HPC INTERNATIONAL SAS

Pollution by volatile PFAS: Health Risks due to vapors and contamination of Ambient Air

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1. Introduction

Since the 1960s PFAS: Per- & Polyfluoro-Alkyl Substances have gradually become since a major environmental problem, also for Public Health, due to their multiple and vast application (historical and still current). This environmental and public health threat has started to be taken into account little by little since the 2010s and strongly in 2022 & 2023. Consequently, PFAS are now found in soils, groundwater, food and water. drinking water as well as in soil gases and ambient air for a family of volatile PFAS, the FTOHs: Fluorotelomer-Alcohols. Between 9,000 and 12,000 synthetic PFAS pollutants have been produced.

PFAS polymers of the "Teflon" type (or PFTE) etc. do not have good bioavailability and are therefore much less toxic than monomeric PFAS. These PFAS monomers are the subject of the work presented herewith. PFAS are known in particular for their toxicological effects of endocrine disruptors, hepatotoxicity, immunotoxicity, their effects on fetal development and for some, carcinogenicity (e.g. PFOA) [1 - 84].

An individual fluorotelomer alcohol molecule is named by the number of carbons that are fluorinated versus the number that are hydrocarbon-based. 8:2 fluorotelomer alcohol for ex. would represent a molecule with 8 fluorinated carbons and a 2 carbon ethyl alcohol group. The general structure of a fluorotelomer alcohol is most commonly $F(CF_2)_nCH_2CH_2OH$, where n is an even number.

An important characteristic of PFAS is their behavior in Environmental Chemistry, because only polyfluorinated PFAS are modified by microbiological bio-transformation into perfluorinated PFAS, which remain totally stable and non-degradable, or even bio-accumulable.

The PFAS pollution sources are multiple and particularly present on industrial sites, which have used these products, sites of former fires or firefighting training, where firefighting foams (AFFF: Anti Fire Fighting Foams, eg at airports) were used. Agricultural land is also a source of PFAS pollution, due to the input of sludge from STEP: Wastewater Treatment Plants which contain accumulated PFAS.

The following (historical) activities can cause PFAS pollution:

- Anti-Fire Trainings,
- Airport or air base military site,
- Fire site and use of AFFF,
- Electrochemical galvanizing,
- Production of "waxed" paper or cardboard,
- Production of Waterproof Textiles,
- Sprays, paints, waterproofing lacquers,
- Production and application of Teflons (PTFE, etc.),
- Petroleum and chemical industry sites and/or production and application of paints, dyes, inks, pigments, chemical waxes and polishing products,
- Solvent applications (garages, dry cleaners, laundries, etc.,
- Landfills and former municipal landfills, etc. (ISDD, ISDND, ISDD, etc.),
- Dyeings & Tanneries,
- Carpets, rugs, fabrics and plastics with flame retardants,
- Production of objects and furniture containing surfaces,
- Production of cleaning products,
- Photographic chemistry (laboratories, and production of papers and films, etc.),
- Production of electronic elements,
- Production and applications of pesticides and biocides,
- Production of cosmetic products,
- Sites having received Sludge from STEP.

2. Environnemental Chemistry

The environmental chemistry of PFAS is particularly important and complicated. There is no group of pollutants showing more complex environmental chemistry than PFAS. In particular, it should be noted that there are more than 9,000 PFAS substances, divided into 33 substance categories. The best known are Perfluoroalkane-sulfonic acids (PFASs), Perfluoroalkyl-carboxylic acids (PFCA), Perfluoroalkyl-phosphates & their esters, Fluorotelomer-alcohols (FTOH), etc. (including more than 32 other groups…). Some of them, eg. PFOA: Perfluoro-octanoic acid and PFOS: Perfluoro-octane-sulfonate (see Fig. 1) are banned (and prohibited in the EC and USA & Canada) by the Stockholm Convention in the category of POPs: Persistent Organic Pollutants. PFOA is carcinogenic. Commercial products mainly contain mixtures.

