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Interreg Baltic Sea Region

Co-funded by the European Union

SUSTAINABLE WATERS EMPEREST

Per- and polyfluoroalkyl substances Problem for all species

Many hazards, one health

Angela Ivask

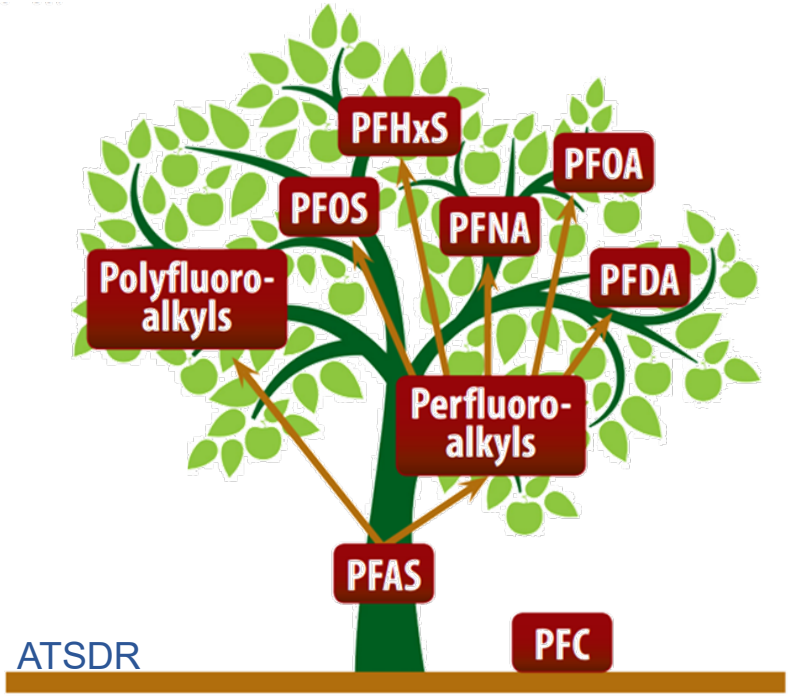
University of Tartu, Institute of Molecular and Cell Biology
Estonian Society of Toxicology

13.02.2024

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Per- and polyfluoroalkyl substances
PFAS

- Non-specific general name of a group of organic and inorganic compounds that contain at least one fully fluorinated methyl or methylene carbon atom
  any chemical with at least a perfluorinated methyl group ($–CF_3$) or a perfluorinated methylene group ($–CF_2–$) is a PFAS
- Perfluoroalkyl substances include fully fluorinated alkyl chain
- Polyfluoroalkyl substances include partly fluorinated alkyl chain
- More than 15 000 compounds according to chemicals databases (PubChem)



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Per- and polyfluoroalkyl substances PFAS

- Heat resistant surfaces
- Stain resistant surfaces (e.g., paper), and fabrics
- Non-sticky food-related surfaces
- Personal care products (emulsifier and viscosity regulator)
- Cleaning products (surfactant properties, film formation)
- Inert and durable lubricants (high durability), ski wax
- Paints, adhesives (additive for paint repellence)
- Pharmaceuticals, plant protection products (enhancer,
- Aerospace, medical, and automotive applications
- Semiconductor industries









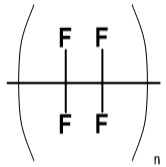


Journal of Water Process Engineering 2020, 38, 101683

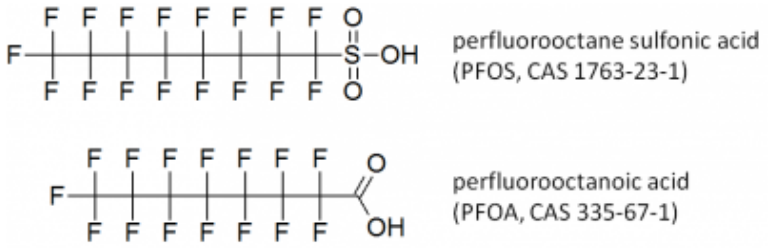
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Per- and polyfluoroalkyl substances
PFAS

- Most widely used in products, **Teflon and Gore-Tex**, is likely **PTFE**, fluoropolymer with repeating structural units



- Historically most environmentally widespread PFASs are **PFOS** and **PFOA**



1938	1947	1951	1969	2000	2009	2011	2020	2023	2025
PTFE by DuPont (Teflon)	PFAS by 3M	C8 or PFAS by DuPont	Gore-Tex (based on PTFE)	Voluntary phaseout of PFOS (US)	PFAS included to Stockholm Convention chemicals	**ECHA** Use of PFOS based foams prohibited	Manufacturing and sales of PFOS prohibited	Manufacturing and sales of PFCAs with C9-C14 prohibited	All uses of PFOA and PFCAs with C9-C14 prohibited

Journal of Water Process Engineering, Volume 38, 2020, 101683; echa.europa.eu

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PFAS problem from DuPont

- Since 1950-s Du Pont had used PFOA “C8” in their Teflon production process in West Virginia plant
- Since 1960-s the company knew that the chemical increases liver size in rats and rabbits
- Since 1970-s it was known that workers had increased PFOA levels in their blood
- Since 1984 the company knew that nearby rivers contain the chemical
- By 1990s it was known that PFOA induces cancer of liver, pancreas and testicles in rats

- Since 1990s Wilbur Tennant in Ohio observed the death of his cattle due to drinking polluted water
- In 1998 he received help from lawyer Rob Bilott to sue DuPont for his cows
- People potentially affected by PFOA become tested for “C8” in their blood along other illnesses
- After 20 years of court, DuPont paid to 3500 people more than 600 million dollars



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PFAS in environment

- Municipal landfills and wastewater treatment plants are the main sources if PFAS to the environment
- “Forever chemicals”: stability of C-F bond
- Transport through air is limited due to low volatility but compounds have been found in
- PFOA and PFOS have relatively good mobility and are the most detected PFASs in aqueous environment and soil

	Surface water	Soil	Sediment	Ground-water	Air	Dust	Human tissue (liver)	logKow (lipophilicity)
PFOA	0.1-800 ng/l	0.002-60 000 ng/g	0.01-800 ng/g	0.5-4000 ng/l	0.001-30 pg/m^3	0.3-400 ng/g	13.6 ng/g	4.3*
PFOS	0.5-100 ng/l	0.04-300 000 ng/g	0.03-3000 ng/g	0.02-5000 ng/l	0.002-100 pg/m^3	0.3-2000 ng/g	102 ng/g	4.5

