHEMICAL PROPERTIES[10]	
Property	**Value**
	664.74 °C
Relative density	1.716 at 20 °C According to OECD TG 109. EU Method A.3. EPA OPPTS 830.7300
Surface tension	15.7 mN/m at 20 °C (1 g/L solution) According to OECD TG 115. EU Method A.5. DIN EN 14370
Auto-flammability	No self-ignition reaction up to a temperature of 400 °C According to EU Method A.16
Flash point	No flash point obtained for the test substance up to a reflux temperature of 97.9 °C. According to ASTM D93-02
Dissociation constant	No dissociation constant obtained from the titration curves. According to OECD TG 112. EPA OPPTS 830.7370

7.5. Manufacture and uses

7.5.1. Quantities

Table 5: Quantities

AGGREGATED TONNAGE (PER YEAR)[11]				
☐ 1 – 10 t	☒ 10 – 100 t	☒ 100 – 1000 t	☒ 1000- 10,000 t	☒ 10,000-50,000 t
☒ 50,000 – 100,000 t	☒ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☒ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Table 6: Overview of uses

USES	Use(s)
Uses as intermediate	Confidential
Formulation	Confidential
Uses at industrial sites	Confidential
Uses by professional workers	Confidential
Consumer Uses	Confidential

[11] REACH Registration dossier (https://echa.europa.eu/en/registration-dossier/-/registered-dossier/20210)

Article service life	Confidential

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

There is no harmonised classification for Amphoteric Fluorinated Surfactant.

7.6.2. Self-classification

There are no hazard classes mentioned in the C&L Inventory.

7.7. Environmental fate properties

7.7.1. Degradation

When assessing the degradation pattern of a substance, one should in principle attempt to elucidate the entire degradation pattern of that substance as far and as detailed as possible. However, because complete degradation (mineralisation) of an organic compound is always a complex multi-step process, a complete determination is most of the time not feasible and not appropriate in the framework of the persistence assessment of that substance. Indeed, in this framework one should focus on the parent compound(s) and on those degradation products that potentially meet the (v)P criteria as defined in annex XIII of the Reach Regulation. Therefore, the eMSCA focused in this substance evaluation on the stability of the parent compound AFS and on the identification of the degradation products that are likely to be formed in real environmental conditions and that are expected to meet the (v)P criteria.

Based on the data presented in the registration dossier(s) and on information retrieved from open scientific literature, the eMSCA concludes that the parent compound AFS is not persistent but that several degradation products, which are successively formed during (bio)degradation, meet at least the P criterion.

In the series of degradation products that are successively formed, the following poly-and perfluorinated compounds are considered most relevant, as they are detected in field and laboratory studies, and they are sufficiently stable to potentially cause health effects on humans and/or higher organisms:

- 6:2 fluorotelomer sulfonamide (6:2 $FTSO_2NH_2$).
- 6:2 fluorotelomer sulfonate (6:2 FTS) / 6:2 fluorotelomer sulfonic acid (6:2 FTSA).
- 6:2 fluorotelomer alcohol (6:2 FTOH).
- 6:2 fluorotelomer carboxylic acid (6:2 FTCA).
- Perfluoroheptanoic acid (PFHpA).
- Perfluorohexanoic acid (PFHxA).

7.7.1.1. Abiotic degradation

7.7.1.1.1. Hydrolysis

Table 7: Hydrolysis (with parent compound AFS)

SUMMARY OF STUDIES ON ABIOTIC DEGRADATION - HYDROLYSIS		
Method	**Results**	**References / Remarks**
According to OECD TG 111: Hydrolysis as a Function of pH	Recovery (in %): pH 4: ≥ 95 - ≤ 120 at 50 °C after 5 d pH 7: ≥ 101 - ≤ 113 at 50 °C after 5 d pH 9: ≥ 97 - ≤ 119 at 50 °C after 5 d	REACH Registration dossier: Unpublished study report, 2012a Reliability 1 (Key study) Test material: AFS GLP Transformation products: not specified.
According to OECD TG 111: Hydrolysis as a Function of pH	Recovery (in %): pH 4: ≥ 93.5 - ≤ 101 at 25 °C after 5 d pH 4: ≥ 95.3 - ≤ 109 at 40 °C after 5 d pH 4: ≥ 90.3 - ≤ 106 at 55 °C after 5 d pH 7: ≥ 87.6 - ≤ 107 at 25 °C after 5 d pH 7: ≥ 88.3 - ≤ 106 at 40 °C after 5 d pH 7: ≥ 91.3 - ≤ 106 at 55 °C after 5 d pH 9: ≥ 87.9 - ≤ 107 at 25 °C after 5 d pH 9: ≥ 83.7 - ≤ 100 at 40 °C after 5 d pH 9: ≥ 77.3 - ≤ 99.3 at 55 °C after 5 d	REACH Registration dossier: Unpublished study report, 2014a Reliability 1 (Supporting study) Test material: AFS GLP Transformation products: not specified.

More than 95% of AFS could be recovered after 5 days in a hydrolysis test (OECD TG 111; Unpublished study report, 2012a) at 50 °C and at different pH values. In another hydrolysis test (OECD TG 111; Unpublished study report, 2014a), more than 77.3% of the Substance could be recovered after 5 days at different temperatures and at different pH values. Therefore, it can be concluded that hydrolysis takes place at least very slowly, and that this transformation process does not lead to a classification as not P for AFS.

7.7.1.1.2. Phototransformation/photolysis

No information available.

7.7.1.2. Biodegradation

7.7.1.2.1. Biodegradation in water and sediment

Table 8: Screening studies (with parent compound AFS)

SUMMARY OF SCREENING STUDIES ON BIODEGRADATION IN WATER		
Method	**Results**	**References / Remarks**
Test type: ready biodegradability According to OECD TG 301 B: CO_2 Evolution Test Test system: activated sludge, industrial (adaptation not specified) Oxygen: aerobic	Degradation: 47% degradation after 28 d (CO_2 evolution) Potentially (v)P	REACH Registration dossier: Unpublished study report, 2012b Reliability 1 (Key study) Test material: AFS GLP Toxicity control: Yes Reference substance (Benzoic acid, Sodium salt): > 60% degradation by day 14
Test type: inherent biodegradability According to OECD TG 302 B: Zahn-Wellens/EMPA Test. EPA OPPTS 835.3200: Zahn-Wellens/EMPA Test Test system: activated sludge (adaptation not specified) Oxygen: aerobic	Degradation: 3.5% degradation after 56 d (DOC removal) Percent degradation of parent chemical: 3.5-15.8 mol%; Time period: 55-56 days	REACH Registration dossier: Unpublished study report, 2015a Reliability 1 (Key study) Test material: AFS GLP Toxicity control: Yes Reference substance (Diethylene glycol): 98.8% degradation on average
Test type: ready biodegradability According to OECD TG 301 D: Closed Bottle Test; EU Method C.4-E: Closed Bottle Test; EPA OPPTS 835.3110; SEPA HJ/T 153-2004 Test system: sewage, predominantly domestic (adaptation not specified) Oxygen: aerobic	Degradation: 26% degradation after 28 d (O_2 consumption) Potentially (v)P	REACH Registration dossier: Unpublished study report, 2012c Reliability 2 (Supporting study) Test material: AFS GLP Toxicity control: Not mentioned. Reference substance (Sodium benzoate): 73.1% degradation by day 14
Test type: ready biodegradability According to OECD TG 306: Biodegradability in Seawater	Degradation: 68% degradation after 28 d (COD)	REACH Registration dossier: Unpublished study report, 2017 Reliability 1 (Supporting study)

SUMMARY OF SCREENING STUDIES ON BIODEGRADATION IN WATER		
Method	**Results**	**References / Remarks**
Test system: natural marine water Oxygen: aerobic		Test material: AFS GLP Toxicity control: Not mentioned. Reference substance (Acetic acid, Sodium salt): 81% degradation as maximal value

The registration dossier mentions four screening tests for biodegradation in water performed with AFS.

The first study is a ready biodegradability test (OECD TG 301 B), in which 47 % degradation was observed after 28 days, based on CO_2 evolution (Unpublished study report, 2012b). The pass level of 60% is not reached. Validity criteria for the reference control were met. AFS can therefore considered to be not readily biodegradable. Nevertheless, the observed percentage of biodegradation in this study is substantial.

The second study is an inherent biodegradability test (OECD TG 302 B), in which 3.5% degradation was observed after 56 days, based on DOC removal (Unpublished study report, 2015a). Validity criteria for the reference control were met. However, the study had an abnormally long duration of 56 days.

The third study is a ready biodegradability test (OECD TG 301 D). For this study, 26% degradation was noted after 28 days, based on O_2 consumption (Unpublished study report, 2012c). The pass level of 60% is not reached. Validity criteria for the reference control were met. AFS can therefore considered to be not readily biodegradable. Nevertheless, the observed percentage of biodegradation in this study is substantial.

A ready biodegradability test in seawater was presented in the registration dossier as final study (OECD TG 306; Unpublished study report, 2017). This study showed 68% degradation after 28 days, based on chemical oxygen demand, thus exceeding the pass level of 60%. Validity criteria for the reference control were met. The fact that the pass level is met for this study, and the high percentage of biodegradation observed, are both indications for AFS to be ready biodegradable.

When taking a closer look at the molecular structure of AFS, the experimentally found degradation pattern can easily be explained. The substantial degradation that is observed in the ready tests takes place on the non-fluorinated carbon atoms, and this breakdown process occurs readily. On the contrary, the carbon-fluorine bonds are much more difficult to break, and biodegradation of this highly fluorinated part of AFS proceeds at least very slowly. Although the parent compound breaks down quite readily, there are several (highly fluorinated) degradation products which show a very persistent character.

7.7.1.2.2. Biodegradation in soil

No information available.

7.7.1.3. Formation of degradation products

<u>6:2 FTAB ➔ 6:2 $FTSO_2NH_2$</u>

In a study by Moe *et al*. (2012), the environmental fate of a 6:2 fluorotelomer sulfonamide alkylbetaine (6:2 FTAB) is studied in detail. This 6:2 FTAB is a compound with a similar

structure as Amphoteric Fluorinated Surfactant, as it contains the same fluorinated moiety and a similar non-fluorinated tail (the betaine part). The authors studied the degradation of 6:2 FTAB under UV-light to examine the effect of photolysis under arctic mimicking conditions. In this way, the authors demonstrated that under these favourable conditions, relevant amounts of 6:2 $FTSO_2NH^-$ are formed in less than 1 week time. In the same study, also the *in vivo* transformation of 6:2 FTAB in blue mussel (*M. edulis*) and European turbot (*S. maximus*) was examined. 6:2 FTAB underwent deacetylation and demethylation in mussel and turbot, with formation of several metabolites, including 6:2 fluorotelomer sulfonamide. Further, the presence of 6:2 fluorotelomer sulfonamide was qualitatively demonstrated by analysis of soil samples taken near a firefighting facility, indicating that under real field conditions 6:2 FTAB is degraded to 6:2 $FTSO_2NH_2$. These results are in line with the ready biodegradability studies performed with AFS and they demonstrate that, after release into the environment, degradation of AFS will occur to a relevant extent, and that formation of 6:2 $FTSO_2NH^-$ is to be expected.

