baua:
Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin
Federal Institute for Occupational
Safety and Health

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Ammonium 2,2,3 trifluor-3-(1,1,2,2,3,3-hexafluoro-3-trifluormethoxypropoxy), propionate

EC No 480-310-4

Evaluating Member State(s): Germany

Dated: 22 December 2020

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Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2017

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

The Substance, Ammonium 2,2,3 trifluor-3-(1,1,2,2,3,3-hexafluoro-3-trifluormethoxypropoxy), propionate (ADONA) was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB properties

- Wide dispersive use

- Exposure of environment

During the evaluation another concern was identified. The additional concern was:

- High mobility in water and soil and a possible impact on drinking water sources

The assessment under substance evaluation was targeted on the environmental and ecotoxicological properties of the substance.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

There are no other processes known.

3. CONCLUSION OF SUBSTANCE EVALUATION

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

Table 1

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
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

4. FOLLOW-UP AT EU LEVEL

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

4.1.1. Restriction

ADONA is a member of the group of per-and polyfluoroalkyl substances (PFAS). PFAS are highly persistent in the environment (or degrade to highly persistent degradation products) and have potential to contaminate groundwater, surface water and soil.

The presence of the substances in the environment is practically irreversible, and pose an unacceptable risk to the environment and humans. A broad restriction of PFAS (including ADONA) will be the most appropriate risk management measure to minimize concentrations of these persistent substances in the environment.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

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

Not applicable, see section 4.

5.2. Other actions

Regulation out of REACH is possible (e.g. Groundwater Directive or EU Water Framework Directive).

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

Indication of a tentative plan is not a formal commitment by the evaluating Member State. A commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier should be made via the Registry of Intentions.

Table 2

Follow-up		
Follow-up action	Date for intention	Actor
Annex XV dossier for restriction (broad restriction for substance group PFAS)	2021	Germany, the Netherlands, Norway, Sweden and Denmark

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Ammonium 2,2,3 trifluor-3-(1,1,2,2,3,3-hexafluoro-3-trifluormethoxypropoxy), propionate (ADONA) was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB properties

- Wide dispersive use

- Exposure of environment

During the evaluation also another concern was identified. The additional concern was:

- High mobility in water and soil and a possible impact on drinking water sources.

The assessment under substance evaluation was targeted on the environmental and ecotoxicological properties of the substance.

Table 3

Evaluated endpoints	
Endpoint evaluated	Outcome/conclusion
s	Taking together all available information a full PBT assessment with consideration of the knowledge from the PFOA-PBT assessment cannot be performed. The substance will most probably fulfil the (v)P criterion of REACH Annex XIII. The bioaccumulation potential cannot be refuted based on the lessons learned from the PFOA PBT assessment. Based on the data for environmental toxicity, the substance does not fulfil the T criterion. The registration dossier presently lacks toxicological information relevant to humans. Thus, the data are not sufficient to conclude or to refute on the PBT-properties of the substance.
Wide dispersive use	Wide dispersive use was evaluated due to a concern regarding the suspicion that ADONA occurs as relevant impurity in the final polymers. ADONA is present in trace limits in the final fluoropolymers. The eMSCA concludes that a wide dispersive use of ADONA itself does not occur since there is only one manufacturing site that at the same time is the only site of industrial use within the EU. However, a wide dispersive release via fluoropolymers that may contain trace levels of ADONA cannot be excluded. Concern not fully refuted.
Exposure to the environment	Actions already taken by the registrants are considered as important risk management measures by the eMSCA to ensure a low risk of environmental exposure. However, ADONA is still released into air and waste water in a relevant amount. Further risk management measures for further reduction of local releases by the manufacturer are needed. During processing of polymers, ADONA decomposes to a shorter chain perfluorinated ether (identity claimed confidential by the registrant). According to the registrant there are minor releases into air and water at the manufacturing site. It is not known by the eMSCA if the degradation product is created also at downstream users sites during processing of fluoropolymers and during the use of articles and mixtures containing fluoropolymers manufactured with ADONA. Further risk management is needed as the degradation product is expected to have similar concerns (persistent and highly mobile).

Mobility	The low adsorption potential of the substance indicates a high mobility in water and soil.

7.2. Procedure

The Substance, Ammonium 2,2,3 trifluor-3-(1,1,2,2,3,3-hexafluoro-3-trifluormethoxypropoxy), propionate (ADONA) was included in the Community Rolling Action Plan for substance evaluation 2015-2017 which was published on 17 March 2015 and was scheduled for evaluation in 2017. The Member State Competent Authority of Germany was appointed to carry out the evaluation.

In the assessment, environmentally relevant endpoints have been considered. Potential risks to human health have not been assessed.

Regarding the suspected environmental effects of ADONA, the eMSCA focused on the PBT properties, the mobility and on exposure assessment in this substance evaluation. The evaluation was based on the registration dossier, peer-reviewed publications from the scientific literature and on personal communication with the registrant.

In July 2017, a meeting with the registrant took place. The registrant provided further data on uses.

