One Health: PFAS substances between certainties and uncertainties

Risk analysis and open issues for a group of pervasive contaminants

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ONE HEALTH: the new operational definition adopted by WHO, FAO, OIE, UNEP (11/12/2021)

Integrated and **unifying** approach

Recognizes that the health of humans, domestic and wild animals, plants and the environment (including ecosystems) are closely linked and **interdependent**

Involves multiple sectors, disciplines, and components of society

Food safety is largely One Health. Should be protected FROM FARM TO FORK:
- From *living organisms* that produce food
- To how food is produced, packaged, consumed

Is the priority approach (EFSA ONE Conference june 2022) to analyze, assess and manage complex problems involving ecosystems, agrifood, supply chains, human health

LIKE PFAS

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One Health: environment - other living things – food - humans,

And then

For PFAS, food is the main conduit between the environment and our bodies

- Contamination of agri-food chains is the main way of exposure to environmental releases of PFAS for the population (EFSA 2020)

- Because of the persistence and mobility of these substances, contamination is *widespread* and *pervasive*

- Certain kinds of foods, such as eggs and fish, are particularly vulnerable due to environmental dynamics (e.g., through water bodies) and the *peculiar type of bioaccumulation* (protein binding) of these contaminants

- Remember the importance of water, especially for PFOA (EFSA 2020): as food in itself and essential element of foods

***From the fields* (irrigation, watering, aquaculture)**
***To the table* (baking, cooking..)**

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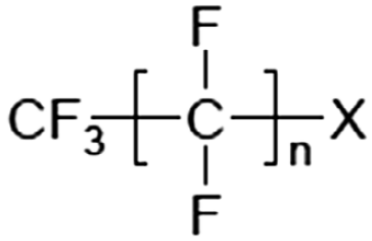
The big PFAS family

1) perfluoroalkyl substances, especially perfluoroalkyl acids (PFAA) such as carboxylates (PFCA) e sulfonates (PFSA), as well as perfluoroalkanes sulfonamides;
2) polyfluoroalkyl substances such as monomers fluorotelomers - alcohols (FTOH), olefin e iodides - as well as the acids of polyfluoroalkyl ethers. *All* are formed by

- A hydrophobic **alkyl chain**, R, of variable length (typically C4–C16) and a **hydrophilic group**, X. The hydrophobic part can be **fluorinated** completely [R=F(CF2)n-] or partially. When *fluorination is complete* = **proper perfluoralkyl substances.**



General structure of PFAS

- **The exceptional strength of the C–F bond determines the special properties of these substances, which have motivated their massive production and use**

As well as their persistence

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Properties

Amphiphilic substances
Can act as surfactants, non-ionic, cationic or anionic.
Anionic substances include perfluoroalkane sulfonic acids (PFSA), including perfluorooctane sulfonate (PFOS), and perfluoroalkyl carboxylic acids (PFCA), including perfluorooctanoic acid (PFOA)

$F(CF_2)n\text{-}CH_2CH_2\text{-}X$

Fluorotelomers

- **PFAS partially fluorinated (polyfluoroalkyl substances) which can be *precursors* of perfluoroalkyl substances such as PFOS e PFOA;**

which currently represent the contaminants of greatest concern for persistence and toxicity

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Uses

Textiles, carpets, paints, coating materials (also food-contact materials, e.g., microwave popcorn bags) military and aerospace equipment, fire-fighting foams, industrial applications, surfactants emulsifiers, cosmetics and other personal care products.

- PFAS are 4700, yet only a few had, so far, large production volumes
- *Some numbers on production volume* (*EFSA 2018*):

- in 1970-2002 produced **122.500 t PFOS, of which 26.500 was classified as industrial waste;**

- (2006) Estimated global annual production of PCFA: 4000-8000 t, of wich **3,600-5700 t PFOA-**ammonium

Major producers: **USA** and **Belgium**, also important **Italy and Japan**

(*EEA, 2019*) potential release of PFAS from more than **100.000 sites in the EU.**