<u>6:2 $FTSO_2NH_2$ ➔ 6:2 FTS + 6:2 FTCA</u>

In open scientific literature, many papers can be found that describe the abiotic and biotic degradation processes that can take place with poly-and perfluorinated sulfonamides. Most of the time, the first step in the degradation of sulfonamides is the breaking of the S-N bond. One may assume that the specific chemical structure of the fluorinated chain in the sulfonamide (either a perfluorinated chain or a 6:2 fluorotelomer chain) will hardly influence the chemical reaction taking place at the sulfonamide functionality. Therefore, it is reasonable to accept that the reaction mechanism that is proposed by D'Eon *et al*. (2006) and by Martin *et al*. (2006) will also operate with AFS. The reaction mechanism proposed by these authors is represented in Figure 1.

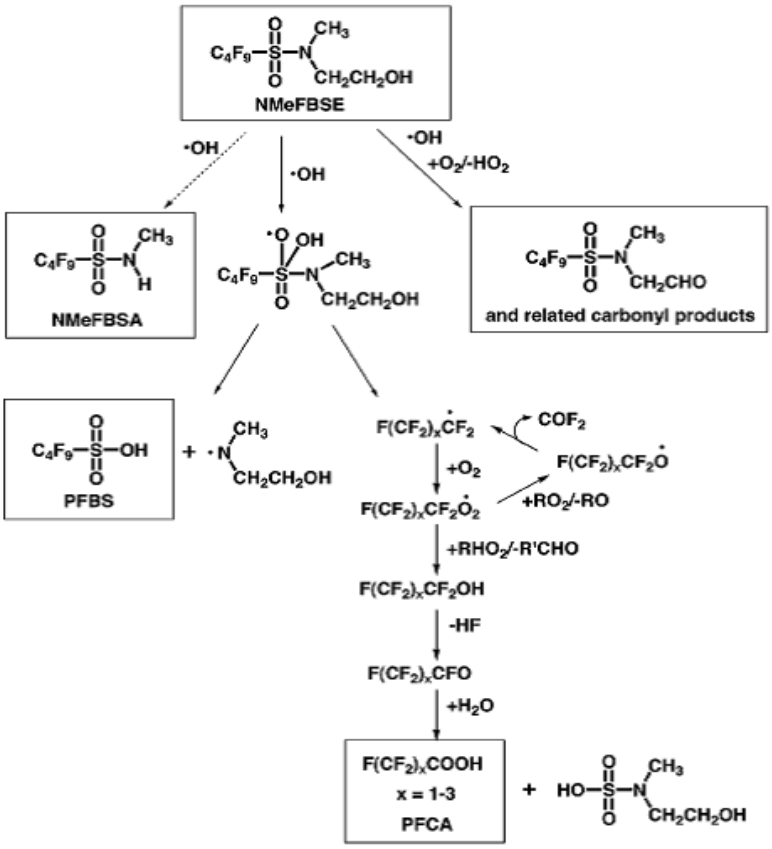

Figure 1: Proposed degradation scheme of highly fluorinated sulphonamide (D'Eon *et al.*, 2006)

Applying the proposed reaction mechanism to the AFS case, the eMSCA concludes that in real environmental conditions, and as a result of the degradation of 6:2 $FTSO_2NH_2$, 6:2

FTS(A) will be formed (see reaction scheme on the left), and probably also 6:2 FTCA (see reaction scheme on the right). It should be noted that the degradation process was monitored under laboratory conditions which tend to considerably accelerate the degradation process compared to real field conditions. It is therefore impossible to assess the rate of these degradation reactions in the environment, but one may safely assume that, after long residence periods, the proposed degradation products 6:2 FTS(A) and 6:2 FTCA will be formed to a relevant extent.

The transformation of 6:2 fluorotelomer sulfonamide into 6:2 fluorotelomer sulfonate is not only found in the gas phase, but it is also reported to occur in (micro)organisms. This reaction is for example also observed in rats (Xie *et al*., 2009), in wastewater treatment plant (WWTP) sludge (Rhoads *et al*., 2008), and in marine sediment (Benskin *et al*., 2013).

Therefore, the eMSCA concludes that in real environmental conditions, degradation will not stop at the sulfonamide stage, but will proceed further, and will result in the formation of 6:2 fluorotelomer sulfonate and other (shorter) fluorinated compounds.

6:2 FTS ➔ PFHxA + PFPeA + PFBA + 5:3 Acid

Wang *et al*. (2011) studied the biotransformation of 6:2 FTS (potassium salt) in activated sludge collected at WWTPs in the USA. The removal of the sulfonate group of 6:2 FTS was considered a rate-limiting step in its biotransformation. The reason why 6:2 FTS is relatively resistant to microbial desulfonation is not yet clear. A potential explanation may be that 6:2 FTS is a rather rigid molecule that cannot easily reach the active site of a sulfonate-α-hydroxylase. As a result of the slow transformation of 6:2 FTS, only small amounts of further degradation products could be observed in this study after 90 days: 1.5 % of PFPeA, 1.1 % of PFHxA, 0.14 % of PFBA and 0.12 % of 5:3 acid was detected. In comparison with biotransformation resulting in PFPeA and PFHxA, 5:3 acid was regarded as descending from a 'minor pathway'. This study confirms that, in the long run, perfluorinated carboxylic acids (PFCAs) will be formed in sludge. On the other hand, because of the slow transformation of 6:2 FTS, one can also expect that 6:2 FTS-concentrations may become substantial and health effects of this compound should be examined.

6:2 FTS ➔ PFHpA + PFHxA + PFPeA + 5:3 Acid

A study of Zhang *et al*. (2016) examined aerobic and anaerobic biotransformation of 6:2 FTS (potassium salt) in river sediment collected in the USA. Biotransformation of 6:2 FTS occurred quite rapidly in aerobic sediment, with a half-life of less than 5 days. After 90 days the formation of 21 mol% of PFPeA, 20 mol% of PFHxA, 16 mol% of 5:3 Acid and 0.55 mol% of PFHpA was observed. On the contrary, 6:2 FTS showed no biotransformation in anaerobic sediment after 100 days. Degradation of the sulfonate moiety under these conditions was also regarded as the rate-limiting step in the biotransformation of 6:2 FTS. This study confirms that the presence of O_2 is a crucial factor in the degradation of 6:2 FTS. In upper oxygen rich sediment layers, degradation of 6:2 FTS will take place quite readily with formation of PFCAs like PFHxA and PFHpA. In lower anaerobic sediment layers, 6:2 FTS will hardly break down, and will show a persistent character.

6:2 FTS ➔ PFCAs

Yang *et al*. (2014) studied the degradation of 6:2 FTS (potassium salt) in advanced oxidation processes. In this way, it is possible to examine in a very short time (i.e., a few hours) how 6:2 FTS will degrade in the air compartment. It is evident that in real environmental conditions this degradation will occur at a much lower rate, nevertheless it is to be expected that all the PFCAs (C_7-PFCA ➔ C_2-PFCA) will be formed after long residence times. The UV/H_2O_2 method seemed to be most effective way to speed up the degradation process, with only 9.6 % 6:2 FTS remaining after one hour. If only UV light is applied, degradation is also observed but at a rate 2 to 3 orders of magnitude slower.

A degradation pathway is proposed (Figure 2) in which desulfonation and carboxylation led to the formation of PFHpA. PFHxA could also immediately be formed via the intermediate unstable alcohol $C_6F_{13}OH$. Consecutive CF_2 flake off-processes led to a gradual unzipping of the perfluorinated chain until complete mineralisation was achieved.

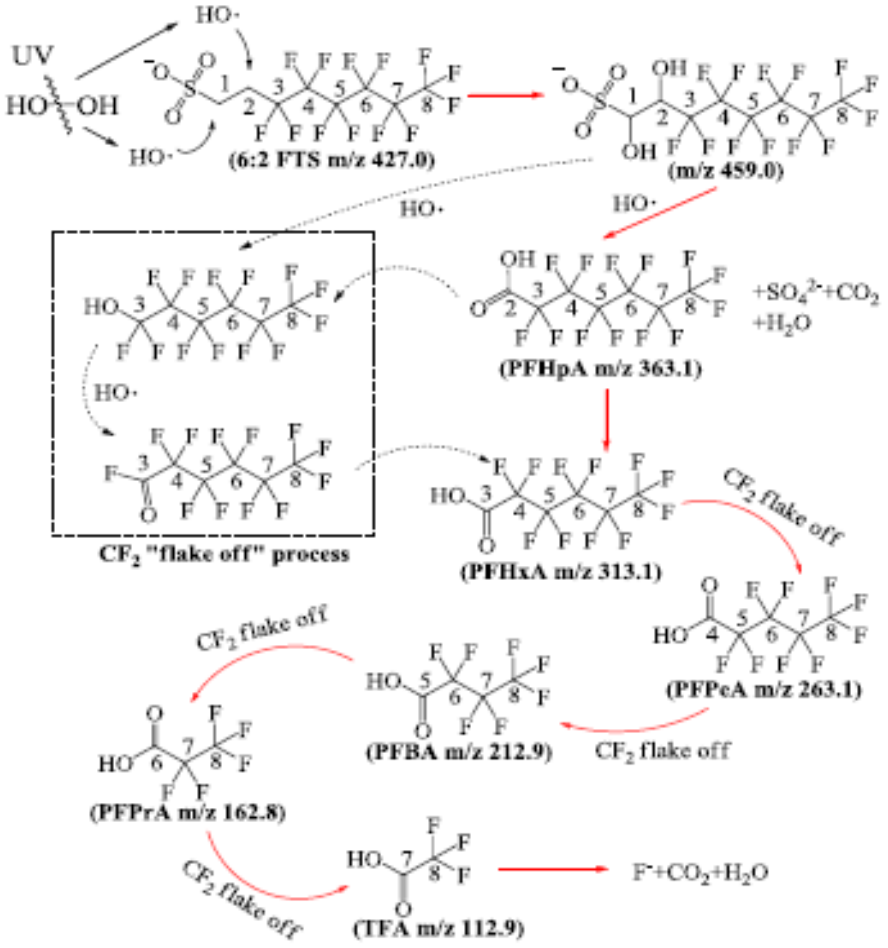

Figure 2: Proposed degradation pathway of 6:2 FTS in a UV/H_2O_2 system (Yang *et al*., 2014)

(6:2 FTAB ➔) 6:2 FTS ➔ 6:2 FTCA ➔ PFHxA + PFPeA + PFBA + 4:2 FTUA

Shaw *et al*. (2019) studied degradation of 6:2 FTAB and 6:2 FTS (ammonium salt) by the *Gordonia* sp. strain NB4-1Y. After only 1 week (168 h), 99.9 % of 60 µM 6:2 FTS and 70.4 % of 60 µM 6:2 FTAB was degraded by NB4-1Y. A degradation scheme was proposed (Figure 3), in which 6:2 FTAB is transformed to 6:2 FTS and/or 6:2 FTOH until formation of 6:2 fluorotelomer acid (6:2 FTCA), and 6:2 fluorotelomer unsaturated acid (6:2 FTUA). Thereafter two distinct pathways are identified, a major and a minor pathway.

The major pathway, in which more than 50 mol% of metabolites were produced after 168 hours, involves formation of 5:2 ketone and ultimate degradation towards the short chain perfluorocarboxylic acids PFHxA and PFPeA. The minor pathway, which covered less than 1.0 mol% of produced metabolites, involves formation of 5:3 fluorotelomer carboxylic acid (5:3 FTCA) and ultimate degradation towards PFBA and 4:2 fluorotelomer unsaturated acid (4:2 FTUA). Since degradation of 6:2 FTAB only yielded low concentrations of PFHxA and PFPeA (0.026 mol% of PFHxA and 0.001 mol% of PFPeA) after 168 hours, one can argue that degradation to these compounds occurs, but it will proceed very slowly.