The evaluating MSCA concluded that ADONA is suspected to be mobile in water and soil. The concern regarding persistency was also confirmed.

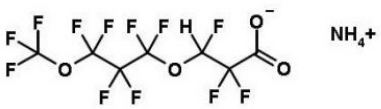
7.3. Identity of the substance

Table 4: Substance identity.

Public name:	ammonium 2,2,3 trifluor-3-(1,1,2,2,3,3-hexafluoro-3-trifluormethoxypropoxy), propionate
EC number:	480-310-4
CAS number:	-
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	$C_7H_5F_{12}NO_4$
Molecular weight range:	395.1 g/mol
Synonyms:	ADONA

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

Structural formula:



7.4. Physico-chemical properties

Table 5

Overview of physicochemical properties.	
Property	Value
Physical state at 20°C and 101.3 kPa	Colourless liquid (visual inspection)*
Vapour pressure	1.9 kPa at 20°C (OECD 104, dynamic method)
Water solubility	miscible, ≥500 g/L (The substance is used as an aqueous solution)
Partition coefficient n-octanol/water (Log Kow)	1.3 at 25 °C and pH 7.1 (Ionic substance, log P for anion only, OECD 117 HPLC method)
Granulometry	n.a. (waiving in accordance with column 2 of REACH Annex VII)

* study used for the determination of physical-chemical property was conducted with a 30% aqueous solution of the substance.

7.5. Manufacture and uses

7.5.1. Quantities

Table 6

Aggregated tonnage (per year)				
☒ 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

ADONA is mainly used as a processing aid for the production of fluoropolymers. ADONA is present in trace levels in the final polymers. Fluoropolymers are widely used, e.g in food contact materials.

Table 7

Overview of uses	
	Use(s)
Uses as intermediate	-
Formulation	-
Uses at industrial sites	Use as industrial processing aid for fluoropolymer production
Uses by professional workers	-
Consumer Uses	Occurs in trace levels in the final polymers
Article service life	-

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

No entry in Annex VI of CLP Regulation available.

7.6.2. Self-classification

- In the registration(s):
  - Acute Tox. 4 (H302)
  - Eye irrit. 2 (H319)
  - Skin Sens. 1B (H317)

No additional hazard classes have been notified in addition in the C&L inventory.

7.7. Environmental fate properties

7.7.1. Degradation

7.7.1.1. Abiotic degradation

7.7.1.1.1. Hydrolysis

Hydrolysis was tested in a OECD TG111 study. The registrant concludes that ADONA is hydrolytically stable at pH 4, 7 and 9 and the half-life was extrapolated to be >1 year.

Table 8

Summary of studies on hydrolysis			
Method	Results	Reliability	Reference
OECD Guideline 111 (Hydrolysis as a Function of pH)	Preliminary test (50°C) % decomposition after 5 days: pH 4: ≤ 0.05 % pH 7: 0.27 – 1.12 % pH 9: ≤ 0.22 % half-life > 1 year	Rel. 2 (key study)	Registration dossier

7.7.1.1.2. Phototransformation / photolysis

No relevant information available.

7.7.1.2. Biodegradation

7.7.1.2.1. Screening tests

Biodegradation of ADONA was tested in one screening test. Only 6 % degradation was shown within 28 days (see Table 9).

Table 9

Summary of screening tests			
Method	Results	Reliability	Reference
OECD Guideline 301 B (Ready Biodegradability: CO2 Evolution Test) Non-adapted inoculum	degradation of test substance: 6 % after 28 days (CO2 evolution) Toxicity control: 36 % degration in 14 days Reference substance: 74 % degradation by day 14	1 (key study)	Registration dossier

7.7.1.2.2. Simulation tests

No simulation test is available.

7.7.1.2.3. Estimated data

An estimation of degradation half-lives via US EPA EPIsuite was performed by Gomis et al. (Gomis et al., 2015). BIOWIN3 outputs were converted into half-lives with the conversion scheme proposed by Aronson and co-workers (Aronson et al., 2006). The half-lives were estimated for the neutral form of ADONA. For water and for soil, half-lives of 240 days were estimated. Nevertheless, the authors note that the predictive power of BIOWIN3 for per- and polyfluoroalkyl substances is limited.

Based on BIOWIN v4.10 the substance (neutral form of ADONA) is considered to be potentially persistent or very persistent:

BIOWIN 1: –1.3106 (does not biodegrade fast)

BIOWIN 2: 0 (does not biodegrade fast)

BIOWIN 3: 1.3495 (recalcitrant)

BIOWIN 4: 2.7802 (weeks)

BIOWIN 5: 0.3642 (not readily degradable)

BIOWIN 6: 0 (not readily degradable)

BIOWIN 7: –0.9944 (does not biodegrade fast)

Ready biodegradability prediction: no

According to REACH guidance document R.11, a substance is potentially persistent or very persistent if the following screening criteria are fulfilled: BIOWIN 2 value < 0.5 and BIOWIN 3 value < 2.25 or BIOWIN 6 value < 0.5 and BIOWIN 3 value < 2.25. The values for ADONA are well below these screening criteria.