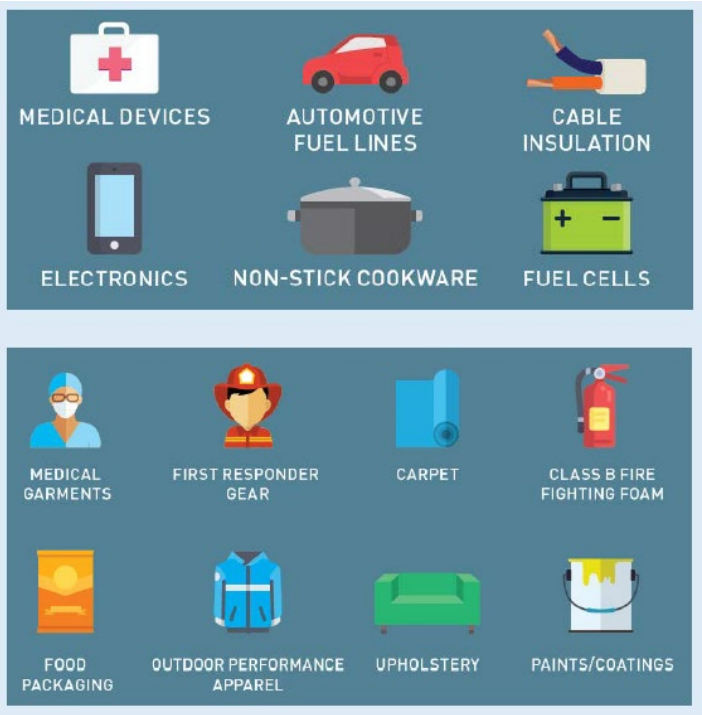
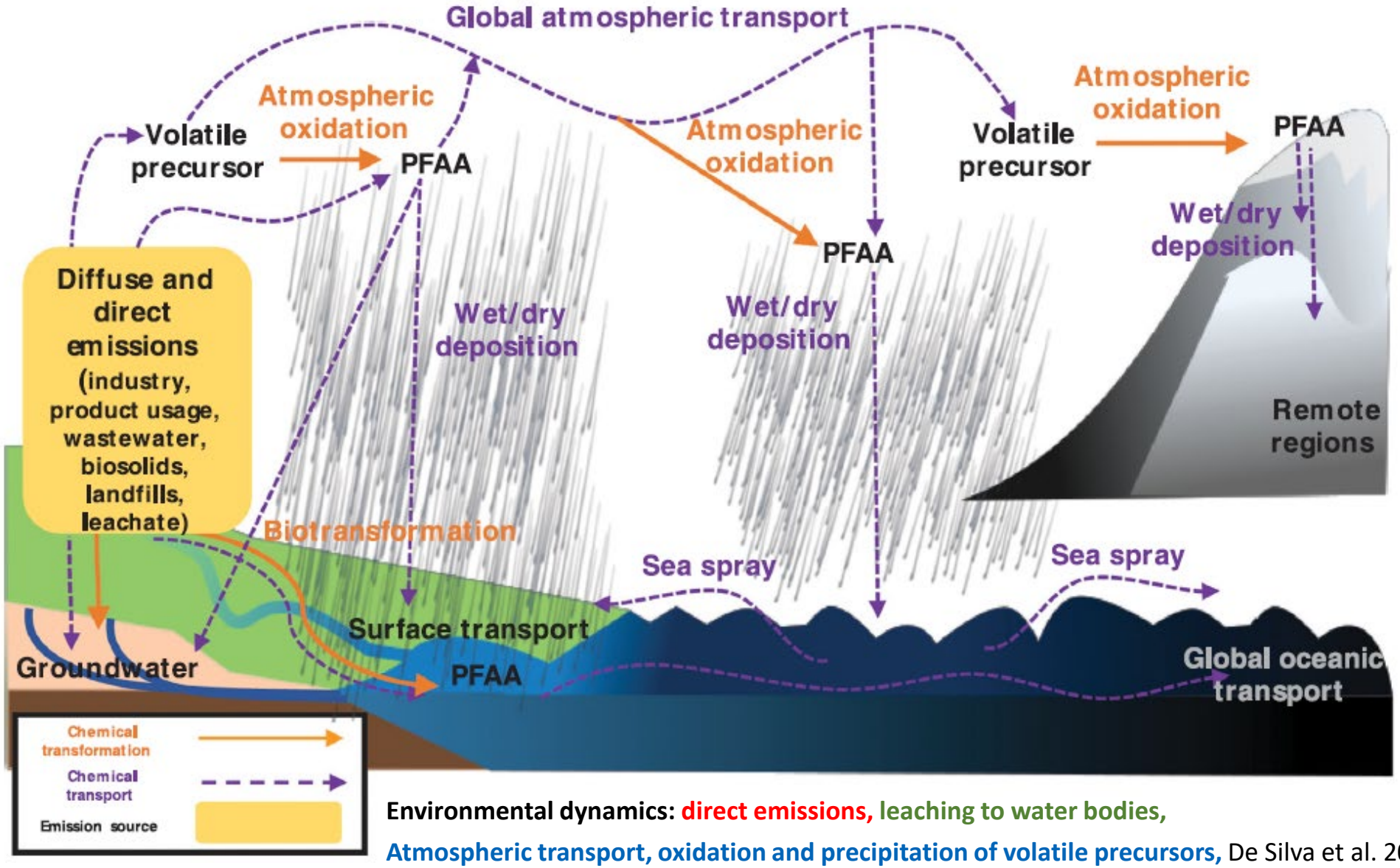