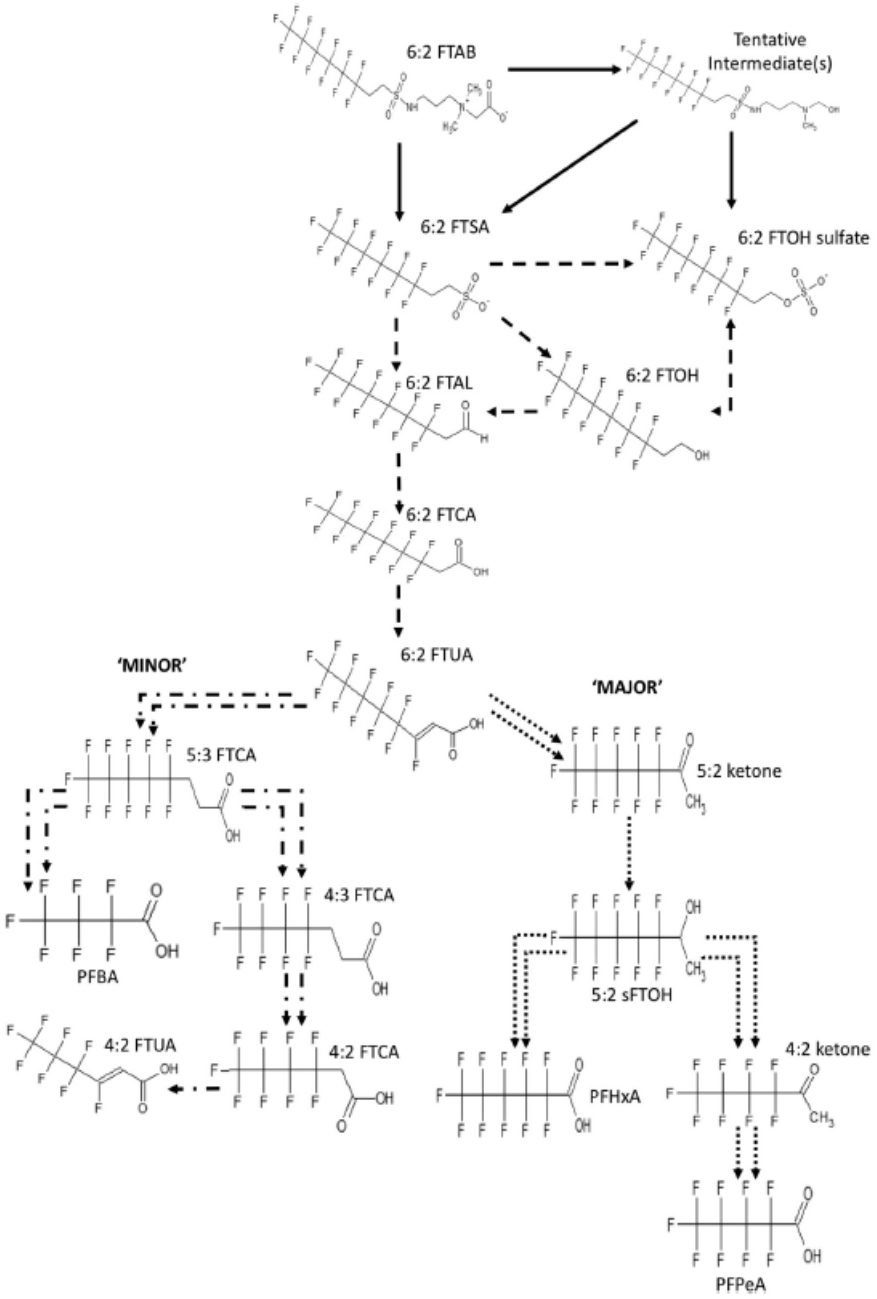

Figure 3: Proposed degradation pathway of 6:2 FTS and 6:2 FTAB by *Gordonia* sp. strain NB4-1Y (Shaw *et al*., 2019)

7.7.1.4. Conclusion

The parent compound AFS is hydrolytically stable. Although the pass level is only reached once (for the OECD TG 306 study) in the available ready and inherent biodegradability studies, substantial degradation is nevertheless observed in all these tests. It is therefore considered that degradation mainly takes place on the non-fluorinated chain of the parent compound. The first degradation product of AFS that shows a considerable persistent character under specific conditions (e.g., anaerobic sediment) is 6:2 FTS(A). This substance can degrade further, depending on the conditions in the various environmental compartments, to a whole series of poly-and perfluorinated compounds. Based on the expected persistence and hazardous properties, the perfluorinated acids PFHpA and PFHxA are the most relevant.

7.7.2. Environmental distribution

7.7.2.1. Adsorption / Desorption

Table 9: Adsorption / Desorption

SUMMARY OF STUDIES ON DISTRIBUTION: ADSORPTION / DESORPTION		
Method	**Results**	**References / Remarks**
According to OECD TG 121: Estimation of the Adsorption Coefficient (K_{oc}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC) Test type: HPLC estimation method Test system: soil and sewage sludge	Adsorption coefficient: Soil: K_{oc} = 2 190 Log K_{oc} = 3.34 Sewage sludge: K_{oc} = 2 090 Log K_{oc} = 3.32	REACH Registration dossier: Unpublished study report, 2012d Reliability 1 (Key study) Test material: AFS GLP

An experimental log K_{oc}-value (via HPLC estimation method) of 3.34 was determined for AFS in soil, and an experimental log K_{oc}-value of 3.32 was determined in the same manner for AFS in sewage sludge (Unpublished study report, 2012d). The Substance therefore shows a medium potential for adsorption. Furthermore, the Substance has a moderate to low water solubility (107 mg/L).

This experimental value is consistent with the Log K_{oc}-value(s) estimated by the eMSCA in EPI Suite (EPIWEB v4.1; KOCWIN v2.00), at least with the Log K_{oc}-value of 3.6599 derived from the Molecular Connectivity Index (MCI) Method. The Log K_{oc}-value of -0.6065 derived from the K_{ow} Method is largely different from the experimental values mentioned for AFS above, this because the log K_{ow} estimated by EPI Suite is also quite low (-2.12; EPIWEB v4.1; KOWWIN v1.68).

7.7.2.2. Volatilisation

There is no experimentally determined Henry's Law Constant available in the registration dossier. A Henry's Law Constant of 2.88 x 10^{-17} Pa-m^3/mole at 25 °C was calculated by the eMSCA in EPI Suite (EPIWEB v4.1; HENRYWIN v3.20 (Bond Method)). The Substance is therefore expected to have a low tendency to volatilize. The vapour pressure of AFS is indicated to be <10^{-6} Pa at 20 °C, which indicates that partitioning to the air will be negligible.

7.7.2.3. Distribution modelling

According to the Level III Fugacity Model (EPIWEB v. 4.1), the Substance will mainly distribute to soil (94%).

	Mass amount (%)	Half-Life (hr)	Emissions (kg/hr)
Air	3.45e-006	4.53	1 000
Water	4	4.32e+003	1 000
Soil	94	8.64e+003	1 000
Sediment	1.95	3.89e+004	0

Persistence time: 8.15e+003 hr

However, when emissions of AFS are exclusively modelled to water, most of the Substance will be distributed to water (67.3%).

	Mass amount (%)	Half-Life (hr)	Emissions (kg/hr)
Air	1.64e-022	4.53	0
Water	67.3	4.32e+003	1 000
Soil	2.12e-015	8.64e+003	0
Sediment	32.7	3.89e+004	0

Persistence time: 1.26e+003 hr

According to the modelled results above, both soil and water can be important environmental compartments for AFS.

7.7.3. Bioaccumulation

7.7.3.1. Aquatic bioaccumulation

Table 10: Aquatic bioaccumulation

SUMMARY OF STUDIES ON BIOACCUMULATION (AQUATIC)		
Method	**Results**	**References / Remarks**
No guideline mentioned. Subset of fish from the OECD TG 210 study used to determine bioconcentration factor values. *Oncorhynchus mykiss* Test type: flow-through Test medium: aqueous (freshwater) BCF = (Concentration in Fish Tissue) / (Concentration in Test Solution)	Day 45 BCF: ≥ 0.637 - ≤ 3.01 L/kg (Whole body w.w.) (Mean, measured total solids concentrations) Day 90 BCF: ≥ 0.41 - ≤ 1.18 L/kg (Whole body w.w.) (Mean, measured total solids concentrations)	REACH Registration dossier: Unpublished study report, 2012e Reliability 2 (Supporting study) Test material: AFS GLP

Experimental bioconcentration factor (BCF) values were derived for AFS with *Oncorhynchus mykiss* (previously named *Salmo gairdneri*). The study is considered supporting, as it was not performed according to a specific guideline for assessing bioaccumulation. A subset of fish from the OECD TG 210 study (Unpublished study report, 2012e) was used to determine bioconcentration factor values. Maximal BCF values varied from 1.18 L/kg (day 90) to 3.01 L/kg (day 45). Neither of the measured bioconcentration factor values exceeded 2 000 L/kg. Therefore, AFS is not bioaccumulative for aquatic organisms.

A BCF-value of 3.162 L/kg wet-wt was calculated by the eMSCA in EPI Suite (EPIWEB v4.1; BCFBAF v3.01 (regression-based method)). An experimental log K_{ow}-value of 1.35 at 25 °C is presented in the registration dossier (According to OECD TG 123, Slow-Stirring Method). The log K_{ow} of -2.12 estimated by the eMSCA in EPI Suite (EPIWEB v4.1, KOWWIN v1.68) is even much lower than the experimentally determined value. Both the experimental and estimated log K_{ow}-values do not meet the screening criterion of 4.5 regarding aquatic bioaccumulation.

7.7.3.2. Terrestrial bioaccumulation

No experimental study is available on terrestrial bioaccumulation. An estimation in EPI Suite (EPIWEB v4.1; KOAWIN v1.10) resulted in a log K_{oa}-value of 17.815. When filling in the experimental log K_{ow}-value of 1.35 as input into the EPI Suite model, the calculated log K_{oa} becomes even higher, and a log K_{oa}-value of 21.285 can be derived. The Log K_{oa}-value is therefore much higher than 5, however the log K_{ow}-value is below 2, which

indicates that the screening criteria for bioaccumulation in air-breathing organisms are not fulfilled for AFS.

Toxicokinetic data (see Table 18) are available for the Substance. A saturation in absorption was observed in the first study (OECD TG 417), as the bioavailability of the Substance decreased as the doses were set higher. Also, a small degree of accumulation in males was observed after 14 days of exposure, however not in females. In the second study (no guideline), a plasma steady state concentration was reached by day 4, and a preferential partitioning of the Substance into the liver was noted.

