Analysis of the most appropriate risk management option (RMOA)

Substance Name: Tetrafluoroethylene

EC Number: 204-126-9

CAS Number: 116-14-3

Authority: The Health and Safety Authority

Date: October 2018

Cover Note

Tetrafluoroethylene was screened by IE in the third manual screening round in 2016. The screening verified the initial concern of carcinogenicity based on the observed effects in the available OECD 453 studies. Tetrafluoroethylene does not have a harmonised classification and there are significant variations in the self-classification of tetrafluoroethylene in the classification and labelling inventory. It is therefore proposed to prepare an Annex VI dossier for harmonised classification as Carc. 1B.

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NOTE: This annex contains confidential information

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1 IDENTITY OF THE SUBSTANCE

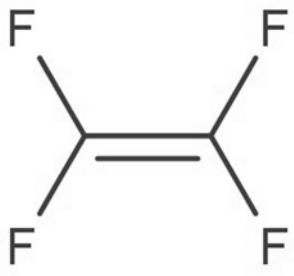
1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	Tetrafluoroethylene
IUPAC name (public):	1,1,2,2-tetrafluoroethylene
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	C_2F_4
Molecular weight or molecular weight range:	100.02 g/mol
Synonyms:	Ethen, tetrafluor-; Ethene, tetrafluoro- (9CI); Ethylene tetrafluoride; Ethylene, tetrafluoro- (8CI); Eurotard FS-200; Fluon; KT-300M; KT-600M; KTL-450A; KTL-4N; KTL-610; KTL-630; KTL-8F; KTL-8N; KTL-8N(U); KTL-9S; Neoflon; Perfluorethen; Perfluorethylen; Perfluoroethene; Perfluoroethylene; RE-L; SEFLOR; Tefzel; Tetrafluorethen; Tetrafluorethylen; Tetrafluoroethene; Tetrafluoroethylene; TFE

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

Structural formula:



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2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

RMOA		☐ Risk Management Option Analysis (RMOA) other than this RMOA
REACH Processes	Evaluation	☐ Compliance check, Final decision
		☐ Testing proposal
		☐ CoRAP and Substance Evaluation
	Authorisation	☐ Candidate List
		☐ Annex XIV
	Restri -ction	☐ Annex XVII
Harmonised C&L		☐ Annex VI (CLP) (see section 3.1)
Processes under other EU legislation		☐ Plant Protection Products Regulation Regulation (EC) No 1107/2009
		☐ Biocidal Product Regulation Regulation (EU) 528/2012 and amendments
Previous legislation		☐ Dangerous substances Directive Directive 67/548/EEC (NONS)
		☐ Existing Substances Regulation Regulation 793/93/EEC (RAR/RRS)
(UNEP) Stockholm convention (POPs Protocol)		☐ Assessment
		☐ In relevant Annex

Other processes/ EU legislation	☐ Other (provide further details below)

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

Tetrafluoroethylene does not have a harmonised classification.

3.1.2 Self classification

- In the registration:
  - Flam. Gas 1 – H220: Extremely flammable gas
  - Carc. 1B – H350: May cause cancer
  - STOT SE 2 – H371: May cause damage to organs (kidney, inhalation)

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:
  - Carc. 2 – H351: Suspected of causing cancer
  - STOT SE 2 – H371: May cause damage to organs (kidney) (inhalation)
  - STOT RE2 – H373: May cause damage to organs (kidney)

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

None currently proposed.

3.1.4 CLP Notification Status

Table: CLP Notifications

	CLP Notifications[1]
Number of aggregated notifications	9
Total number of notifiers	640

3.2 Additional Hazard Information

3.2.1 Environment

Tetrafluoroethylene (TFE) is an unstable, colourless, highly flammable gas. It is very slightly soluble in water. Any TFE released into the environment is expected to be distributed to the atmosphere, where it will quickly degrade to carbon dioxide and hydrogen fluoride.

In the aquatic environment, hydrolysis of TFE will not occur and it is not prone to rapid biodegradation and bioaccumulation. TFE will not adsorb significantly to soils and sediments. The predicted toxic concentrations of TFE to either aquatic or terrestrial organisms are considerably higher than the solubility level of TFE in water.