However, there are some limitations for the predictions of perfluorinated compounds with BIOWIN. This is because the training data set is incompletely implemented for perfluorinated carbon chains. Nevertheless, as it is considered that the perfluorinated carbon chain is expected to be very stable but is not properly included in the BIOWIN model, it can be concluded that the persistence of perfluorinated substances will be underestimated by the BIOWIN predictions.

7.7.1.3. Summary and discussion on degradation

ADONA is hydrolytically stable at pH 4, 7, and 9.

The substance is not readily biodegradable as shown by a screening test. Only 6 % degradation was shown within 28 days. The lack of biodegration is also supported by QSAR predictions.

At temperatures above 190 °C which is used for processing of the polymers, ADONA decomposes to a shorter chain perfluorinated ether (identity claimed confidential by the registrant).

ADONA belongs to the group of perfluoroether carboxylic acids. These substances are structurally similar to perfluoroalkyl carboxylic acids (e.g. perfluorooctanoic acid), with an acidic functional group attached to a per- and polyfluoroether chain instead of a perfluoroalkyl chain. Under environmentally relevant conditions, perfluoroether chains are similarly resistant to abiotic (photolysis, reactions with OH radicals, and hydrolysis) and biotic degradation as the perfluoroalkyl chains (Wang et al., 2015).

The stability of organic fluorine compounds has been described in detail by Siegemund et al. (Siegemund et al., 2000): “When all valences of a carbon chain are satisfied by fluorine, the zig-zag-shaped carbon skeleton is twisted out of its plane in the form of a helix. This situation allows the electronegative fluorine substituents to envelope the carbon skeleton completely and shield it from chemical attack. Several other properties of the carbon-fluorine bond contribute to the fact that highly fluorinated alkanes are one of the most stable organic compounds. These include polarisability and high bond energies, which increase with increasing substitution by fluorine. The influence of fluorine is greatest in highly fluorinated and perfluorinated compounds. Properties that are exploited commercially include high thermal and chemical stability”.

Based on their molecular properties perfluorinated compounds can be expected to be poorly degradable. A number of perfluoroalkyl substances have been concluded as very persistent under the SVHC process[2]. This includes: PFOA and its ammounium salt, C9-C14 PFCAs as well as the ammonium and sodium salts of C9 and C10 PFCA, perfluorobutane sulfonic acid (PFBS) and its salts, perfluorohexanesulfonic acid (PFHxS) and its salts, and 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, its salts and its acyl halides.

In conclusion, the eMSCA concludes that ADONA most probably fulfils the P and the vP criteria of REACH Annex XIII.

7.7.2. Environmental distribution

ADONA is an ionisable substance which will dissociate in soils and surface waters to form ammonium ions, which are subject to nitrogen cycling in the environment, and DONA anions. The adsorption of the DONA anions was determined according to OECD 121 guideline using the HPLC method. The log Koc was estimated to be < 1.3 at 20 °C (Registration dossier). The value indicates that the substance has a low adsorption potential to organic carbon in soil and sewage sludge.

ADONA was found in the rivers Rhine and Waal in concentrations between 79 – 347 pg/L (Heydebreck, 2017). This indicates further occurence of uses or releases of ADONA in Germany not only in the vicinity of the production site. The Bavarian State Office for Health and Food Safety continuously investigated perfluoroalkyl substances in drinking water of one administrative district (Altötting) from November 2016 until autumn 2018. The concentrations of DONA (dissociated anion from ADONA) were at or below the detection limit (≤ 0.004 µg/L) at all sampling points. However, the authority also stated that wells known to be polluted with per-and polyfluoroalkyl substances (PFASs) were not used anymore, instead, the drinking water was used from other wells (Bavarian State Office for Health and Food Safety, 2018).

7.7.3. Bioaccumulation

[2] https://echa.europa.eu/de/candidate-list-table

Table 10

Studies on aquatic bioaccumulation			
Method	Result	Remark	Reference
Cyprinus carpio aqueous (freshwater) flow-through Total uptake duration: 34 d	BCF: 0.094 whole body w.w. (Time of plateau: 34 d)(steady state) (34d BCF of ADONA at a concentration of 0.1 mg/L active ingredient was 0.094 ± 0.0071.)	1 (reliable without restriction) key study experimental result Test material: ADONA	Registration dossier

The given log KOW is 1.3. ADONA is completely dissociated under environmentally relevant conditions, and the substance potentially binds to proteins, as outlined below. For these reasons, the low log KOW of ADONA cannot be considered as a sufficiently valid descriptor to rule out a bioaccumulation potential. Other mechanisms than the sole partitioning of ADONA to lipids may drive bioaccumulation (e.g. binding to proteins).