7.7.3.3. Conclusion

It is concluded that the parent compound Amphoteric Fluorinated Surfactant (AFS) does not fulfil the B-criterion for aquatic organisms. Experimental and estimated BCF- and log K_{ow}-values do not meet the requirements for aquatic bioaccumulation. Very high log K_{oa}-values could be estimated for AFS, however in combination with the low log K_{ow}-values, this is not a trigger for bioaccumulation in air-breathing organisms.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

7.8.1.1. Fish

7.8.1.1.1. Short-term toxicity to fish

Table 11: Short-term effects on fish

SUMMARY OF SHORT-TERM TOXICITY STUDIES ON FISH		
Method	**Results**	**References / Remarks**
According to OECD TG 203: Fish, Acute Toxicity Test *Oncorhynchus mykiss* Test type: static Test medium: freshwater	96h LC_{50} > 712 mg_{AFS}/L (nominal) based on mortality. 96h LC_{50} > 120 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on mortality	REACH Registration dossier: Unpublished study report, 2012f Reliability 1 (Key study) Test material: AFS GLP
According to OECD TG 203: Fish, Acute Toxicity Test; EPA OPPTS 850.1075: Freshwater and Saltwater Fish Acute Toxicity Test; SEPA. HJ/T 153-2004 *Danio rerio* Test type: static Test medium: freshwater	96h LC_{50} > 150 mg/L (nominal) based on mortality. 96h LC_{50} > 145 mg/L (meas. arithm. mean) based on mortality.	REACH Registration dossier: Unpublished study report, 2012g Reliability 2 (Supporting study) Test material: AFS GLP

A fish toxicity study performed with *Oncorhynchus mykiss* (previously named *Salmo gairdneri*) according to OECD TG 203 is indicated to be the key study for short-term toxicity to fish on AFS (Unpublished study report, 2012f). The solution with total fluorinated solids

included 28.0% AFS, 1.4% of impurity 1, and <0.2% of impurity 2. The test media pH ranged from 7.6 to 8.3. The nominal exposure series was 0, 44.5, 89.0, 178, 356 and 712 expressed as mg_{AFS}/L; and 0, 13.1, 26.2, 52.3, 105 and 209 expressed as $mg_{total\ fluorinated\ solids}$/L. Mean measured concentrations were 0, 11.4, 22.6, 42.4, 87.4 and 120 expressed as $mg_{total\ fluorinated\ solids}$/L. Mortality or sublethal effects were not observed within the exposure period of 96 hours, not for the control group and not for any the tested groups. As no mortality was observed, the 96h LC_{50}-value (nominal) was > 712 mg_{AFS}/L, and the 96h LC_{50}-value (meas. arithm. mean) was > 120 $mg_{total\ fluorinated\ solids}$/L.

A supporting study regarding fish acute toxicity in *Danio rerio* (previously named *Brachydanio rerio*) according to OECD TG 203, is also available in the registration dossier (Unpublished study report, 2012g). Also here, mortality was not observed during the exposure period of 96 hours. The 96h LC_{50}-value (nominal) was set at > 150 mg/L, and the 96h LC_{50}-value (meas. (arithm. mean)) was indicated to be > 145 mg/L.

Conclusion: There is no indication of short-term toxicity to fish, as all 96h LC_{50}-values are above 1 mg/L.

7.8.1.1.2. Long-term toxicity to fish

Table 12: Long-term effects on fish

SUMMARY OF LONG-TERM TOXICITY STUDIES ON FISH		
Method	**Results**	**References / Remarks**
According to OECD TG 210: Fish, Early-Life Stage Toxicity Test. EPA OPPTS 850.1400: Fish, Early-Life Stage Toxicity Test *Oncorhynchus mykiss* Test type: flow-through Test medium: freshwater	90d NOEC = 5.86 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on first and last day of hatching. 90d NOEC = 13.4 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on egg hatching, first day of swim-up, larval survival and abnormalities at thinning and test end, length, and wet weight at test end. 90d LOEC = 13.4 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on first and last day of hatching. 90d LOEC > 13.4 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on egg hatching, first day of swim-up, larval survival and abnormalities at thinning and test end, length, and wet weight at test end.	REACH Registration dossier: Unpublished study report, 2012e Reliability 1 (Supporting study) Test material: AFS GLP

A fish early-life stage toxicity study was recently performed with *Oncorhynchus mykiss* (previously named *Salmo gairdneri*) according to OECD TG 210 (Unpublished study report, 2012e). The solution with total fluorinated solids included 28.0% AFS, 1.4% of impurity 1, and <0.2% of impurity 2. The test media pH ranged from 7.6 to 8.3. The nominal exposure series was 0, 3.23, 6.46, 12.9, 25.5 and 51.0 expressed as mg_{AFS}/L; and 0, 0.95, 1.9, 3.8, 7.5 and 15 expressed as $mg_{total\ fluorinated\ solids}$/L. Mean measured concentrations were 0, 0.648, 1.21, 2.69, 5.86 and 13.4 expressed as $mg_{total\ fluorinated\ solids}$/L. Based on the first and last day of hatching, a 90d NOEC of 5.86 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) and a 90d LOEC of 13.4 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) could be derived. When observing potential effects on egg hatching, first day of swim-up, larval survival, abnormalities, length, and wet weight, this resulted in a 90d NOEC of 13.4 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) and a 90d LOEC of > 13.4 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean).

Conclusion: There is no indication of long-term toxicity to fish, as all 90d NOEC-values are above 1 mg/L.

7.8.1.2. Aquatic invertebrates

7.8.1.2.1. Short-term toxicity to aquatic invertebrates

Table 13: Short-term effects on aquatic invertebrates

SUMMARY OF SHORT-TERM TOXICITY STUDIES ON AQUATIC INVERTEBRATES		
Method	**Results**	**References / Remarks**
Equivalent or similar to OECD TG 202: Daphnia sp. Acute Immobilisation Test *Daphnia magna* Test type: static Test medium: freshwater	48h EC_{50} > 712 mg_{AFS}/L (nominal) based on immobility. 48h EC_{50} > 122 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on immobility.	REACH Registration dossier: Unpublished study report, 2012h Reliability 1 (Key study) Test material: AFS GLP
Equivalent or similar to OSPAR/PARCOM Protocols on Methods for the Testing of Chemicals Used in the Offshore Industry 2006 Part A: A sediment bioassay using an amphipod Corophium sp. *Corophium volutator* (aquatic arthropod) Test type: static Test medium: saltwater	10d LC_{50} > 13 419 mg/kg dry sediment (nominal) based on mortality. 10d NOEC = 4 192 mg/kg dry sediment (nominal) based on mortality. 10d LOEC = 13 419 mg/kg dry sediment (nominal) based on mortality.	REACH Registration dossier: Unpublished study report, 2015b Reliability 1 (Key study) Test material: AFS GLP

An acute immobilisation test on AFS equivalent to OECD TG 202 performed with *Daphnia magna* is available in the registration dossier (Unpublished study report, 2012h). The solution with total fluorinated solids included 28.0% AFS, 1.4% of impurity 1, and <0.2% of impurity 2. The test media pH was 8.1-8.2 at the start and 8.3 at the end. The nominal exposure series was 0, 44.5, 89, 178, 356 and 712 expressed as mg_{AFS}/L; and 0, 13.1, 26.2, 52.3, 105 and 209 expressed as $mg_{total\ fluorinated\ solids}$/L (also nominal). Mean measured concentrations were 0, 9.18, 16.7, 33.9, 97.3 and 122 expressed as $mg_{total\ fluorinated\ solids}$/L. The lowest nominal concentration, which resulted in 100% immobility at the end of the test period, was greater than 712 mg_{AFS}/L (48h EC_{50} > 712 mg_{AFS}/L, nominal). Expressed in total fluorinated solids, this corresponds to a concentration greater than 122 $mg_{total\ fluorinated\ solids}$/L (48h EC_{50} > 122 $mg_{total\ fluorinated\ solids}$/L, meas. arithm. mean).

A second study on AFS, according to an unknown guideline, was performed with the aquatic arthropod *Corophium volutator* (Unpublished study report, 2015b). The test media pH ranged from 7.84 to 8.31. Nominal concentrations were 0, 127, 409, 1 311, 4 192 and 13 419 mg/kg dry sediment, and were 0, 95, 305, 977, 3 125 and 10 000 mg/kg wet sediment. A very high 10d LC_{50}-value of > 13 419 mg/kg dry sediment was obtained (based on mortality, as well as a 10d NOEC of 4 192 mg/kg dry sediment, and a 10d LOEC of 13 419 mg/kg dry sediment (all nominal)). The study also had a long duration of 10 days (whereas the equivalent to OECD TG 202 study was performed for 48 hours).

Conclusion: There is no indication of short-term toxicity to aquatic invertebrates, as all 48h EC_{50} / 10d LC_{50}-values are above 1 mg/L or mg/kg.

7.8.1.2.2. Long-term toxicity to aquatic invertebrates

Table 14: Long-term effects on aquatic invertebrates

SUMMARY OF LONG-TERM TOXICITY STUDIES ON AQUATIC INVERTEBRATES		
Method	**Results**	**References / Remarks**
According to OECD TG 211: *Daphnia magna* Reproduction Test; EPA OPPTS 850.1300: Daphnid Chronic Toxicity Test *Daphnia magna* Test type: semi-static Test medium: freshwater	21d EC_{50} > 13.5 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on adult survival. 21d NOEC = 3.18 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on total number of live young produced per surviving female at the end of the study. 21d LOEC = 6.42 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on total number of live young produced per surviving female at the end of the study.	REACH Registration dossier: Unpublished study report, 2012i Reliability 1 (Supporting study) Test material: AFS GLP

A long-term toxicity study on AFS according to OECD TG 211 performed with *Daphnia magna* is available in the registration dossier (Unpublished study report, 2012i). A percentage total fluorinated solids of 29.4% was used in the test solutions. The test media pH ranged from 7.9 to 8.3 in the different test solutions. The nominal exposure series was 0, 3.38, 6.76, 13.5, 26.7 and 53.4 expressed as mg_{AFS}/L; and 0, 0.994, 1.99, 3.97, 7.85 and 15.7 expressed as $mg_{total\ fluorinated\ solids}$/L (also nominal). Mean measured concentrations were 0, 0.619, 1.50, 3.18, 6.42 and 13.5 expressed as $mg_{total\ fluorinated\ solids}$/L. The study resulted in the derivation of a 21d EC_{50} larger than 13.5 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean, based on adult survival), a 21d NOEC of 3.18 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean, based on total number of live young per surviving female), and a 21d LOEC of 6.42 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean, based on total number of live young per surviving female).

Conclusion: There is no indication of long-term toxicity to aquatic invertebrates, as all 21d NOEC-values are above 1 mg/L.

7.8.1.3. Algae and aquatic plants

Table 15: Effects (short-term and long-term) on algae and aquatic plants

SUMMARY OF TOXICITY STUDIES ON ALGAE AND AQUATIC PLANTS		
Method	**Results**	**References / Remarks**
According to OECD TG 201: Alga, Growth Inhibition Test; EPA OPPTS 850.5400: Algal Toxicity, Tiers I and II *Raphidocelis subcapitata* Test type: static	72h EC_{50} > 136 mg_{AFS}/L (nominal) based on growth rate. 72h EC_{50} > 31.6 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on growth rate. 72h NOEC = 17 mg_{AFS}/L (nominal) based on biomass, yield, growth rate, each based on cell count.	REACH Registration dossier: Unpublished study report, 2012j Reliability 1 (Key study) Test material: AFS GLP

SUMMARY OF TOXICITY STUDIES ON ALGAE AND AQUATIC PLANTS		
Method	**Results**	**References / Remarks**
Test medium: freshwater	72h NOEC = 3.43 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) based on biomass, yield, growth rate, each based on cell count.	

Secondly, a toxicity study on *Raphidocelis subcapitata* (previously named *Selenastrum capricornutum* and *Pseudokirchneriella subcapitata*) is available with AFS, performed according to OECD TG 201 (Unpublished study report, 2012j). The solution with total fluorinated solids included 28.0% AFS, 1.4% of impurity 1, and <0.2% of impurity 2. Study endpoints were growth rate, biomass, and yield. The test media pH ranged from 7.57 to 8.20. The nominal exposure series was 0, 8.5, 17, 34, 68 and 136 expressed as mg_{AFS}/L; and 0, 2.5, 5, 10, 20 and 40 expressed as $mg_{total\ fluorinated\ solids}$/L. Mean measured concentrations were 0, 1.80, 3.43, 7.19, 15.8 and 31.6 expressed as $mg_{total\ fluorinated\ solids}$/L. Based on the growth rate, a 72h EC_{50} of > 136 mg_{AFS}/L (nominal) and a 72h EC_{50} of > 31.6 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean) could be derived. Based on the endpoints biomass, yield and growth rate (each based on cell count), this resulted in a 72h NOEC of 17 mg_{AFS}/L (nominal) and a 72h NOEC of 3.43 $mg_{total\ fluorinated\ solids}$/L (meas. arithm. mean).

