

**From:** [PC](#)  
**To:** [Coffin Butte Landfill Appeals](#)  
**Subject:** LU-24-027 testimony  
**Date:** Monday, October 6, 2025 4:15:22 PM  
**Attachments:** [PFAS Pam Castle LFG Testimony Final .pdf](#)  
[PFAS Pam Castle - Adamopoulos et al 2025.pdf](#)  
[PFAS Pam Castle - Andrews et al 2023.pdf](#)  
[PFAS Pam Castle - Costello and Lee 2024.pdf](#)  
[PFAS Pam Castle - Fenton et al 2021.pdf](#)  
[PFAS Pam Castle - Lin et al 2024.pdf](#)  
[PFAS Pam Castle - Tolaymat et al 2023.pdf](#)  
[PFAS Pam Castle - Reetz et al 2025.pdf](#)

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Attached is a PDF of my testimony regarding PFAS in landfill gas  
File Name = PFAS Pam Castle LFG Testimony Final

The seven references cited are attached as PDFs and have file names formatted as:  
"PFAS Pam Castle - " followed by the author names and year (as referenced in the testimony)

Best,

Pam Castle

Commissioners Malone, Shepherd and Wyse,

My name is Pam Castle and I live at 993 NW Cypress Avenue in Corvallis some eight miles from Coffin Butte Landfill - I have a Master's in pharmacology/toxicology, taught college biology for approximately 20 years, and testified before the Benton County Planning Commission in opposition to the expansion of the landfill. The following is a modification of that testimony.

Until recently, landfill leachate presented the largest concern surrounding PFAS (the “forever” chemicals getting lots of scrutiny because of their multitude of dangers) escaping landfills. Recently, the potential for long-range distribution of PFAS from landfills via landfill gas (LFG) has spurred its examination. It is likely that, given the enormous plumes of fugitive LFG escaping Coffin Butte Landfill, PFAS are spreading across the region. On October 6, I submitted written testimony regarding odor issues at my home. What I smell on foggy days are the signature odors of landfills – the rotten cabbage smell from hydrogen sulfides and a sweet solvent smell. It is not a stretch to think that when we smell landfill odor not only are we breathing in a potpourri of VOCs, we are breathing in PFAS.

PFAS present health risks to plants, animals, and humans. Since landfills concentrate PFAS, allowing more PFAS to be trucked in and concentrated at Coffin Butte Landfill where it escapes via two main routes is irresponsible and risky.

## PFAS in Landfill Gas (LFG)

A 2024 study of PFAS escape at three landfills in Florida found the 32 – 76% of total fluorine (one way to measure PFAS is to measure fluorine) that escaped via LFG was at least as great or greater than the 24 – 68% that escaped in leachate. They concluded it is likely that LFG is a major route of PFAS entering the environment (Lin, et al. 2024).

As seen in Figure 1, a 2023 Tolaymat et al. 2023 review paper reported that of the yearly total mass of PFAS entering landfills, 6% escaped via LFG while 10% escaped via leachate.

### Summary:

LFG is a significant route for PFAS to escape landfills and enter the atmosphere where they can be deposited in water and onto soils.