The registrants provide one study on aquatic bioaccumulation according to OECD 305 with the test organism Cyprinus carpio. The study is a GLP compliant study in a flow-through system. Two test concentrations were tested (1 mg/L and 0.1 mg/L) and verified by analytical monitoring. At none of the concentrations used for testing mortality or adverse effects were observed. A depuration phase was not conducted as the BCF after the uptake phase of 34 days was below 10 in both test concentrations (BCF (0.1 mg/L)= 0.094; BCF (1 mg/L)= 0.074). The study is reliable without restriction and does not indicate a bioaccumulation potential in fish.

However, bioconcentration values in water breathing organisms may not be the most relevant endpoint to consider. For instance perfluorooctanoic acid (PFOA) shows a low bioaccumumulation potential in fish but field studies show, that air-breathing organisms are more likely to biomagnify PFOA compared to water breathing organisms. Elevated levels of PFOA in human blood and a half-life in humans of 2-4 years lead to the conclusion that PFOA is bioaccumulative (European Chemicals Agency, 2013).

A review (Ng and Hungerbühler, 2014) investigated compiled data from various studies on tissue distribution. Liver and blood and thus protein rich compartments are important for the accumulation of perfluoroalkyl acids (PFAAs). However, the picture is not consistent for all PFAAs. Also phospholipids may be a potential sink. Arnot and Gobas developed a model in order to predict bioaccumulation of partially charged organic compounds in phospholipids (Arnot and Gobas, 2004). They also successfully predicted the BCFs of perflouroalkyl carboxylates (PFCAs). This shows that also phospholipids could be a potential sink. In their review Ng and Hungerbühler (2014) investigated absorption to phospholipids and absorption to proteins by comparing two models for bioaccumulation. The first model, mentioned by Arnot and Gobas (2004) is based on absorption in phospholipids. The second developed by Ng and Hungerbühler is based on protein binding, i.e. albumin binding, the binding to liver fatty acid binding proteins and organic anion transporters (Ng and Hungerbühler, 2013). The authors conclude that both models were able to predict part of the observed bioaccumulation (Ng and Hungerbühler, 2014).

Furthermore, the review (Ng and Hungerbühler, 2014) elucidates the structural properties of PFCAs and perflourinated sulfonic acids (PFSAs) which may govern their absorption:

- Seen from lab and field data, accumulation increases with chain length and depends on the acidic headgroup. Sulfonic acids show a higher accumulation than carboxylic acids with the same chain length.
- The increase of accumulation with chain length complies with the model of Arnot and Gobas i.e. the chain length dependence of the membrane/water partitioning coefficient.

- The pattern of chain length and protein binding (see for instance (Bischel et al., 2010)) is more complex:
    - The binding affinity to albumin levels off for PFAAs with 6-9 perfluorinated carbons, probably due to steric hindrance and a less flexible tail than hydrocarbontails.
    - Liver fatty acid binding proteins are highly tissue specific and may not all be able to bind PFAAs due to the stiffness of the fluorocarbon chain similarly to albumin. However, one type of liver fatty acid binding protein only expressed in mammals has been reported to bind bulkier ligands and is a potential binding site even for longer chained PFAAs with up to 11 perfluorinated carbons.
    - Organic anion transporters are a class of proteins ubiquitously expressed. Studies with a wide range of perfluorinated chain lengths with renal excretion and reabsorption proteins of rats and humans (Weaver et al., 2010; Yang et al., 2010) show a chain length dependent affinity peaking at 7-8 and 9 respectively.

Gender as well as species-specific expression of organic anion transporters might explain the differences in half-lives as observed for PFOA. They function either as an aid for uptake or elimination depending on their position on the apical or basolateral membrane side. Some organic anion transporters are responsible for reabsorption from urine to blood. The activity of human reabsorption transporters activity was far more pronounced than for rats (Weaver et al., 2010; Yang et al., 2010). ADONA has six perfluorinated carbon atoms, whereas PFOA (which is concluded to be bioaccumulative (B)) has seven perfluorinated carbon atoms. Concluding from the observations described above the chain length of ADONA should not hinder protein binding. However, in contrast to the PFCAs with which the above described observations have been made, ADONA contains two ether bonds.

In conclusion, ADONA may bind to proteins in a similar way as other perfluorinated substances. It may be potentially re-absorbed and may thus have a slower elimination half-life. Thus, ADONA may be accumulating in human blood.

7.7.3.1. Elimination half-lives in humans and animals

Half-lives of ADONA are available for several organisms and humans and listed in

Table 11. No threshold for defining a substance of being bioaccumulative above a certain half-life is available. For being able to compare half-lives of ADONA with half-lives of a substances which is already known to be bioaccumulative (benchmarking), data for PFOA were also included in the table. The clearance time of ADONA in mice, rats, monkeys and humans is an order of a magnitude lower compared to PFOA.