Conclusion: There is no indication of short-term and long-term toxicity to algae and aquatic plants, as all 72h EC_{50} / 72h NOEC-values are above 1 mg/L.

7.8.1.4. Sediment organisms

No data available.

7.8.1.5. Other aquatic organisms

No data available.

7.8.1.6. Conclusion

The lowest short-term freshwater LC/EC_{50}-value is the algae 72h EC_{50}-value of > 31.6 $mg_{total\ fluorinated\ solids}$/L. The lowest freshwater NOEC is the invertebrate 21d NOEC of 3.18 $mg_{total\ fluorinated\ solids}$/L. Both values indicate that the T-criterion is not met for AFS.

7.8.2. Terrestrial compartment

7.8.2.1. Toxicity to soil macro-organisms

Table 16: Effects (short-term and long-term) on soil macro-organisms

SUMMARY OF TOXICITY STUDIES ON SOIL MACRO-ORGANISMS		
Method	**Results**	**References / Remarks**
According to OECD TG 207: Earthworm, Acute Toxicity Tests. EU Method C.8: Toxicity for Earthworms - Artificial Soil Test. EPA OPPTS 850.6200: Earthworm Sub chronic Toxicity Test. SEPA. HJ/T 153-2004 *Eisenia fetida* (annelid)	14d LC_{50} > 1 000 mg/kg soil dw (meas. initial) based on mortality.	REACH Registration dossier: Unpublished study report, 2012k Reliability 2 (Supporting study) Test material: AFS

Substrate: artificial soil		GLP

A toxicity study on AFS according to OECD TG 207, using the annelid *Eisenia fetida* as test species, is available in the registration dossier (Unpublished study report, 2012k). No mortality was observed at the highest exposure concentration of 1 000 mg/kg soil dw. The 14d LC_{50} is therefore > 1 000 mg/kg soil dw (meas. initial).

Conclusion: There is no indication of short-term and long-term toxicity to soil macro-organisms.

7.8.2.2. Toxicity to terrestrial plants

No data available.

7.8.2.3. Toxicity to soil micro-organisms

No data available.

7.8.2.4. Toxicity to other terrestrial organisms

No data available.

7.8.3. Microbiological activity in sewage treatment systems

7.8.3.1. Toxicity to micro-organisms in sewage treatment systems

Table 17: Effects (short-term and long-term) on micro-organisms in sewage treatment systems

SUMMARY OF TOXICITY STUDIES ON MICRO-ORGANISMS (SEWAGE TREATMENT)		
Method	**Results**	**References / Remarks**
According to OECD TG 209: Activated Sludge, Respiration Inhibition Test Test organisms (species): activated sludge. Test medium: freshwater	3h NOEC = 100 mg a.i./L (nominal) based on respiration rate.	REACH Registration dossier: Unpublished study report, 2012l Reliability 1 (Key study) Test material: AFS GLP

The environmental part of the registration dossier also mentions a respiration inhibition test with activated sludge according to OECD TG 209 (Unpublished study report, 2012l). The 3h NOEC was stated to be 100 mg a.i./L (nominal), which is the highest concentration tested, at which also no significant respiration inhibition of the activated sludge was observed. It was also noted in the registration dossier that testing at higher concentrations was not possible due to excessive foaming.

Conclusion: There is no indication of short-term and long-term toxicity to micro-organisms in sewage treatment systems.

7.8.4. PNEC derivation and other hazard conclusions

Not assessed.

7.8.5. Conclusions for classification and labelling

Based on the available data, AFS (considering its properties as parent compound) should not be classified for the environment.

Acute Toxicity:

All L(E)C_{50}s > 1 mg/L ➔ No classification warranted for acute aquatic toxicity.

Chronic Toxicity:

NOECs are available for all 3 trophic levels and are all > 1 mg/L ➔ No classification warranted for chronic aquatic toxicity.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

Table 18: Toxicokinetics (absorption, metabolism, distribution, and elimination)

SUMMARY OF STUDIES ON TOXICOKINETICS			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 417: Toxicokinetics; EPA OPPTS 870.7485: Metabolism and Pharmacokinetics Test species: Rat (Crl:CD(SD)), both sexes	Group 1: single exposure by gavage, 30 mg/kg bw Group 2: single exposure by gavage, 1 000 mg/kg bw Group 3: IV, 5 mg/kg bw Group 4: 14d oral gavage (daily), 30 mg/kg bw	Indication of saturation in absorption (Bioavailability of test substance ↓ as dose ↑) Small degree of accumulation in males following 14d of exposure (not in females) Elimination, half-life: 28-38h in males and 21-38h in females (Across different dose groups)	REACH Registration dossier: Unpublished study report, 2015c Reliability 1 (Key study) Test material: AFS GLP
No guideline mentioned. Test species: Rat (Crl:CD(SD)), both sexes	Gavage Duration of exposure: 7d Doses: 0 and 30 mg/kg bw/d	Plasma steady state concentration: reached by day 4. Test substance preferentially partitioned into the liver	REACH Registration dossier: Unpublished study report, 2012m Reliability 2 (Supporting study) Test material: AFS Non-GLP

Two studies on toxicokinetics are available in the registration dossier. In a first study (OECD TG 417; Unpublished study report, 2015c), the test substance accumulated to a small degree in males after 14 days of exposure by repeated oral gavage. However, no accumulation was observed in female rats. In a second study, for which no guideline was mentioned (Unpublished study report, 2012m), it became apparent that AFS preferentially partitioned to the liver of male and female rats.

7.9.2. Acute toxicity and Corrosion/irritation

7.9.2.1. Acute toxicity via oral route

Table 19: Acute toxicity after oral administration

SUMMARY OF STUDIES ON ACUTE TOXICITY - ORAL			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 425: Acute Oral Toxicity: Up-and-Down Procedure; EPA OPPTS 870.1100: Acute Oral Toxicity Test species: Rat (Crl:CD(SD)), female	Gavage Doses (nb. of animals tested): 175 (1), 550 (1), 1 750 (3) and 5 000 (3) mg/kg bw Obs. period: 14d	LD_{50}: 3 129 mg/kg bw based on act. ingr. Mortality: all animals died at 5 000 mg/kg bw (no mortality observed at the lower dose levels) Clinical signs: at 1 750 mg/kg bw: ataxia at 5 000 mg/kg bw: ataxia, decreased muscle tone, moribundity, low or prostrate posture. BW: no treatment-related effects Necropsy: no test substance-related effects	REACH Registration dossier: Unpublished study report, 2011 Reliability 1 (Key study) Test material: AFS No vehicle GLP

In an acute oral toxicity study, following OECD TG 425, performed on female rats (Unpublished study report, 2011) a LD_{50} of 3 129 mg/kg bw was derived (based on act. ingr.). All animals exposed to 5 000 mg/kg bw died, however no mortality was observed at the lower doses.

Conclusion: AFS is not acutely toxic via the oral route.

7.9.2.2. Acute toxicity via inhalation route

Table 20: Acute toxicity after inhalation exposure

SUMMARY OF STUDIES ON ACUTE TOXICITY - INHALATION			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 403: Acute Inhalation Toxicity; EPA OPPTS 870.1300: Acute Inhalation Toxicity; EEC Method B.2 Directive 92/69/EEC;	Aerosol Conc.: 5.6 ± 0.90 mg/L 1 exposure group (5 males and 5 females) Duration of exposure: 4h	4h LC_{50}: > 5.6 mg/L air based on total atmospheric concentration. 4h LC_{50}: > 2.6 mg/L air based on non-volatile components. Mortality: No mortality occurred during the study period	REACH Registration dossier: Unpublished study report, 2012n Reliability 1 (Key study) Test material: AFS Vehicle: air

SUMMARY OF STUDIES ON ACUTE TOXICITY - INHALATION			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
MAFF Japan Agricultural Chemicals Regulation Laws 2-1-3 Notification 12-Nousan-8147 and Notification 13 Seisan 1739 Test species: Rat (Crl:CD(SD)), both sexes	Obs. period: 14d	Clinical signs: one male showed laboured breathing. BW: all animals gained weight during the observation period. Necropsy: no treatment-related effects	GLP

An acute inhalation toxicity study performed with rats (OECD TG 403; Unpublished study report, 2012n) resulted in a 4h LC_{50} higher than 5.6 mg/L air, based on total atmospheric concentration, which is also the only tested dose level (and a 4h LC_{50} higher than 2.6 mg/L air, based on non-volatile components).

Conclusion: AFS is not acutely toxic via the inhalation route.

7.9.2.3. Acute toxicity via dermal route

Table 21: Acute toxicity after dermal administration

SUMMARY OF STUDIES ON ACUTE TOXICITY - DERMAL			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 402: Acute Dermal Toxicity; EPA OPPTS 870.1200: Acute Dermal Toxicity; EEC Method B.3 Directive 92/69/EEC Test species: Rat (Crl:CD(SD)), both sexes	Coverage: Semi-occlusive Dose: 5 000 mg/kg bw 1 exposure group (5 males and 5 females) Duration of exposure: 24h Obs. period: 14d	24h LD_{50}: > 5 000 mg/kg bw based on act. ingr. Mortality: No mortality occurred during the study period Clinical signs: hyperkeratosis was observed in 3 females at days 6 and 7 of obs. period. Necropsy: no treatment-related effects	REACH Registration dossier: Unpublished study report, 2012o Reliability 1 (Key study) Test material: AFS No vehicle GLP

The acute dermal toxicity study performed on rats, resulted in a 24h LD_{50} higher than 5 000 mg/kg bw (based on act. ingr.). This was also the only dose tested (OECD TG 402; Unpublished study report, 2012o).

Conclusion: AFS is not acutely toxic via the dermal route.

7.9.2.4. Skin irritation / Corrosion

Table 22: Skin irritation / Corrosion

SUMMARY OF STUDIES ON SKIN IRRITATION AND CORROSION			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 404: Acute Dermal Irritation / Corrosion; EPA OPPTS 870.2500: Acute Dermal Irritation Test species: Rabbit (New Zealand White), male *In vivo*	Coverage: Semi-occlusive Skin: Shaved Amount applied: 0.5 mL. 1 exposure group (3 animals) Duration of exposure: 4h Obs. period: Directly after patch removal + 30-60 min, 24h, 48h and 72h after patch removal	Mean erythema score (24, 48 and 72h): 0/4 (score of 1 immediately after patch removal for 2 animals, and score of 1 after 30-60 min for 2 animals) Mean edema score (24, 48 and 72h): 0/4	REACH Registration dossier: Unpublished study report, 2012p Reliability 1 (Key study) Test material: AFS No vehicle GLP

The skin irritation study, in which 0.5 mL of AFS was applied on shaved skin of rabbits, showed no substantial skin irritation (OECD TG 404; Unpublished study report, 2012p). Erythema was only observed for some animals, and at some time points in the beginning (directly and 30-60 min after patch removal). After 24h of patch removal, erythema was no longer noted. Edema was not observed throughout the observation period.

Conclusion: AFS is not irritating for the skin.