Image source: Jessica Bowman. American Chemistry Council



Environmental dynamics: direct emissions, leaching to water bodies,

Atmospheric transport, oxidation and precipitation of volatile precursors, De Silva et al. 2021

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Environmental fate

Release into the environment occurs at all stages: production, use, disposal

- Municipal **wastewater treatment plants** and **waste landfills** are important direct sources of PFAS, especially in aquatic ecosystems

- **Transport**: (**persistent, mobile, toxic substances**):

atmospheric fall-out even at considerable distance from emission sources.

Long-range transport in water bodies (one or more PFAS identified in more than 90% of EU rivers). Possibility of contaminating drinking water.

- **Patcghy contamination**: a diffuse background and hot spots, also quite extensive (municipalities in the Vicenza provincial area)

- PFAS and **circular economy: use of sludge as fertilizer and manure;**

Reuse of materials with high levels of PFAS;

Emission of volatile precursors from uncertainers (*EEA, 2019*)

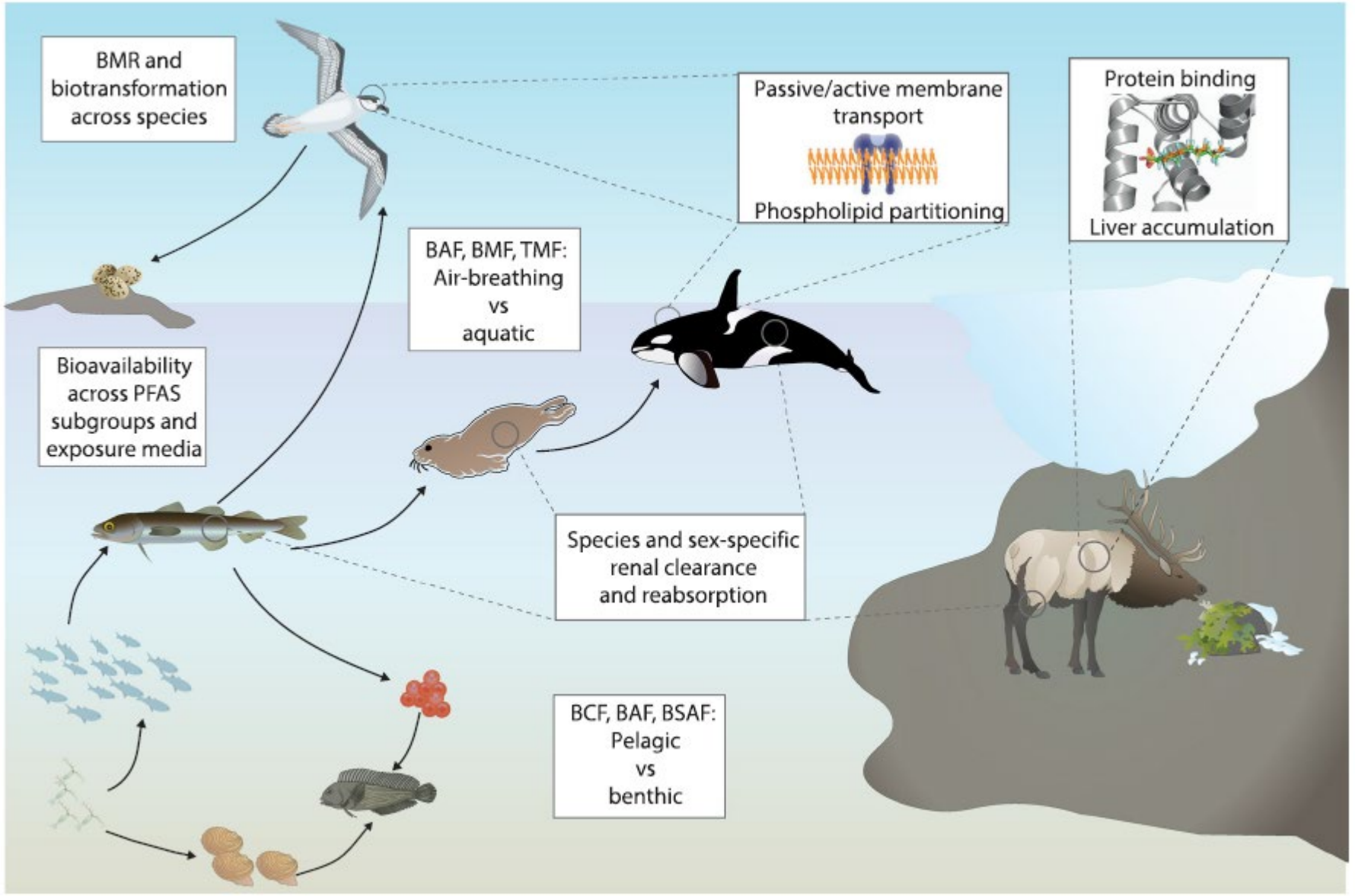
Bioaccumulation processes in ecosystems

Parameters:

BCF = bioconcentration factor (from water); BAF = bioaccumulation factor (organism vs. water, including all routes of exposure: feeding, contact..);
BSAF = biota-sediment accumulation factor (organisms in contact with sediment);
BMF = biomagnification factor (in trophic chains);
TMF = trophic magnification factor (in an organism relationship between the concentration of a substance and the place in the trophic chain);
BMR = basal metabolism;
