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Scientific Director of HPC-Group International

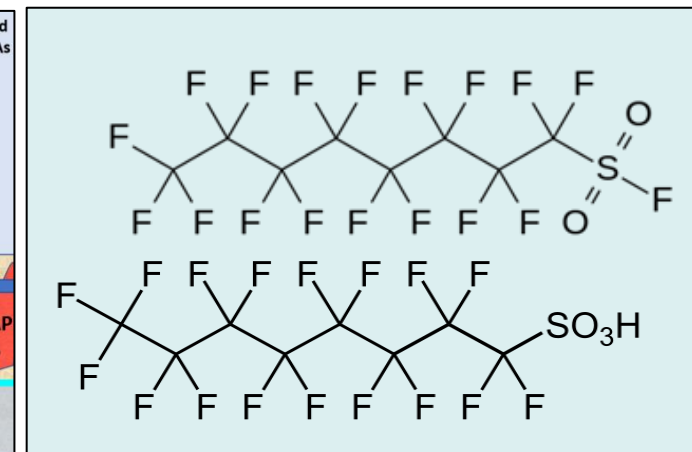
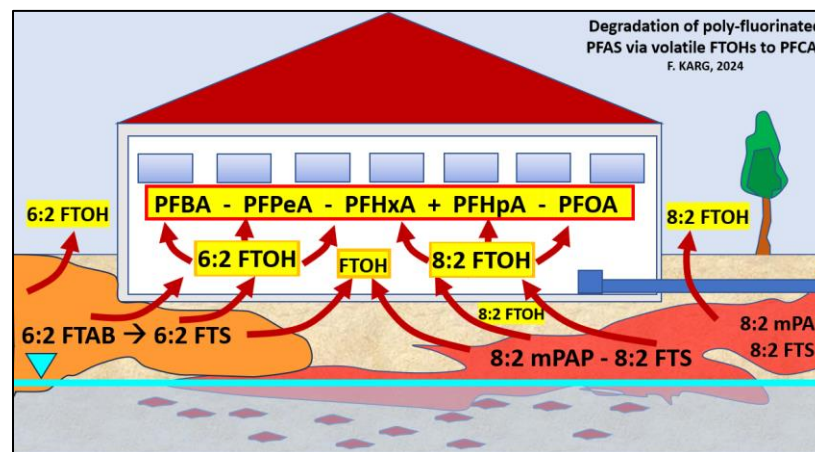
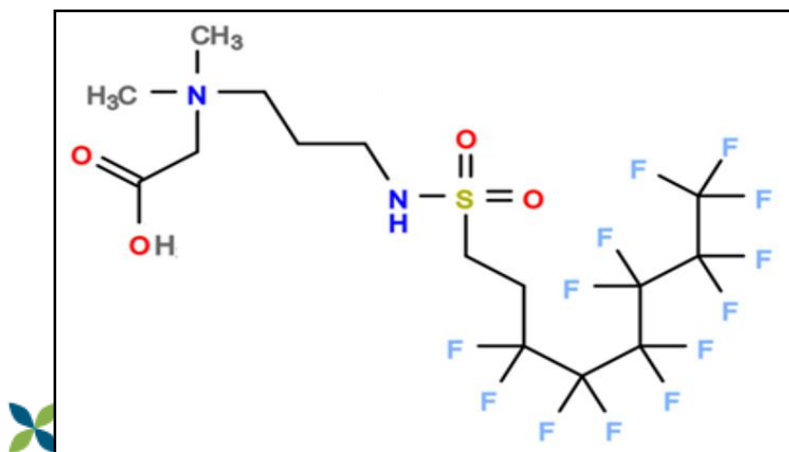
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Human Health Risk Assessment via Toxicological Exposure Risk Quantification (HHRA & TERQ) concerning Bio-transformation Chains of poly-fluorinated PFAS to per-fluorinated PFAS and Top Assay Application

Evaluation des risques sanitaires et toxicologiques (EQRS & ARR) des PFAS
concernant les chaines de bio-transformation des PFAS poly-fluorés vers les PFAS
per-fluorés et application du Top Assay

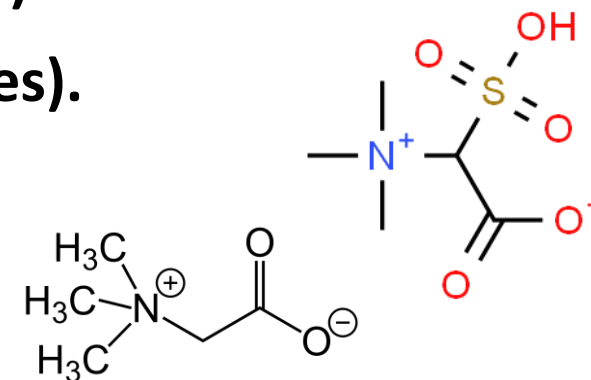
Dr. (PhD) Frank Karg / Scientific Director of HPC-Group (INOGEN JV) and
CEO-President of HPC INTERNATIONAL / France, Germany, Switzerland, Hungary, Balkan, etc.

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PFAS (Fluorinated Tensioactifs) contain **hydrophile groups** (strong solubility):

- **Non-ionic** (for ex. Polyethylene glycols, Acrylamide Oligomers).
- **Anionic** (for ex., Sulfonates, Sulfates, Carboxylates, Phosphates).
- **Cationics** (for ex., Quarternary Ammonium).
- **Amphoters** (for ex., Betaines & Sulfo-betaines): base + acid.



- **Commercial products** mainly contain **mixtures**.
- **The long chain fluoro-telomeres (> C₈)** used as substitutes for PFOS (prohibited) and PFOA **are transformed into PFOA in the subsoil.**
- Short-chain PFAS' (< C₆) can't be transformed into PFOA or PFOS.

In
minimum
33
Categories

1. **Perfluoroalkane-sulfonic-acids (PFASs),**
2. Perfluoroalkane-sulfonats (salts),
3. Perfluoroalkane-sulfinic-acid/sulfonates,
4. Perfluoro-cycloalkane-sulfonic-acids & derivats,
5. Perfluoroalkane-sulfonamids (FASAs),
6. Perfluoroalkane-sulfonamide & quaternary ammonium salts,
7. Acrylate de perfluoroalkane-sulfonamide (MeFASACs),
8. Perfluoroalkane-sulfonamide methylacrylates,
9. Perfluoroalkane-sulfonamide phosphates,
10. Perfluoroalkane-sulfonyl halogenureas,
11. Different polyfluoroalkyl-sulfur compounds,
12. **Perfluoroalkyl-carboxyl-acids (PFCA),**
13. Perfluoroalkyl-carboxyl-acids,
14. Perfluoroalkyl-alcohols/cetones,
15. Halogenurea perfluoroalkyl-carboxylic acids,
16. Perfluoroalkyl-halogenureas,
17. Perfluoroalkyl-ethers,
18. Perfluoroalkyl-amines,
19. Perfluoroalkyl-amino-acides/salts/esters,
20. **Perfluoroalkyl-phosphates,**
21. Perfluoroalkyl-acrylate,
22. Perfluoroalkyl-methacrylates,
23. Other Perfluoroalkyl-carboxylic esters,
24. Perfluoroalkyl-heterocyclic Compounds,
25. Perfluoroalkyl-silanes,
26. **Fluorotelomer-alcools,**
27. Fluorotelomer halogenides,
28. Fluorotelomer sulfonates, sulfonyl chlorides and sulfonamides,
29. Fluorotelomer Acrylates,
30. Fluorotelomer Methylacrylates
31. Other Fluorotelomer Acrylates
32. Fluorotelomer phosphates,
33. Other fluorotelomers.

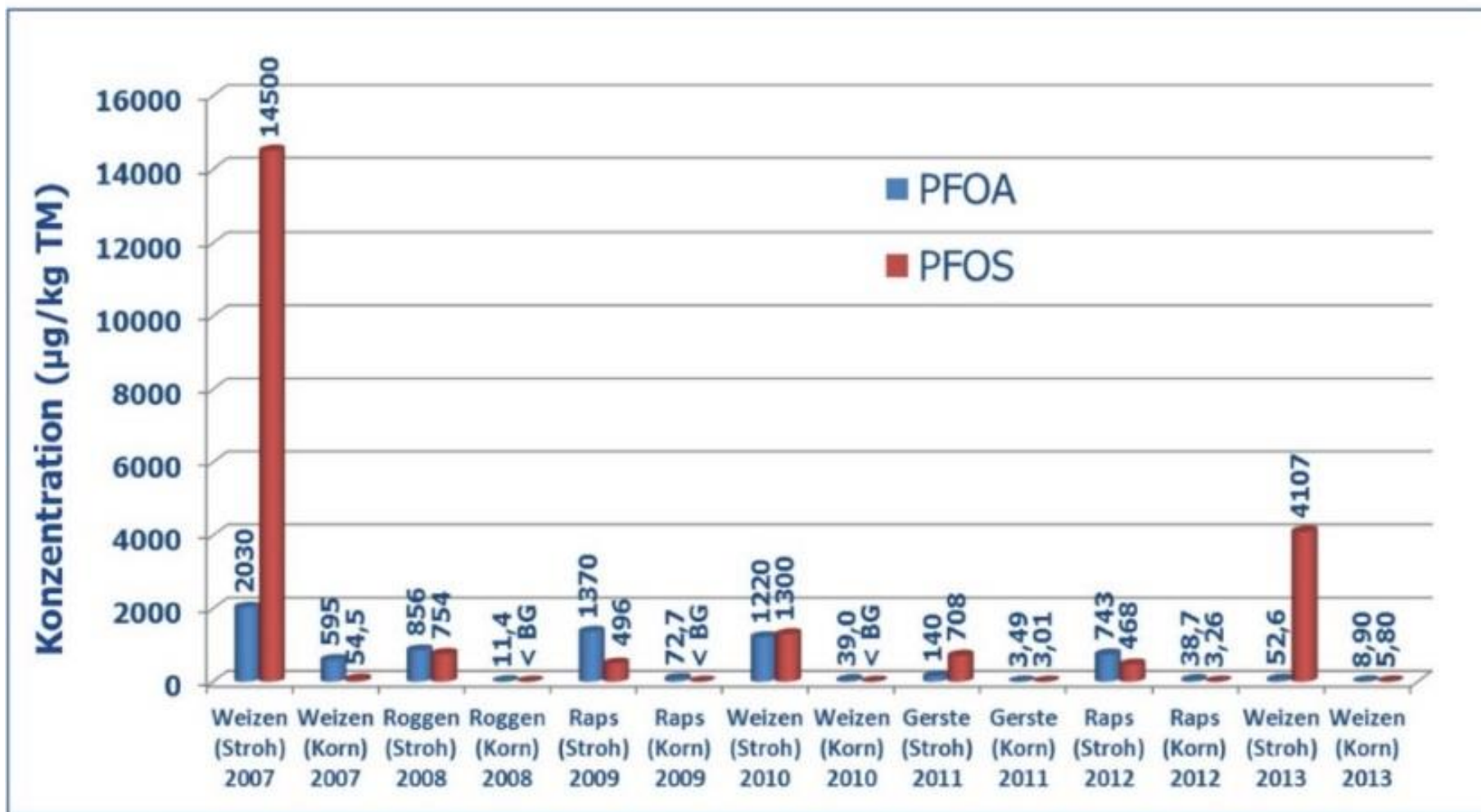
**In total > 9 000 – 12 000 PFAS
are existing !**

PAP Contamination Sources
(Polyfluorinated alkyl phosphate esters)
in Housing & Food packaging and
Biotransformation & Hydrolysis



Source/Quelle: TAXVIG et al. 2014

WWTP sludge on agriculture Land → PFOA & PFOS in German Crop

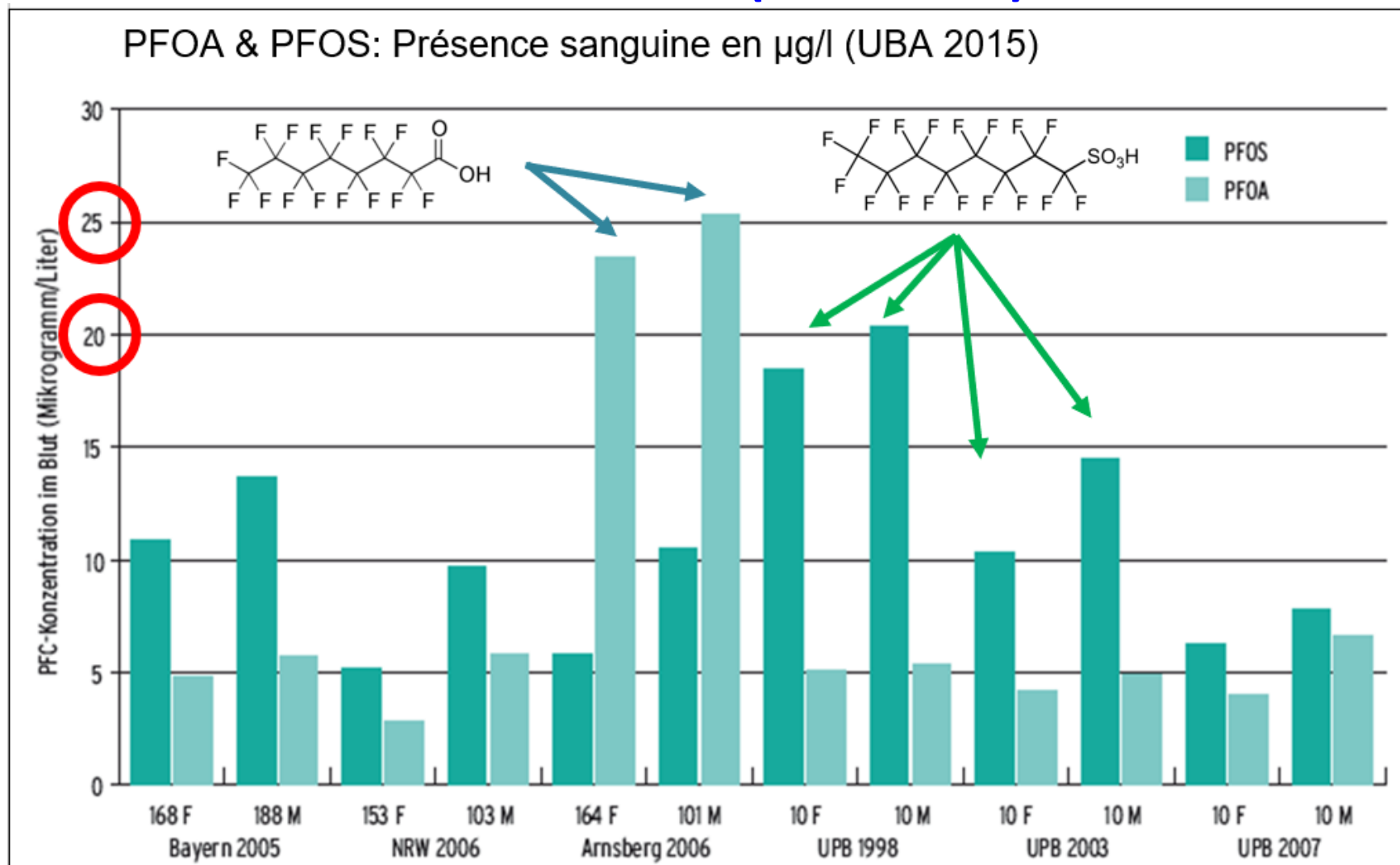


Regulations: EC : Food-Stuff (Meat & Fisch)