* Limited measurement

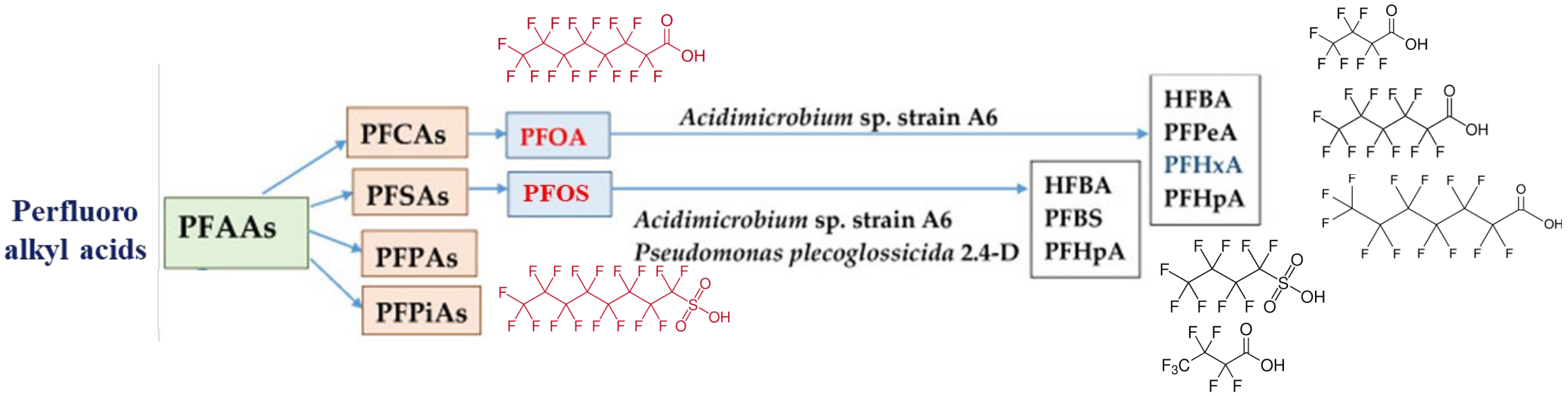
Interstate Technology and Regulatory Council, based on 2012-2022 articles
Report from Danish Environmental Protection Agency 2015

Drinking water	500 ng/l for all PFAS (Europe)	100 ng/l (Canada)	70 ng/l (US Health Advisory)	0.004 ng/l US EPA (interim)

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PFAS in environment

- Although PFASs are resistant to biodegradation, limited biological breakdown may take place (~65% of PFAS) that does not lead to total mineralization
- The terminal degradation products of PFOA and PFOS may be PFCAs (e.g., perfluorohexanoic acid [PFHxA]) and PFSAs (e.g., perfluorohexane sulfonate [PFHxS]), which are more water soluble than the original compound and very persistent
- PFAS biological removal in WWTP is not efficient