TMF = trophic magnification factor

[De Silva et al. 2021]

With these parameters, it is possible to **identify indicator organisms in a specific ecosystem**



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Bioaccumulation: specific aspects

- The trophic chains of *birds* and *marine mammals* show TMFs with *steeper regression curves* (TMF much greater at higher trophic levels)

- *Fish* trophic chains show TMF with *much less steep* regression curves (more even distribution of TMF).

- PFOS and many other PFAS can biomagnify to a high degree in trophic chains of *terrestrial vertebrates*: elimination through lung-air exchange negligible vs. effective elimination in water through the *gills*

- (*Guerranti et al., 2017: project PREVIENI*) Poor bioaccumulation of PFOA and PFOS in organisms at *low-to-medium levels* of trophic chains (earthworms, barbs, coot eggs) was seen in a WWF oasis downstream of a polluted site (landfill in Bussi sul Tirino, PE) compared to an oasis upstream of the same site

In contrast, heavy metals, fat-soluble persistent contaminants (PBDEs, PCBs), and the phthalate metabolite MEHP showed evident bioaccumulation in these same organisms

Bioaccumulation mechanisms

For lipophilic contaminants (e.g., Dioxins, PCB, PBDE), the simple *partition between lipids and water* (indicated by their octanol-water partition coefficient) provides an indicator for the propensity to bioaccumulate.
This *is not* the case for PFAS

- Compared with fat-soluble contaminants, the bioaccumulation of PFAS is still less understood: **preferential partitioning in serum proteins** appears to be (at least one of) the key mechanisms