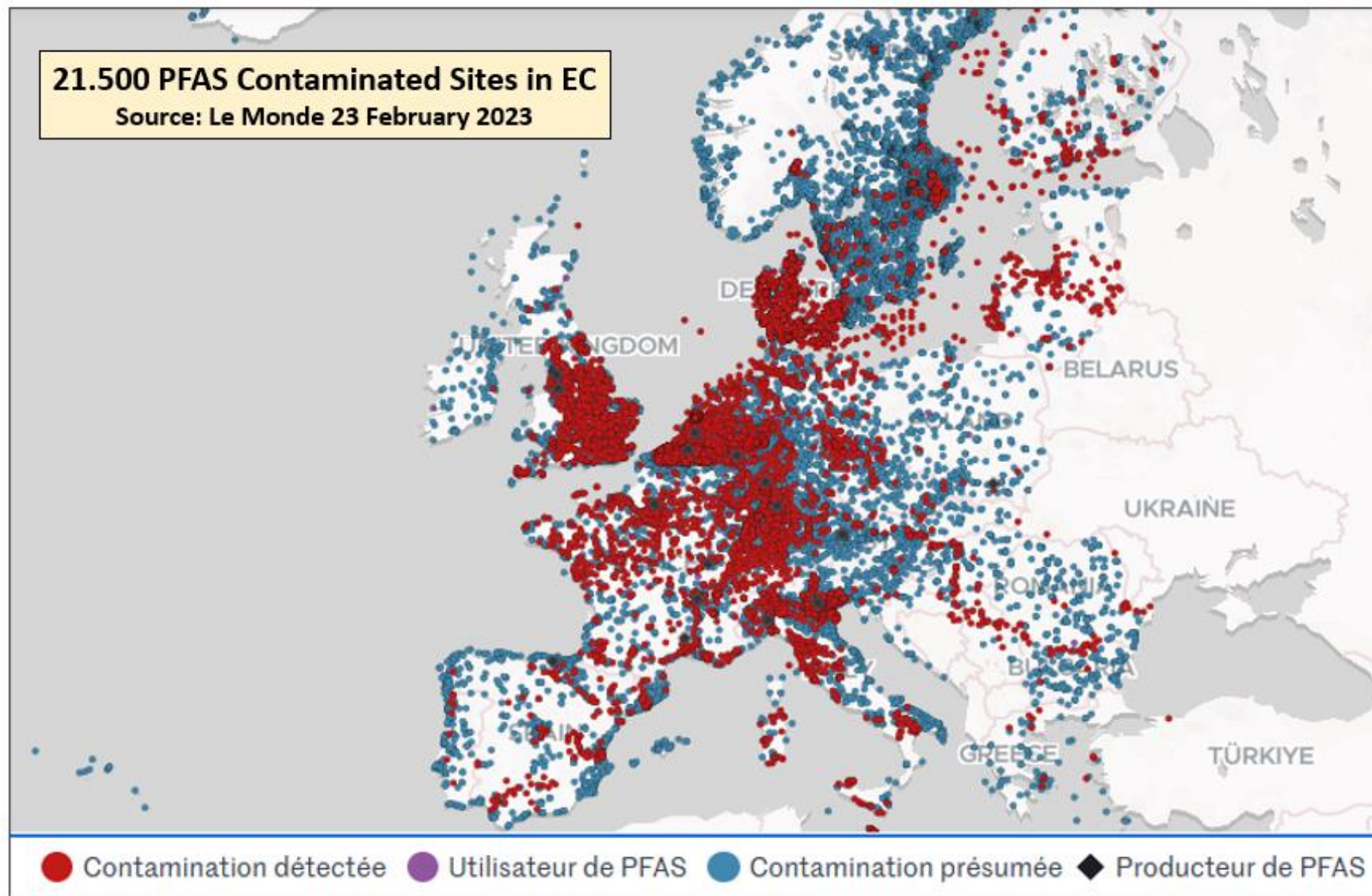
- **EC-Regulation EC 2022/2388 of 07.12.2022, concerning PFAS-Limits in Food-Stuff from 01.01.2023.**
In [µg/kg] (Table simplified)

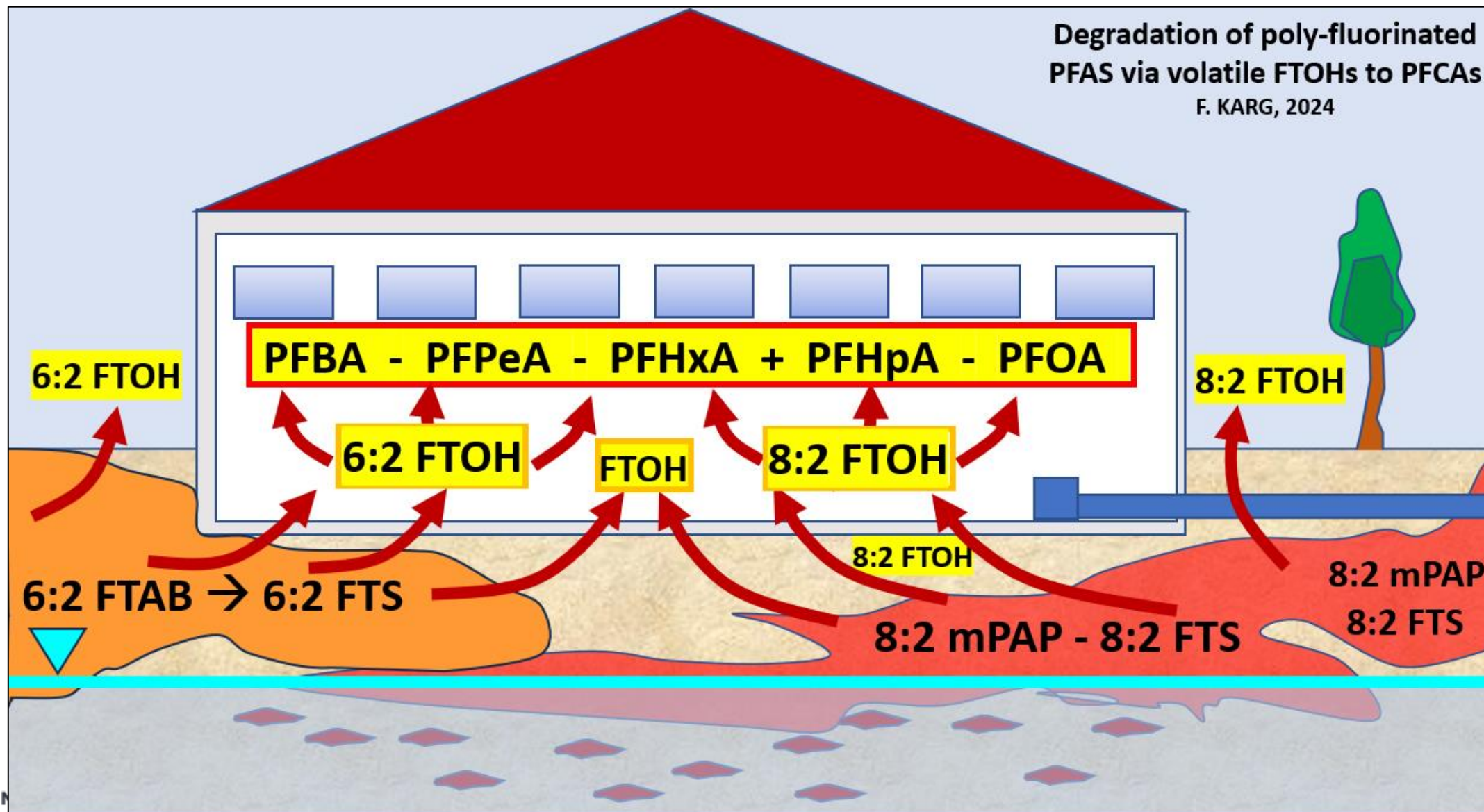
Food-Stuff		PFOS	PFOA	PFNA	PFHxS	Total PFOS, PFOA, PFNA & PFHxS
10.1	Eggs	1,0	0,30	0,70	0,30	1,7
10.2.1.1	Fish	2,0	0,20	0,50	0,20	2,0
10.2.1.2	Other Fishes (b)	7,0	1,0	2,5	0,20	8,0
10.2.1.3	Other Fisches ©	35	8,0	8,0	1,5	45
10.2.2	Crustacea & Mollusks	3,0	0,70	1,0	1,5	5,0
10.3.1	Meat: Cattle, Pig, Poultry	0,30	0,80	0,20	0,20	1,3
10.3.2	Meat: Cheep	1,0	0,20	0,20	0,20	1,6
10.3.3	Offal: Cattle, Pig, Poultry, Cheep	6,0	0,70	0,40	0,50	8,0
10.3.4	Venison (excepted Bear)	5,0	3,5	1,5	0,60	9,0
10.3.5	Offal from Venison (excepted Bear)	50	25	45		

PFAS in Blood (UBA 2015):

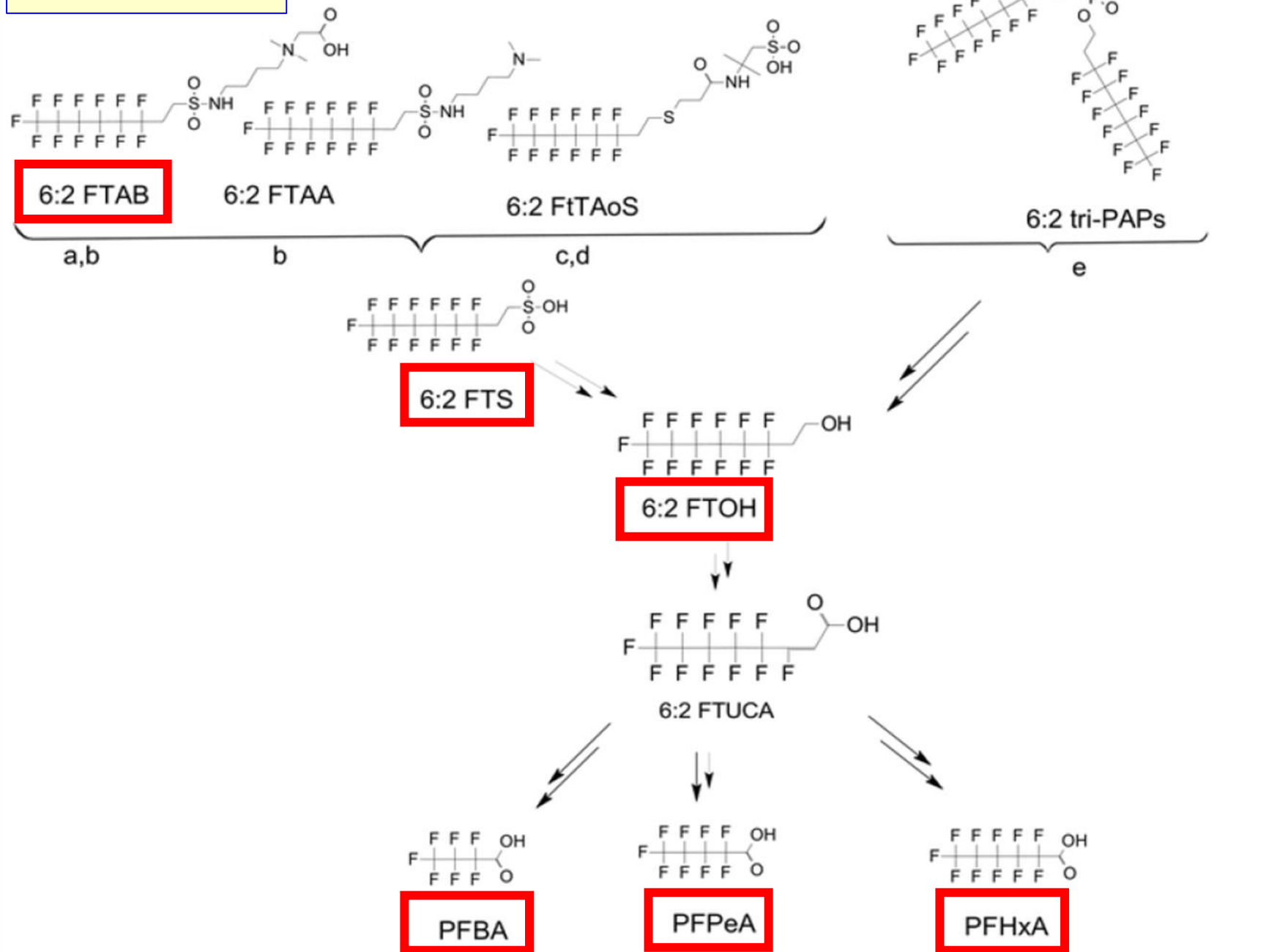


**PFAS:
Situation
Beginning
2023**





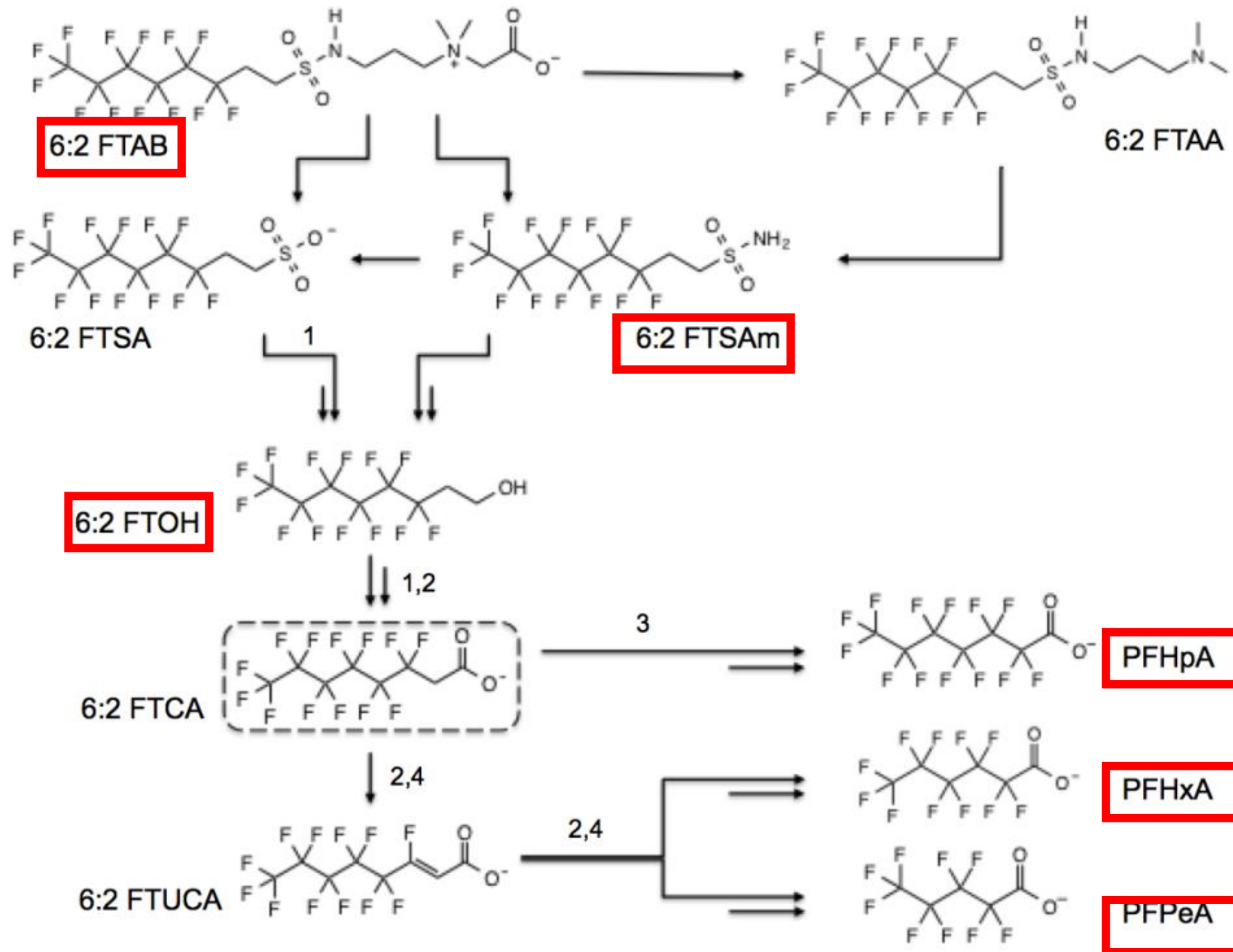
6:2-FTAB



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**6 :2 FTAB:
Degradation
via 6 :2 FTS and 6 :2
FTOH to per-
fluorinated PFBA,
PFPeA & PFHxA**