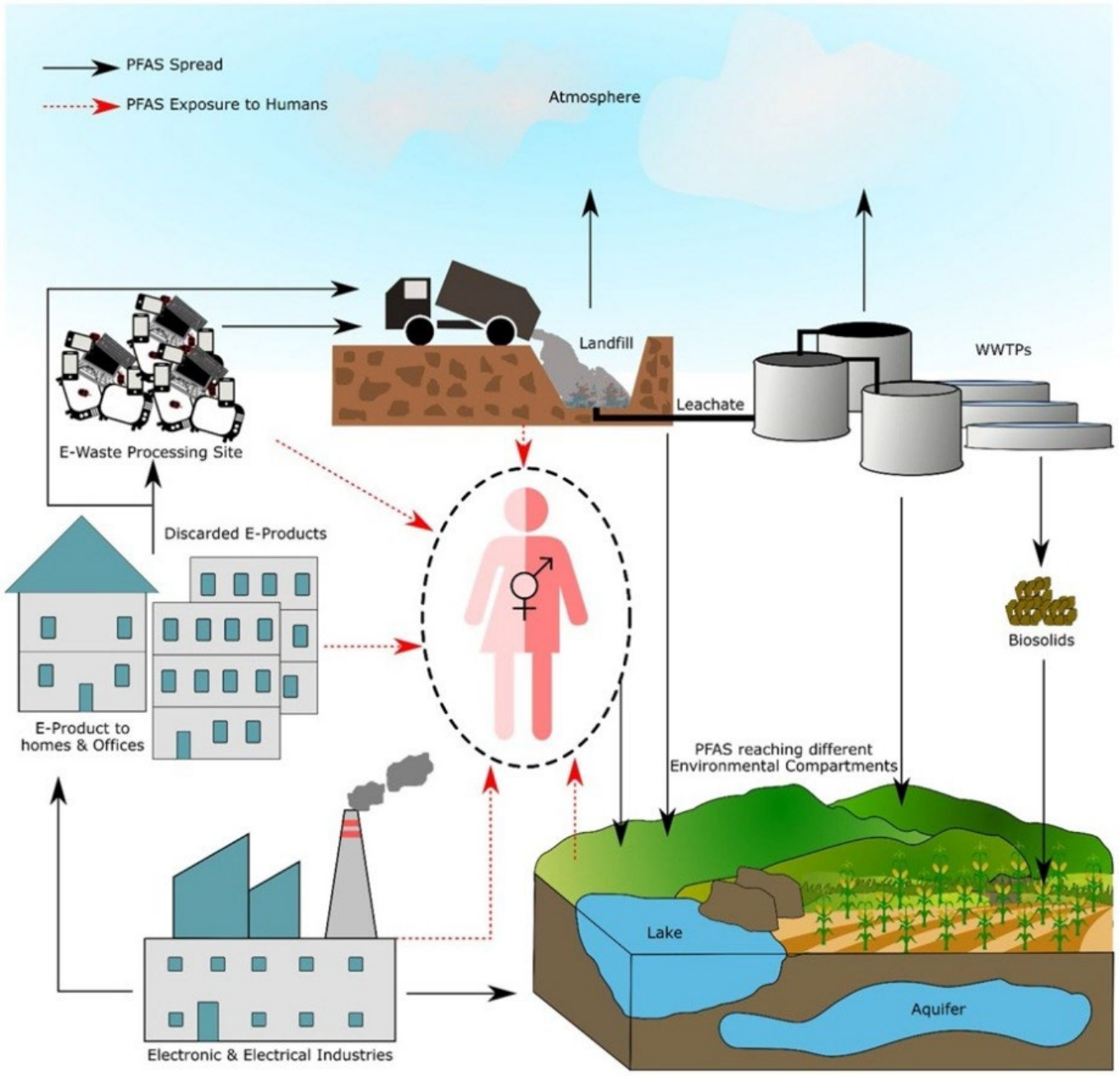


Toxics. 2023,11(5): 446

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PFAS in environment

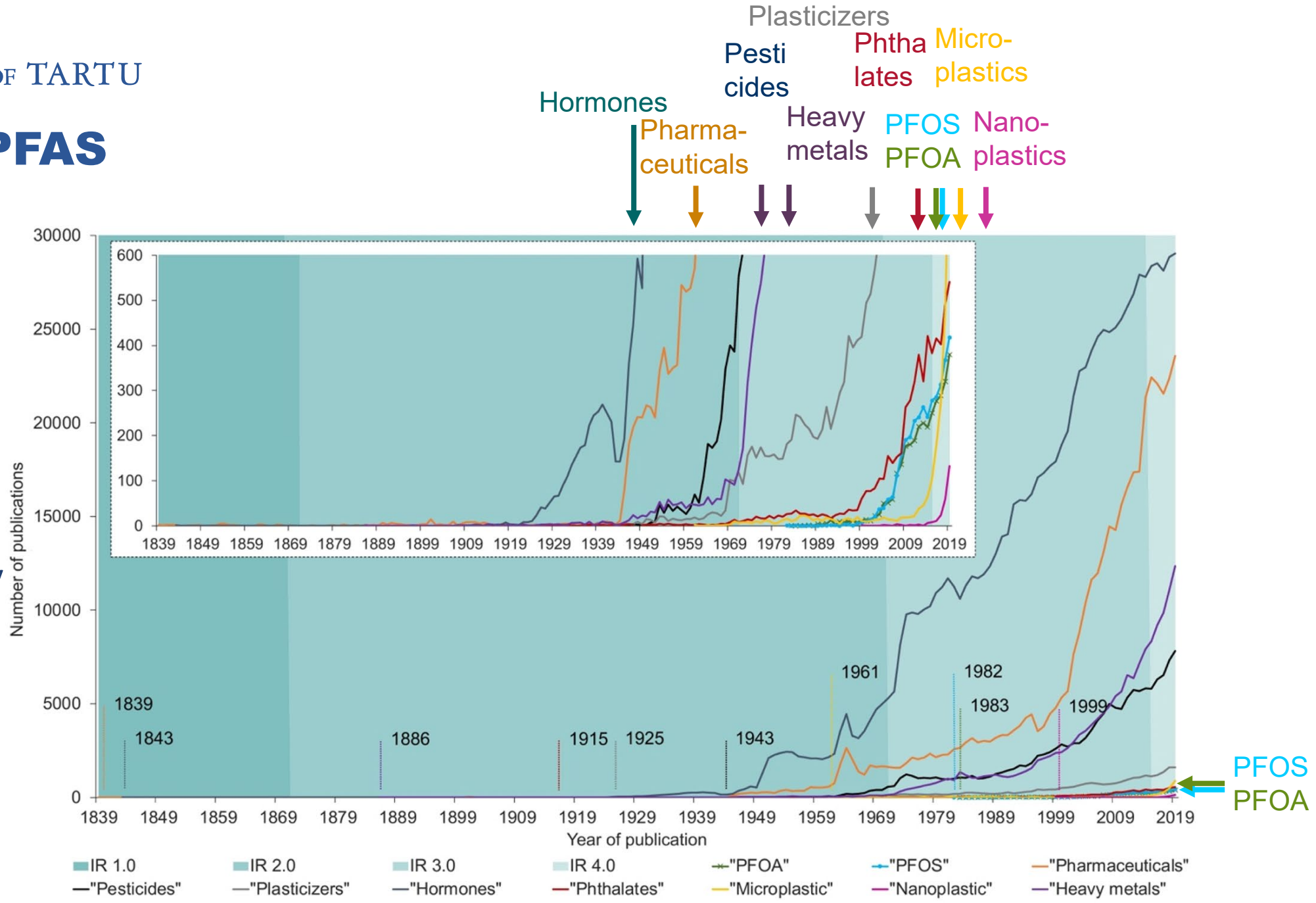
- Various exposure pathways to human and wildlife
- Resulting toxicological effects...



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Toxicity of PFAS

- Research articles related with PFAS toxicity have been published since 2000-s
- However, the number is relatively low compares with other toxicological research

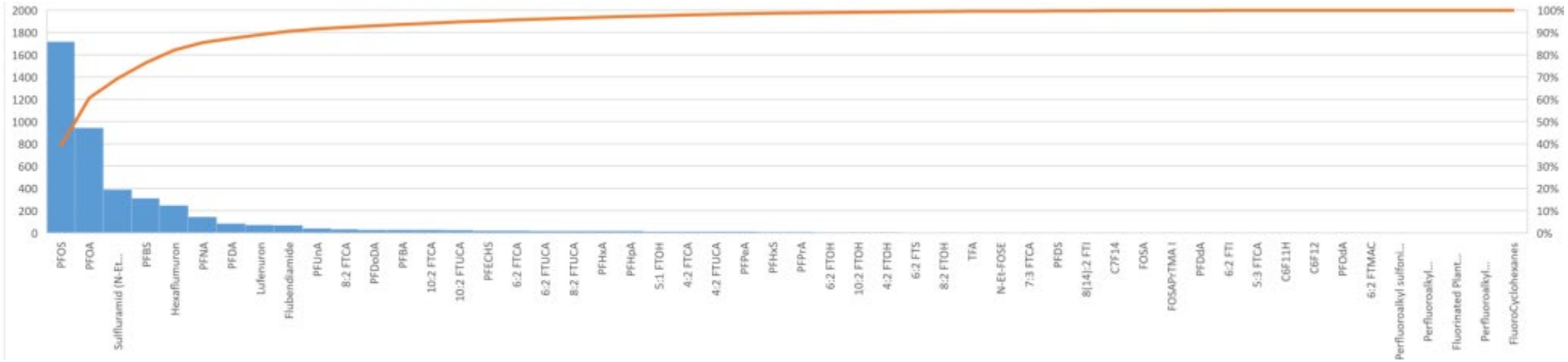


npj Clean Water 2023, 6:57

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Ecotoxicological effects of PFAS

- Most data available for PFOS and PFAS

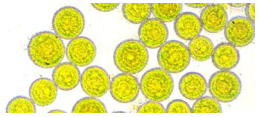


Environmental Toxicology and Chemistry 2021, 40: 564-605

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Ecotoxicological effects of PFAS