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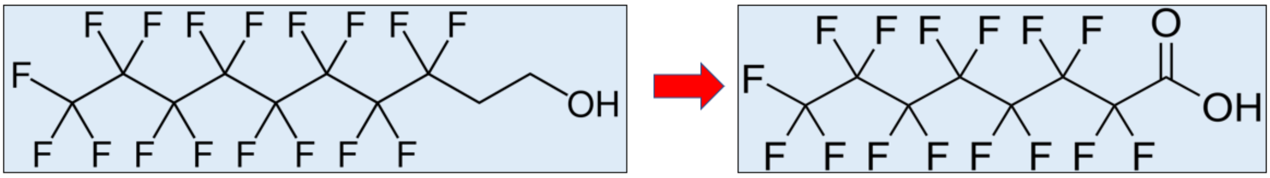

Fig. 1: Bio-transformation of 8:2-FTOH to carcinogenic PFOA

The reason for the high water solubility associated with lipophilia is based on the fact that there are PFAS:

- Anionics (e.g. sulfonates, sulfates, carboxylates and phosphates),
- Cationic (e.g. quaternary ammonium),
- Amphoteres (e.g. betaines and sulfo-betaines): base + acid and
- Non-ionic (eg polyethylene glycols, acrylamide oligomers).

It is very important to emphasize, that not fully fluorinated poly-fluorinated PFAS ("Precursors") can be converted by bio-transformation into persistent and fully fluorinated chemicals, the per-fluorinated PFAS [87 – 94]. Complete microbiological degradation of PFAS has not yet been demonstrated.

The following diagram shows an example of the biotransformation of polyfluorinated alkyl phosphates (PAP) in soils and groundwater to volatile fluorotelomer alcohols (FTOH) which subsequently migrate into soil gases and into the ambient air. Subsequently, the FTOHs are transformed microbiologically into stable per-fluorinated PFAS. For example ; 6:2-FTOH is biotransformed into PFHxA and PFPeA and 8:2-FTOH into PFOA, PFHpA, PFHxA and 2H-PFOA (see the following Figs.).