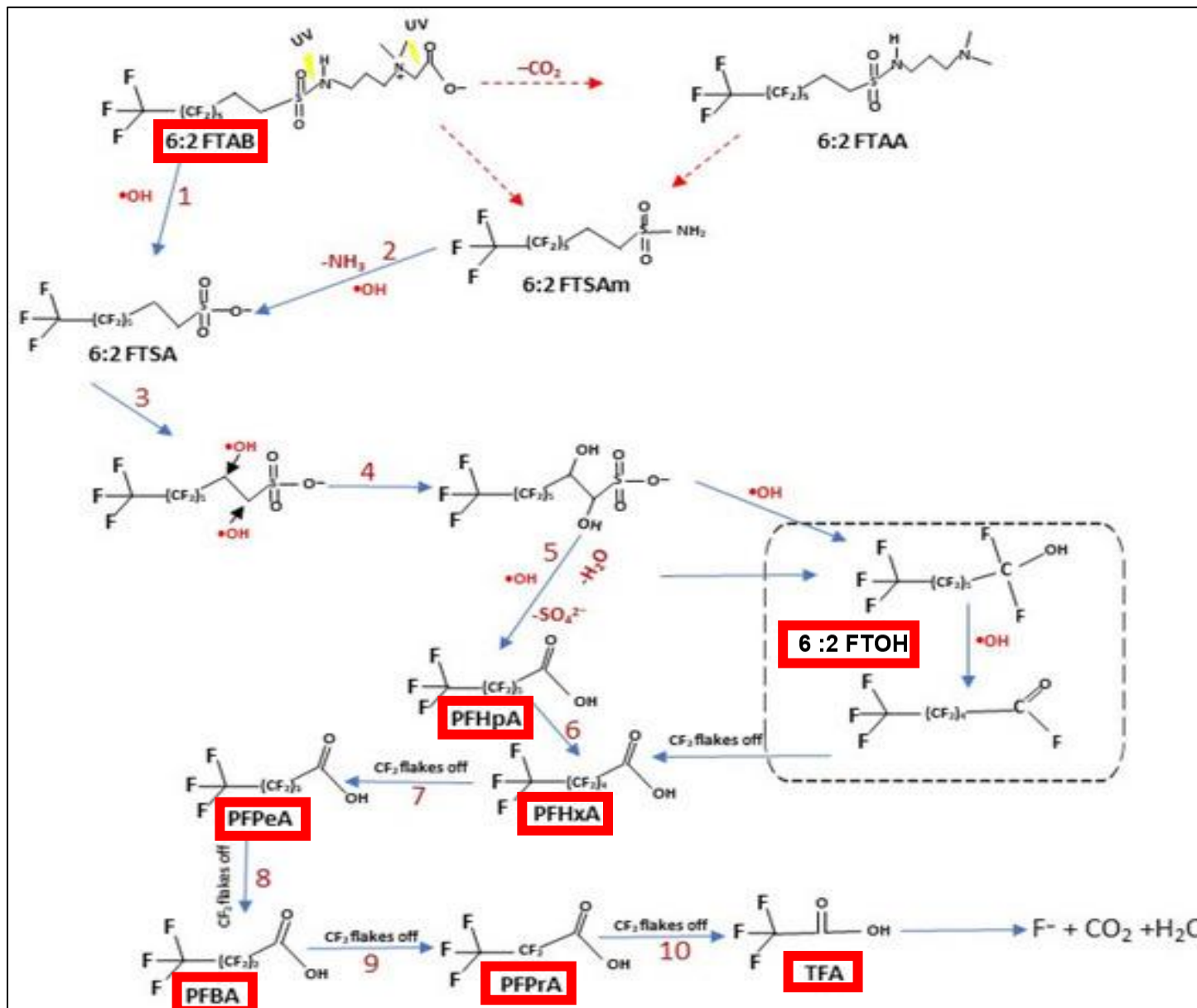
(LaFond et al. 2023, D.M.J.
Shaw et al. 2019 ,Ying Shi,
2018 and V. Mendeza et. al.
2022)



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**6 :2 FTAB:
Photolysis
via
6 :2 FTSA and
6 :2 FTOH to
perfluorinated PFAS:
PFBA, PFPeA and
PFHxA**

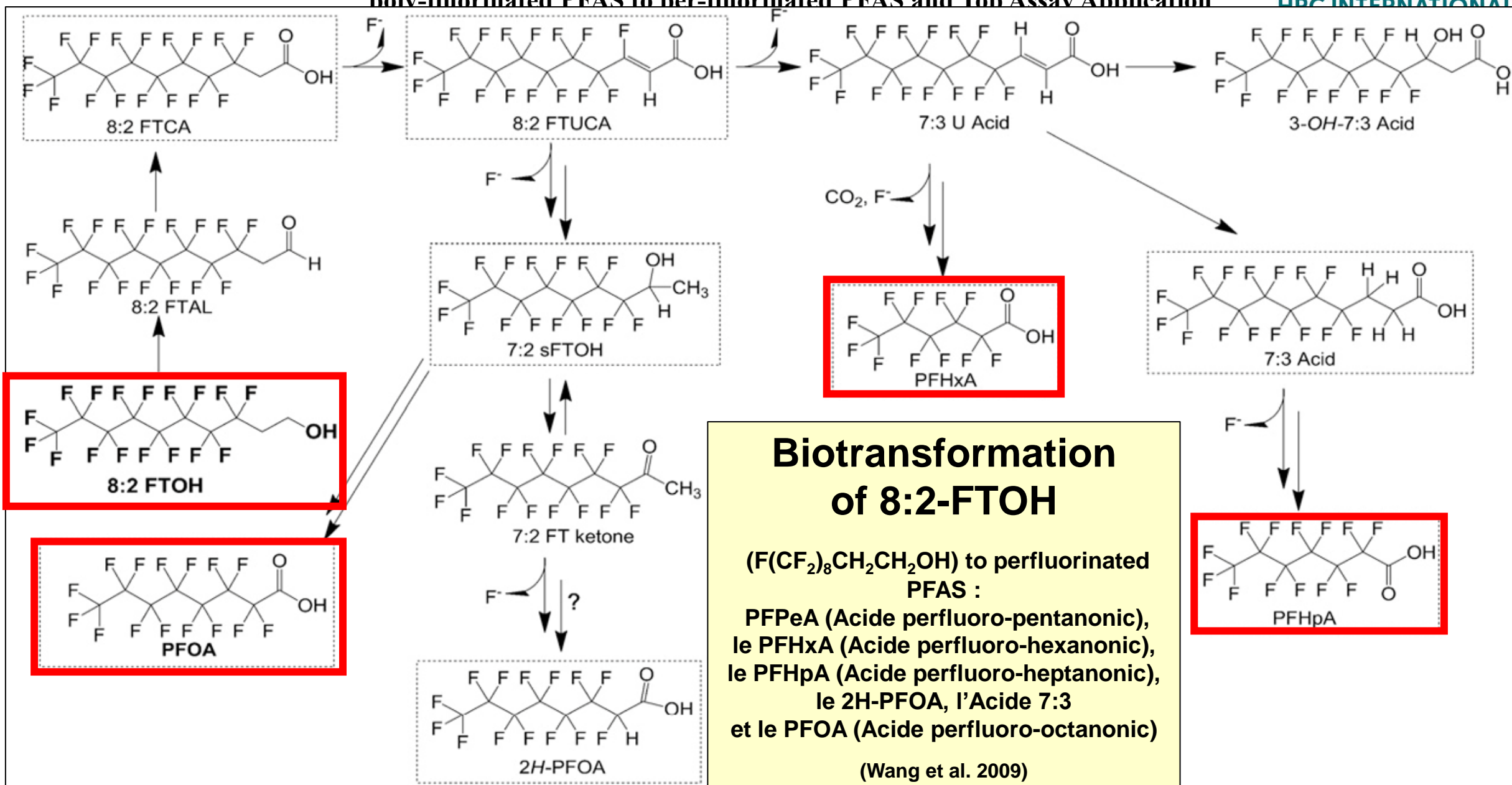
(Lennard John Trouborst:
2016)

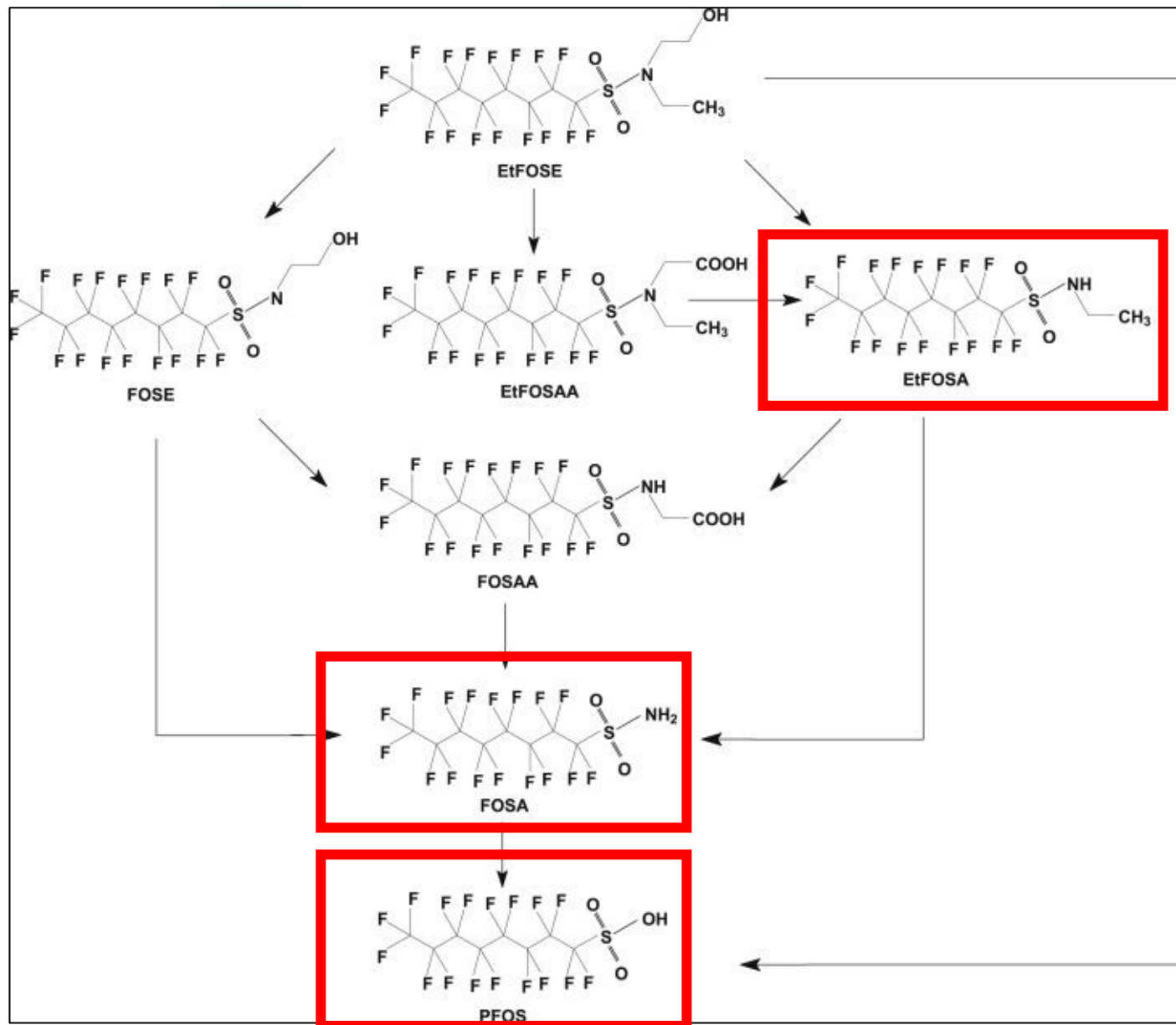


**6 :2 FTAB
Photolysis:**

**via 6:2 FTOH to
PFHxA, PFPeA, PFBA,
PFPrA & TFA**

(Naveed, A. et al 2024)