TFE is only expected to occur in air, as it is highly unstable with a high vapour pressure and only slightly soluble in water, it is unlikely to have a potential impact on man via the environment. However, as a fluoropolymer, it may warrant further consideration as part of the overall examination of short chain fluorinated carbonaceous compounds.

3.2.2 Human Health

3.2.2.1 Carcinogenicity

Animal data:

Two 2-year carcinogenicity studies conducted in accordance with OECD 453 with rats and mice are reported in the registration data.

In the first study reported, groups of 60 male and female Fischer 3544/N rats were administered TFE by inhalation at 0, 156, 312 or 625ppm (males) and 0, 312, 625 or 1250 ppm (females) for 6 hours per day, 5 days a week for 104 weeks. At the end of the study period there was a reduced survival rate in high dose males and in all treated females. An increased incidence of renal tubule adenomas was observed in mid and high dose males and high dose females. In

[1] C&L Inventory database, http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database (accessed 11th December 2017)

the liver there was an increased incidence of hepatocellular carcinomas in mid dose males and low and mid dose females, and hepatocellular adenomas in females in all dose groups. The incidence of haemangiosarcoma was increased in females of the mid and high dose group and the incidence of mononuclear cell leukaemia was increased in low dose males and all treated females. A slight increase in the incidence of testicular interstitial cell adenomas was observed in mid and high dose males, however it is noted that this is a common lesion in aging rats so the significance of this finding is unclear.

In the second study reported, groups of 58 male and female B6C3F1 mice were administered TFE by inhalation at 0, 312, 625 or 1250 ppm. At the end of the study period the survival rate in both sexes was decreased when compared with the control. Hepatocellular carcinomas were also increased in all treated males and females. An increased incidence of haemangioma and haemangiosarcoma was observed in all treated animals when compared with concurrent control and historical control data. There was an increased incidence of histiocytic sarcomas in lung and liver in all treated animals.

Human data:

The registration data includes results from a multi-centre cohort mortality study which examined the exposure of 4773 workers at six production sites across Europe and North America to TFE and ammonium perfluoro-octanoate (APFO) and the incidence of cancers. The standard mortality rates for the workers were increased for cancers of the liver and kidney and for leukaemia. However there are some limitations with the data in particular the cofounding effect of APFO which is also reported to induce liver, leydig cell and pancreatic acinar cell tumours in rodents.

3.2.2.2 Genotoxicity

The registration data reports results of a number of in vitro and in vivo genotoxicity studies with TFE.

In vitro, negative bacterial reverse mutagenicity, mammalian cell mutagenicity and a mammalian chromosome aberration assay with TFE are reported.

In vivo, no increase in micronucleated polychromatic erythrocytes was observed in the bone marrow of mice exposure to TFE by inhalation for 6 hours at doses up to 19000 ppm (males) and 28000 ppm (females). In a second micronucleus assay, peripheral blood cells were sampled at the end of a 13 week exposure to TFE at doses up to 5000 ppm. No significant increase in the frequency of micronucleated erythrocytes was observed. In an unscheduled DNA synthesis (UDS) assay in mice, no increase in UDS induction was observed at concentrations up to 160 g/m^3.

Based on the available data TFE is not considered to be genotoxic.

3.2.2.3 Occupational Exposure

Occupational exposure occurs in the primary manufacture of TFE and during the subsequent polymerisation process. Inhalation exposure has been measured in European manufacturing plants at between 0.16 and 6mg/m^3 and between <0.4 and 6.1 mg/m^3 (8hr TWA). Further epidemiological assessments using exposure modelling estimated the highest exposures in the polymerisation areas. TFE exposure in finishing areas of plants was assessed to be low. The introduction of control measures, increasing process automation and other improvements were judged in a 2012 study (Sleeuwenhoek and Cherrie) to have resulted in exposures generally decreasing over time.