7.9.2.5. Eye irritation

Table 23: Eye irritation

SUMMARY OF STUDIES ON EYE IRRITATION			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 405: Acute Eye Irritation / Corrosion; EPA OPPTS 870.2400: Acute Eye Irritation Test species: Rabbit (New	Single exposure Amount applied: 0.1 mL. 1 exposure group (1 male and 2 females) Obs. period: 1, 24, 48 and 72h after treatment	Mean corneal opacity score (24, 48 and 72h): 0/4 Mean iris score (24, 48 and 72h): 0/4 Mean conjunctivae score (24, 48 and 72h): 0/4 Mean chemosis score (24, 48 and 72h): 0/4	REACH Registration dossier: Unpublished study report, 2012q Reliability 1 (Key study) Test material: AFS No vehicle

Zealand White), both sexes *In vivo*	Control: Left eye of each animal not treated	Redness and discharge of conjunctivae observed for 3 animals after 1h	GLP

The eye irritation study, in which 0.1 mL of AFS was applied to the right eye of rabbits (left eye untreated as control), showed no substantial eye irritation (OECD TG 405; Unpublished study report, 2012q). Redness and discharge of conjunctivae was observed for all tested animals after 1h. However, this was no longer noted after 24h of treatment. Iritis, corneal opacity and chemosis of conjunctivae were not observed at any of the time points.

Conclusion: AFS is not irritating for the eyes.

7.9.3. Sensitisation

7.9.3.1. Skin sensitisation

Table 24: Skin sensitisation

SUMMARY OF STUDIES ON SKIN SENSITISATION			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 429: Skin Sensitisation – Local Lymph Node Assay (LLNA); EPA OPPTS 870.2600: Skin Sensitisation Test species: Mouse (CBA / JHsd), female *In vivo*	Conc.: 0, 5, 25, 50 and 100% of tested material No. of animals per dose: 5	Clinical signs: no treatment-related effects Body weight: no treatment-related effects SI: 1.53, 1.44, 0.85 and 0.58 respectively at 5, 25, 50 and 100% (SI of 3.55 in positive control group)	REACH Registration dossier: Unpublished study report, 2012r Reliability 1 (Key study) Test material: AFS Vehicle: dimethyl sulphoxide GLP

A Local Lymph Node Assay (LLNA) performed with mice according to OECD TG 429 (Unpublished study report, 2012r) did not show a statistically significant increase in cell proliferation measurements when compared to the vehicle control group, for any of the tested concentrations. Stimulation index (SI) values were lower than 3 in all experimental groups.

Conclusion: AFS is not sensitizing for the skin.

7.9.3.2. Respiratory sensitisation

No data available.

7.9.4. Repeated dose toxicity

7.9.4.1. Repeated dose toxicity via oral route

Table 25: Repeated dose toxicity after oral administration

SUMMARY OF STUDIES ON REPEATED DOSE TOXICITY - ORAL			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 422: Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test; OECD TG 407: Repeated Dose 28-Day Oral Toxicity Study in Rodents; EPA OPPTS 870.3650: Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test. EPA OPPTS 870.3050: Repeated Dose 28-Day Oral Toxicity Study in Rodents Test species: Rat (Crl:CD(SD)), both sexes	Gavage *Experiment 1:* 5 animals/sex/group, duration of exposure = 28d *Experiment 2:* 5 animals/sex/group, duration of exposure = 28d with 1 month of recovery *Experiment 3:* 10 animals/sex/group, duration of exposure = 30 days prior to and during cohabitation until day 3 postpartum for females showing evidence of copulation (for other animals until day before sacrifice) Conc.: 0, 10, 50 and 200 mg/kg/d Daily	NOAEL: 10 mg/kg bw/d based on: act. ingr. Clinical signs and mortality: no treatment-related effects Food efficiency: no treatment-related effects Haematology: no treatment-related effects Clinical chemistry: no treatment-related effects Neurobehaviour: no treatment-related effects Organ weights: no treatment-related effects Histopathology: *Experiment 1:* Males: increase in hyaline droplets in cortical tubules (kidneys) of mild severity at 200 mg/kg/d and minimal severity at 50 mg/kg/d; minimal to mild degeneration/atrophy of nasal olfactory epithelium of 2/5 animals in both the male and female groups (200 mg/kg/d group) and in 1/5 females (50 mg/kg/d group). *Experiment 2:* Mild chronic progressive nephropathy in two males (200 mg/kg/d group), one of these also had minimal granular casts. No olfactory lesions observed. *Experiment 3:*	REACH Registration dossier: Unpublished study report, 2012s Reliability 1 (Key study) Test material: AFS Vehicle: deionized water GLP

SUMMARY OF STUDIES ON REPEATED DOSE TOXICITY - ORAL			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
		Males (P1): increase in hyaline droplets in cortical tubules (kidneys) of mild severity at 200 mg/kg/d and minimal severity at 50 mg/kg/d; minimal to mild degeneration/atrophy of nasal olfactory epithelium in 3/10 (50 mg/kg/d group) and 2/10 (200 mg/kg/d group) females. In 1 female of the highest dose, the lesions were severe.	
No guideline mentioned. Test species: Rat (Crl:CD(SD)), both sexes	Gavage Conc.: 0, 30, 500 and 1 000 mg/kg/d No. of animals: - Control: 5 males, 5 females - 30 mg/kg/d: 8 males, 8 females - 500 mg/kg/d: 5 males, 5 females - 1 000 mg/kg/d: 5 males, 5 females 5 animals/sex for the main study + 3 animals/sex for the metabolism study (only at 30 mg/kg/d) Duration of exposure: - 6 days for the main study - 7 days for the metabolism study Daily	NOAEL: 1 000 mg/kg bw/d based on: act. ingr. (According to the registration dossier, however, microscopic changes were observed at this highest dose) Clinical signs: no treatment-related effects Gross pathology: Females: no treatment-related effects Males: Kidney dilatation in 2/5 animals (500 mg/kg/d group); kidney discoloration in 2/5 animals and thymus foci in 1/5 animals (1 000 mg/kg/d group). Nose: Degeneration/atrophy of nasal olfactory epithelium in male and female animals (1 000 mg/kg/day group). Also seen in other groups, including control. Liver: Males: Minimal hepatocellular hypertrophy (1 000 mg/kg/day group). Kidneys: Males: Increased accumulation of hyaline droplets in renal tubules (300 and 1 000 mg/kg/day groups). Kidney weight relative to body weight was increased at all dose levels. Brain: Males: Brain weight relative to body weight was	REACH Registration dossier: Unpublished study report, 2012m Reliability 2 (Supporting study) Test material: AFS Vehicle: water Non-GLP

SUMMARY OF STUDIES ON REPEATED DOSE TOXICITY - ORAL			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
		increased (1 000 mg/kg/day group).	

Two studies on repeated dose toxicity via the oral route are available in the registration dossier.

In the Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test, rats were exposed by gavage to AFS at concentrations of 0, 10, 50 and 200 mg/kg/d (treatment groups) (OECD TG 422; OECD TG 407; Unpublished study report, 2012s). Five animals/sex/group were exposed for 28 days (Experiment 1). Five animals/sex/group were treated for 28 days with a 1 month-recovery period (Experiment 2). 10 animals/sex/group received exposure to AFS from 30 days prior to and during cohabitation. This lasted until day 3 postpartum for females showing evidence of copulation, and until the day before sacrifice for males and females showing no sign of copulation.

No treatment-related effects were observed on clinical signs and mortality, food efficiency, haematology, clinical chemistry, neurobehaviour and organ weights. Furthermore, reproductive performance and the offspring remained unaffected.

Some treatment-related effects on histopathology could be noted. In both experiment 1 and 3, histopathological effects could be observed for the kidneys of male animals (increase in hyaline droplets in cortical tubules) at 200 mg/kg/d, and nasal effects for female animals (degeneration/atrophy of nasal olfactory epithelium) at 50 and 200 mg/kg/d. Therefore, a NOAEL of 10 mg/kg bw/d was derived (based on: act. ingr.).

In the second (short-term repeated dose toxicity) study, rats received concentrations of 0, 30, 500 and 1 000 mg/kg/d of AFS by gavage. A main study (duration of 6 days) and a metabolism study (duration of 7 days) were performed. No guideline was mentioned for this study in the registration dossier (Unpublished study report, 2012m), and the study was not performed to GLP principles. Some histopathological effects were noted in the nose of male and female rats in the highest dose group, however minimal effects were also noted in the other groups including control. Effects on males were observed in the liver (1 000 mg/kg/d group) and in the kidneys (300, 500 and 1 000 mg/kg/d group). Also, for males, there was an increased brain weight relative to body weight in the 1 000 mg/kg/d group. The NOAEL was stated to be 1 000 mg/kg bw/d (based on: act. ingr.).

In summary, the first study showed no treatment-related effects on clinical signs and mortality, food efficiency, haematology, clinical chemistry, neurobehaviour and organ weights, also reproductive performance and the offspring remained unaffected. However, several treatment-related effects on histopathology were observed. Nevertheless, degeneration/atrophy of nasal olfactory epithelium was not observed after the recovery period.
The second study showed no treatment-related effects on clinical signs. However, effects were noted for gross pathology, and for the nose, liver, kidneys, and brain.

Conclusion: Based on the available data, the Registrant concluded that AFS is not toxic after repeated exposure and the eMSCA agrees with this conclusion. There is no need to request further information on repeated dose toxicity of the Substance in the framework of this Substance Evaluation.

7.9.4.2. Repeated dose toxicity via inhalation route

No data available.

7.9.4.3. Repeated dose toxicity via dermal route

No data available.

7.9.5. Mutagenicity

Table 26: Mutagenicity: *in vitro*

SUMMARY OF STUDIES ON MUTAGENICITY – *IN VITRO*			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 473: *In Vitro* Mammalian Chromosome Aberration Test; EPA OPPTS 870.5375: *In Vitro* Mammalian Chromosome Aberration Test; EC Directive 2000/32/EC, Annex 4A-B10, No. L 136 Cell type: Human peripheral blood lymphocytes *In vitro*	Conc.: - Preliminary toxicity assay: 10, 50, 100, 250, 500, 1 000, 1 500, 2 810, 5 000 µg/mL - Chromosome assay: 100, 250, 500, 1 000, 2 810, 5 000 µg/mL With and without metabolic activation Metabolic activation system: Aroclor 1254-induced rat liver S9 Controls: DMSO, mitomycin C, cyclophosphamide	Genotoxicity: Negative Cytotoxicity: No (But tested up to precipitating concentrations)	REACH Registration dossier: Unpublished study report, 2012t Reliability 1 (Key study) Test material: AFS Vehicle / Solvent: DMSO GLP
According to OECD TG 471: Bacterial Reverse Mutation Assay. EPA OPPTS 870.5100: Bacterial Reverse Mutation Test. EC Directive 2000/32/EC, Annex 4D-B13/14 No. L136 Species / strain: *S. typhimurium* TA 1535, TA 1537, TA 98 and TA 100 + *E. coli* WP2 uvr A *In vitro*	Conc.: 333, 667, 1 000, 3 333, and 5 000 µg/plate With and without metabolic activation Metabolic activation system: Aroclor 1254-induced rat liver S9 Controls: DMSO, 2-aminoanthracene, benzo[a]pyrene, 2-nitrofluorene, sodium azide, Acridine mutagen ICR-191, 4-nitroquinoline-N-oxide	*S. typhimurium*: - Genotoxicity: Negative - Cytotoxicity: Yes *E. coli*: - Genotoxicity: Negative - Cytotoxicity: No	REACH Registration dossier: Unpublished study report, 2012u Reliability 1 (Key study) Test material: AFS Vehicle / Solvent: DMSO GLP

SUMMARY OF STUDIES ON MUTAGENICITY – *IN VITRO*			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 476: *In Vitro* Mammalian Cell Gene Mutation Test. EPA OPPTS 870.5300: *In Vitro* Mammalian Cell Gene Mutation Test; EU Method B.17: Mutagenicity - In *Vitro* Mammalian Cell Gene Mutation Test Cell type: Mouse lymphoma L5178Y cells *In vitro*	Conc.: - Preliminary toxicity assay: 0.5 – 2 500 µg/mL - Mutation assay: 4h-treatment: 300, 500, 750, 1 000, and 1 250 µg/mL (Without S9 activation) 4h-treatment: 400, 500, 750, 1 000, and 1 250 µg/mL (With S9 activation) 24h-treatment: 5, 15, 25, 50, and 75 µg/mL (Without S9 activation) With and without metabolic activation Metabolic activation system: Aroclor-induced rat liver S9 Controls: 7,12-dimethylbenzanthra-cene, methylmethane-sulfonate	Genotoxicity: Negative Cytotoxicity: Yes	REACH Registration dossier: Unpublished study report, 2012v Reliability 1 (Key study) Test material: AFS Vehicle / Solvent: DMSO GLP

Three *in vitro* studies on genetic toxicity are available in the registration dossier.