- PFAS are *bioavailable* and long-chain PFAA can accumulate in specific biological systems at **levels comparable** to e.g., dioxins and PCB

- Because of their chemical properties, PFAA are associated with **proteins** (e.g., serum albumin) and **membrane phospholipids** rather than intracellular storage lipids

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Bioaccumulation in aquatic trophic chains

Biomagnification is greater in aquatic chains than in terrestrial chains.
Generally, PFAS bioaccumulation increases with increasing perfluoroalkyl chain length and thus *hydrophobicity.*

- Most of the data refer to freshwater fish species (*Teleostei*)
- Data are limited for marine species: further research is needed to determine whether bioaccumulation for freshwater and marine species follows the same parameters
- Bioaccumulation factors from water to Baltic herring (*Clupea harengus*):
  - Perfluoroalkyl carboxylates (PFCA): increase from ~2.0 to 5.3 as chain length increases from 6 to 10 carbon atoms
  - Perfluoroalkylsulfonates (PFSA): increase from 3.3 to 4.1 with increasing chain length from 6 to 8 carbon atoms

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In terrestrial vertebrates

(*Death et al., 2021*) apart from "hot spots," generally *low input* of PFAS in terrestrial food chains. However, (both farmed animals and game) *aggregate exposure* to PFAS through water, air or feed. The relative contribution of these exposures to PFAS concentrations in food is *less studied*.

- Differences among species in **tissue distribution** and **elimination times** were observed but not yet quantifiable.
- **Not in metabolism**, because PFASs persist in organisms without being (or minimally) metabolized

General aspects:

Much higher concentrations in **liver** (and other organs) than in muscle tissue.

Passage in **milk** and **eggs**, as well as to offspring.

If exposure ceases, PFAS concentrations decrease (but data are too limited to define withdrawal times)

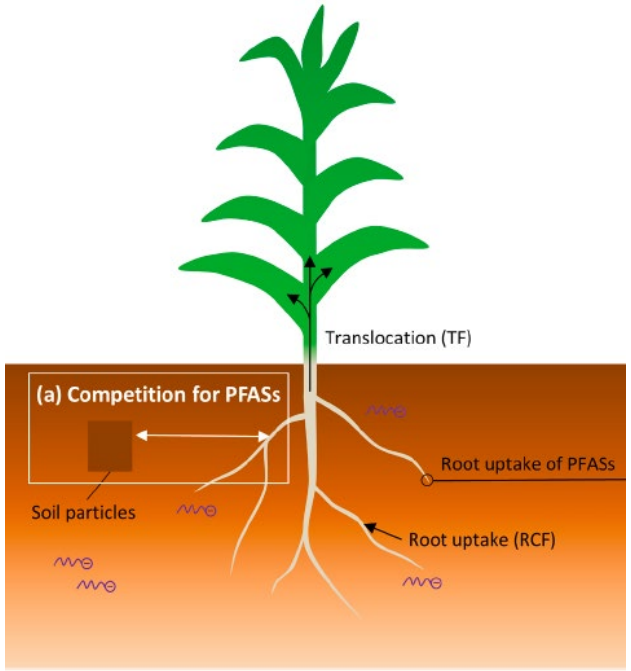
- Toxicity and early biomarkers of effect in farm animals: few data

Bioaccumulation from soil to plants (1)

The soil-plant system plays an important role in PFAS bioaccumulation.
Transfer of PFAS to plants and pastures: from soil, PFAS are absorbed by plant roots

- Uptake into organic material increases with **chain length** however uptake by plants of long-chain PFASs is **limited by** the fraction available in pore water.
- Transfer rates are **higher** for **short-chain** PFAS.

- The rate of transfer **decreases from roots to leaves to fruits**, due to natural barriers within the plants.
- Translocation factors are *inversely related* to PFAS hydrophobicity.
- Nevertheless, PFAS have been **detected in fruit**.