Table 11

Half-Lives of ADONA and PFOA in humans and animals				
Organism	Half-life PFOA (M = male, F = female)	Reference Remark	Half-life ADONA (M = male, F = female)	Reference Remark
Rat	M: 5.6 d, F: 0.08 d	(Ohmori et al., 2003) Mean β-phase of two compartment model with first-order elimination, single IV dose of 48.64 mmol/kg bw	M: 5.8 h, F: 0.86 h	Registration dossier Single IV dose of 28 mg/mL. ADONA was identified in serum and liver samples. First order elimination.
	M: 13 d	(Benskin et al., 2009) β-phase elimination rate, single oral dose, 0.5 mg/kg	Phase 1, phase 2: Males: 0.66 d, 13.3 d; F: 0.12 d, 34.6 d	Registration dossier Biphasic elimination Repeated oral dose: In total 9 mg/kg/day
Mice	M: 22 d, F: 16 d	(Lou et al., 2009) Mean β-phase of one compartment model with first-order elimination, single oral dose of 1 or 10 mg/kg	M: 8,1 h, F: 6.19 h	Registration dossier Single IV dose: 5 mL/Kg body weight of a solution at 5.6 mg/ml. ADONA was identified in serum and liver samples. First order elimination.
Monkey	M: 21 d, F: 33 d	(Butenhoff et al., 2004) Mean β-phase of one-compartment model with first-order elimination, single IV dose of 10 mg/kg	M: 5.7 h, F: 4.2 h	Registration dossier Single IV dose: 28.2 mg test article per kg body weight. First order elimination.
Human workers	M: 3.6 y, F: 3.5 y	(Olsen et al., 2007) Mean β-phase of non-compartment model with first-order elimination, periodic blood samples collected over 5 years	M: 16 – 36 d M: 11 – 44 d	Registration dossier Terminal serum elimination in 3 occupationally exposed workers. Information provided by the registrant during consultation. 6 male employees (aged 21-54) in an area with potential exposure to ADONA.

The half-life of ADONA varies in the species analysed. For PFOA it was found that the half-life in human blood is far higher compared to animals. The reason for the different half-lives in humans and animals is not known. ADONA shows in all studies lower half-lives compared with PFOA. The half-life in human blood was, however, calculated on the basis of altogether nine occupationally exposed workers and ranged between 11 and 44 days. The data may not be sufficient to conclude that ADONA is not bioaccumulating in human blood.

7.7.4. Mobility

ADONA is an ionisable substance which will dissociate in soils and surface waters to form an ammonium ion and a DONA anion. Based on low expected volatility for the ionic components and high water solubility, ADONA will ultimately be present in the aquatic compartment. A log KOC of < 1.3 indicates that the substance has a low adsorption potential to soil and sediments. The high persistence, high water solubility and a low pKa indicate that ADONA also has the ability to be transported readily from river/estuary systems to remote areas over long distances or into the groundwater. Hence, ADONA may

enter groundwater and drinking water resources. Further, the registrant states that ADONA can be removed from surface or groundwater with A-carbon technology.

A study was conducted to measure the ADONA concentration in the vicinity of the production site in 2013 (Schreiber, 2014). The concentration in the upper soil layer reached up to 10.8 µg/kg dry weight. Due to the high mobility of the ADONA-anion concentrations up to 2.1 µg/L could be detected in groundwater after a relatively short period of use. The concentration in the groundwater decreases rapidly down to the detection limit with the distance from the manufacturing site with one exemption. At one sample extraction point, ADONA was found unexpectedly in low concentrations. However, the transportation to that point via groundwater seems not very plausible. Therefore, precipitation from air was discussed by Schreiber. This also could be an indication for the high mobility of ADONA. Three main emission paths were concluded in this study:

- Release of cleared waste water into the river Alz,
- deposition from the air via soil into the groundwater and
- diffuse releases from local point sources on the manufacture site.

Additionally, lysimeter studies and leaching studies in soil columns were performed (Schreiber, 2014). Soil samples were collected in the vicinity of the registrants site in 2013. The studies were performed according to DIN 19528 and DIN 19527. The rate for mobilizing ADONA in different soil types was around 90%. The study concluded also that soils containing a high degree of organic matter showed higher retardation compared with soils containg a lower degree of organic matter.

Lysimeter studies were performed from 2011 to 2013 to analyse the leaching potential of ADONA in three different soils. The lysimeter studies showed contradicting results, e.g. in one lysimeter, ADONA values were measured in concentrations of 20 to 40 ng/L throughout the whole duration of the study. The author concluded that the monolith used may already have been contaminated with ADONA probably via deposition. In another lysimeter, only low amounts of ADONA (4 ng/L) were measured after using a more sophisticated analytical method.

The degradation product of ADONA (formed during fluoropolymer processing steps at high temperature) is released in low volumes to air and water according to the registrant. Interestingly, the same substance was found in a water treatment facility near a fluoropolymer manufacturing plant in the US (Sun et al., 2016). The authors state that there was no meaningful adsorption of this substance and similar perfluorinated ethers to powdered activated carbon. Thus, the degradation product seems to be mobile in water and soil.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

7.8.1.1. Fish

The registrants provided data on the acute toxicity to fish (Table 12). The studies show that ADONA has a low acute toxicity to fish (>100 mg/L). Long term tests are not available.