- **Aqueous exposure**



Algae:
EC_{50} 10 000 – 40 000 µg/L



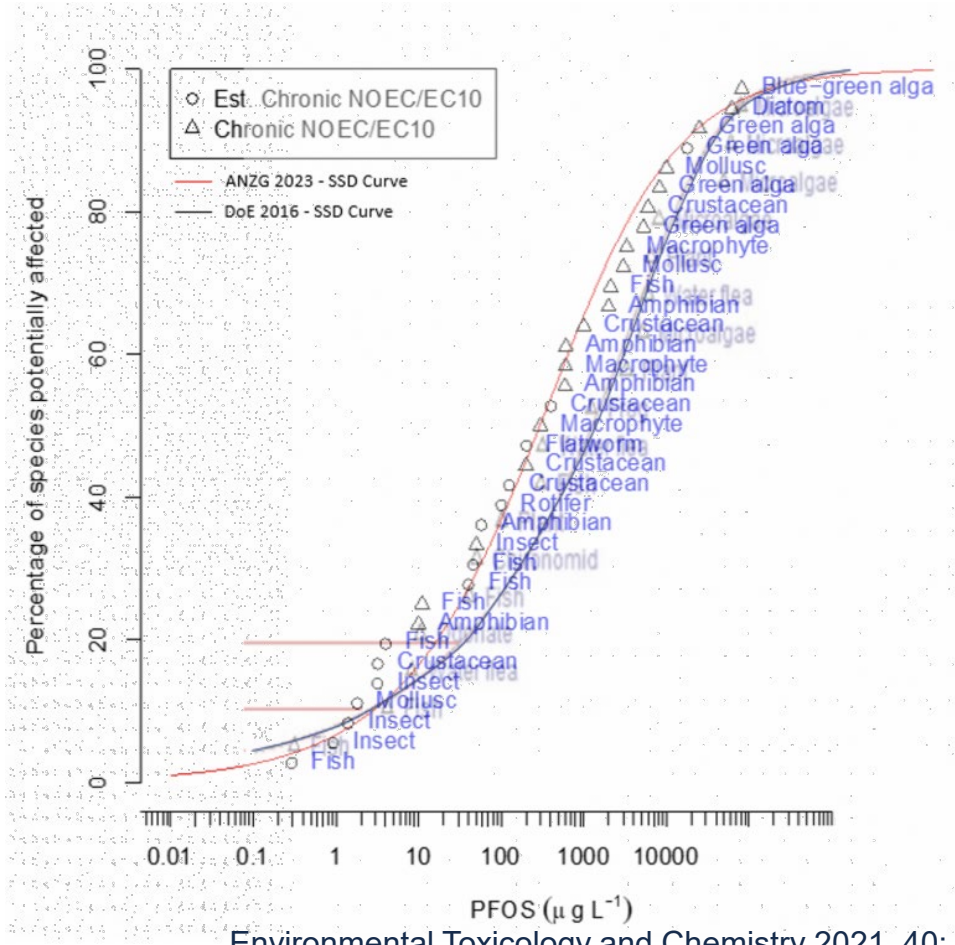
Invertebrates:
Acute toxicity: EC_{50} 0.1 to 195 000 µg/L
- PFAS with longer chain lengths more toxic
- Sulfonates more toxic than carboxylates



Danio rerio

Fish:
Acute toxicity:
PFOA LC_{50} 600 000 – 4000 000 µg/L
PFOS LC_{50} 4200 – 80 000 µg/L
Chronic toxicity:
LOEC 0.7-5600 µg/L
Multigenerational study:
Lower survival at 10 µg/L

	Surface water
PFOA	0.0001-0.8 µg/l
PFOS	0.0005-0.1 µg/l



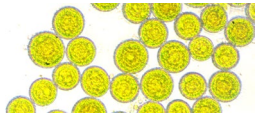
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Ecotoxicological effects of PFAS

	Surface water
PFOA	0.0001-0.8 µg/l
PFOS	0.0005-0.1 µg/l

- **Mode of action in aquatic organisms**



Algae:

Damage of cell membrane and decrease of photosynthesis



Invertebrates:

- At 60 µg/l PFAS production of vitellogenin (**egg yolk protein**) was reduced in *Daphnia magna*
- Vitellogenin level reduced in free-living nematode *Cenorhabditis elegans*
- Alterations of a enzymes important for **lipid metabolism** and insulin signaling pathways.
- **Obesogenic effects** (fat accumulation due to increased fatty acid synthesis)
- Adverse effects on **immune system**



Danio rerio

Fish:

- **Oxidative stress** and mitochondrial toxicity
- **Oxidation of fatty acids**
- **Hormone like effects**: estrogenic activity, binding of PFOA and PFOS to estrogen receptor
- **Decreased egg production** and hatching
- Long-term exposure inducing reduced **thyroid hormone levels**
- **Dysregulation of lipid metabolism** and fatty liver formation

Environmental Toxicology and Chemistry 2021, 40: 564-605

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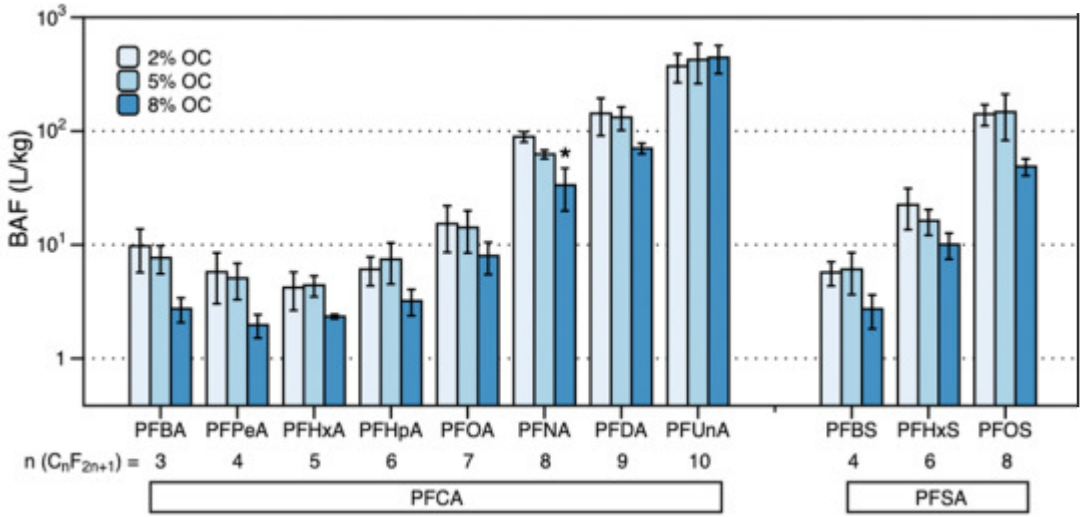
Ecotoxicological effects of PFAS

- **Bioaccumulation of PFAS in aquatic organisms**



- In general, PFAS bioaccumulate depending on their alkyl chain length and functional groups
- Bioaccumulation correlates with log Kow (lipophilicity)

Bioaccumulation of PFAS in aqueous invertebrate *D. magna*



Science of The Total Environment 2023, 866: 161208

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Toxicological effects of PFAS

- **Accumulation of PFAS in humans**
  - PFAS tend to accumulate in human body
  - 3-8 years the half-life of PFOA in human body
  - In rat, accumulation of PFOA was kidney > liver > lung > (heart, whole blood) > testicle > (spleen, brain), and of PFOS liver > heart > kidney > (whole blood) > lung > (testicle, spleen, brain)