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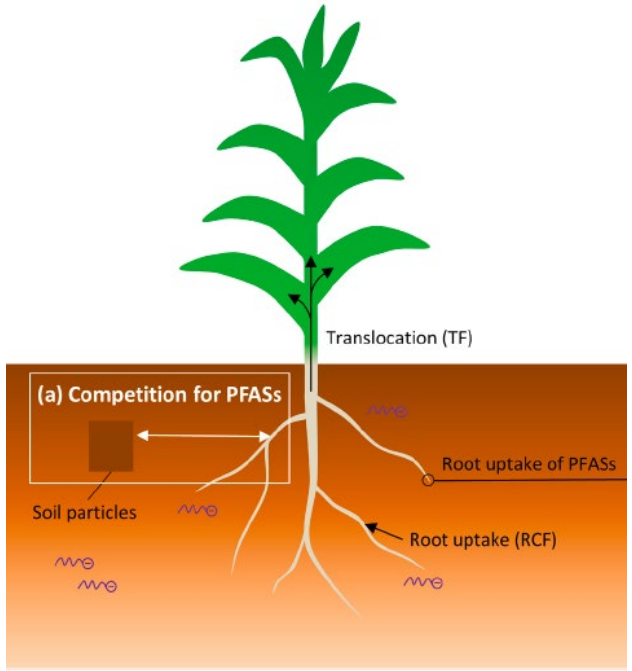
Bioaccumulation from soil to plants (2)

Biomagnification has been observed in natural ecosystems (e.g., from lichen to caribou to wolves), but to a lesser extent than in aquatic food webs involving birds and marine mammals

- In the presence of soil contamination, it is possible to "**map**" transfer to plant and forage foods, integrating (*One health*) :
  - The characterization of the contamination: which PFAS, quantity, distribution
  - - The agronomic characteristics (e.g., irrigation systems, fertilizers)
  - - The mapping of crops present
  - - *Tubers* can be indicators (EFSA, 2020)



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Bioaccumulation in farm animals

Important potential sources are drinking water, pastures, feeds:
agricultural reuse of industrial and urban sludge and effluents indirectly contributes to livestock exposure.

- Water, soil, air, or feed: the contribution of each component of *aggregate* PFAS exposure to PFAS concentrations in food of animal origin is not well characterized.

However, *all of them have to be be considered* in an exposure assessment of food-producing animals

- **Exposure of grazing animals:**

- **Soil ingestion** (significantly higher in sheep than in cattle: EFSA 2011)
- **Forage** exposure to **manure** and **fertilizers** with sludge reuse
- Contamination of water sources and sediments: **leaching** and **overflow** (observed in emergencies with other contaminants: Brescia -PCB- and Valle del Sacco -betaHCH)

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Toxicokinetics

Ingested PFAS are readily absorbed and are not metabolized by animals or humans.
They accumulate in organs and tissues over time progressively.
Maternal transfer to offspring both prenatally (in utero) and postnatally (via breastfeeding)

- After absorption, binding to plasma proteins and distribution to different organs and tissues: bioaccumulation occurs mainly (but not only) in the liver
- In laboratory rodents, the **half-life is much shorter** than in humans
- In humans, the half-life of short-chain PFAS (e.g., PFBA, PFBS, and PFHxA) varies from *a few days to ca. one month*;

for long-chain compounds (e.g., PFOS, PFOA, PFNA, PFDA, PFHxS) it is on the order of **several years**

- The long half-lives of these PFASs result mainly from their interactions with *various transporters involved in the reabsorption processes that occur in the liver, intestine, and kidney*

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But what do PFASs do? Mechanisms of toxicity

- Binding to the nuclear receptor PPARα (lipid and cholesterol metabolism) may explain some of the main effects (*reduced immune response, hepatic steatosis, increased cholesterol, reduced fetal weight*).
- In addition, PFAS may compete with T4 for binding to the hormone transport protein (indirect *thyroid antagonism*)
- **Increased susceptibility of the *developing organism*** (in utero, infancy)

- ❑ Toxicological studies are **important for describing** effects, mechanisms, and target organs;
- ❑ However, **animal-human toxicokinetic differences limit their usefulness** for establishing human health tolerable levels (*health based guidance values* - HBGVs)