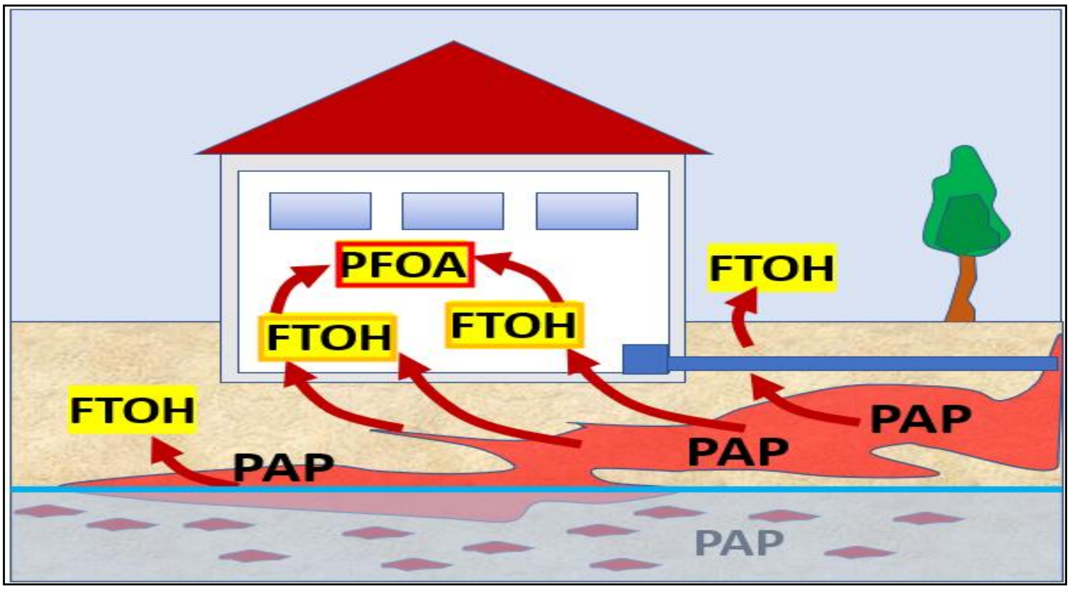

Fig. 2: Example of biotransformation of polyfluorinated alkyl phosphates (PAP) in soils and groundwater to volatile fluorotelomer alcohols (FTOH) and stable per-fluorinated PFAS, such as e.g. carcinogenic PFOA: L. KOPF / HPC, 2017 and F. KARG, 2021 & 2022.

The following diagram shows an example of the biotransformation of 8:2-FTOH ($F(CF_2)_8CH_2CH_2OH$) via intermediate products to stable perfluorinated PFAS, such as PFPA (Perfluoro-pentanonic acid), PFHxA (Perfluoro-pentanonic acid), hexanonic), PFHpA (Perfluoro-heptanonic acid), 2H-PFOA, Acid 7:3 and carcinogenic PFOA (Perfluoro-octanonic acid).