Accumulation of PFAS in human autopsy tissues

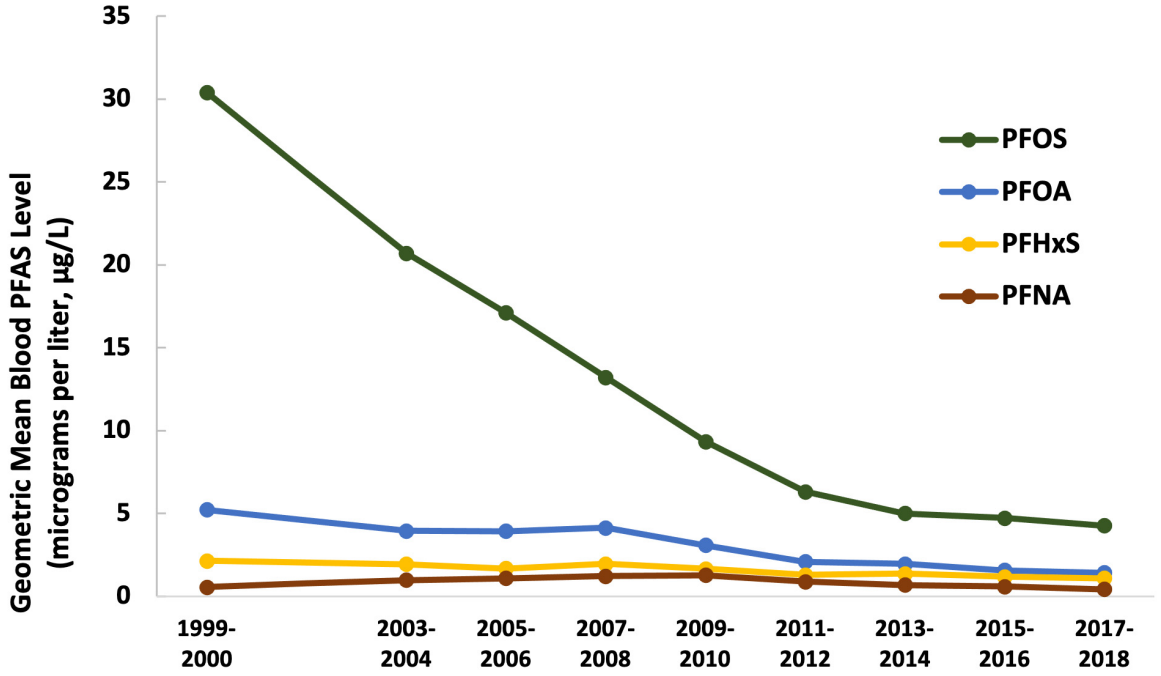
PFAS substance	Mean concentrations ng/g w. w.				
	Liver	Bone	Brain	Lung	Kidney
PFOA	13.6	60.2	<LOD	29.2	2.0
PFOS	102	<LOD	4.9	29.1	75.6
PFHxA	11.5	35.6	18.0	50.1	5.6

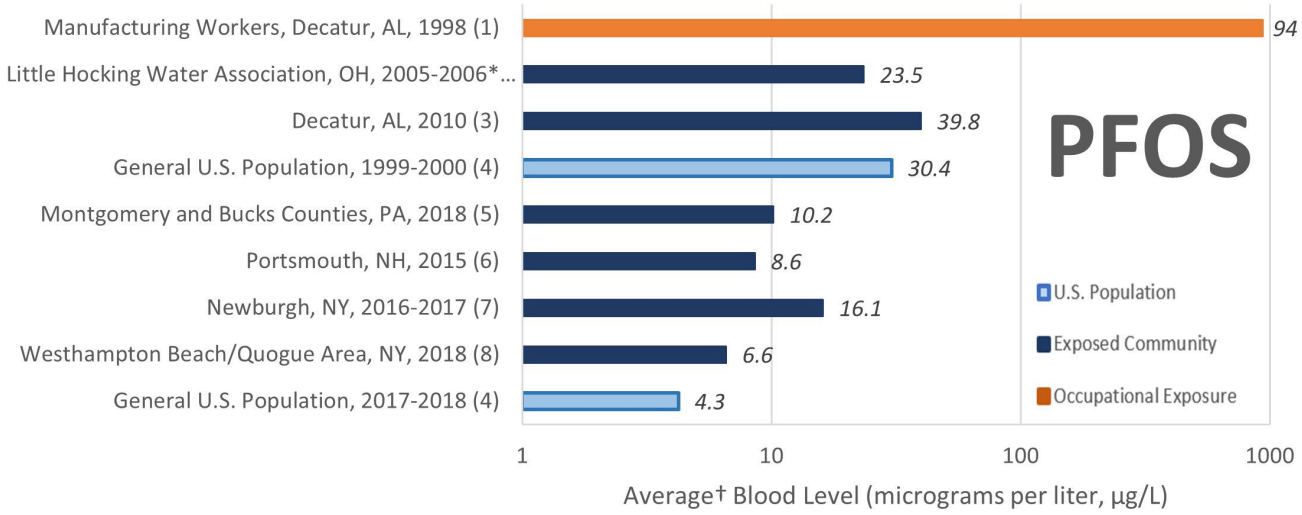
Report from Danish Environmental Protection Agency 2015

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  - With decreased use of PFOS and PFAS, their levels have decreased in humans