PFAS: Environnemental Chemistry

Bio-transformation of EtFOSE, EtFOSA & FOSA to PFOS

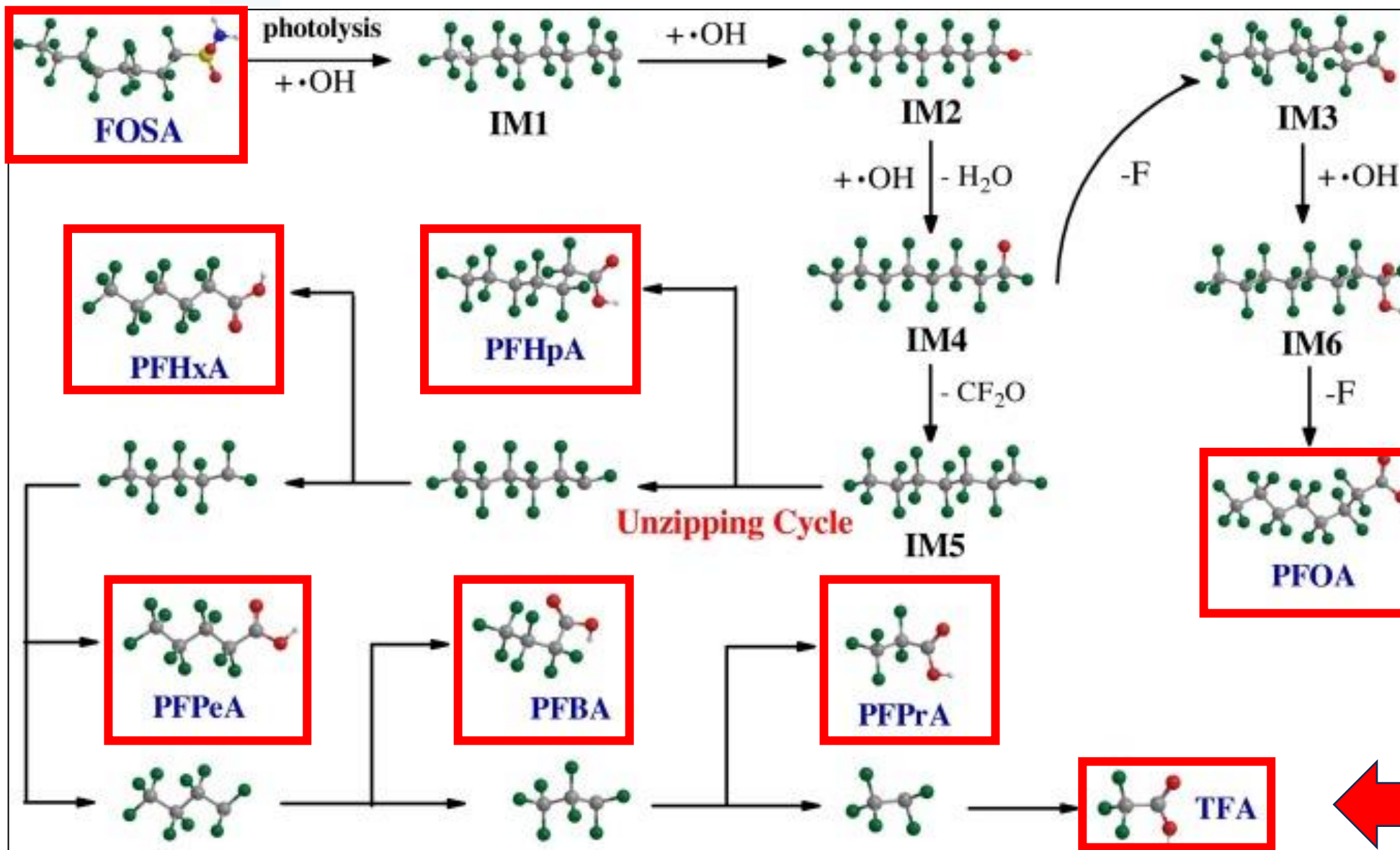
S. Chen et al. 2021

Scotchban FC 807

= 100 % EtFOSA

**Impregnation of
Papers & Textiles**

PFOS

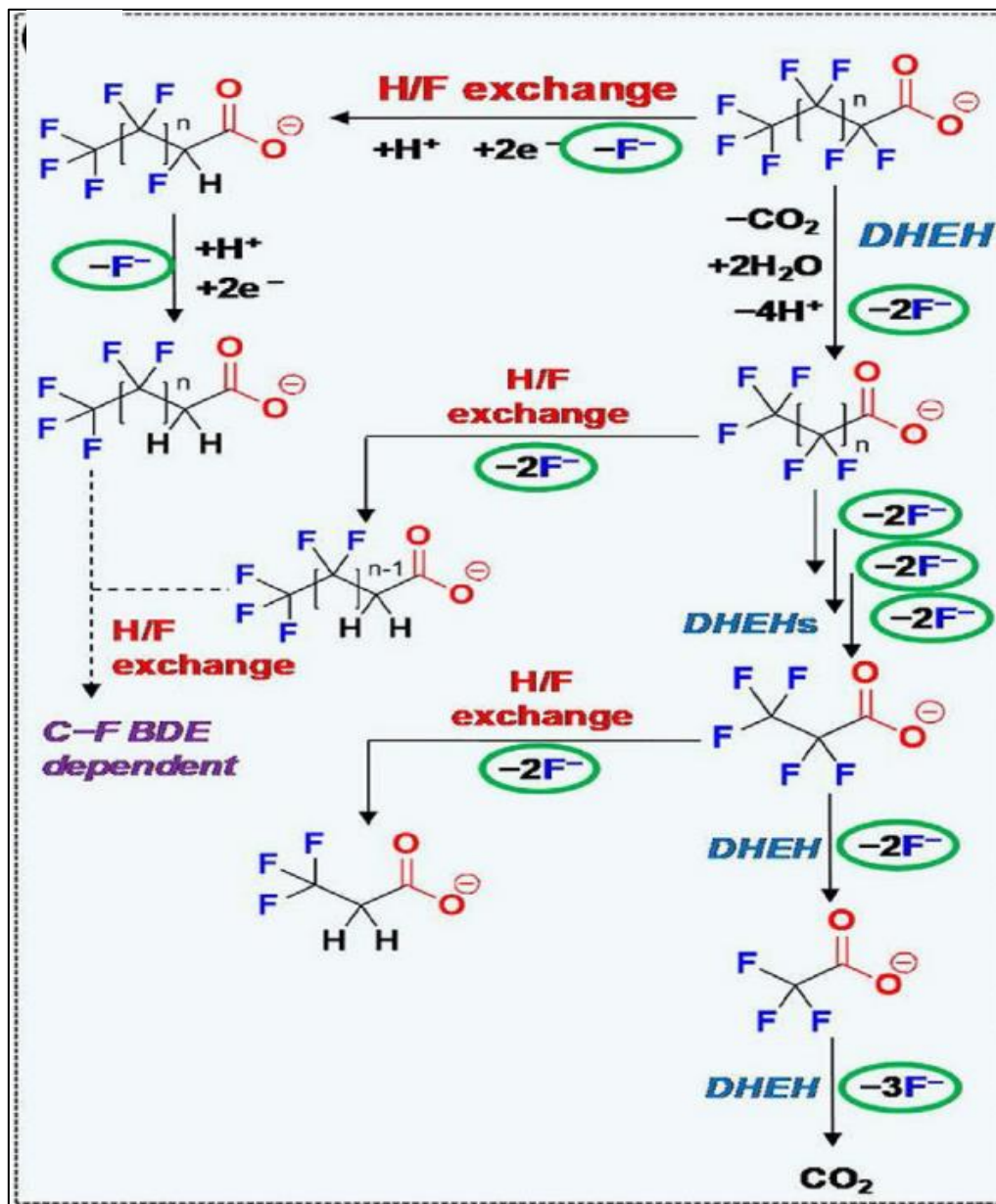


PFAS:
Environmental
Chemistry

**Photolysis
of FOSA to
PFOA, PFNA,
PFHpA, PFHxA,
PFPeA, PFBA,
PFPrA, TFA**

Y. Wang 2020

TFA



PFAS: Environmental Chemistry

Photochemical defluorination of PFBA to TFA

Bentel et al. 2019 & Masruck, A. et al. 2020)

Ultrashort PFAS:

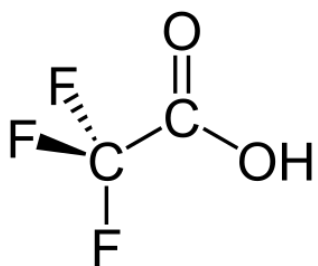
- TFA: Trifluoro acetic acid: CAS: 76-05-1
- TFMS: Trifluoro methane sulfonic acid: CAS: 1493-13-6
- PFES: Penta(per)fluoro ethane sulfonic acid: 354-88-1
- PFPrA: Perfluoro propanonic acid: CAS: 422-64-0
- PFPrS: Perfluoro propane sulfonic acid: CAS: 423-41-6



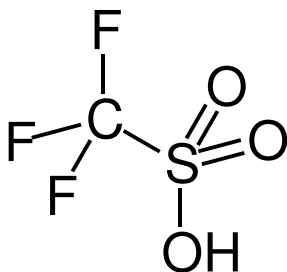
TFA

PFAS: Environmental Chemistry

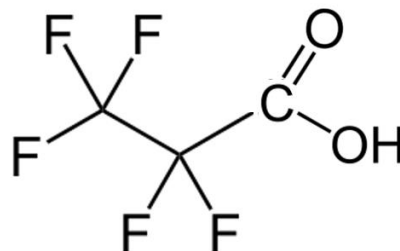
Other (semi) volatile PFAS



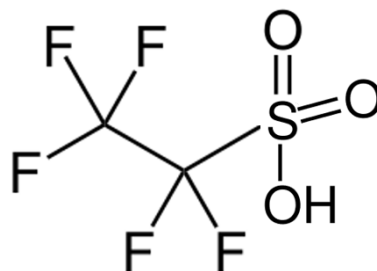
TFA



TFMS



PFPrA



PFES

- **FTOH: Fluorotelomer-alcohols** (4:2-FTOH, 4:3-FTOH, 6:2-FTOH, 6:3-FTOH, 8:2-FTOH, 10:2-FTOH, etc.),
- **FASE: Per-fluoroalkane-sulfamide-ethanols** (par ex. N-MeFOSE, N-EtFOSE),
- **FTI: Fluorotelomer-iodites** (par ex.. 6:2-FTI, 8:2-FTI, 10:2-FTI),
- **FTAC: Fluorotelomere-acrylates** (par ex. 4:2-FTAC, 6:2-FTAC, 8:2-FTAC, 10:2-FTAC),
- **FTMACS: 6:2-Fluorotelomer-methylacrylates** (par ex. 4:2-FTMAC, 6:2-FTMAC, 8:2-FTMAC, 10:2-FTMAC),
- **PFADiI: Perfluoroalkyl-di-iodites** (par ex. PFBuDiI, PFH_xDiI, PFODiI),
- **TFMB: Trifluormethylbenzenes** (z.B. BTFMBB: 1-Brom-3,5-bis(trifluoro-methyl)benzol).

Leaching Increasing or Reduction of of some PFAS-Fluortelomeres by pH-changing

Example: Seawater Intrusion into the Aquifer (HH): Analyses according DIN 38407-42

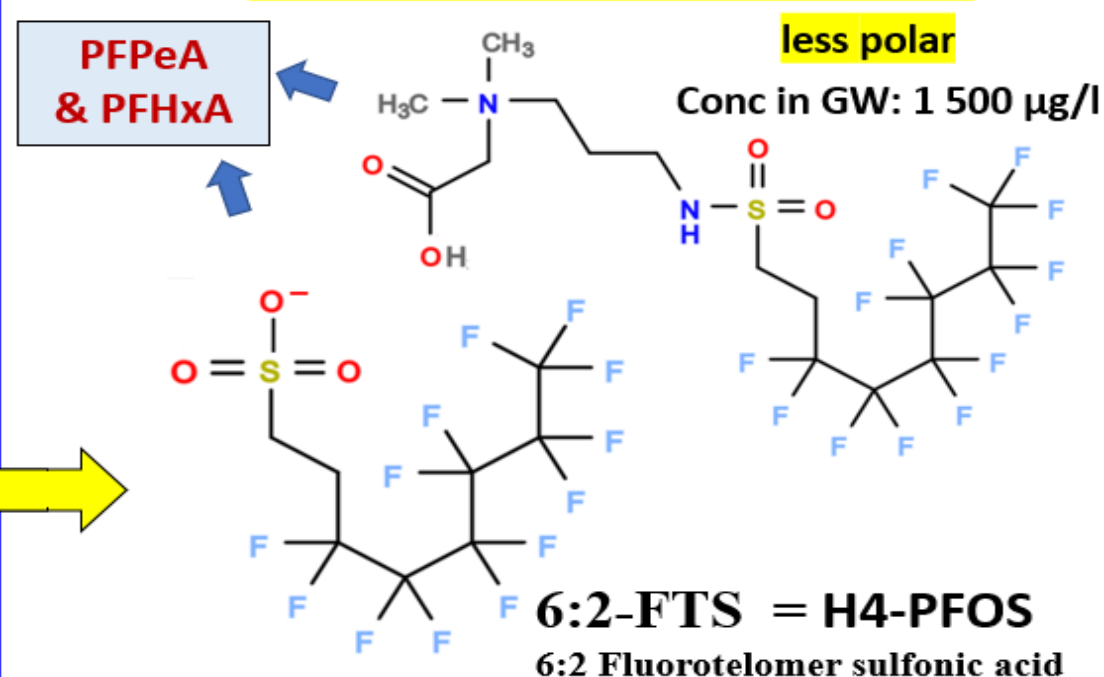
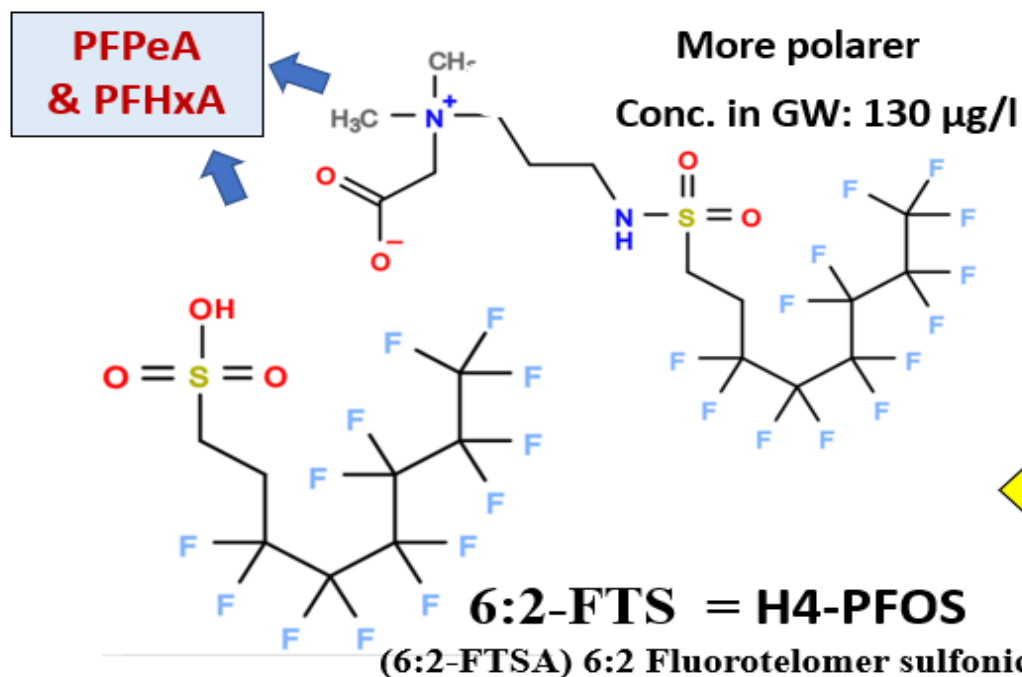
pH 6,7

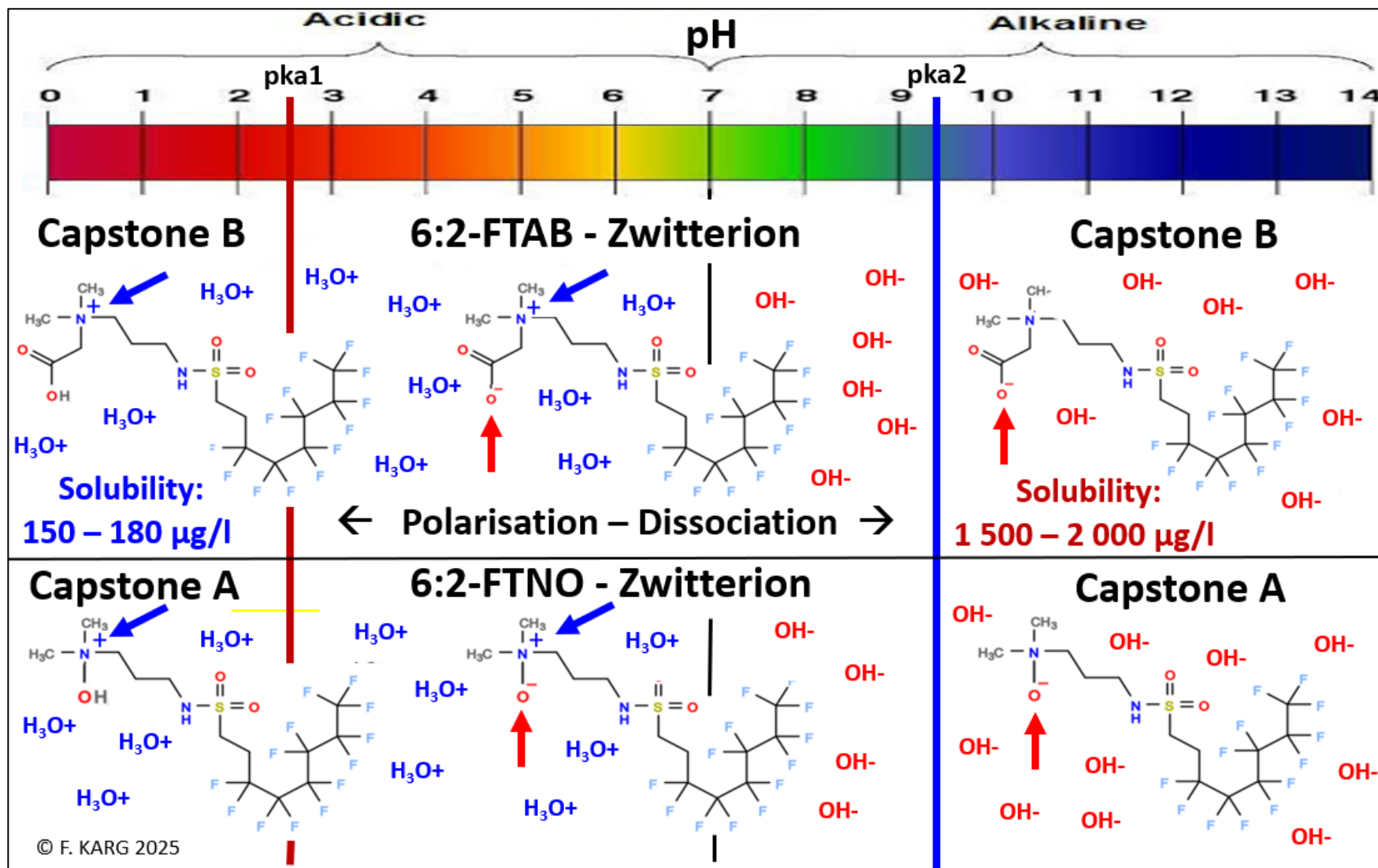
→ zu →

pH 7,3

6:2-FTAB = Capstone B (AFFF)
6:2 Fluorotelomer-sulfonamid-propyl-betain

6:2-FTAB = Capstone B (AFFF)
6:2 Fluorotelomer-sulfonamid-propyl-betain
Factor 11,5 x higher Concentrations



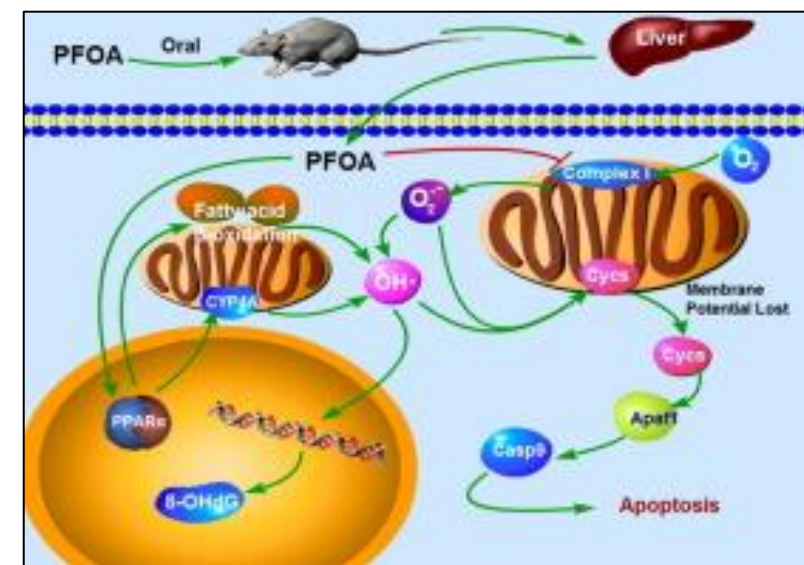


Environmental
Chemistry
according pH of



Toxicology: eg. PFOA et PFOS:

- **Endocrine disruptors** (on the production of steroid hormones, such as reduced testosterone levels, etc.): PFOS + FTOH (Fluoro-telomeric alcohols),
- **Carcinogenicity:** Breast & Testicular Cancer Developments (PFOA):
 - Breast Cancer, if exposure to PFOA + PFOS + BPA + Methylene parabene: Proliferation of epithelial cells & suppression of Apoptosis (Pierozan et al. 2023 & Pesonnen et al. 2024).
- **Teratogenicity** (eg.: levels of androgens or abnormal thyroid hormones, etc.),
- **Immunotoxicity** (via thyroid effects and on the immune system),
- **Neurotoxicity** (hyperactivity disorders, etc.).
As well as other neurological disorders can result.