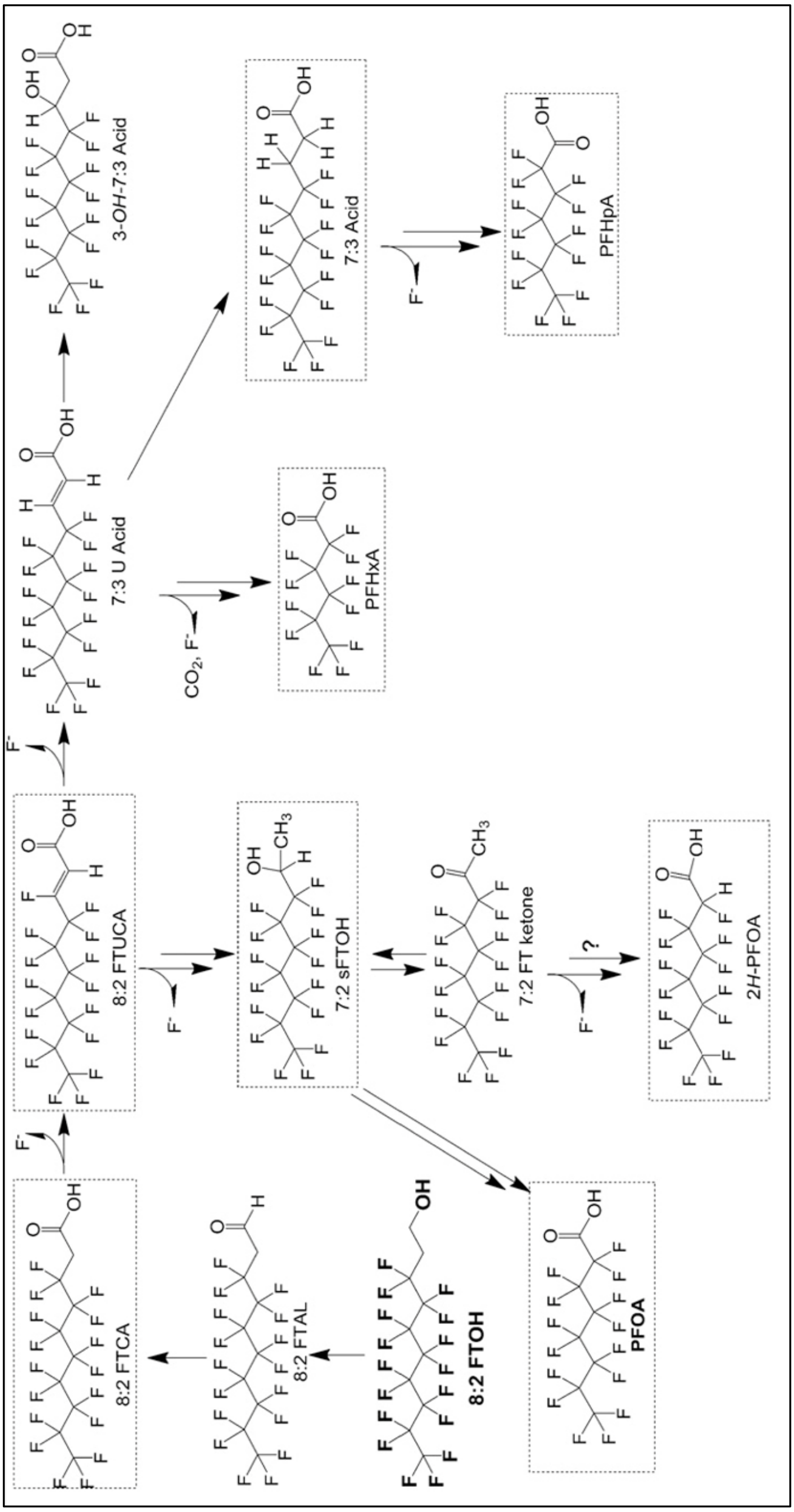

Fig. 3: Example of aerobic biotransformation of 8:2 FTOH ($F(CF_2)_8CH_2CH_2OH$) in soils. Double arrows indicate the formation of stable per-fluorinated substances (Wang et al. 2009, modified).

In the event of a change in pH, some PFAS could become more or less soluble, which also has an impact on the emanations of volatile fluorinated telomeres like FTOH, etc. in soil gases. Some precursors could modify their solubilities (and their extractabilities during chemical analysis procedures).

As it stands today, the analysis of the 20 individual PFAS according to the European Directive 2020/2184 don't integrate FTOHs.

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According to European Directive 2020/2184, which concerns the quality of water for human consumption, the following 20 PFAS are targeted:

Somme des 20 PFAS de la Directive européenne Eau potable 2020 :
- Acide perfluoroctanoïque (PFOA) [5347]
- Acide perfluoroheptanoïque (PFHpA) [5977]
- Acide perfluorohexanoïque (PFHxA) [5978]
- Acide perfluoropentanoïque (PFPeA)[5979]
- Acide perfluorobutanoïque (PFBA) [5980]
- Acide perfluorobutane sulfonique (PFBS) [6025]
- Acide perfluorododécanoïque (PFDoDA) [6507]
- Acide perfluorononanoique (PFNA) [6508]
- Acide perfluorodécanoïque (PFDA) [6509]
- Acide perfluoroundécanoïque (PFUnDA) [6510]
- Acide perfluoroheptane sulfonique (PFHpS) [6542]
- Acide perfluorotridecanoïque (PFTrDA) [6549]
- Acide perfluorodécane sulfonique (PFDS) [6550]
- Acide perfluorooctane sulfonique (PFOS) [6561]
- Acide perfluorohexane sulfonique (PFHxS) [6830]
- Acide perfluoropentane sulfonique (PFPeS) [8738]
- Acide perfluorononane sulfonique (PFNS) [8739]
- Acide perfluoroundécane sulfonique [8740]
- Acide perfluorododécane sulfonique [8741]
- Acide perfluorotridécane sulfonique [8742]

3. Toxic Risks & Health Risk Assessments (TERQ : Toxicological Exposure Risk Quantification)

Exposure to FTOHs specifically has been associated with hepatotoxicity [158 - 160], increased breast cancer cell proliferation [161 - 162], and estrogenic activity [163 - 164]. Some effects on reproduction and development were observed, but these may be due to maternal toxicities [165 - 166].

For the assessment of health risks, toxicological data (TRV: Toxicological Reference Values) must be sought and updated at international level almost on a weekly basis. The most recent TRVs are available mainly in the USA (EPA, etc.), ATSDR and EFSA. ANSES also published PFAS TRVs in 2017, but given the forced advancement of toxicological studies, these TRVs are for the most part already outdated.