Table 12

Effects on fish			
Method	Result	Remark	Reference
Cyprinus carpio freshwater static	LC50 (96 h): > 1012 mg/L act. ingr. (nominal) based on: mortality	1 (reliable without restriction) key study experimental result	Registration dossier

OECD Guideline 203 (Fish, Acute Toxicity Test)	ADONA induced no visible or lethal effects at or below 1012 mg a.i./L (corresponding to 3340 mg/L total product)	Test material: ADONA	
Danio rerio freshwater static OECD Guideline 203 (Fish, Acute Toxicity Test)	LC50 (96 h): > 100 mg/L act. ingr. (nominal) based on: mortality ADONA induced no visible or lethal effects at or below 100 mg a.i./L (corresponding to 334 mg/L total product)	1 (reliable without restriction) key study experimental result Test material: ADONA	Registration dossier

7.8.1.2. Aquatic invertebrates

The registration contains data on the toxicity to aquatic invertebrates (Table 13). The studies show that ADONA has a low toxicity to aquatic invertebrates (>100 mg/L).

Table 13

Effects on aquatic invertebrates			
Method	Result	Remark	Reference
Daphnia magna freshwater static OECD Guideline 202 (*Daphnia sp.* Acute Immobilisation Test)	EC50 (48 h): > 100 mg/L act. ingr. (nominal) based on: mobility (Analytically confirmed nominal concentration of active ingredient based on a content of 29.9% in the test product)	1 (reliable without restriction) key study experimental result Test material: ADONA	Registration dossier
Chironomus riparius freshwater static equivalent or similar to ASTM Standard E729-96 Standard Guide for Conducting Acute Toxicity Tests on Test Materials with Fishes, Macro invertebrates, and Amphibians (2007)	LC50 (96 h): > 1000 mg/L act. ingr. (nominal) based on: larval survival ADONA induced no behavior or lethal effects with 96h EC50 > 1000 mg/L active ingredient (analytically confirmed nominal concentration)	2 (reliable with restrictions) key study experimental result Test material: ADONA	Registration dossier
Daphnia magna freshwater semi-static OECD Guideline 211 (*Daphnia magna* Reproduction Test)	NOEC (21 d): 100 mg/L act. ingr. (nominal) based on: reproduction (ADONA did not adversely affect survival, growth, or reproduction of Daphnia magna at analytically confirmed nominal concentration of 100 mg a.i./L, corresponding to 330 mg/L of total product)	1 (reliable without restriction) key study experimental result Test material: ADONA	Registration dossier

7.8.1.3. Algae and aquatic plants

The registration dossier contains data on the toxicity to algae (Table 14). The studies show that ADONA has a low toxicity to algae (>100 mg/L).

Table 14

Effects on algae and aquatic plants			
Method	Result	Remark	Reference
Pseudokirchnerella subcapitata freshwater static OECD Guideline 201 (Alga, Growth Inhibition Test)	EC50 (96 h): > 100 mg/L act. ingr. (nominal) based on: growth rate (Exposure concentrations were based on nominal concentrations as analytical results showed that concentrations were stable and in agreement with nominal (with and without algae) within 99 - 112% during the 96h test period.) NOEC (96 h): 100 mg/L act. ingr. (nominal) based on: growth rate	1 (reliable without restriction) key study experimental result Test material: ADONA	Registration dossier
Pseudokirchnerella subcapitata freshwater static OECD Guideline 201 (Alga, Growth Inhibition Test)	EC50 (72 h): > 1000 mg/L act. ingr. (nominal) based on: growth rate (Exposure concentrations were based on nominal concentrations as analytical results showed that concentrations were stable and in agreement with nominal (with and without algae) within 96% to 113% during the 96h test period.) EC10 (72 h): > 1000 mg/L act. ingr. (nominal) based on: growth rate	1 (reliable without restriction) key study experimental result Test material: ADONA	Registration dossier

7.8.1.4. Sediment organisms

No relevant information available.

7.8.1.5. Other aquatic organisms

No relevant information available.

7.8.2. Terrestrial compartment

No relevant information available.

7.8.3. Microbiological activity in sewage treatment systems

The registrants provided data on the microbiological activity in sewage treatment systems (Table 15). The studies show that ADONA has a low effect on the microbial activity (> 1000 mg/L).

Table 15

Effects on micro–organisms			
Method	Result	Remark	Reference
activated sludge of a predominantly domestic sewage freshwater static OECD Guideline 209 (Activated Sludge, Respiration Inhibition Test)	EC50 (3 h): > 1000 mg/L act. ingr. (nominal) based on: respiration rate (The 3h EC50 of ADONA for inhibition of respiration rate exceeded the nominal concentration of 3340 mg/L total product, which corresponds to 1000 mg/L active ingredient. 3h NOEC of ADONA = 1000 mg/L active ingredient.)	1 (reliable without restriction) key study experimental result Test material: ADONA	Registration dossier

7.8.4. PNEC derivation and other hazard conclusions

A PNEC was not derived by the registrant because no effects were observed in freshwater and sewage treatment plants.