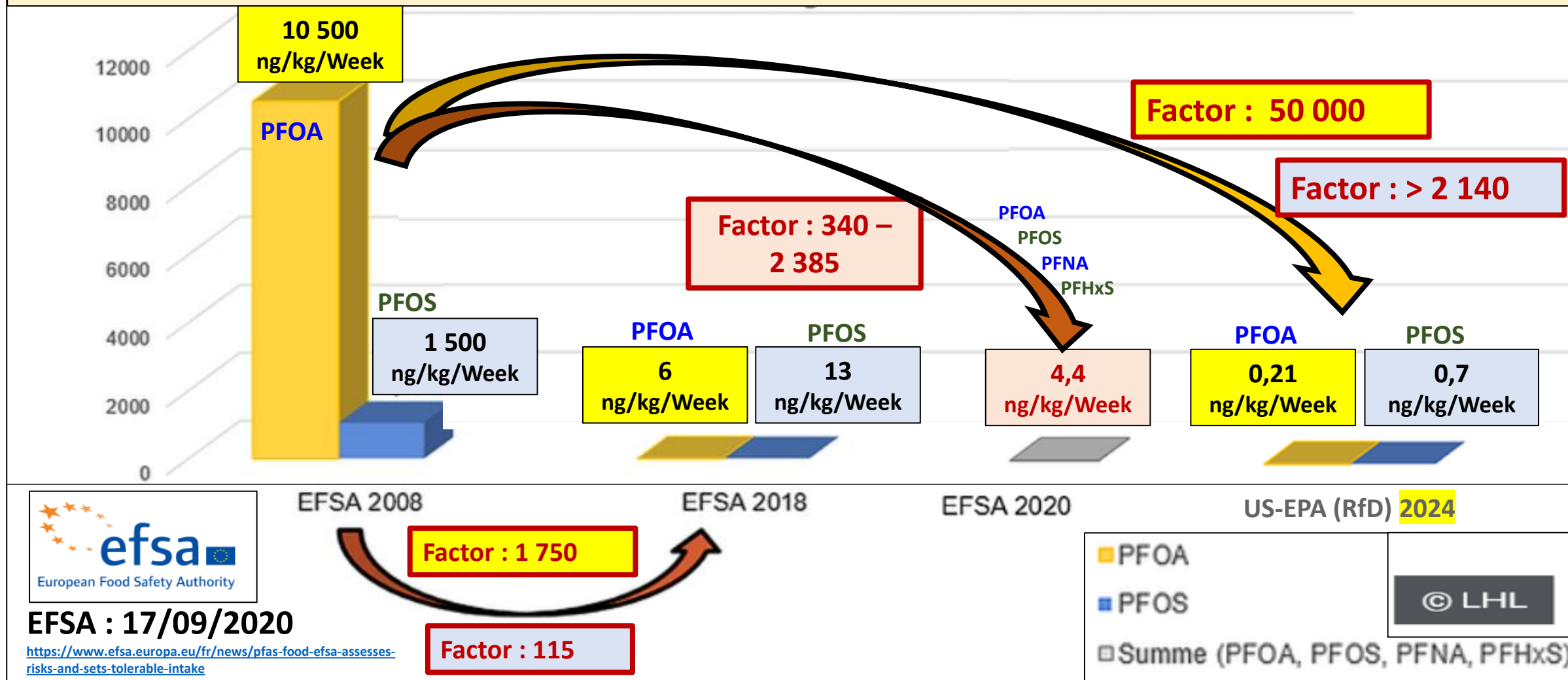
Molecular mechanisms of PFOA-induced Toxicity

Toxicological Effects of PFAS : Résumé

PFAS	Hepato- toxic	Teratogen	Repro- toxic	Immuno- toxic	Hemato- toxic	Endocrine disruptor (Thyroid)	Neurotoxic	Tumors
Perfluorcarboxylic acids								
PFBA								
PFPeA								
PFHxA								
PFHpA								
PFOA								
PFNA								
PFDA								
PFUnA								
PFDaA								
Perfluorsulfonic acids								
PFBS								
PFHxS								
PFOS								
Ethersulfonates								
ADONA								
HFPO-DA Genx								
Laboratory animal studies			Evaluated effect			Negative		

VTR: EFSA & US-EPA : PFOA & PFOS : Consideration of Higher Toxicity

TWI & TDI: Tolerable Weekly & Daily Intake: 2008 – 2020 & 2024



Toxicological Dose – Effect Values: 1/2

ANSES: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail / France (2017)

ATSDR: Agency for Toxic Substances and Disease Registry

EFSA: European Food and Safety Authority (EC)

IRIS : Integrated Risk Information of Substances (U.S.-EPA)

UBA : Umweltbundesamt (Germany)

BfR: Bundesinstitut für Risikobewertung (Germany)

OEHHA : Office of Environmental Health Hazard Assessment

WHO: World Health Organization (OMS)

RIVM : Netherlands Environmental & Health Institute

MDHHS: Michigan Department of Health and Human Services, Division of Environmental Health

TCEQ: Texas Commission on Environmental Quality

NJ-DWQIHES: New Jersey Drinking Water Quality Institute Health Effects Subcommittee

Bil, W. et al. 2020 : Toxicological Equivalence factors on PFOA RfD

SLU: Swedish University of Agricultural Sciences

Subst.	CAS Nr.	Cancero-genic / not can-cero-genic	Chronic toxicological value			Testing Species / Study Type	Sigle	Security Factor & Origin	Organi-sation
			Exposure pathway	Target organ	Value				
PFBA	375-22-4	NC	oral	Hepatic	1 µg/kg/d	Rate	RfD	POD _{HED} / 900	TCEQ 2023 US-EPA IRIS 2022
			inhalation	Hepatic	3,5 µg/m ³	Rate	RfC	from oral value	TCEQ 2023
PFPeA	2706-90-3	NC	oral	Hepatic	0,5 µg/kg/d	Rate	RfD	POD _{HED} / 90	TCEQ 2023
PFHxA	307-24-4	NC	oral	Hepatic	0,5 µg/kg/d	Rate	RfD	POD _{HED} / 90	TCEQ 2023 US-EPA IRIS 2023
PFHpA	375-85-9	NC	oral	Hepatic	25 ng/kg/d	Rate	DJT	Extrapolation of DJT of Health Canada	ANSES 2017 TCEQ 2023
PFOA	335-67-1	NC	oral	Hematologic	0,86 ng/kg/d	Rate	TDI	BMDL 5	UBA 2023 BFR & EFSA 2018
				Hepatic, Mammar, Hematologic	12 ng/kg/d	Mice	RfD	LOAEL / (81 * 300)	TCEQ 2023
				Immune, develop-mental and cardio-vascular	0,03 ng/kg/d	Epidemi-ologic	RfD	Several studies	US-EPA 2024 [7]
			inhalation	Hepatic	4,1 ng/m ³	Rate	RfC	NOAEL / (81 * 3 000)	TCEQ 2023
		C	oral	Testicular tumors	2,52 x 10 ⁻⁶ (ng/kg/d) ⁻¹	Epidemi-ologic	SF	-	New Jersey 2017
				Renal Cell Carcinoma	0,0293 (ng/kg/d) ⁻¹	Epidemi-ologic	SF	-	US-EPA 2024 [7]
PFNA	375-95-1	NC	oral	Hematologic	2,5 ng/kg/d	Mouse	RfD	NOAEL / 300	US-EPA IRIS 2019 / New Hampshire DES 2019
			inhalation	Lung, respiratory system	28 ng/m ³	Rate	RfC	NOAEL / (81 * 30 000)	US-EPA IRIS 2019 TCEQ 2023
PFBS	375-73-5	NC	oral	Hematologic and renal	1,4 µg/kg/d	Rate	RfC	NOAEL / (142*300)	TCEQ 2023
			inhalation		4,9 µg/m ³	Rate	RfC	from oral value	TCEQ 2023

Toxicological Dose – Effect Values: 2/2

ANSES: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail / France (2017)

ATSDR: Agency for Toxic Substances and Disease Registry

EFSA: European Food and Safety Authority (EC)

IRIS : Integrated Risk Information of Substances (U.S.-EPA)

UBA : Umweltbundesamt (Germany)

BfR: Bundesinstitut für Risikobewertung (Germany)

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Bil, W. et al. 2020 : Toxicological Equivalence factors on PFOA RfD

SLU: Swedish University of Agricultural Sciences

Subst.	CAS Nr.	Cancero-genic / not cancero-genic	Chronic toxicological value			Testing Species / Study Type	Sigle	Security Factor & Origin	Organi-sation
			Exposure pathway	Target organ	Value				
PFDA	335-76-2	NC	oral	Hepatic	15 ng/kg/d	Rate	RfD	LOAEL / (81 * 1 000)	TCEQ 2023
				Immune / developmental	0,002 ng/kg/d	Rate	RfD	BMDL / 30	US-EPA IRIS 2024
			inhalation	Hepatic	53 ng/m ³	Rate	RfC	from oral value	TCEQ 2023
PFHxS	355-46-4	NC	oral	Hematologic and thyroïdal	3,8 ng/kg/d	Rate	RfC	LOAEL / (263*300)	TCEQ 2023
			inhalation		13 ng/m ³	Rate	RfC	from oral value	TCEQ 2023
PFHpS	375-92-8	NC	oral	Hepatic	0,43 ng/kg/d	Rate	TDI	Potency Factor : 0,6-2	UBA 2020, EFSA 2018, BfR 2018
PFOS	1763-23-1	NC	oral	Hepatic	1,86 ng/kg/d	Monkey	TDI	NOAEL	UBA 2020 BfR & EFSA 2018
				Decreased birth weight and increased cholesterol	0,1 ng/kg/d	Human epidemiologic	RfD	POP / 10	US-EPA 2024
			inhalation	Thyroidal, neurological and foetal development	81 ng/m ³	Rate	RfC	from oral value (23 ng/kg/j)	TCEQ 2023
		C	oral	Hepatic	39,5 (mg/kg/d) ⁻¹	Rate	SF	-	US-EPA 2024
PFOA	754-91-6	NC	oral	Mammary glands	12 ng/kg/d	Mice	RfD	As PFOA: NOAEL / (81 * 300)	TCEQ 2023
			inhalation		4,1 ng/m ³	Rate	RfC	As PFOA NOAEL/ (81 * 3 000)	TCEQ 2023
6:2-FTOH	647-42-7	NC	oral	Hepatotoxic	43 ng/kg/d	Rate	RfD	RPF based on PFOA's RfD x 0,02	RIVM / Bil et al. 2020 & 2021
8:2-FTOH	678-39-7	NC	oral	Hepatotoxic	21,5 ng/kg/d	Rate	RfD	RPF based on PFOA's RfD x 0,04	RIVM / Bil et al. 2020 & 2021
			oral		1,5 x 10 ³ ng/kg/d	Rate	RfD	RfD assimilated to PFOA transformation Product 8:2-FTOH & Inhalation: 20 m ³ /d	SLU 2018 (Sweden) (Ingestion based on EFSA 2008)

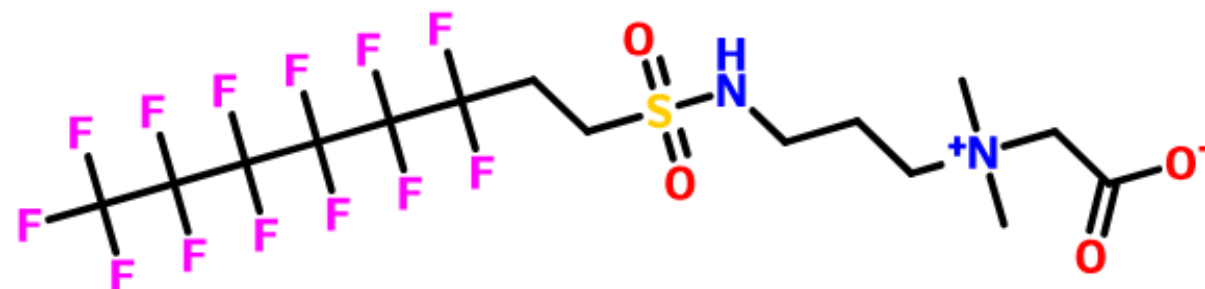
Toxicological Dose – Effect Values: ECHA 2013: 6:2-FTAB (Capstone B)

Toxicité	Type de limite	Limite
Toxicity (systemic)	NOAEL	10 mg/g/jour
Reprotoxicity	NOAEL	10 mg/g/jour
Neurotoxicity	NOAEL	200 mg/kg/jour
Genotoxicity		Non



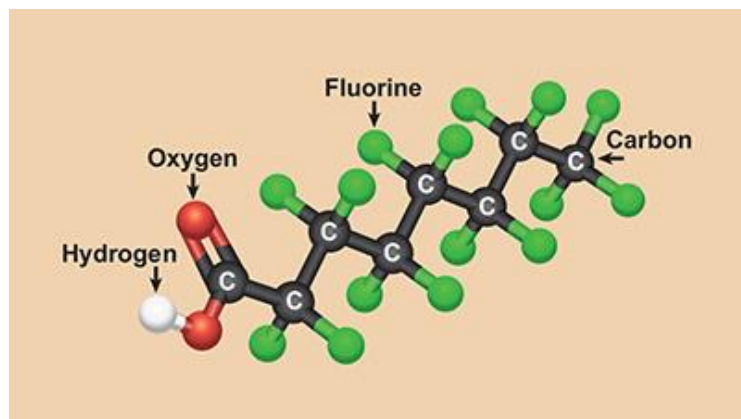
RfD or TDI: 0,3 – 1 mg/kg/d ?

Capstone B



Toxicological Dose – Effect Values: Example: Bil et al. (2020-21) (NL):

**RPF : Relative Potency Factors,
based on Toxicity Equivalence
Factors based on PFOA**



**Warning: RPFs are only usable
cable for hepatotoxicity !**

Per- and polyfluorinated congeners	RPF
Sulfonic acids	
PFBS	0.001
PFPeS*	$0.001 \leq \text{RPF} \leq 0.6$
PFHxS	0.6
PFHpS*	$0.6 \leq \text{RPF} \leq 2$
PFOS	2
PFDS*	2
Carboxylic acids	
PFBA	0.05
PFPeA*	$0.01 \leq \text{RPF} \leq 0.05$
PFHxA	0.01
PFHpA*	$0.01 \leq \text{RPF} \leq 1$
PFOA	1
PFNA	10
PFDA*	$4 \leq \text{RPF} \leq 10$
PFUnDA	4
PFDoDA	3
PFTTrDA*	$0.3 \leq \text{RPF} \leq 3$
PFTeDA	0.3
PFHxDA	0.02
PFODA	0.02
Ether carboxylic acids	
HFPO-DA	0.06
ADONA	0.03
Telomer alcohols	
6:2 FTOH	0.02
8:2 FTOH	0.04

^a RPF values using relative liver weight increase as input. RPFs are presented for 14 perfluoroalkyl acids (PFAAs) and two PFAA precursors (the telomer alcohols).

*RPF based on read-across.