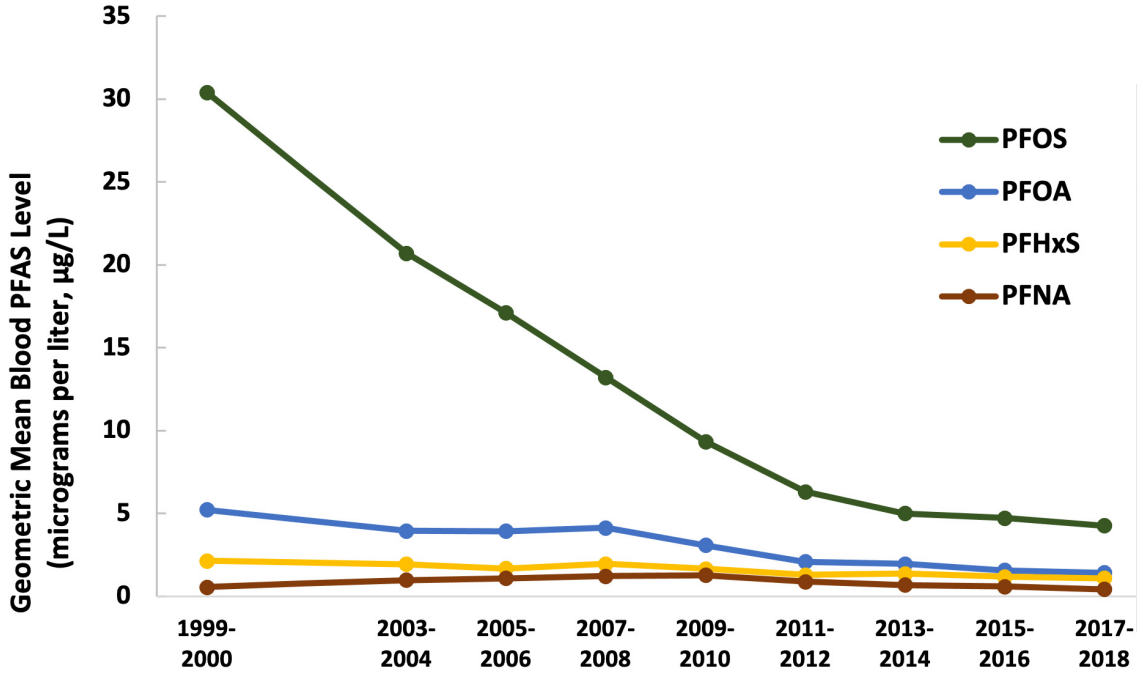


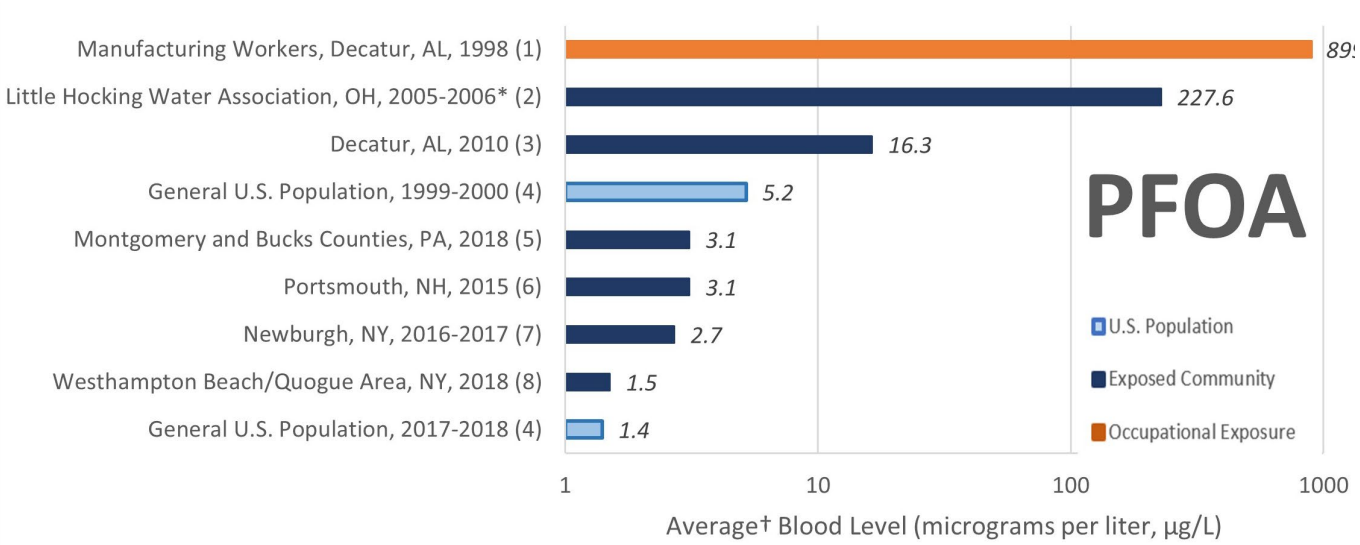
ATSDR, 2024

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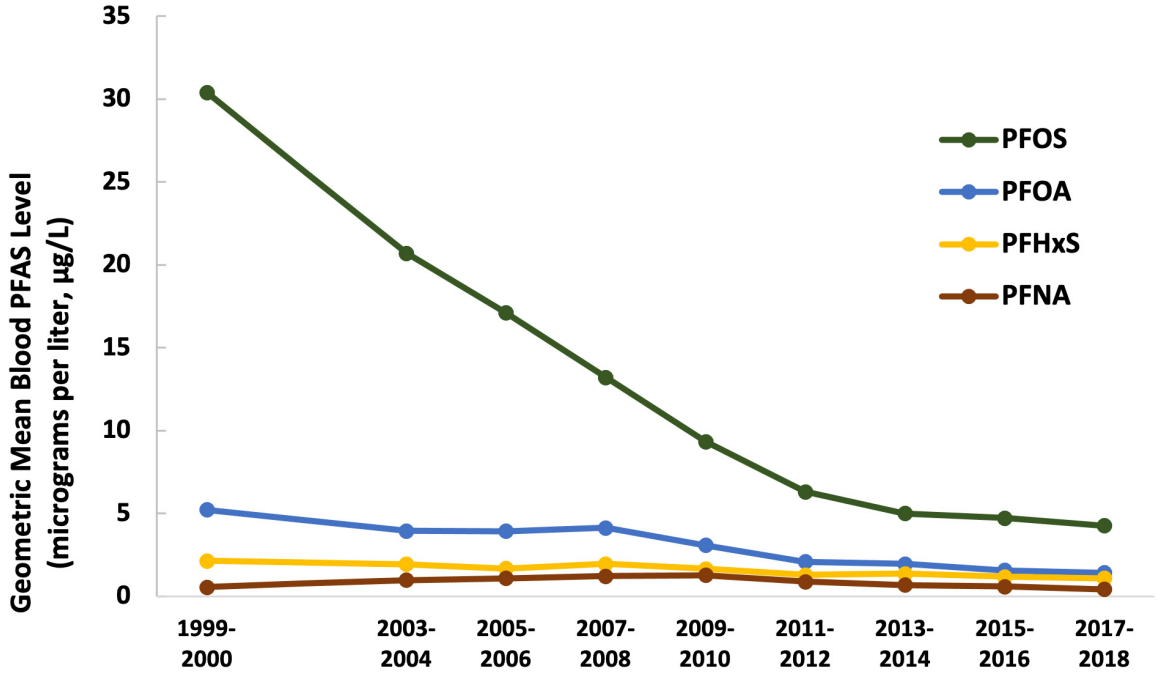


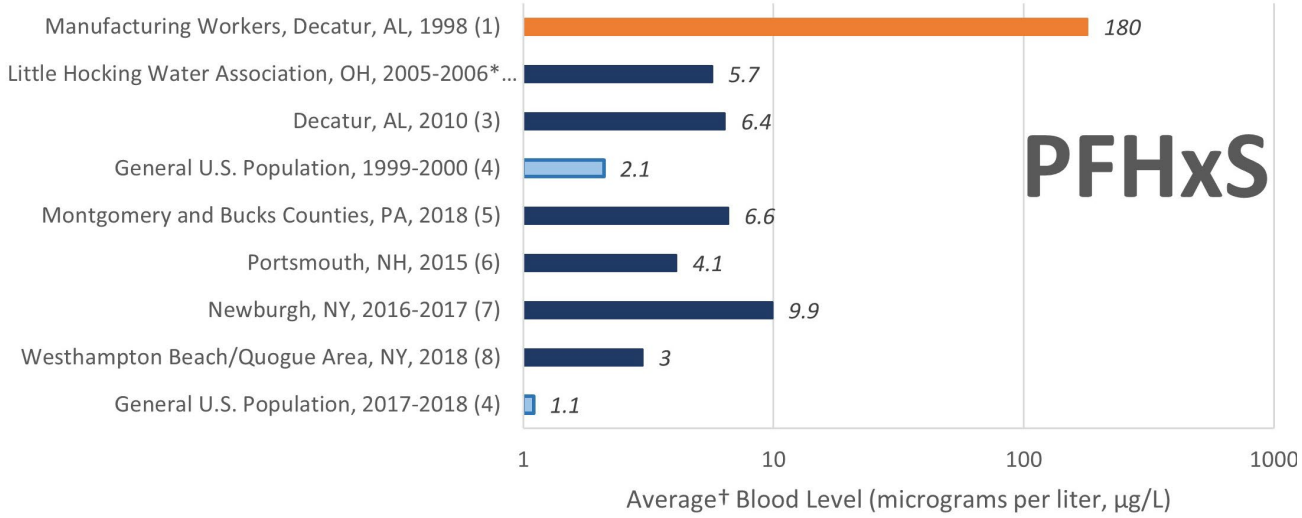
ATSDR, 2024

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Toxicological effects of PFAS