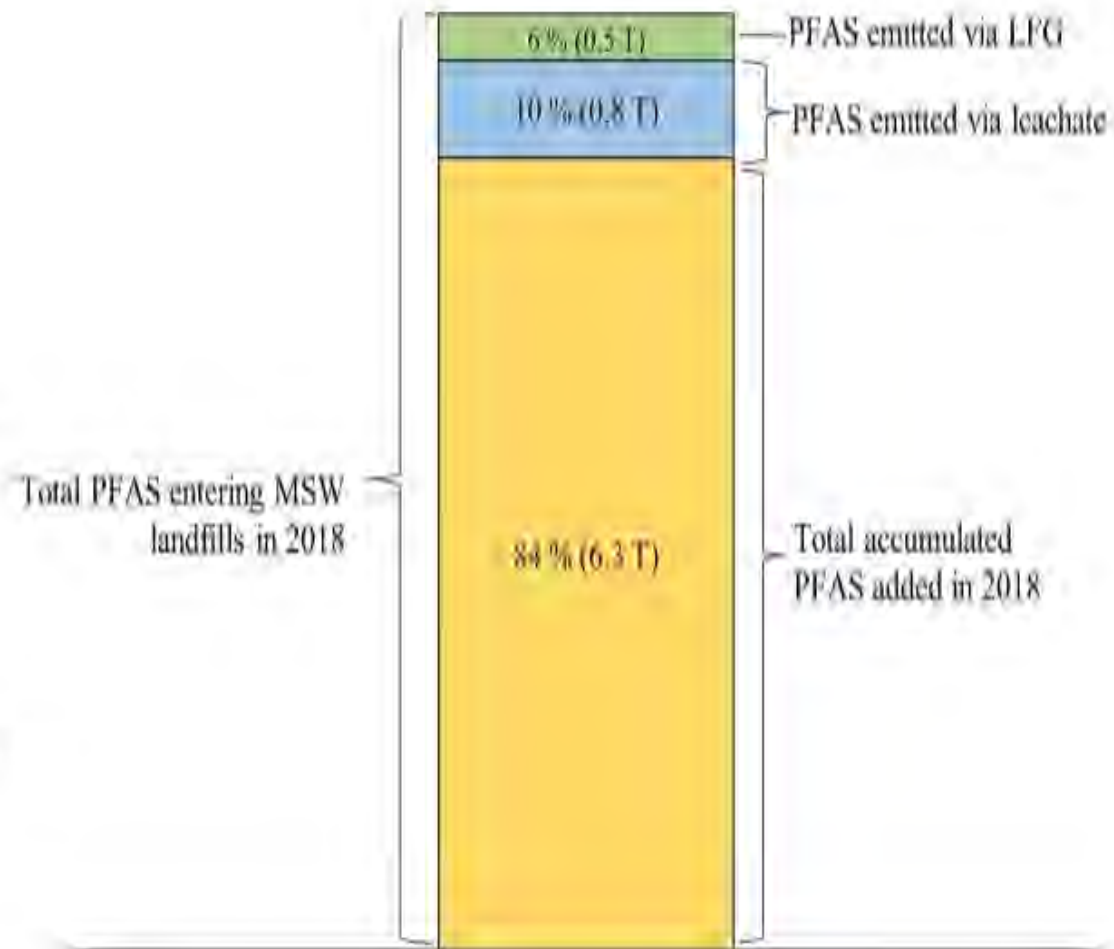


**Figure 1.** The fate of PFAS entering landfills

It is important to note that even though some LFG is captured and burned at flares, flares do not burn at high enough temperatures to mineralize PFAS into an inert salt. Flares do not mitigate PFAS.