Abkürzung	Substanz	CAS-Nummer	TEF
PFBA	Perfluorbutansäure	375-22-4	0.05
PFPeA	Perfluorpentansäure	2706-90-3	0.05
PFHxA	Perfluorhexansäure	307-24-4	0.01
PFHpA	Perfluorheptansäure	375-85-9	1
PFOA	Perfluoroctansäure	335-67-1	1
PFNA	Perfluornonansäure	375-95-1	10
PFDA	Perfluordecansäure	335-76-2	10
PFUnDA	Perfluorundecansäure	2058-94-8	4
PFDoDA	Perfluordodecansäure	307-55-1	3
PFTTrDA	Perfluortridecansäure	72629-94-8	3
PFTeDA	Perfluortetradecansäure	376-06-7	0.3
PFHxDA	Perfluorhexadecansäure	67905-19-5	0.02
PFODA	Perfluoroctadecansäure	16517-11-6	0.02
PFBS	Perfluorbutansulfonsäure	375-73-5	0.001
PFPeS	Perfluorpentansulfonsäure	2706-91-4	0.6
PFHxS	Perfluorhexansulfonsäure	355-46-4	0.6
PFHpS	Perfluorheptansulfonsäure	375-92-8	2
PFOS	Perfluoroctansulfonsäure	1763-23-1	2
PFDS	Perfluordecansulfonsäure	335-77-3	2
HFPO-DA (GenX)	Perfluor(2-propoxypropansäure)	62037-80-3	0.06
ADONA	Perfluoro-4,8-dioxa-3H-nonansäure	958445-44-8	0.03
6:2-FTOH	6:2 Fluortelomeralkohol	647-42-7	0.02
8:2-FTOH	8:2 Fluortelomeralkohol	678-39-7	0.04
Capstone B	Capstone B	34455-29-3	0.001
Capstone A	Capstone A	80475-32-7	0.05
PFOSA (=FOSA)	Perfluoroctansulfonamid	754-91-6	2
4:2-FTS	4:2-Fluortelomer-sulfonsäure	757124-72-4	0.2
6:2-FTS	6:2-Fluortelomer-sulfonsäure	27619-97-2	0.2
8:2-FTS	8:2-Fluortelomer-sulfonsäure	39108-34-4	1
PFNS	Perfluornonansulfonsäure	68259-12-1	10
EtFOSA	N-Ethylperfluoroctansulfonamid	4151-50-2	2
MeFOSA	N-Methylperfluoroctansulfonamid	31506-32-8	2
EtFOSAA	N-Ethylperfluoroctansulfonamidoessigsäure	2991-50-6	2
MeFOSAA	N-Methylperfluoroctansulfonamidoessigsäure	2355-31-9	2

VTR / TEF: Switzerland (2024)

Toxicity Equivalence Factors



No	<u>TRD: Toxicological Reference Dose</u> <u>Choice Criteria</u>	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 Organism	1 Organism	
3	Several Organisms shows similar TRD (+/- 50 %)	> 3 Organisms	2 Organism	1 Organism	
4	Age of base Study	≤ 15 years	15 – 25 years	< 25 years	
5	Mechanistic toxicological basement Study (for ex. Genotoxicity):	Epidemiology	Mammal	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	No		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	No		Yes	
13b	Transposition: Animal to Human	No	Yes		
13c	Transpositions : From in-Vitro	No		Yes	
13d	Transpositions : From in-Silico	No		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	

TOF: Total Organo Fluorine

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= PFAS Monomers & Polymers +
other organo-fluorine Compounds;
Pesticides, Pharmaceuticals, etc.
→ → → *No Compound Identification !*

AOF: Adsorbable Organic Fluorine

= PFAS Monomers & Polymers +
other organo-fluorine Compounds;
Pesticides, Pharmaceuticals, etc.
→ → → *No Compound Identification !*

NTA: Non-Target Analysis = Semi-quantitative Identification of up to
12 000 Compounds: PFAS Monomers

QTA: Quantitative Target
Analysis = up to 20-700 Com-
pounds: PFAS Monomers

QTA+TA; after TOP Assay (20-
200 Compounds: PFCA including
transformed polyfluorinated PFAS)

Recommended PFAS Parameters (min.) + 5 PFAS ultrashort PFAS

PFAS	LQ Eaux		CAS	VTR	Dir. CE EP2020/ 2184	AM 20/06/23 France
PFBA (perfluorobutanonic acid)	ng/l	1	375-22-4			
PFPeA (perfluoropentanonic acid)	ng/l	5	2706-90-3			
PFHxA (perfluorohexanonic acid)	ng/l	1	307-24-4			
PFHpA (perfluoroheptanonic acid)	ng/l	1	375-85-9			
PFOA lineare (perfluorooctanonic acid)	ng/l	1	335-67-1			
PFOA ramifié (perfluorooctanonic acid)	ng/l	1	335-67-1			
PFOA total (perfluorooctanonic acid)	ng/l	1	335-67-1			
PFNA (perfluorononanonic acid)	ng/l	1	375-95-1			
PFDA (perfluorodecanonic acid)	ng/l	1	335-76-2			
PFUnDA (perfluoroundecanonic acid)	ng/l	1	2058-94-8			
PFDoDA (perfluorododecanonic acid)	ng/l	2	307-55-1			
PFTTrDA (perfluorotridecanonic acid)	ng/l	1	72629-94-8			
PFTeDA (perfluorotetradecanonic acid)	ng/l	1	376-06-7			
PFHxDA (perfluorohexadecanonic acid)	ng/l	2	67905-19-5			
PFODA (perfluorooctadecanonic acid)	ng/l	1	16517-11-6			
PFBS (perfluorobutane sulfonic acid)	ng/l	1	375-73-5			
PFPeS (perfluoropentane sulfonic acid)	ng/l	1	2706-91-4			
PFHxS lineaire (perfluorohexane sulfonic acid)	ng/l	1	355-46-4			
PFHxS ramifié (perfluorohexane sulfonic acid)	ng/l	1	355-46-4			
PFHxS total	ng/l	1	355-46-4			
PFHpS (perfluoroheptane sulfonic acid)	ng/l	1	375-92-8			
PFOS lineaire (perfluorooctane sulfonic acid)	ng/l	1	1763-23-1			
PFOS ramifié (perfluorooctane sulfonic acid)	ng/l	1	1763-23-1			
PFOS total (acide perfluorooctane sulfonic acid)	ng/l	1	1763-23-1			
PFDS (perfluorododecane sulfonic acid)	ng/l	1	335-77-3			
4:2 FTS (4:2 fluorotelomer sulfonic acid) H4-PFOS	ng/l	1	757124-72-4			
6:2 FTS (6:2 fluorotelomer sulfonic acid)	ng/l	1	27619-97-2			
8:2 FTS (8:2 fluorotelomer sulfonic acid)	ng/l	1	39108-34-4			
10:2 FTS (acide 10:2 fluorotelomer sulfonique)	ng/l	1	120226-60-0			
MePFOSAA (N-méthylperfluorooctane sulfonamide acetic)	ng/l	1	2355-31-9			
EtFOSAA (acide N-éthylperfluorooctane sulfonamide acétique)	ng/l	1	2991-50-6			
PFOSA (perfluoro-n-octanesulfonamide)	ng/l	2	754-91-6			
PFOSA ramifié (perfluoro-n-octanesulfonamide)	ng/l	2	754-91-6			
PFOSA total (perfluoro-n-octanesulfonamide)	ng/l	2	754-91-6			
MeFOSA lineaire (N-méthylperfluorooctanesulfonamide) (MePFOSA)	ng/l	1	31506-32-8			
6:2-FTAB (6 :2 fluorotelomer sulfonamido propyl betaine) Capstone B	ng/l	10	34455-29-3			

PFAS	LQ Eaux		CAS	VTR	Dir. CE EP2020/ 2184	AM 20/06/23 France
MeFOSA ramifié (N-méthylperfluoro-n-octanesulfonamide) (MePFOSA)	ng/l	1	31506-32-8			
MeFOSA total (N-méthylperfluoro-n-octanesulfonamide) (MePFOSA)	ng/l	1	31506-32-8			
8:2 DiPAP (8:2 polyfluoroalkyl phosphate diester)	ng/l	1	678-41-1			
HFPO-DA (hexafluoropropyleneoxide dimer acid) / Gen X	ng/l	1	13252-13-6			
EtFOSA lineaire (N-éthylperfluorooctanesulfonamide) (EtPFOSA)	ng/l	1	4151-50-2			
EtFOSA ramifié (N-éthylperfluorooctanesulfonamide) (EtPFOSA)	ng/l	1	4151-50-2			
EtFOSA totale (N-éthylperfluorooctanesulfonamide) (EtPFOSA)	ng/l	1	4151-50-2			
MeFBSAA (perfluorobutanesulfonamide (N-méthyl) acetate)	ng/l	5	159381-10-9			
5:3-FTCA: 5:3 fluorotélomer carboxylic acid	ng/l	1	914637-49-3			
6:2-FTCA: 6:2 fluorotélomer carboxylic acid	ng/l	5	53826-12-3			
8:2 FTUCA (2H-perfluoro-2-decenoïque acid)	ng/l	1	70887-84-2			
DONA (4,8-dioxa-3H-perfluorononanonic acid) ADONA	ng/l	1	919005-14-4			
MeFBSA (n-méthylperfluorobutanesulfonamide)	ng/l	1	68298-12-4			
PFBSA (perfluorobutanesulfonamide)	ng/l	1	30334-69-1			
PFECHS (perfluoro-4-éthylcyclohexanesulfonic acid)	ng/l	1	646-83-3			
PFNS (perfluorononane sulfonic acide)	ng/l	1	68259-12-1			
PFDoDS (perfluorododecane sulfonic acid)	ng/l	1	79780-39-5			
6:2 phosphate fluorotelomérique diester. 6:2 diPAP	ng/l	10	57677-95-9			
6:2 8:2 phosphate fluorotelomérique diester 6:2 8:2 diPAP	ng/l	10	943913-15-3			
PFHxSA (perfluorohexanesulfonamide)	ng/l	1	41997-13-1			
PFUnDS (perfluoroundecane sulfonic acid)	ng/l	2	749786-16-1			
PFTTrDS (perfluorotridecane sulfonic acid)	ng/l	2	791563-89-8			
EtFOSE (2-(N-éthylperfluoro-1-octanesulfonamido)-ethanol)	ng/l	5	1691-99-2			
MeFOSE (2-(N-méthylperfluoro-1-octanesulfonamido)-ethanol)	ng/l	5	24448-09-7			
NFDHpA (Nonafluoro-3,6-dioxaheptanoïque acid)	ng/l	1	151772-58-6			
PFMPA (Perfluoro-3-méthoxypropanoïque acid)	ng/l	1	377-73-1			
PFMBA (perfluoro-4-méthoxybutanoïque acid)	ng/l	1	863090-89-5			
C6O4 (Perfluoro([5-méthoxy-1,3-dioxolan-4-yl]oxy)acetic acid)	ng/l	10	1190931-41-9			
6:2-FTOH (6:2 fluorotelemer alcohol) FHET	ng/l	20	647-42-7			
8:2-FTOH (8:2 fluorotelemer alcohol) FOET	ng/l	10	678-39-7			

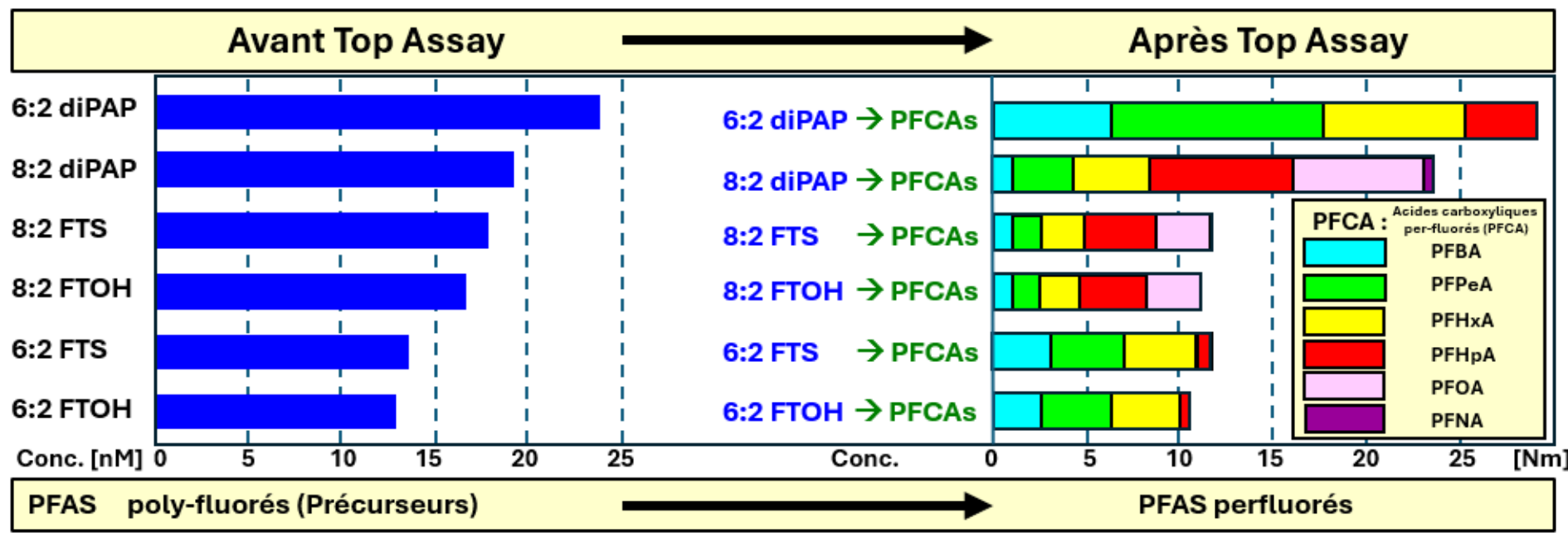
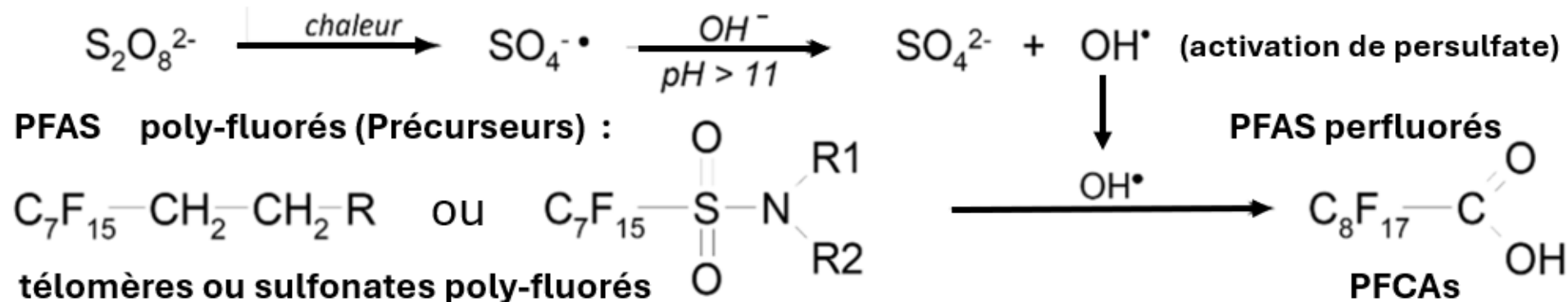
PFAS Ultrashorts :

TFA (trifluoroacetic acid)	ng/l	10				
PFPrA (perfluoropropanoïque acid)	ng/l	10				
TFMS (trifluoromethanesulfonic acid)	ng/l	10				
PFES (perfluoroethanesulfonic acid)	ng/l	10				
PFPrS (perfluoropropanesulfonic acid)	ng/l	10				