The first *in vitro* genetic toxicity test was performed with human peripheral blood lymphocytes according to OECD TG 473 (Unpublished study report, 2012t). Concentrations of AFS ranged from 10 to 5 000 µg/mL for the preliminary toxicity assay, and from 100 to 5 000 µg/mL for the chromosome assay. The assay was negative for the induction of chromosome aberrations in the absence and presence of S9-activation. Validity criteria regarding vehicle controls, untreated negative controls and positive controls were fulfilled.

Another *in vitro* genetic toxicity study using *S. typhimurium* and *E. coli* as test species was performed according to OECD TG 471 (Unpublished study report, 2012u). AFS was used in concentrations from 333 to 5 000 µg/plate. Cytotoxicity was noted for the *S. typhimurium* strain TA100, both with and without S9 metabolic activation, beginning at a concentration of 3 333 µg/plate. For *E. coli* no cytotoxicity was observed. No test substance precipitation was apparent. Genotoxicity was scored as negative for both the *S. typhimurium* and *E. coli* strains, with and without metabolic activation. Validity criteria regarding vehicle controls, untreated negative controls and positive controls were fulfilled.

Mouse lymphoma L5178Y cells were used as study subject in the third *in vitro* genetic toxicity study according to OECD TG 476 (Unpublished study report, 2012v). Concentrations of AFS ranged from 0.5 to 2 500 µg/mL for the preliminary toxicity assay, and for the mutation assay from 300 to 1 250 µg/mL in the 4h-treatment (with and without metabolic activation) and from 5 to 75 µg/mL in the 24h-treatment (without metabolic activation). Genotoxicity was negative with and without metabolic activation. Cytotoxicity was however positive, at ≥ 2 500 µg/mL (4h-treatment) and starting from a concentration of ≥ 500 µg/mL (24h-treatment), in the preliminary toxicity assay. Validity criteria regarding vehicle controls and positive controls were fulfilled. Validity of untreated negative controls was not examined.

In summary, all three *in vitro* studies on mutagenicity indicate that the Substance is negative for genotoxicity. Cytotoxicity is only observed for the *S. typhimurium* strain in the second study, and for mouse lymphoma cells in the third study; but not for the human peripheral blood lymphocytes in the first study, and not for the *E. coli* strain in the second study.

Conclusion: AFS does not exert mutagenic properties *in vitro*.

Table 27: Mutagenicity: *in vivo*

SUMMARY OF STUDIES ON MUTAGENICITY – *IN VIVO*			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 474: Mammalian Erythrocyte Micronucleus Test Test species: Mouse (Crl:CD1(ICR)), both sexes *In vivo*	Gavage Single exposure Conc.: 0, 500, 1 000, and 2 000 mg/kg/d No. of animals: - 0, 500 and 1 000 mg/kg/d: 5 animals/sex/group - 2 000 mg/kg/d: 7 animals/sex/group Obs. period: Directly after exposure + until 72h after exposure Controls: Cyclophosphamide; Conc.: 30 mg/kg/d	Genotoxicity: Negative Toxicity: No	REACH Registration dossier: Unpublished study report, 2014b Reliability 1 (Key study) Test material: AFS Vehicle: Deionized water GLP

An *in vivo* genetic toxicity study was performed with mice according to OECD TG 474 (Unpublished study report, 2014b). AFS was administered in concentrations of 0, 500, 1 000, and 2 000 mg/kg/d by gavage as a single exposure. Genotoxicity was negative and no toxicity was noted in the study. No biologically relevant increases in micronuclei were observed from peripheral blood reticulocytes (RETs) of the bone marrow. Validity criteria regarding vehicle, negative and positive controls were fulfilled.

Conclusion: AFS does not exert mutagenic properties *in vivo*.

7.9.6. Carcinogenicity

No data available.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

Table 28: Toxicity to reproduction (fertility and developmental toxicity)

SUMMARY OF STUDIES ON REPRODUCTIVE TOXICITY			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 422: Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test. EPA OPPTS 870.3650: Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test Test species: Rat (Crl:CD(SD)), both sexes	Gavage *Experiment 1:* 5 animals/sex/group, duration of exposure = 28d *Experiment 2:* 5 animals/sex/group, duration of exposure = 28d with 1 month of recovery *Experiment 3:* 10 animals/sex/group, duration of exposure = 30 days prior to and during cohabitation until day 3 postpartum for females showing evidence of copulation (for other animals until day before sacrifice) Conc.: 0, 10, 50 and 200 mg/kg/d Daily	NOAEL (P0): 10 mg/kg bw/d based on: act. ingr. NOAEL (F1): 200 mg/kg bw/d based on act. ingr. Clinical signs and mortality: no treatment-related effects Food efficiency: no treatment-related effects Haematology: no treatment-related effects Clinical chemistry: no treatment-related effects Neurobehaviour: no treatment-related effects Organ weights: no treatment-related effects Histopathology: *Experiment 1:* Males: increase in hyaline droplets in cortical tubules (kidneys) of mild severity at 200 mg/kg/d and minimal severity at 50 mg/kg/d; minimal to mild degeneration/atrophy of nasal olfactory epithelium of 2/5 animals in both the male and female groups (200 mg/kg/d group) and in 1/5 females (50 mg/kg/d group). *Experiment 2:* Mild chronic progressive nephropathy in two males (200 mg/kg/d group), one of these also had minimal granular casts. No olfactory lesions observed. *Experiment 3:* Males (P1): increase in hyaline droplets in cortical tubules (kidneys) of mild severity at 200 mg/kg/d and minimal severity at 50 mg/kg/d; minimal to mild	REACH Registration dossier: Unpublished study report, 2012s Reliability 1 (Key study) Test material: AFS Vehicle: deionized water GLP

SUMMARY OF STUDIES ON REPRODUCTIVE TOXICITY			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
		degeneration/atrophy of nasal olfactory epithelium in 3/10 (50 mg/kg/d group) and 2/10 (200 mg/kg/d group) females. In 1 female of the highest dose, the lesions were severe. Reproductive performance (P0): no treatment-related effects General toxicity (F1): no treatment-related effects	

In a Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test, rats were exposed by gavage to AFS at concentrations of 0, 10, 50 and 200 mg/kg/d (treatment groups) (OECD TG 422; Unpublished study report, 2012s). Five animals/sex/group were exposed for 28 days (Experiment 1). Five animals/sex/group were treated for 28 days with a 1 month-recovery period (Experiment 2). 10 animals/sex/group received exposure to AFS from 30 days prior to and during cohabitation. This lasted until day 3 postpartum for females showing evidence of copulation, and until the day before sacrifice for males and females showing no sign of copulation.

No treatment-related effects were observed on clinical signs and mortality, food efficiency, haematology, clinical chemistry, neurobehaviour and organ weights.

Some treatment-related effects on histopathology could be noted. In both experiment 1 and 3, histopathological effects could be observed for the kidneys of male animals (increase in hyaline droplets in cortical tubules) at 200 mg/kg/d, and nasal effects for female animals (degeneration/atrophy of nasal olfactory epithelium) at 50 and 200 mg/kg/d. Therefore, a NOAEL (P0) of 10 mg/kg bw/d was derived (based on: act. ingr.). No effects were observed regarding reproductive performance (P0) and general toxicity of the offspring (F1). The NOAEL (F1) for reproductive toxicity was set equal to 200 mg/kg bw/d, which is also the highest concentration tested.

In summary, no treatment-related effects on clinical signs and mortality, food efficiency, haematology, clinical chemistry, neurobehaviour and organ weights were observed. However, several treatment-related effects on histopathology were observed. No treatment-related effects were observed regarding reproductive performance (P0) and general toxicity (F1).

Conclusion: Based on the available data, the Registrant concluded that AFS is not reprotoxic and the eMSCA agrees with this conclusion. Sufficient information is available for this endpoint. There is no need to request further information on reproductive toxicity of the Substance in the framework of this Substance Evaluation.

7.9.8. Specific investigations: Neurotoxicity

Table 29: Neurotoxicity

SUMMARY OF STUDIES ON NEUROTOXICITY			
Method	**Administration / exposure and doses / concentrations**	**Results**	**References / Remarks**
According to OECD TG 422: Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test; OECD TG 407: Repeated Dose 28-Day Oral Toxicity Study in Rodents; EPA OPPTS 870.3650: Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test. EPA OPPTS 870.3050: Repeated Dose 28-Day Oral Toxicity Study in Rodents Test species: Rat (Crl:CD(SD)), both sexes	Gavage *Experiment 1:* 5 animals/sex/group, duration of exposure = 28d *Experiment 2:* 5 animals/sex/group, duration of exposure = 28d with 1 month of recovery *Experiment 3:* 10 animals/sex/group, duration of exposure = 30 days prior to and during cohabitation until day 3 postpartum for females showing evidence of copulation (for other animals until day before sacrifice) Conc.: 0, 10, 50 and 200 mg/kg/d Daily	NOAEL: 200 mg/kg bw/d based on: act. Ingr. Neurobehavioural parameters: no treatment-related effects (See table 25 and table 28 for more elaborate explanations on the other results derived from the study)	REACH Registration dossier: Unpublished study report, 2012s Reliability 1 (Supporting study) Test material: AFS Vehicle: deionized water GLP

This study (Unpublished study report, 2012s) has already been discussed in section 7.9.4.1. (Repeated dose toxicity via oral route) and in section 7.9.7. (Toxicity to reproduction (effects on fertility and developmental toxicity)). Additionally, a NOAEL for neurotoxicity of 200 mg/kg bw/d (based on: act. ingr.) was derived, which is also the highest concentration tested.

Conclusion: Based on the available data, the Registrant concluded that AFS is not a selective neurotoxicant and the eMSCA agrees with this conclusion. Sufficient information is available for this endpoint. There is no need to request further information on neurotoxicity of the Substance in the framework of this Substance Evaluation.

7.9.9. Hazard assessment of physico-chemical properties

Not assessed.

7.9.10. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

Not assessed.

7.9.11. Conclusions of the human health hazard assessment and related classification and labelling

Based on the available data, AFS (considering its properties as parent compound) should not be classified for human health.