In the case of FTOHs present in soils, groundwater and soil gases, it will also be imperative to carry out FTOH investigations in the ambient air of buildings with sensitive uses (ERP: Schools, Nurseries, etc.) or residential, on the basis of quantification thresholds (or at least for the detection thresholds), of the order of 4 – 8 ng/m3, in order to have a good exploitable basis for the EQRS: Quantitative Assessment of Health Risks.

A first simplified risk assessment approach is possible via existing limit values, e.g. in Germany, or published by the European Community. In Germany there are limit values for drinking water, soil and groundwater.

The US-EPA considers that the majority of exposure today comes from drinking water, outside of polluted sites, due to the lack of monitoring and treatment of PFAS. According to Directive (EU) 2013/39/EU "Water Framework" (WFD), concerning PFOS & derivatives (and other priority substances) an Environmental Quality Standard (EQS-MA) of 0.65 ng/l for surface waters and 0.13 ng/l for waters from the marine environment (and EQS-MAC: Maximum Allowable Concentrations) has been set.

It is important to note that a simple application of the Limit Values, generic and individual within the framework of a simplified risk assessment does not take into account specific exposure scenarios and exposures to mixtures (“Cocktails”) pollutants with, at a minimum, taking into account the additivity of the risks of pollutants having the same targets and toxicological effects. Consequently, it is preferable to carry out EQRS (or ARR, HRA, TERQ), which corresponds well to the French Methodology for the Management of Polluted Sites, according to the note from the Ministry in charge of the Environment, of 04/19/ 2017.

Another important aspect is that only an EQRS (or ARR, TERQ, HRA) will make it possible to define Health Compliance Control Values, in the form of MAC (Maximum Admissible Concentration) for maximally acceptable Excess Individual Risks (of cancer): ERI < 10E-5 or a Systemic Risk Index of IR < 1 (= DJE / DJT: Daily Exposure Dose over the Tolerable Daily Intake). Regarding the EQRS: Quantitative Assessment of Health Risks, the basis is either the measurement of concentrations in the exposure media, or the modeling of the transfer of pollutants from one compartment to another (e.g. pollutants in groundwater or from the ground to the gases of the ground and the ambient air. An important step in the EQRS is the choice of TRVs (Toxicological Reference Values), because their evolution is rapid.

For example, the 2017 ANSES PFAS guide includes certain TRVs for PFAS, but given the many TRV publications to date, these values are partially outdated, and in particular much more restrictive to date. A Tolerable Weekly Intake (DHT) of 4.4 ng/kg/Week (or the Tolerable Daily Intake (TDI) of 0.63 ng/kg/d for PFAS: PFOA, PFOS, PFNA & PFHxS) has been published by EFSA, 09/17/2020. In 2020, toxicity equivalence factors with respect to PFOA were also published by W. Bil et al. in the form of RPF: Relative Potency Factors, existing also for some FTOHs.

In order to ensure the correct choice of TRVs for PFAS, it is recommended to apply scientific selection criteria and not national criteria. Fig. The following shows criteria for choosing the applicable TRVs, in order to take into account the best toxicological knowledge concerning the dose-effect relationships of PFAS.