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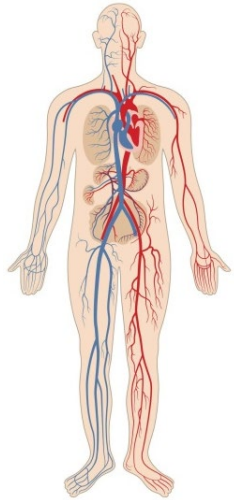
Epidemiological data

For some of the PFAS of greatest concern, particularly PFOS and PFOA, human epidemiological data have accumulated in recent years and have been the basis for recent risk assessments (see EFSA 2020)

- The effects identified in animal models have since been **generally confirmed in humans**
- Good quality epidemiological studies have been published in the last decade
- EFSA's latest risk assessment (2020) is based **primarily on human data**



Persistent, unmetabolized PFAS: *levels in serum/plasma* are a good indicator of body burden

"PREVIENI" study (first biomonitoring in Italy): PFOS (mainly) and PFOA levels widespread in the population with a wide distribution of values (La Rocca et al., 2014, 2015)

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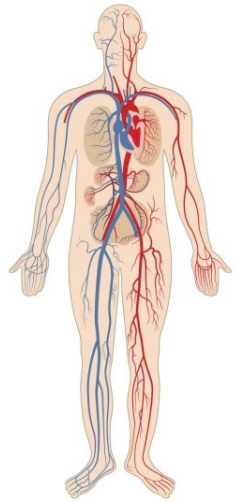
Epidemiological data (2)

- Based on available animal and human studies, **effects on the immune system (reduced vaccine response in children)** were considered the basis for risk assessment (EFSA 2020)

- Other effects worthy of attention and on which data are increasing:

- **Increased cholesterol levels**, imbalances in glucose and lipid metabolism: increased risk of aspects of metabolic syndrome?
- Decreased **thyroid function**
- Reduced **fetal growth**



They may be important for a TWI update.

Note: PFAS toxicity: rather than direct damage to DNA/cells (as in "good ol'time" toxicology)

Incorrect modulation/programming of tissue functioning/development even at very low doses

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Risk Characterization (EFSA 2020)

❑ Four long-chain PFAS most important* for food safety (PFOA, PFOS, PFNA, PFHxS).

* Persistence, prevalence, as well as data availability

- The 4 substances exhibit similar **bioaccumulation properties and toxic effects**

- **weekly dose** (not daily because these are substances that bioaccumulate and give rise to a "body burden") **tolerable group (= for the sum of the 4 PFAS)**

4.4 nanograms/kg body weight

Tolerable dose = pragmatic intake limit (considering scientific evidence and uncertainties) *to define whether at the population level there is a concern*

Risk Characterization (EFSA 2020)

While considering uncertainties due to incomplete data, the exposure levels of large parts of the European population are **above the tolerable dose**, highlighting a health risk;

Most important foods (**contamination x consumption**)

Fish, eggs, water (for PFOA) and also **fruit**

Other PFAS-rich sources of **limited consumption** (**liver, game**) may be *indicators of contamination*

Children (the population *most vulnerable* to the effects of PFAS) are also the *most exposed* segment of the population (also because they eat more daily in relation to body weight)

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Risk Characterization (EFSA 2020): About food sources

- **Fish and seafood** overall the most important source; pay attention also to shellfish (e.g., mussels, clams): *sedentary and filter-feeding organism;*

and *fish in contact with sediments* (Gallocchio et al. 2022): carp, tench, barbel

- Much more limited data for marine fish
- **Eggs**: higher levels in eggs from *free-range farms* because they are more exposed to the environment (Gazzotti et al., 2021)
- High consumption of **eggs and/or fish and/or liver and kidney** is correlated with body burden (study on European adolescents, Richterova et al., 2023)
- Lower contamination of *organically grown vegetables*

Hypothesis: co-formulants and packaging of plant protection products - whose use is limited in organic products (Piva et al., 2023)

- **drinking water** predominates *in high exposure scenarios* associated with water supply contamination cases

less important in *background exposure of the general population*, except for PFOA

Risk Characterization: comments

- Children: average intake about **two times higher** than adults:

also emerged clearly from *the Istituto Superiore di Sanità risk assessment of food-related exposure in the Veneto area* affected by PFOA contamination (Istituto Superiore di Sanità, 2019).