7.8.5. Conclusions for classification and labelling

The acute toxic effects for fish, daphnia and algae are all above 100 mg/L. The chronic toxic effects for daphnia and algae are both above 1 mg/L (for fish no chronic data available). Classification and labelling for aquatic environment is not justified.

7.9. Human Health hazard assessment

Not evaluated.

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.11. PBT and vPvB assessment

Persistence

ADONA is hydrolytically stable and not readily biodegradable. No simulation test is available. Based on BIOWIN predictions ADONA is expected to be (very) persistent.

The substance belongs to the group of perfluoroether carboxylic acids. These substances are structurally similar to perfluoroalkyl carboxylic acids (e.g. perfluorooctanoic acid), with an acidic functional group attached to a per- and polyfluoroether chain instead of a perfluoroalkyl chain. Under environmentally relevant conditions perfluoroether chains are similar resistant to abiotic and biotic degradation as the perfluoroalkyl chains.

The stability of organic fluorine compounds has been described in detail by Siegemund et al. (Siegemund et al., 2000): “When all valences of a carbon chain are satisfied by fluorine, the zig-zag-shaped carbon skeleton is twisted out of its plane in the form of a helix. This situation allows the electronegative fluorine substituents to envelope the carbon skeleton completely and shield it from chemical attack. Several other properties of the carbon-fluorine bond contribute to the fact that highly fluorinated alkanes are one of the most stable organic compounds. These include polarisability and high bond energies, which increase with increasing substitution by fluorine. The influence of fluorine is greatest in highly fluorinated and perfluorinated compounds. Properties that are exploited commercially include high thermal and chemical stability”.

Based on their molecular properties, perfluorinated compounds can be expected to be poorly degradable. A number of perfluoroalkyl substances have been concluded as very persistent under the SVHC process.

Hence, ADONA is expected to be very persistent.

Bioccumulation

Based on the findings and data it cannot be concluded that the substance is not bioaccumulative. An OECD 305 study with carp does not indicate a bioaccumulation potential in fish.

However, bioconcentration values in water breathing organisms may not be the most relevant endpoint to consider. As shown for PFOA, there is a low bioaccumulation potential in fish but elevated levels of PFOA in human blood and a half-life in humans of 2-4 years. The clearance time of ADONA in mice, rats and monkeys is an order of a magnitude lower compared to PFOA. Two studies with occupationally exposed workers show a half-life of 11-44 days. No threshold for defining a substance of being bioaccumulative above a certain half-life is available.

Observations with PFAAs show a chain length dependent binding to proteins. ADONA may bind to proteins similary. It may be potentionally re-absorbed and may thus have a slower elimination half-life in human blood. Thus, ADONA may be accumulating in human blood. The bioaccumulation assessment cannot be concluded based on the currently available information.

Toxicity

Based on the NOEC for aquatic invertebrates of 100 mg/L, the substance does not fulfil the toxicity criterion of 0.01 mg/L. Furthermore, short-term toxic effects for fish, aquatic invertebrates and algae are all above 100 mg/L. Hence, the screening threshold value of 0.1 mg/L is not fulfilled. The substance does not fulfil the T criterion based on environmental toxicity.

Mobility

ADONA is an ionisable substance which will dissociate in soils and surface waters to form an ammonium ion and a DONA anion. The low adsorption potential of the anion indicates a high mobility in soil and water. Its environmental distribution properties make ADONA mobile in the aquatic environment. Due to the global water cycle, the aqueous compartments are all well connected, e.g. rivers and oceans. Once ADONA has entered the environment, e.g. in a surface water body, there is no natural barrier to prevent ADONA from being distributed to oceans and thus a wide spread occurs far from the point source. Additionally, with no natural barriers ADONA can reach groundwater and in consequence drinking water. Drinking water would then be a source of direct exposure of humans.

Overall conclusion

Taking together all available information, a full PBT assessment, with consideration of the knowledge from the PFOA-PBT assessment, cannot be performed. The substance will most probably fulfil the (v)P criterion of REACH Annex XIII. The bioaccumulation potential cannot be refuted based on the lessons learned from the PFOA PBT assessment. Based on the data for environmental toxicity, the substance does not fulfil the T criterion. The registration dossier presently lacks toxicological information relevant to humans. Thus, the data are not sufficient to conclude or to refute on the PBT-properties of the Substance.

Additionally, ADONA is mobile in soil and water. A broad restriction of PFAS (including ADONA) will be the most appropriate risk management measure to minimize concentrations of these persistent substances in the environment.

7.12. Exposure assessment

7.12.1. Environment

Assessment of exposure was conducted based on information in the registration dossier, the CSR and information provided by the registrant. Furthermore, publicly available

monitoring data was also taken into account. Since most of the available information are confidential, only a generic summary of the exposure assessment is presented here.