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[2]

4.1 Tonnage and registration status

Table: Tonnage and registration status

From ECHA dissemination site	
Registrations	☒ Full registration(s) (Art. 10) ☐ Intermediate registration(s) (Art. 17 and/or 18)
Total tonnage band for substance (excluding volume registered under Art 17 or Art 18, or directly exported)	10,000-100,000 tpa

[2] Dissemination site accessed on 11th December 2017

4.2 Overview of uses

Table: Uses

	Use(s)
Uses as intermediate	Use of monomer in polymerisation processes at industrial sites; Polymer preparations and compounds
Formulation	Formulation into mixture; Use in closed process; Polymer preparations and compounds
Uses at industrial sites	Use of monomer in polymerisation processes; Polymer preparations and compounds; manufacture of oligomers, fluoroelastomers and fluoropolymers, which include polytetrafluoroethylene (PTFE); Use of reactive processing aid; Manufacture of plastics products, including compounding and conversion
Uses by professional workers	Use of the polymer formulated from TFE monomer. Use in closed process. Chemical production in closed process or processes with equivalent containment conditions
Consumer Uses	None
Article service life	(as polymer) Films and fibres; bearings and gaskets; nonstick coatings for cooking utensils; waterproof and breathable membranes for clothing; protective coatings on carpets

4.3 Additional information

Tetrafluoroethylene is a halogenated olefin that occurs as a colorless, odorless gas at room temperature. It is practically insoluble in water. TFE is very flammable and at high pressures it may polymerize easily without an inhibitor, especially if heated or in the presence of oxygen (IARC 1979, NTP 1997). Because of its instability, it requires tight controls when handling, and registrants report that it is transferred to on-site polymerization units by direct pipeline at EU manufacturing sites.

It is manufactured in a four stage process involving the separate production of hydrogen fluoride and chloroform, which are subsequently reacted in the presence of antimony trifluoride to produce chlorodifluoromethane. The chlorodifluoromethane is pyrolysed at >650^{o}C to produce TFE.

TFE is used primarily in the synthesis of fluoropolymers, particularly the homopolymer polytetrafluoroethylene (PTFE or Teflon) (IARC 1979, HSDB 2009). TFE is also used as a copolymer to make fluorinated ethylene-propylene resins with hexafluoropropylene as a copolymer, perfluoroalkoxy resins with perfluoropropyl vinyl ether as the copolymer, and ethylene-tetrafluoroethylene resins. TFE is used in the production of low-molecular-mass compounds and intermediates, such as iodoperfluoroalkanes, and it reacts with perfluoronitrosoalkanes to produce nitroso rubbers (HSDB 2009). TFE was also used in the past in food-product aerosols, though this use has now been discontinued.

5 JUSTIFICATION FOR THE RISK MANAGEMENT OPTION

5.1 Need for (further) risk management

Table: SVHC Roadmap 2020 criteria

	Yes	No
a) Art 57 criteria fulfilled?	X*	
b) Registrations in accordance with Article 10?	X	
c) Registrations include uses within scope of authorisation?	X	
d) Known uses not already regulated by specific EU legislation that provides a pressure for substitution?	X	

*Currently the substance does not have a harmonized classification, though the registrants classify as Carc 1B.

5.2 Identification and assessment of risk management options

5.2.1 Harmonised CLH

Tetrafluoroethylene is used primarily as a monomer in the industrial production of polymers and at a limited number of manufacturing sites. TFE does not have a harmonised classification with the evidence suggesting classification as Carc. 1B H350. However, it is noted that more than two thirds of notifiers to the Classification and Labelling Inventory do not self classify as Carc 1B.

According to the CLP Regulation substances may be classified as category 1A carcinogens “if they are known to have carcinogenic potential for humans, classification is largely based on human evidence”. The available human data do not sufficiently demonstrate a causal relationship between exposure to TFE and human cancer.

In order to classify a substance as category 1B for carcinogenicity, classification can be based on evidence in experimental animals demonstrating a causal relationship between the agent and an increased incidence of malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories under different protocols.

In an inhalation carcinogenicity study with TFE in rats an increased incidence of renal tubule and hepatocellular neoplasms in both sexes, and increased incidences of haemangiosarcomas and mononuclear cell leukaemia in females was observed. In an inhalation carcinogenicity study in mice with TFE, increased incidences of liver haemangiomas and haemangiosarcomas, hepatocellular neoplasms and histiocytic sarcomas were observed.