No	TRD: Toxicological Reference Dose Choice Criteria	Appreciation			
		Favorable	Correct	Not favorable	Exclusion
1	Variability of indicated TRD	(+/- 0 %)	≤ (+/- 30 %)	> (+/- 30 %)	
2	Class (potential) Carcinogenic: EC: Class 3/ US-EPA: Class B2, C / IARC: Group 1	3 Organisms : CE, US-EPA, IARC, etc.	2 Organisms	1 Organisms	
3	Several Organisms shows similar TRD (+/- 50 %)	➢ 3 Organisms	2 Organisms	1 Organism	
4	Age of base Study	≤ 15 a	15 – 25 a	< 25 a	
5	Mechanistic toxicological basement Study (for ex. Genotoxicity):	Epidemiology	Mamifer	In-Vitro / In-silico	
6	Basement Study : Klimisch Quality Criteria	Class 1	Class 2	Class 3	Class 3
7	Verified Purity of Compound	Yes	< 95 %	No	
8	Excipient potentially toxic	Non		Yes	
9	Presence of population without exposure (test witness)	Yes		No	
10	General Quality Criteria (Klimisch) of toxicological effect studies	Standardized Study (OCDE, UE, US EPA, FDA, etc.)	Standardized Study without Details, but correctly documented	Document insufficient for evaluation, systematic deficiencies	
11	POD : Point of Departure	Quantified Epidemiological Data, BMLD, etc. (PBPK)	NOAEL sensitive NOAEL	LOAEL sensitive, LOAEL, Other	
12	Uncertainty (or Assessment) Factors	1 – 100	> 100 – 1000	> 1 000 – 10 000	> 10 000
13a	Transpositions: Between Exposure Pathways	Non		Yes	
13b	Transposition: Animal to Human	Non	Yes		
13c	Transpositions : From in-Vitro	Non		Yes	
13d	Transpositions : From in-Silico	Non		Yes	
14	Study time-representatively	≥ chronic (> 180 d)	sub-chronic (90 d) to chronic (180 d)	< sub-chronic (< 90 d)	
15	Integration of bio-disponibility / Bio-resorption capacity (ex.: DIN 19 738)	Yes	Not known (100 %)	Known, but not considered	

Fig. 12: TRV selection criteria (F. KARG 2022)

The following table shows some TRVs (Dose-Effect Values) for FTOHs:

Compound	Inhalation Systemic	Ingestion Systemic	Considered Effect	Tests	Uncertainty (Security) Factor	Reference
6:2 FTOH: Fluorotelomer alcohol		**RfD** (based on PFOA TDI: 6 ng/kg/week: 0,86 ng/kg/d / RPF 0,02): **43 ng/kg/d**	**Hepato-toxic**	**Rat**	**Relative Potency Factor: RPF = 0,02**	**Bil et al. 2020: (RfD based on PFOA TDI: UBA 2020, EFSA 2018 & BfR 2018)**
8 : 2 FTOH: Fluorotelomer alcohol		**RfD** (based on PFOA TDI: 6 ng/kg/week: 0,86 ng/kg/d / RPF 0,04 **):** **21,5 ng/kg/d**	**Hepato-toxic**	**Rat**	**Relative Potency Factor: RPF = 0,04**	**Bil et al. 2020: (RfD based on PFOA TDI: UBA 2020, EFSA 2018 & BfR 2018)**
8 : 2 FTOH: Fluorotelomer Alcohol	**RfC : 1,5 x 10^6 pg/kg/d**	**RfD assimilated to PFOA as biotransformation end-product: 1,5 µg/kg/d**	**Hepato-toxic**	**Rat**		**SLU 2017 (Ingestion based on EFSA 2018)**

Fig. 13: Choice of certain TRVs according to the criteria in Fig. 7 (F. KARG 2022):

A complementary step to the EQRS (or ARR, TERQ, HRA) is the definition of health compliance control values, in the form of MACs (Maximum Admissible Concentrations) by integrating an additivity of the risks of pollutants concerning the same targets and toxicological effects, for maximally acceptable Excess Individual Risks (of cancer): ERI < 10E-5 or a Systemic Risk Index of IR < 1 (= DJE / DJT: Daily Exposure Dose over Tolerable Daily Dose). MACs are commonly used in the form of Sanitary Control Values, in order to verify or co-develop corrective action objectives, or even depollution objectives. Management measures, e.g. depollution are based in France on a Management Plan, a definition of the Source Zones of concentrated pollution and then a Cost-Benefit Balance Sheet of the different management and treatment methods and technologies to ensure tolerable toxicological risks.

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