ADONA is manufactured for the use as a processing aid in the production of fluoropolymers. The aqueous solution of ADONA serves as an emulsifier. Losses are mainly through incineration of ADONA or decomposition products in the off gas from production or of waste streams. Based on high water solubility, ADONA will ultimately be present in the aquatic compartment. During drying processes the ammonium salt of ADONA is released with the off-gas as ammonia and the acid DONA. If present in the atmosphere, the high water solubility of both ADONA and DONA indicates removal with atmospheric precipitation. According to the registrant, long-distance transport by air is not expected. Long-range transport refers to the atmospheric transport of air pollutants for a distance greater than 100 kilometres (United Nations, 1997).

A study was conducted to measure the ADONA concentration in the vicinity of the production site in 2013 (Schreiber, 2014). For more details see chapter 7.7.4.

Three main emission paths were concluded in this study:

- Release of cleared waste water into the river Alz,
- Deposition from the air via soil into the groundwater and
- diffuse releases from local point sources on the manufacture site.

According to the EFSA opinion on food contact materials, ADONA should only be used in the polymerisation of fluoropolymers processed at temperatures higher than 280 °C for at least 10 minutes and in the polymerisation of fluoropolymers for being processed at levels up to 30% and temperatures higher than 190 °C into polyoxymethylene polymer for repeated use articles only. According to the registrant, ADONA is not present in these final articles after the heat treatment and a wide dispersive release of ADONA via products and articles could be excluded.

ADONA degrades at temperatures > 190°C to the main degradation product – a shorter chain perfluorinated ether (identity claimed confidential by the registrant). According to the registrant, this degradation product is released via air and water at low concentrations. It is not known whether the degradation product is created also at downstream users sites at fluoropolymer processing and during the use of articles and mixtures containing fluoropolymers manufactured with ADONA. Information regarding the physical chemical properties of the degradation product and its fate and behaviour is not available.

Conclusion

Based on the available information the eMSCA concludes that ADONA is released into the environment via air and water at the manufacturing site, although there are many mitigation measures by the manufacturer. This may be problematic in the vicinity of the production site. The eMSCA therefore recommends implementation of further measures for further reduction of local releases by the manufacturer.

Additionally, a wide dispersive release via fluoropolymers that may contain trace levels of ADONA cannot be excluded. Detailed information regarding the ADONA concentration in final fluoropolymers containing articles is not available.

During processing of polymers, ADONA decomposes to a shorter chain perfluorinated ether. There are releases into air and water at the manufacturing site. Releases of the degradation product into the environment should be minimised both during processing steps and during manufacturing or handling of related articles at downstream user’s sites.

7.13. Risk characterisation

ADONA shows a low toxicity to the environmental species tested. The acute toxic effects for fish, daphnia and algae are all above 100 mg/L. The chronic toxic effects for daphnia and algae are both above 1 mg/L (for fish no chronic is data available).

However, the substance may be bioaccumulating in human blood in a similar way as PFOA. Two studies with occupationally exposed workers show a half-life of 11-44 days which is far lower compared with the half-life of PFOA in human blood. However, no threshold for defining a substance of being bioaccumulative above a certain half-life is available. It may be potentially re-absorbed and may thus have a slower elimination half-life in human blood. Thus, ADONA may be accumulating in human blood.

ADONA is used as a processing aid during the manufacture of fluoropolymers. Releases occur to air and waste water. ADONA decomposes at temperatures occuring during processing of fluoropolymers to a shorter chain perfluorinated ether. This processing is conducted at the manufacturing site, but could be possible at downstream users sites, too. A low adsorption potential of short chain perfluorinated ethers was shown by Sun et al. (Sun et al., 2016).

ADONA is very persistent and mobile, and the concern for being bioaccumulative in human blood could not be ruled out. A broad restriction of PFAS (including ADONA) will be the most appropriate risk management measure to minimize concentrations of these persistent substances in the environment.

7.14. References

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7.15. Abbreviations

ADONA	ammonium 2,2,3 trifluor-3-(1,1,2,2,3,3-hexafluoro-3-trifluormethoxypropoxy), propionate
BCF	bioconcentration factor
CSR	Chemical Safety Report
DONA	2,2,3 trifluor-3-(1,1,2,2,3,3-hexafluoro-3-trifluormethoxypropoxy), propionate anion / 2,2,3 trifluor-3-(1,1,2,2,3,3-hexafluoro-3-trifluormethoxypropoxy), propionic acid
EC50	Half maximal effective concentration
EFSA	European Food Safety Authority
eMSCA	evaluating member state competent authority
LC50	Half maximal lethal concentration
NOEC	no observed effect concentration
PBT	persistent, bioaccumulative, toxic
PFAA	perfluoroalkyl acids
PFAS	per-and polyfluoroalkyl substances
PFCA	perfluoroalkyl carboxylic acid/ perflouroalkyl carboxylates
PFSA	perfluoroalkyl sulfonic acid/ perfluoroalkyl sulfonates
PFOA	Perfluorooctanoic acid
SVHC	Substance of very high concern
vPvB	very persistent, very bioaccumulative