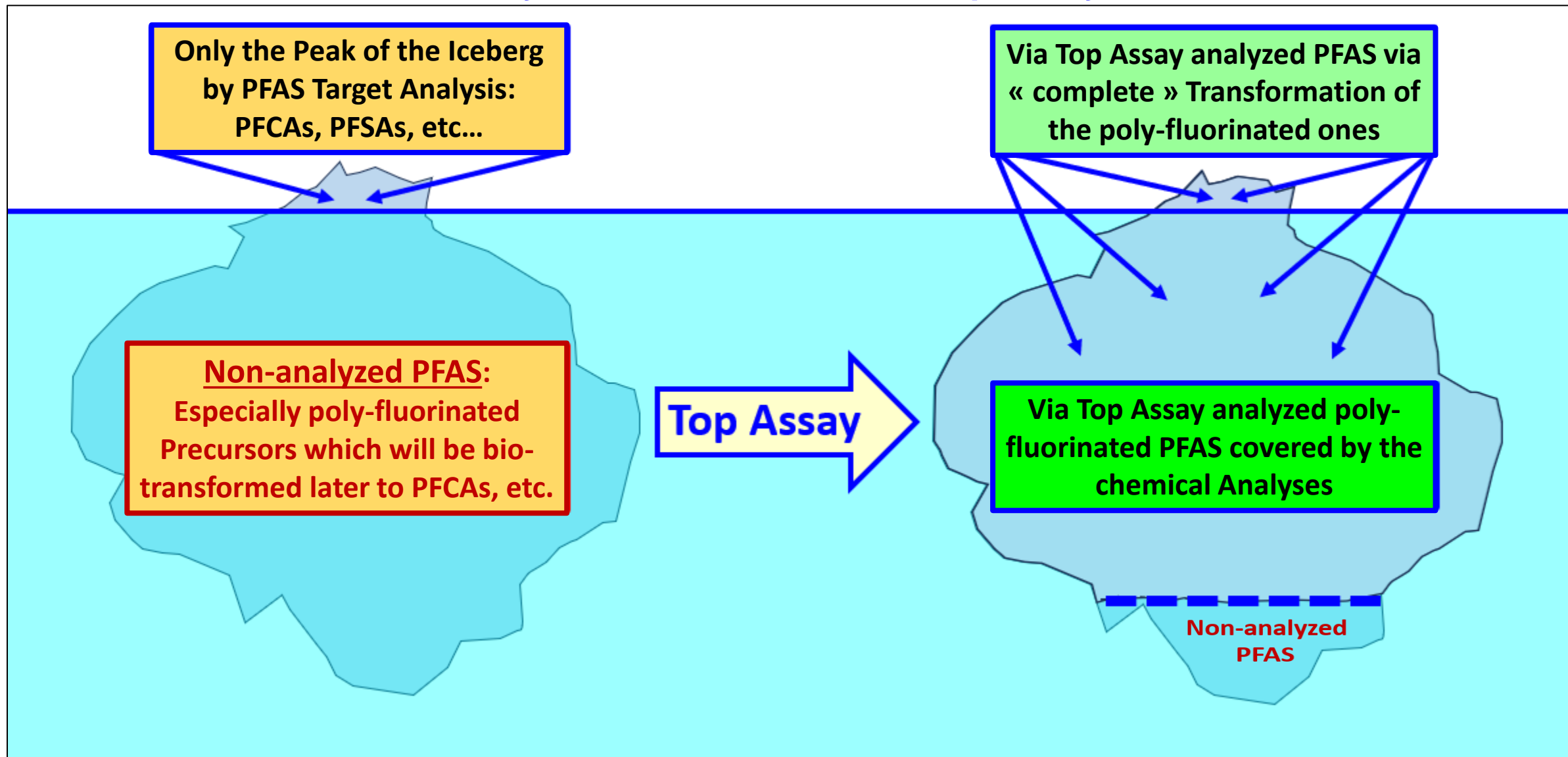
Considering of
all
poly-fluorinated
PFAS as final
per-fluorinated
PFCAs

Top Assay Total Oxidizable Precursor

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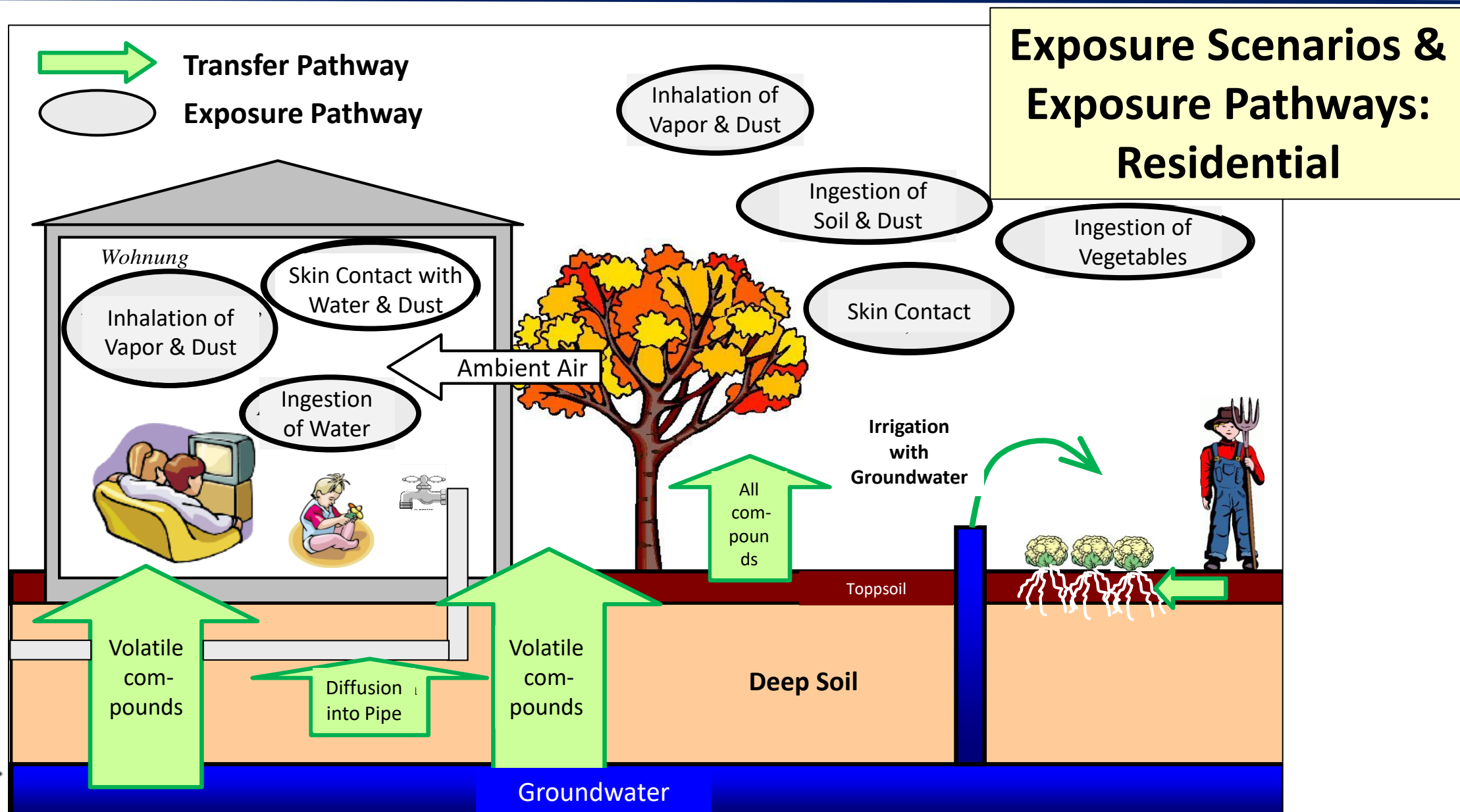


Analyses PFAS sans et avec Top Assay

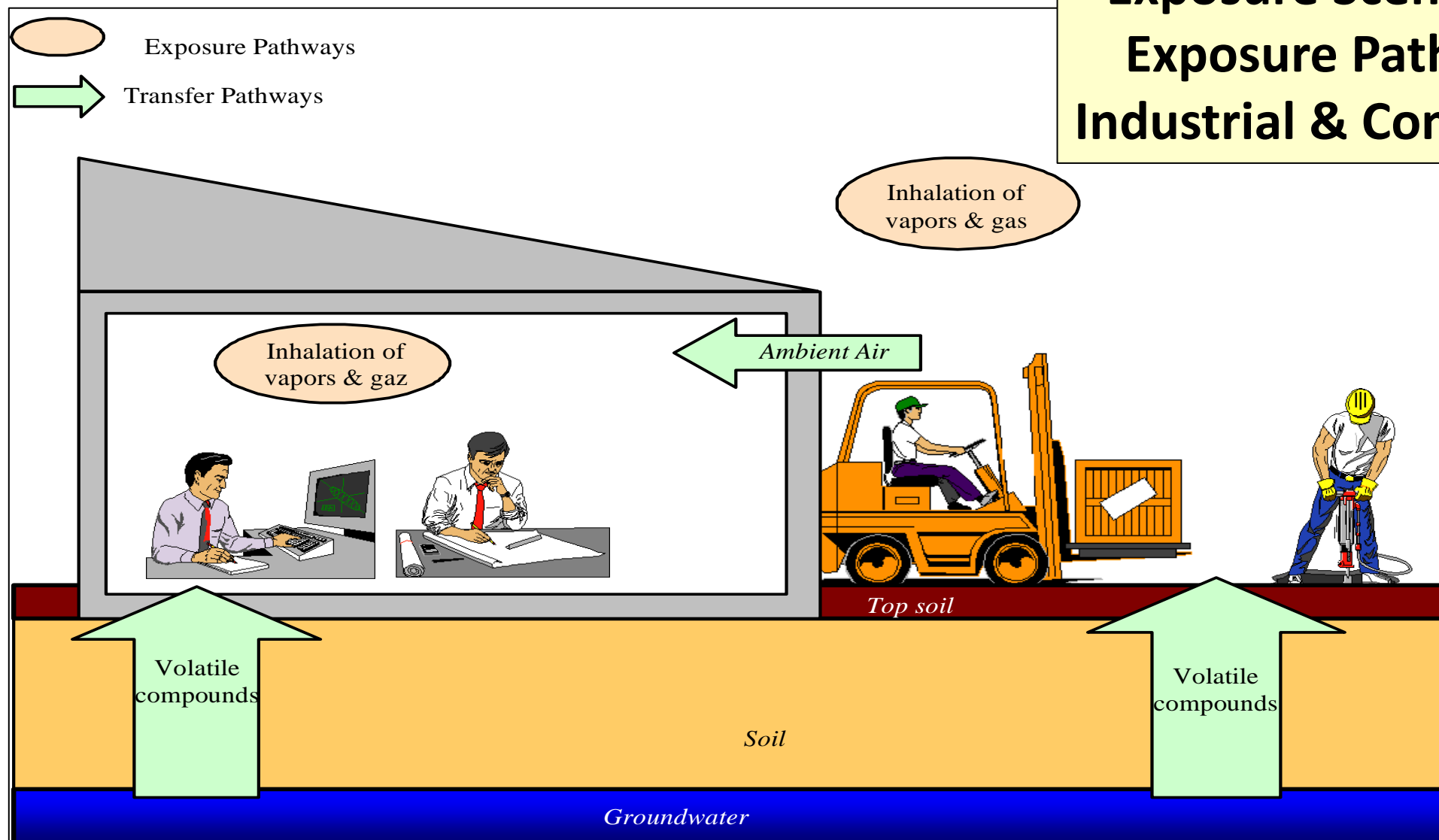


Generic Table Limit Values versus site specific TERQ-HRA: Health Risk Assessment

Characteristics	Site-specific HRA-based Remediation Goals	Generic Table Limit Values
Site specific Approach: <ul style="list-style-type: none"> ➤ For ex. Germany: BBodSchV § 15 (4): GFS, St2W... ➤ For ex. France: C-19/04/2017 ➤ Belgium, NL, CH, DK, Italy, UK, Spain, HU. 	Yes	No
Site specific consideration of geological & Hydrogeological Context (GW-Protection....::	Yes	No -to-> rarely
Site specific consideration of pollutant Cocktails (Precursors, FTOH, etc.)	Yes	No
Consideration of Site and Case specific Remediation Goals	Yes	No
Optimization of Remediation Needs: technically & economically	Yes	Not at all
Sustainable approach with possible Site use restrictions, confinement, in-situ Remediation, etc.	Yes, site specific Remediations Scenarios are possible	Mostly not, by demanding of excavation and P&T, etc.

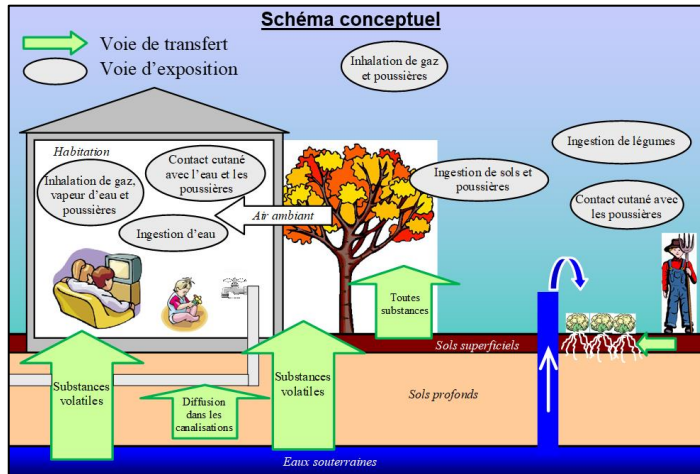


Exposure Scenarios & Exposure Pathways: Industrial & Commercial



Human Health Risk Assessment via Toxicological Exposure Risk Quantification (HHRA & TERQ) concerning Bio-transformation Chains of poly-fluorinated PFAS to per-fluorinated PFAS and Top Assay Application

Exposure Scenarios & Exposure Pathways



Exposure Scenario / Exposure Pathways		Industry & Commerce	Parcs & Sports	Kinder-gartens	Residential (collective) et Schools	Agri-culture & Food Production	Residential with individual Gardens
Inhalation	Respiration of Vapors & Gas: Soil Gas / Vapor → Ambient Air (indoor & outdoor)	Yes	Yes	Yes	Yes	Yes	Yes
	Respiration of Dust	Yes	Yes	Yes	Yes	Yes	Yes
	Respiration of vapors during hot shower*	(Yes)	(Yes)	No	Yes	No	Yes
Ingestion	Passive Ingestion (Children & Adults) or active (Children) of contaminated soil	Yes	Yes	Yes	Yes	Yes	Yes
	On-site produced Food ingestion	No	No	No	No	Yes	Yes
	Ingestion of contaminated Tap Water*	(Yes)	(Yes)	No	Yes	Yes	Yes
Dermal	Direct Skin Contact of contaminated Soil	Yes	Yes	Yes	Yes	Yes	Yes
	Skin Contact of Tap Water during shower or Bath*	(Yes)	(Yes)	No	(Yes)	Yes	Yes
	Skin Contact during Bath in surface water or pumped Groundwater	No	Yes	No	(No)	(No)	(Yes)

(*) : in case of pollution Impact to Drinking Water Pipes

TERQ-HRA: Health Risk Assessment: Exposure Quantification (Example: Oral Exposure)

Exposure Quantification: Ingestion of soils, water or food:

$$DED_{ing} = C_m \cdot \frac{Q_{ing}}{P} \cdot F_a \cdot \frac{Ex}{Ve} \cdot F_{exa} \cdot F_{exd}$$

DED_{ing} = Daily Exposure Dose [mg/kg/d]

C_m = Concentration Pollutants Concentration in the exposure medium : C_{soil} [mg/kg],
C_{water} [mg/l], C_{food} [mg/kg]

Q_i = Ingested Soil quantity and/or food [kg/d] or water [L/d], distinct from the
Adults (Q_{ing.A}) and the Children (Q_{ing.C})

P(a) = Adult Body Weight [70 kg]

P(e) = Child Body Weight [15 kg]

F_a = Absorption Factor (if failing: 100 % = [1])

Ex = Exposure years in Lifetime (Adult or Child) [y]

Ve = Lifetime: Adult or Child [y]. In case of carcinogenic Pollutants: Ve = Ex [y]

F_{exa} = Yearly Exposure [d/365 d]

F_{exd} = Daily Exposure [hrs/24 hrs]

TERQ-HRA: Health Risk Assessment: Exposure Quantification (Example: Inhalation Exposure)

Exposure Quantification: Example Inhalation of Dust, Vapors & Gas:

$$DED_{ing} = C_{air} \cdot \frac{Q_{inh}}{P} \cdot F_a \cdot \frac{Ex}{V_e} \cdot F_{exa} \cdot F_{exd}$$

DED_{ing} = Daily Exposure Dose [mg/kg/d]

C_{air} = Pollutants Concentration in the exposure medium : C_{air} [mg/m³], including dust,

Q_i = Inhaled Air quantity [m³/d], distinct from the Adults (Q_{ing.A}), the Children (Q_{inh.}), women, men and activities.