These findings are supported by the IARC monograph in which it was concluded that, based on the available two-year carcinogenicity studies in F344/N rats and B6C3F1 mice, there was clear evidence of carcinogenic activity and sufficient

evidence in experimental animals for the carcinogenicity of TFE respectively (NTP, 1997; IARC 2016).

Therefore, there is sufficient evidence to support a harmonised classification of TFE as Carc. 1B. The primary risk management step for TFE is the preparation of an Annex VI dossier for harmonisation of the substances classification.

The registered uses of Tetrafluoroethylene are industrial only and in a limited number of EU based sites, and as a monomer intermediate.

Control of worker exposure to TFE is currently regulated on an EU wide basis by Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work. It has been noted in the 2012 Sleeuwenhoek and Cherrie study that the introduction of control measures, increasing process automation and other improvements have resulted in exposures generally decreasing over time. However, harmonisation of the substances classification as a Cat 1b Carcinogen will ensure it's inclusion within the scope of Directive 2004/37/EC governing carcinogens and mutagens at work. Enforcement of this and existing worker protection legislation by the relevant national authorities in these jurisdictions should continue to ensure workers are not subjected to an unacceptable risk by ensuring that in so far as is technically possible, manufacture and use in a closed system and the exposure of workers is reduced to as low a level as is technically possible.

In addition, TFE may need to be considered as part of the overall assessment into short-chained fluorinated carbonaceous compounds.

5.3 Conclusions on the most appropriate risk management option

Tetrafluoroethylene does not have a harmonised classification, and the Classification & Labelling Inventory indicates more than two thirds of notifications do not self classify as Carc 1B.
Harmonised classification of Tetrafluoroethylene as Carc. 1B H350 would ensure coherent communication in the supply chain and trigger additional and improved risk management actions by all companies and workers using this substance particularily under Directive 2004/37/EC. As a primary step in improved worker safety, it is concluded to submit a CLH dossier for a harmonised classification for this substance.

Enforcement of Directive 2004/37/EC (carcinogens or mutagens at work) and existing worker protection legislation by the relevant national authorities in the jurisdictions where manufacture and polymerization of TFE occurs should continue to ensure workers are not subjected to an unacceptable risk.

TFE may also need to be considered as part of the ongoing work of the working group for short-chained fluorinated carbonaceous compounds.

5.4 References

1. ECETOC (2003). Tetrafluoroethylene. (CAS No. 116-14-3). JACC No. 42. Brussels: European Centre for Ecotoxicology and Toxicology of Chemicals.

2. IARC. (1979). Some monomers, plastics and synthetic elastomers, and acrolein. IARC 19:1-513

3. IARC (2017). Some Chemicals Used as Solvents and in Polymer Manufacture: Tetrafluoroethylene. 110:111-140

4. NTP (2014). NTP Tetrafluoroethylene. Report on carcinogens, thirteenth edition. 12:401-402

5. NTP (1997). NTP toxicology and carcinogenesis studies of tetrafluoroethylene (CAS No. 116-14-3) in F344 rats and B6C3F1 mice (inhalation studies). Natl Toxicol Program Tech Rep Ser, 450:1-321. PMID: 12594525

6. HSDB (2017). Tetrafluoroethylene. Hazardous substance database (HSDB). Available from https://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+844

7. ECHA (2017) Dissemination site: Tetrafluroethylene. Available from https://www.echa.europa.eu

8. Sleeuwenhoek and Cherrie (2012): Exposure assessment of tetrafluoroethylene and ammonium perfluorooctanoate 1951–2002. Journal of Environmental Monitoring

9. Consonni, Straif, Symons, Tomenson, van Amelsvoort, Sleeuwenhoek, Cherrie, Colombo, Farrar and Bertazzi (2013): Cancer Risk Among Tetrafluoroethylene Synthesis and Polymerization Workers. American Journal of Epidemiology, Volume 178, Issue 3, 1 August 2013, Pages 350–358