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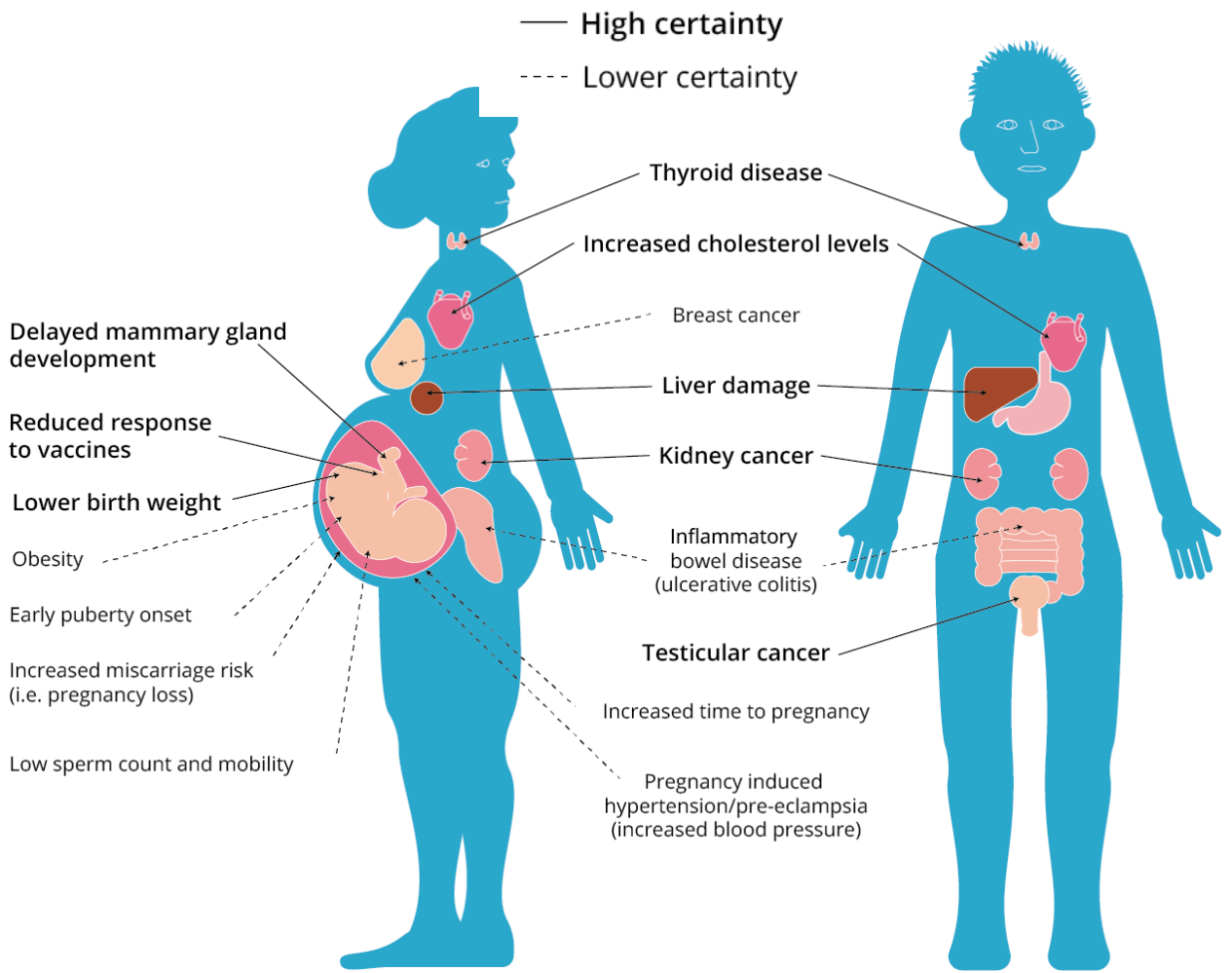
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Toxicological effects of PFAS

- **Effects of PFAS in humans**

  Effects involve:

  - **Reproductive effects** such as decreased fertility or increased high blood pressure in pregnant women
  - **Developmental** effects or **delays** in children: low birth weight, accelerated puberty
  - **Increased risk** of pancreatic, prostate, kidney, testicular **cancers**
  - Risk of **fatty liver** and hepatocellular carcinoma
  - Reduced vaccine response
  - **Interference** with the body's **natural hormones**
  - **Increased** cholesterol levels and/or **risk of obesity**
  - Suspected health effects depend on exposure concentration:
    susceptibility to vaccines < increased cancer risk < developmental alterations <low birth weights



US National Toxicology Program, 2016

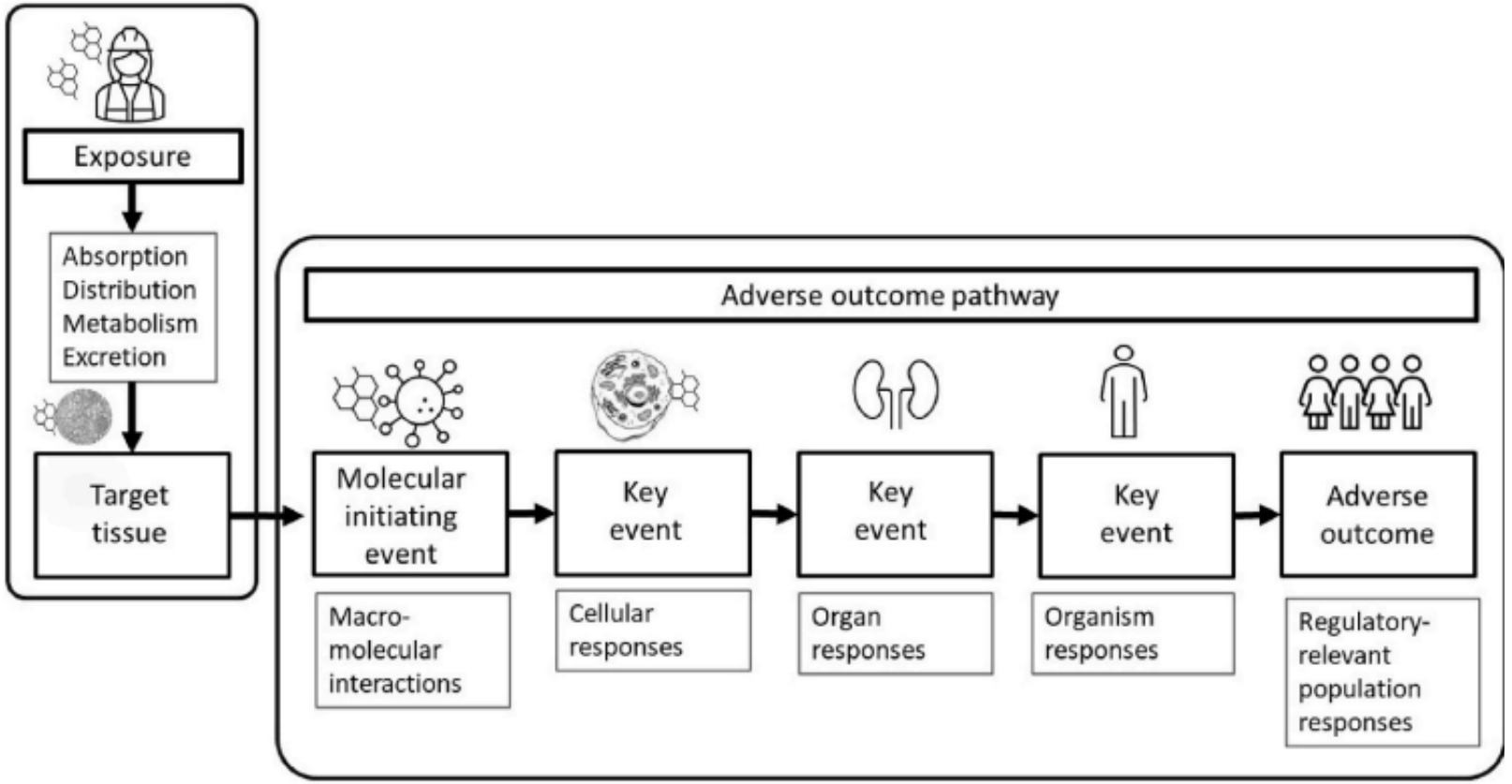
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Toxicological effects of PFAS