P(a) = Adult Body Weight [70 kg]

P(e) = Child Body Weight [15 kg]

F_a = Absorption Factor (if failing: 100 % = [1])

Ex = Exposure years in Lifetime (Adult or Child) [y]

V_e = Lifetime: Adult or Child [y]. In case of carcinogenic Pollutants: V_e = Ex [y]

F_{exa} = Yearly Exposure [d/365 d]

F_{exd} = Daily Exposure [hrs/24 hrs]

TERQ-HRA: Health Risk Assessment: Exposure Quantification (Example: Dermal Exposure)

Exposure Quantification: Dermal Contact: Soil, Dust, Water, etc.:

$$DED_{ing} = Cm \cdot CM \cdot \frac{A_{exp.}}{P} \cdot Fa \cdot \frac{Ex}{Ve} \cdot Fexa \cdot Fexd$$

DED_{ing} = Daily Exposure Dose [mg/kg/d]

Cm = Pollutants Concentration in the exposure medium : C_{soil} [mg/kg],
C_{water} [mg/l], C_{dust} [mg/kg]

CM = Contact with media Mass [mg/m²]

A_{exp.} = Exposed Skin surface: Adults, Winter, Summer, etc. [m²]

P(a) = Adult Body Weight [70 kg]

P(e) = Child Body Weight [15 kg]

Fa = Absorption Factor (if failing: 100 % = [1])

Ex = Exposure years in Lifetime (Adult or Child) [y]

Ve = Lifetime: Adult or Child [y]. In case of carcinogenic Pollutants: Ve = Ex [y]

Fexa = Yearly Exposure [d/365 d]

Fexd = Daily Exposure [hrs/24 hrs]

TERQ-HRA: Health Risk Assessment:

Acceptable & Unacceptable Risks:

- Individual Cancer Risk : $ICR \leq 10^{-5}$

$$ICR = DED \bullet UR$$

Daily Exposure Dose (mg/kg/d) • Unit Risk or Slope Factor (mg/kg/d)⁻¹

- Non-Cancer-Risk: Risk Index: $RI \leq 1$

$$RI = DED / TDI$$

Daily Exposure Dose (mg/kg/d) / Toxic Reference Dose
or TDI, ADI, RfD etc. (mg/kg/d) per toxicological target Organ

Acceptable Risks (for ex.: ICR Individual Cancer Risk):

- **WHO:** WHO: World Health Organisation, M. Younes: International Symposium “Exposure and Risk Assessment with Respect to Contaminated Soil”, Munich from February 28 & 29/1996: **Acceptable Individual Cancer Risk: $ICR = 10^{-5}$** (= 1 additional Cancer per 100 000 Persons),
- **Austria:** UBA_{AT}: Umweltbundesamt (2011): **Acceptable Cancer Risk: $ICR = 10^{-5}$,**
- **UK:** DEFRA: Department for Environment, Food and Rural Affairs (2002): Report CLR9TOX1-10: **Acceptable Cancer Risk: $ICR = 10^{-5}$,**
- **Canada:** According HEALTH CANADA (2002) : “Atlantic Provinces” (NS, NB, PEI, and Nfld./Lab.): **Acceptable Cancer Risk: $ICR = 10^{-5}$,**
- **France:** MEDD: Circular from April 2017: **Acceptable Cancer Risk: $ICR = 10^{-5}$,**
- **Germany:** Bundesanzeiger BA 161a from August 28/1999 : Toxicological Screening Level (PW) for **Acceptable Cancer-Risk: $ICR = 10^{-5}$, Proved intervention level: $ICR = 5 \bullet 10^{-5}$**
- **Italy:** Decreto 52/2006 from 2006: **Acceptable Cancer Risk: $ICR = 10^{-5}$,**
- **Netherlands:** RIVM (2001): Document 711701 025 Re-Evaluation of Human-Toxicological Maximum Permissible Risk levels: **Acceptable Cancer Risk: $ICR = 10^{-5}$,**
- **Switzerland:** Vollzugshilfe zur Altlastenverordnung / Herleitung von Konzentrationswerten BAFU: 29.01.2014. **Acceptable Cancer Risk: $ICR = 10^{-5}$,**
- **USA:** DOH: **Acceptable Cancer Risk: $ICR = 10^{-6} - 10^{-4}$.** In the most cases and States an **Acceptable Cancer Risk of $ICR = 10^{-5}$** is used.
- **Australia, Hong-Kong, Denmark, Japan, New Zealand, Norway, Sweden: $ICR = 10^{-5}$** is used.

Combined Exposure to multiple Chemicals:

According IPCS & WHO : 2009 etc.(+ lots of other Authors: US-EPA, etc.):
to be differentiated between:

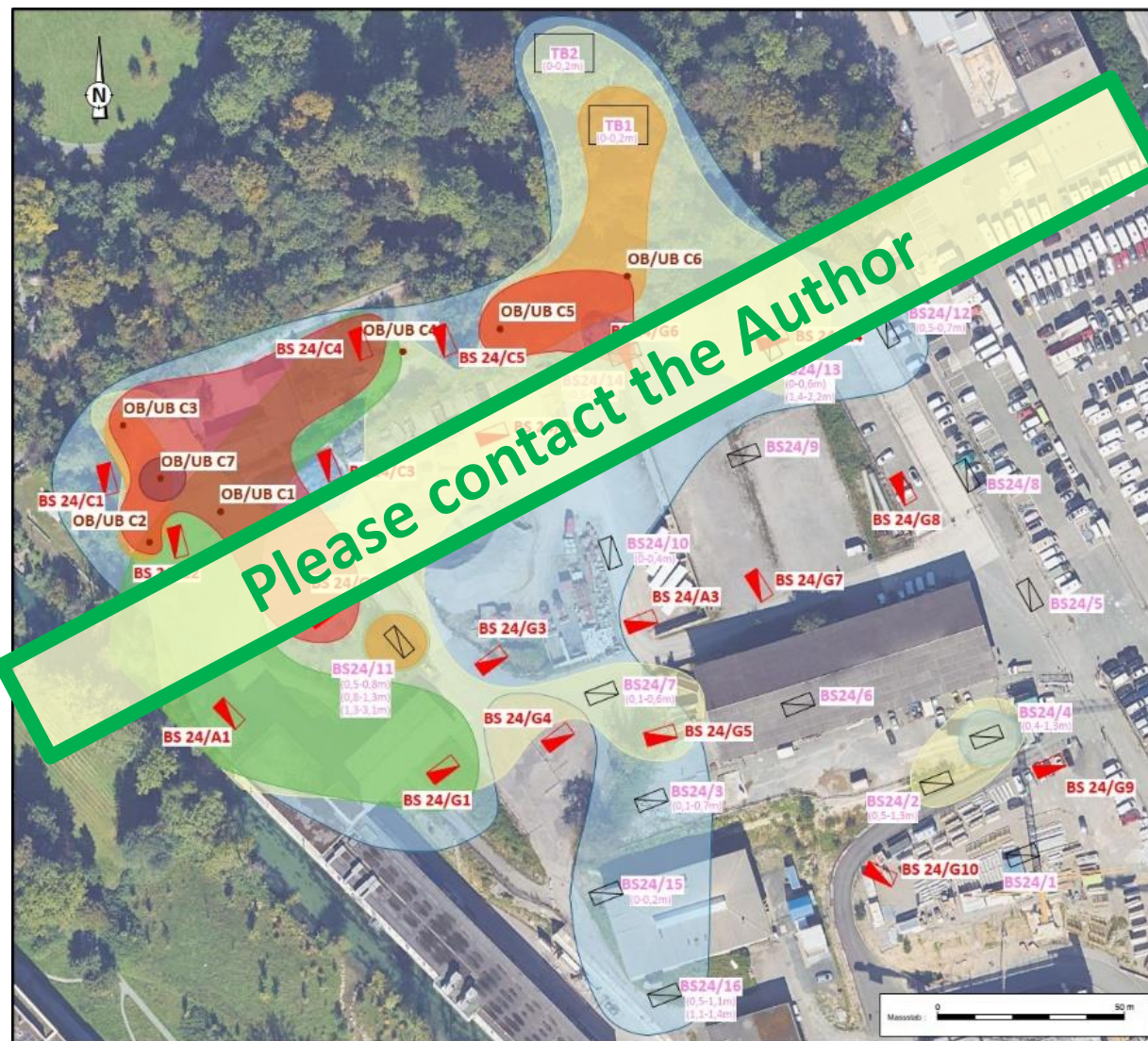
A. Aggregate Exposure of a single Chemical via all pathways,

B. Cumulative Exposure with combined Risk to multiple Chemicals:

- Identification of a Group of Chemicals with **the same mechanism of Toxicity (or Target Tissues & Organs) = MOA: Common Toxic Mode of Action**
- **“Dose Addition is assumed for different MOA Subgroups”**

(In this case the slope of the dose-response curve of a Chemical is not altered)

Example Exceeding of site specific Remediation Goals:



Individual Residential site Use with private Garden



PFHpA $\geq 0,002 \text{ mg/kg}^{(1)}$



PFOA $\geq 0,0004 \text{ mg/kg}^{(1)}$



PFNA $\geq 0,0004 \text{ mg/kg}^{(1)}$



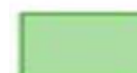
PFHxS $\geq 0,0004 \text{ mg/kg}^{(1)}$



PFOS $\geq 0,0004 \text{ mg/kg}^{(1)}$

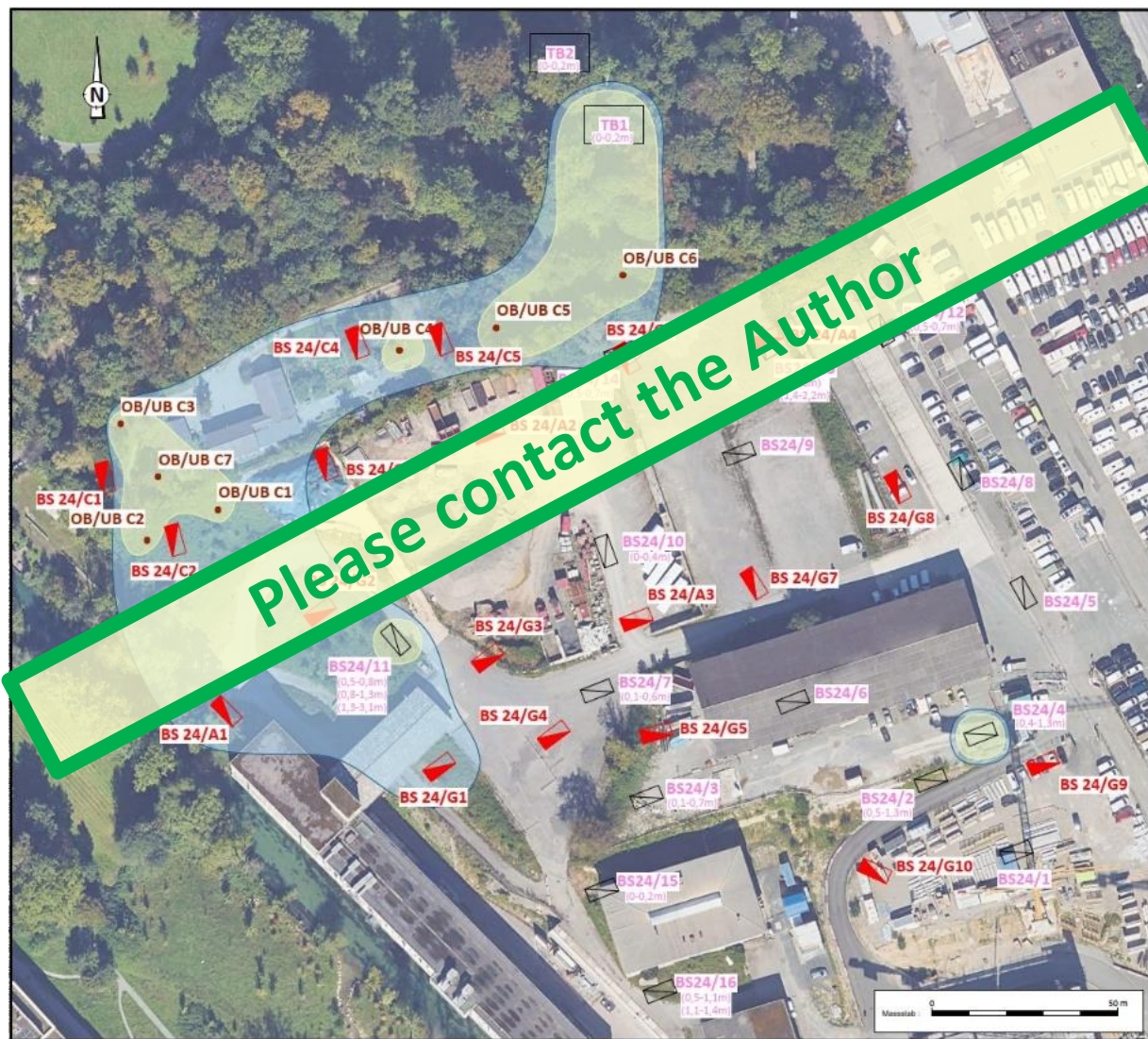


PFHpS $\geq 0,0004 \text{ mg/kg}^{(1)}$

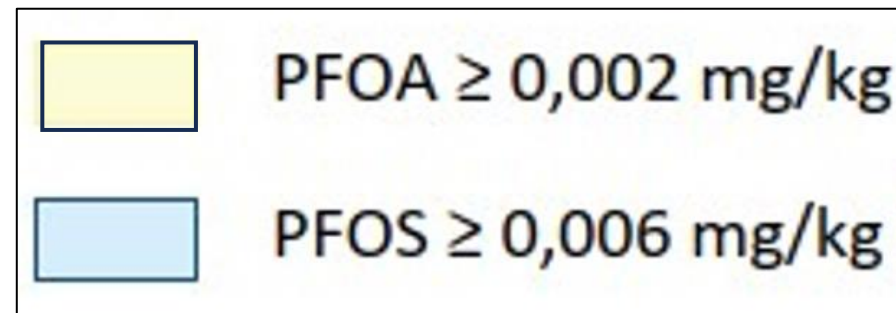


PFOSA $\geq 0,002 \text{ mg/kg}^{(1)}$

Example Exceeding of site specific Remediation Goals: Soil



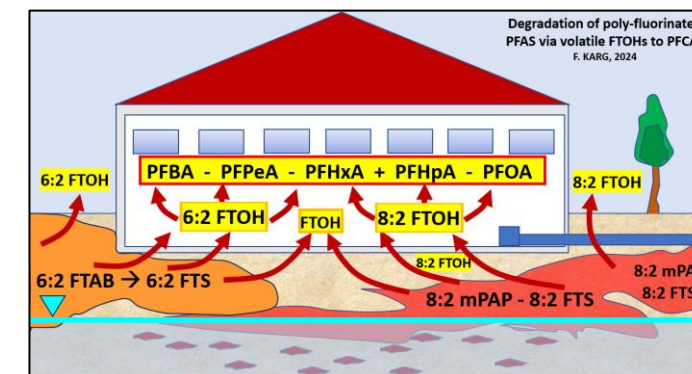
Green space and Sports Areas:



Conclusion:

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- About > 9 000 – 12 000 Compounds are existing.
- PFAS are very Soluble but also Bio-accumulable.
- Per- and polyfluoroalkyl substances (PFAS) are non-volatile, excepted volatile FTOH: Fluorotelomer Alcohols and some ultra-short PFAS.
- Polyfluorinated PFAS are bio-transformed into stable Perfluorinated PFAS.
- Thousands of sites polluted by PFAS: Fire-Fighting sites (as on airports, etc.), industrial sites, agriculture land with WWTP Sludge, etc. are existing.
- Site Investigations and TERQ Health Risk Assessments are necessary !
 - ➔ Generic Table Threshold Levels should be avoided, because of site specific uses & Pollutant Cocktails.
 - ➔ A site-specific Definition of TERQ-Remediation Goals should be preferred instead of *generic Table Threshold Levels* for Health Risk Assessments concerning the site-specific Pollutant Cocktails.
 - ➔ Toxicological Exposure Risk Reference Values (VTR) should be chosen by Scientific Criteria only.
 - ➔ Exceeding of Site-specific Remediation Goals for acceptable Risks can be mapped for Remediation Plans.



Management of PFAS: Per- & Polyfluoro-Alkyl Substances: Environmental Contaminations & Health Risk

Thank You !

Questions? Remarks? Requests?

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