- PFOS and PFOA account for the **large share of overall dietary exposure** (PFOS 66% and PFOA 21%) compared to the other two long-chain PFAS, PFNA, and PFHxS

- Consumption of **locally produced foods** increases body burden

  - *proximity to "hotspots" of contamination* (Richterova et al., 2023)

  - Also confirmed by the risk assement carried out by Istituto Superiore di Sanità (2019):

factors associated with high exposure to PFOA

  - use of **private wells** for drinking water supply

  - consumption of food, especially of **animal origin**, that is **locally produced and/or self-produced**

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PFASs enter EU food control system

Based on the evaluation of EFSA:

Regulation (EU) 2022/2388 (7/12/2022)

Maximum residue limits for the sum of the four Pfas in food of animal origin:

Eggs; fish meat, by species and considering marine and freshwater species separately*; crustaceans and bivalve molluscs; meat and offal of cattle, sheep, pigs and poultry; meat and offal of game*

Therefore, PFAS **must finally be included** in official controls and self-control systems therefore:

inclusion in contaminant control plans,

validated analytical methods, reference laboratories...

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IS EVERYTHING ALL RIGHT?
NOT EVERYTHING...

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Food contact materials

PFAS in food contact materials: **plastic tableware, microwave cooking bags, Teflon substitutes:**

How serious is the problem? EFSA has not performed an assessment, yet

However, every now and then the precautionary principle applies

(5/3/2024: Food Safety Magazine)

The European Parliament and Council have reached a provisional agreement on the **Packaging and Packaging Waste Regulation** (PPWR), which would require all packaging used in the EU to be recyclable, set restrictions on plastic packaging, and **ban the use of per- and polyfluoralkyl substances (PFAS) in food contact packaging**.

Parliament and Council must formally approve the agreement before the requirements enter into force.

Important knowledge gaps

PFAS are *many*

Medium- and short-chain PFASs could be proposed to replace PFAS of greater concern, BUT

Limited knowledge on persistence, toxicology, and ability to contaminate food =

certainly less persistent, probably less toxic,

but probably **not entirely innocent.**

Data needed, however

Circular economy: persistent and mobile PFAS can be **unwanted hosts** (e.g., manure and fertilizer with sludge reuse)

Reliable methods to degrade them?

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PFAS and «ONE HEALTH»

How do PFAS get to foods?

Characterize the main determinants of exposure for living organisms-plants and animals-from which our food originates:

irrigation, manures, fertilizers, feed, drinking water, aquaculture facilities

(the EFSA opinion is also somewhat lacking on this)

For the prevention of health risks from dietary exposure to PFAS: **a One Health vision "from farm to fork"**

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PFAS and «ONE HEALTH»

For the control and prevention of PFAS food contamination: “From farm to fork“

Take action on the main sources of exposure of food-producing animals, namely **drinking water and feedstuffs**

Collect and evaluate **scientific evidence** to **set limits** in these matrices, also considering **interspecies differences**

v. Position paper FOSAN - Ente di ricerca sugli Alimenti e la Nutrizione, 2023, «*Valori limite di PFAS nelle acque di abbeverata in relazione ai rischi di potenziale bioaccumulo negli animali da reddito*»

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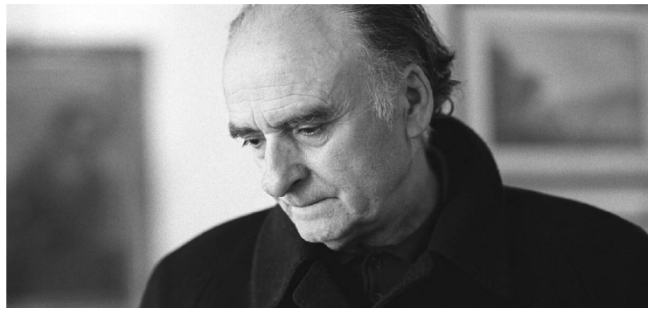
(Andrea Zanzotto 1921-2011)



In questo progresso scorsoio
non so se vengo ingoiato
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We hope to have interested you, goodbye!

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