- **Adverse outcome pathways**

  Events leading to toxicological outcome

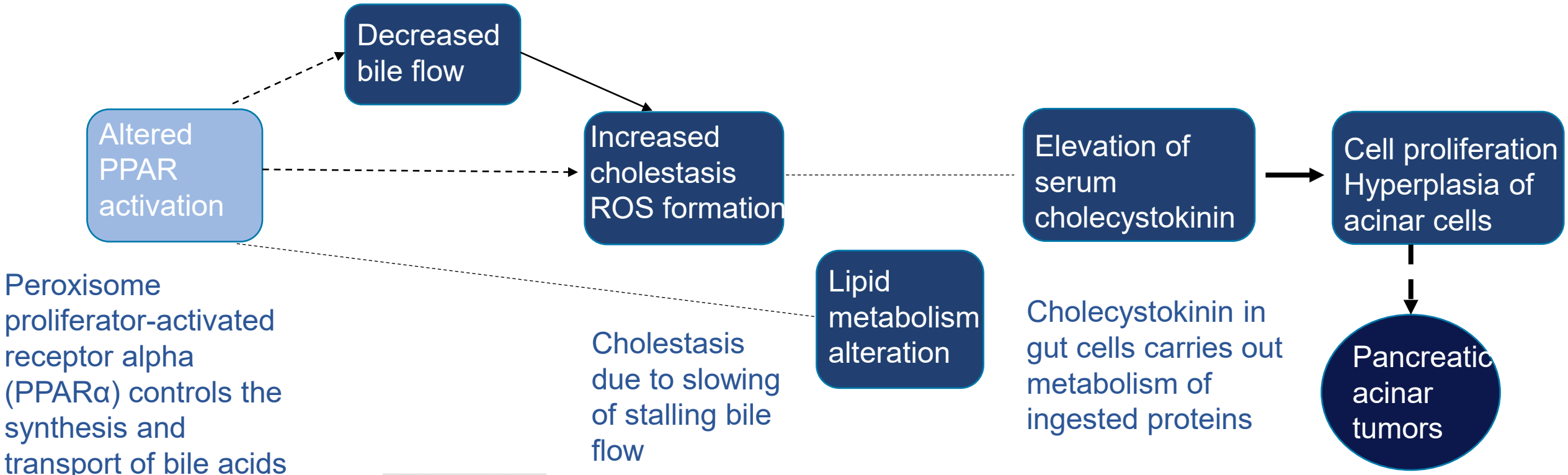
  Knowledge-based managed by the US EPA

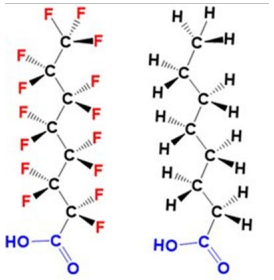


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Toxicological effects of PFAS

- **Two adverse outcome pathways identified**





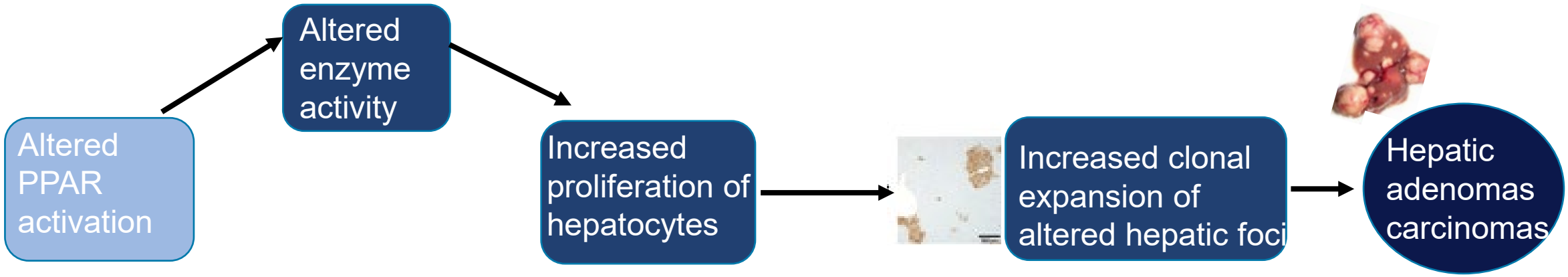
- Increased risk for **pancreatic cancer**
- **Increased** cholesterol levels and/or **risk of obesity**

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Toxicological effects of PFAS

- **Two adverse outcome pathways identified**

Non-adjacent
Adjacent
MIE — Molecular initiating event
KE — Key event
AO — Adverse outcome



Peroxisome proliferator-activated receptor alpha (PPARα) activation leading to increased β-oxidation of fatty acids, which increases liver lipid content

Increased activity of acyl coenzyme A oxidase, peroxisomal beta-oxidase, carnitine acetyl transferase, catalas

Growth factors for hepaptocytes – cytokines, tumor necrosis factor, released

Cells similar to fetal hepatoblasts (bipotential) appear

Continued activation of PPARα is necessary for focal enlargement and the formation of tumors

- Risk of **fatty liver** and hepatocellular carcinoma

In 2023, IARC (International Agency for Research on Cancer) classified:
PFOA as *carcinogenic to humans* (Group 1)
PFOS as *possibly carcinogenic to humans* (Group 2B)

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Challenges related with understanding the effects of PFAS on humans and wildlife

- Currently available is information on limited number of PFASs
- Organisms exposed to PFASs during their whole life, all scenarios not possible to test
- PFASs present as mixture and mixture toxicity is unknown
- Measurement of low concentrations of PFASs, both in the environment as well in tissues
- Understanding toxicokinetics of PFASs
- New mechanisms of biological action to be discovered

Environ Toxicol Chem 2021, 40: 564-605

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Thank you for listening

Interreg Baltic Sea Region

Co-funded by the European Union

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