7.10. Assessment of endocrine disrupting (ED) properties

7.10.1. Endocrine disruption – Environment

In the conclusion document for EC No 241-527-8[12] and EC No 218-407-9[13], the German CA concluded that the available data clarifies that PFHxA acts as an ED for the environment in accordance with the Endocrine Disruptor (ED) definition of the World Health Organisation (WHO). However, there is no official identification of PFHxA as ED by RAC or MSC.

6:2 FTS(A) is a degradation product of AFS. Based on the available information in literature (see below), a concern for thyroid hormones disruption was identified during substance evaluation in 2018.

Developmental toxicity

6:2 FTAB, a structurally related substance and precursor to 6:2 FTS (as described in section 7.7.1.3.), has been shown to induce **developmental toxicity in zebrafish embryos**.

Shi *et al*. (2018) performed a study on developmental toxicity induced by 6:2 FTAB. For this purpose, zebrafish (*Danio rerio*) embryos were exposed to different concentrations of 6:2 FTAB (0, 5, 10, 20, 40, 60, 80, and 100 mg/L) from 6 to 120 hours post-fertilization (hpf) in 6-well plates. In the tail region some morphological defects were observed. In the 20 and 40 mg/L 6:2 FTAB-treated groups, embryos exhibited rough-edged skin/fins. Furthermore, a large number of apoptotic cells was observed in the tail area of the 40 mg/L 6:2 FTAB-treatment group. Some embryos (10% and 23.3% of the 20 and 40 mg/L 6:2 FTAB-treatment group, respectively) were also observed to have uninflated swim bladders at 120 hpf. Since 6:2 FTAB is quickly metabolized (Moe *et al*., 2012; described in section 7.7.1.3.), the developmental toxicity induced by 6:2 FTAB, as demonstrated in this study, might (partly) be caused by one of its metabolization products.

Effects of excessive thyroid hormones administration

Excessive **administration of thyroid hormones was seen to cause similar effects on zebrafish embryos** as the effects that were induced by 6:2 FTAB in the study of Shi *et al*. (2018).

[12] Substance Evaluation Conclusion Document on EC No 241-527-8. 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl acrylate. April 2023. Evaluating Member State: Germany. https://echa.europa.eu/documents/10162/5c201ae4-8b10-ca18-df24-7ae5a7f83e37

[13] Substance Evaluation Conclusion Document on EC No 218-407-9. 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl methacrylate. April 2023. Evaluating Member State: Germany. https://echa.europa.eu/documents/10162/15a5aaeb-0159-d730-c4f7-66c8dd85a8b4

Brown (1997) studied the influence of excessive administration of thyroid hormones on the development of the zebrafish and the Mexican axolotl (*Ambystoma mexicanum*). Zebrafish larvae were continuously exposed to 30 nM T4 starting from 11 days post-fertilization (dpf). The T4-treatment resulted in an early onset of fin development; pectoral fins of zebrafish larvae were seen to develop as early as the appearance of the unpaired fins. Pectoral fins of the T4-treated group were also seen to be larger than those of the control group, at the same stage. The Mexican axolotl also showed such an early onset of morphological changes. An addition of 30 nM T4 to the water of axolotls was performed starting from 14 dpf. Gills of T4-treated Mexican axolotls increased proportionately in size with the animal's growth and quickly resembled adult gills.

Liu and Chan (2002) also performed a study on the effects of excessive administration of thyroid hormones on the development of zebrafish embryos. An important observed effect was a deflation of the swim bladder by 5 dpf, after exogenous treatment of zebrafish embryos with 30 nm T4. The swim bladder was buoyant at 4 dpf, but a reduction of volume in the air chamber, due to exogenous exposure to T4, resulted in a deflation 24 hours later. Furthermore, T4-treatment led to an altered pigmentation in zebrafish embryos. Melanophores over the dorsal surface of the swim bladder in the T4-treated group showed an abnormal small, fragmented pattern, likely caused by the aggregation of melanin.

Similar effects were seen after treatment of zebrafish embryos from 0 to 120 hpf with 500 µM T3, such as deflated swim bladders and reductions in melanophore size and density (Jomaa *et al*., 2014).

7.10.2. Endocrine disruption - Human health

Not assessed.

7.10.3. Conclusion on endocrine disrupting properties (combined/separate)

At first it was considered that the ED concern was not clarified for a relevant degradation product of AFS, i.e., 6:2 fluorotelomer sulfonate (6:2 FTS), and that additional information needed to be generated. A Draft Decision was written to address the concern regarding 'potential endocrine disruptor' for 6:2 fluorotelomer sulfonate (6:2 FTS), a degradation product of AFS. The intention was to request an Amphibian Metamorphosis Assay (AMA) according to OECD TG 231 with Potassium 6:2 fluorotelomer sulfonate (K-6:2 FTS). The Draft Decision was referred to the Member State Committee (MSC) on 12 May 2020.

However, due to the restriction (proposal) for "Undecafluorohexanoic acid (PFHxA), its salts and related substances" that was then submitted, the Draft Decision for AFS was withdrawn after the MSC-70 meeting on 8 July 2020. This is because AFS was formally acknowledged as a 'related substance' to PFHxA. AFS is therefore included in the restriction (proposal) for PFHxA.

Furthermore, in April 2023, in the conclusion document for EC No 241-527-8[14] and EC No 218-407-9[15], the German CA concluded that the available data clarifies that PFHxA acts as an ED for the environment in accordance with the Endocrine Disruptor (ED) definition of the World Health Organisation (WHO). However, there is no official identification of PFHxA as ED by RAC or MSC.

[14] Substance Evaluation Conclusion Document on EC No 241-527-8. 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl acrylate. April 2023. Evaluating Member State: Germany. https://echa.europa.eu/documents/10162/5c201ae4-8b10-ca18-df24-7ae5a7f83e37

[15] Substance Evaluation Conclusion Document on EC No 218-407-9. 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl methacrylate. April 2023. Evaluating Member State: Germany. https://echa.europa.eu/documents/10162/15a5aaeb-0159-d730-c4f7-66c8dd85a8b4

The eMSCA decided to conclude the substance evaluation of AFS, thereby leaving the ED concern of 6:2 FTS unresolved. While the eMSCA has a concern regarding the ED properties of 6:2 FTS, the eMSCA does not consider it proportionate to follow up on these with further information requirements or potential SVHC identification according to Art. 57 as it is expected that the two substances (AFS and 6:2 FTS) fall under the scope of the restriction of PFHxA and precursors, thereby ultimately limiting their further impact on the environment.

7.11. PBT and vPvB assessment

As indicated earlier in this assessment report, not only the PBT/vPvB properties of the parent compound Amphoteric Fluorinated Surfactant (AFS) are evaluated, but also the PBT/vPvB profile of the degradation products, in particular the relevant degradation product Perfluoroheptanoic acid (PFHpA).

Parent compound Amphoteric Fluorinated Surfactant (AFS)

For the parent compound AFS, several biodegradability studies are available (three ready tests and one inherent biodegradability test) (See section 7.7.1.2). Although the pass level is only reached once (for the OECD TG 306 study) in the available ready and inherent biodegradability studies, the extent of observed biodegradation is always substantial. Also taking into consideration the chemical structure of the parent compound, primary degradation should occur quite readily. Therefore, the eMSCA considers that the parent compound AFS does not meet the P-criterion.

The highest measured BCF-value for AFS is 3.01 L/kg and the measured log K_{ow}-value of AFS amounts to 1.35. Since this measured log K_{ow}-value is less than 2, it is considered that AFS is not bioaccumulative, nor for aquatic organisms, nor for terrestrial organisms.

A series of ecotoxicity studies with the parent compound AFS on fish, aquatic invertebrates, algae, and earthworms were executed. In none of these studies substantial toxicity was observed, and the T-criterion is not fulfilled.

A series of studies regarding toxicity to human health were performed with the parent compound AFS. The T-criterion is not fulfilled for any of these studies.

In summary, it is concluded that the parent compound Amphoteric Fluorinated Surfactant (AFS) is not a PBT/vPvB substance.

Relevant degradation product Perfluoroheptanoic acid (PFHpA)

Perfluoroheptanoic acid and its salts (EC No: -; CAS No: -) is identified as an SVHC, meeting the criteria of Article 57 (c), hazard class toxic for reproduction category 1B; (d), persistent, bioaccumulative and toxic (PBT); (e), very persistent and very bioaccumulative (vPvB); and (f), equivalent level of concern having probable serious effects to human health and to the environment. Agreement in MSC has been reached on 28 November 2022. For the full argumentation regarding the SVHC identification, the eMSCA refers to the Member State Committee Support Document (ECHA Member State Committee, 2022). On 17 January 2023, "Perfluoroheptanoic acid and its salts" was included as an SVHC in the Candidate List for eventual inclusion in Annex XIV (ECHA Decision, 2022).

Considering the implication of the identification of "Perfluoroheptanoic acid and its salts" as an SVHC, for substances which transform and/or degrade to PFHpA, this is reported in Chapter R.11 (ECHA, 2017: ECHA Guidance on PBT/vPvB assessment, p. 25):

'If a registered substance contains a constituent, impurity or additive or transforms/degrades to a substance which is in the Candidate List because of meeting the

PBT and/or vPvB criteria, the registrant must conclude his substance to meet the PBT or vPvB criteria accordingly.'

7.12. Exposure assessment

Not applicable.

7.13. Risk characterisation

Not applicable.

7.14. References

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7.15. Abbreviations

act. ingr.:	active ingredient
AFS:	Amphoteric Fluorinated Surfactant
AMA:	Amphibian Metamorphosis Assay
BCF:	Bioconcentration factor
Bw:	body weight
CA:	competent authority
C&L:	Classification & Labelling
CLP:	Classification, Labelling and Packaging
Conc.:	concentration
DW:	dry weight
ED:	Endocrine Disruptor
eMSCA:	evaluating Member State Competent Authority
EU:	European Union
4:2 FTUA:	4:2 fluorotelomer unsaturated acid
5:3 FTCA:	5:3 fluorotelomer carboxylic acid
6:2 FTAB:	6:2 fluorotelomer sulfonamide alkylbetaine
6:2 FTCA:	6:2 fluorotelomer carboxylic acid
6:2 FTOH :	6:2 fluorotelomer alcohol
6:2 FTS :	6:2 fluorotelomer sulfonate
6:2 FTSA :	6:2 fluorotelomer sulfonic acid
6:2 $FTSO_2NH_2$:	6:2 fluorotelomer sulfonamide
6:2 FTUA :	6:2 fluorotelomer unsaturated carboxylic acid
GLP:	Good Laboratory Practice
K-6:2 FTS:	Potassium 6:2 fluorotelomer sulfonate
LC_{50}:	concentration that is lethal for 50 % of the tested organisms.
LD_{50}:	dose that is lethal for 50 % of the tested organisms.
LLNA:	local lymph node assay
MCI:	molecular connectivity index
MSC:	Member State Committee
Nb. or No.:	number

NOAEL:	no observed adverse effect level
Obs.:	observation
OECD:	Organisation for Economic Co-operation and Development
OPPTS:	Office of Prevention, Pesticides and Toxic Substances, US EPA
PBT:	Persistent, Bioaccumulative and Toxic
PFBA:	perfluorobutanoic acid
PFCA:	perfluorinated carboxylic acid
PFHpA:	perfluoroheptanoic acid
PFHxA:	perfluorohexanoic acid
PFPeA:	perfluoropentanoic acid
RAC:	Committee for Risk Assessment
RET:	reticulocytes
SEAC:	Committee for Socio-economic Analysis
SD:	Sprague-Dawley
SI:	stimulation index
SVHC:	Substance of Very High Concern
TG:	Test Guideline
vPvB:	very Persistent and very Bioaccumulative
WWTP:	wastewater treatment plant