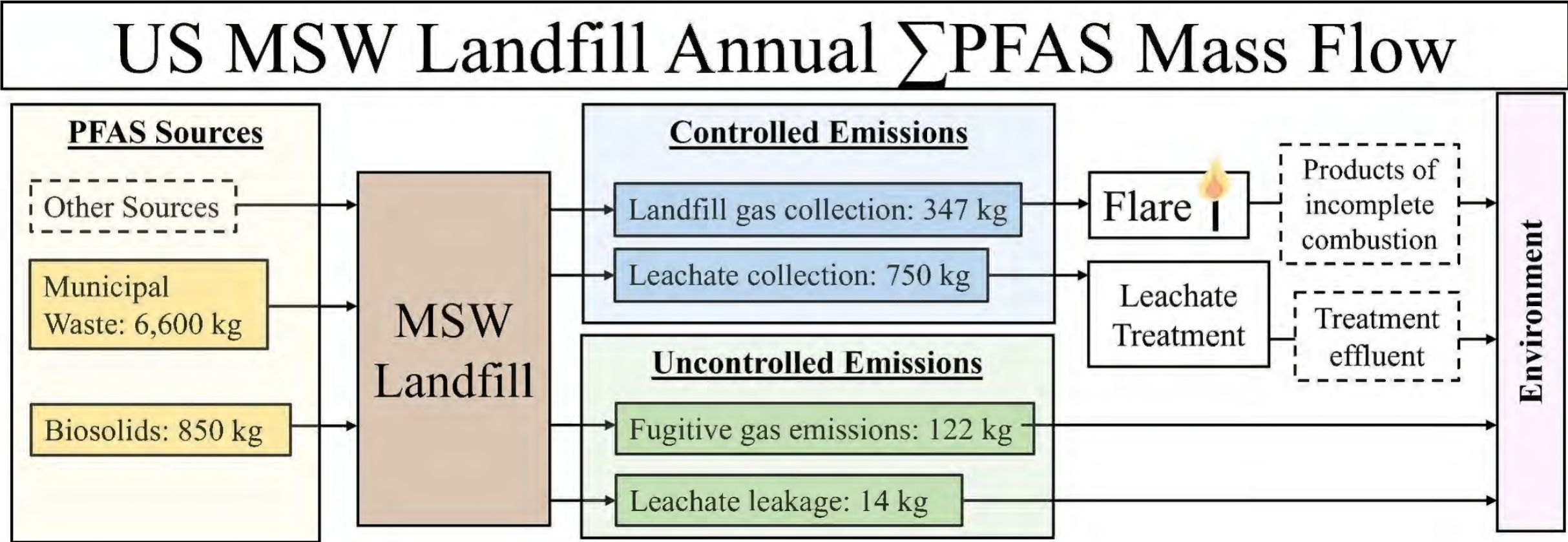


**Figure 2.** Flowchart of annual PFAS entering and leaving landfills (Tolaymat et al. 2023).

## **The four main sources of PFAS entering the atmosphere, soil, and water are:**

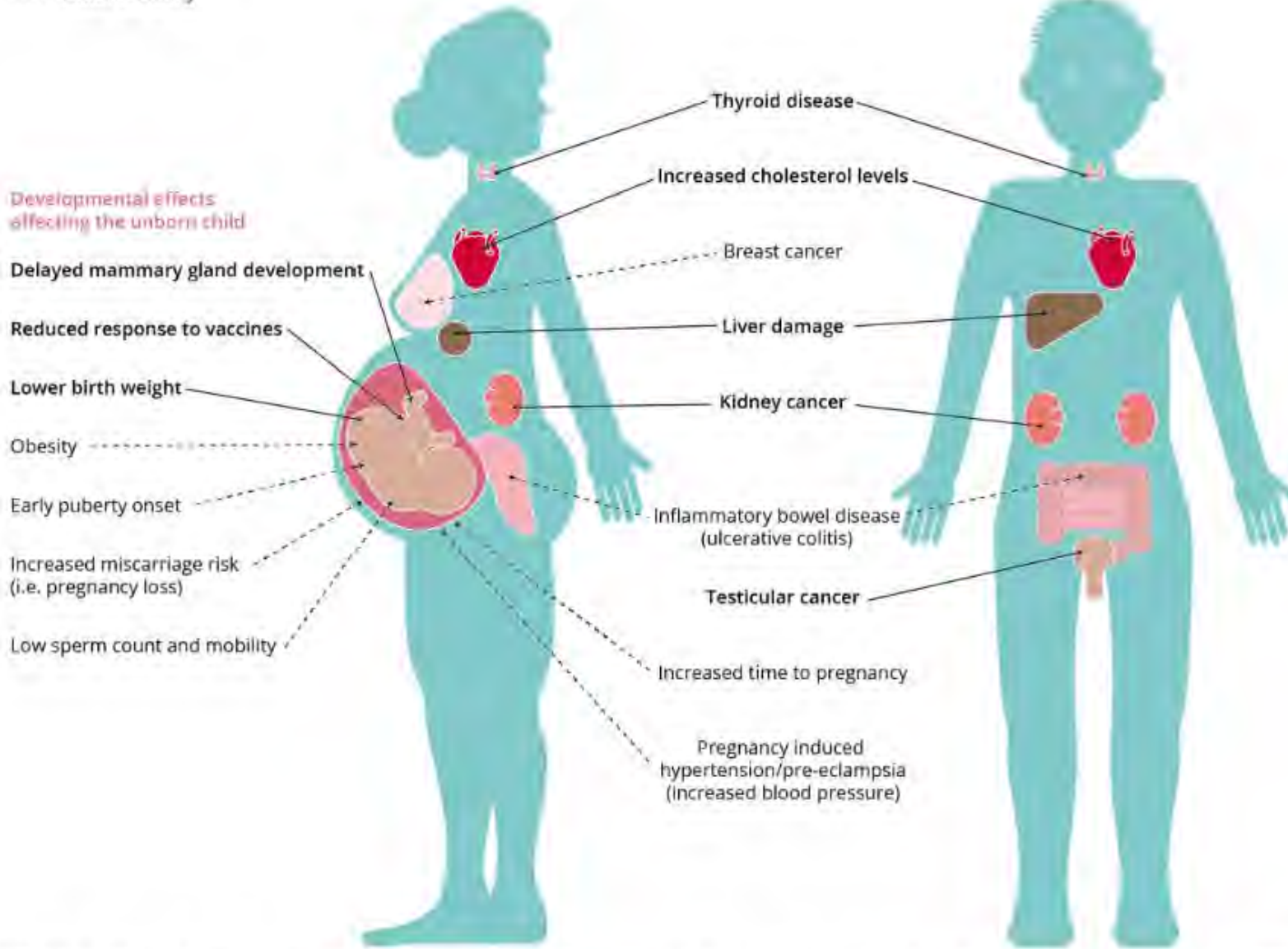
- Manufacturing sites
- Places where firefighting activities take place (aqueous film-forming foam use)
- Landfills – landfill leachate and LFG (like at Coffin Butte Landfill)
- Wastewater treatment plant (WWTP) biosolid applications to soil- like what happens in the region after millions of gallons of landfill leachate are sent from Coffin Butte Landfill to the Corvallis and Salem WWTPs to be processed with municipal sewage – WWTP processes do not mitigate PFAS. Those PFAS either end up in biosolids spread on area fields or in effluent that is released into the Willamette River.

The PFAS in those biosolids can stay with that soil, enter groundwater, or become airborne and transported elsewhere.

(Reetz et al. 2025)

# PFAS present human health risks – expanding landfill increases the risk to us all

— High certainty  
---- Lower certainty



Health risks of high certainty:

Developmental effects on the fetus – delayed mammary gland development, reduced response to vaccines due to immunotoxicity, and lower birth weight.

Cancers – Kidney and testicular

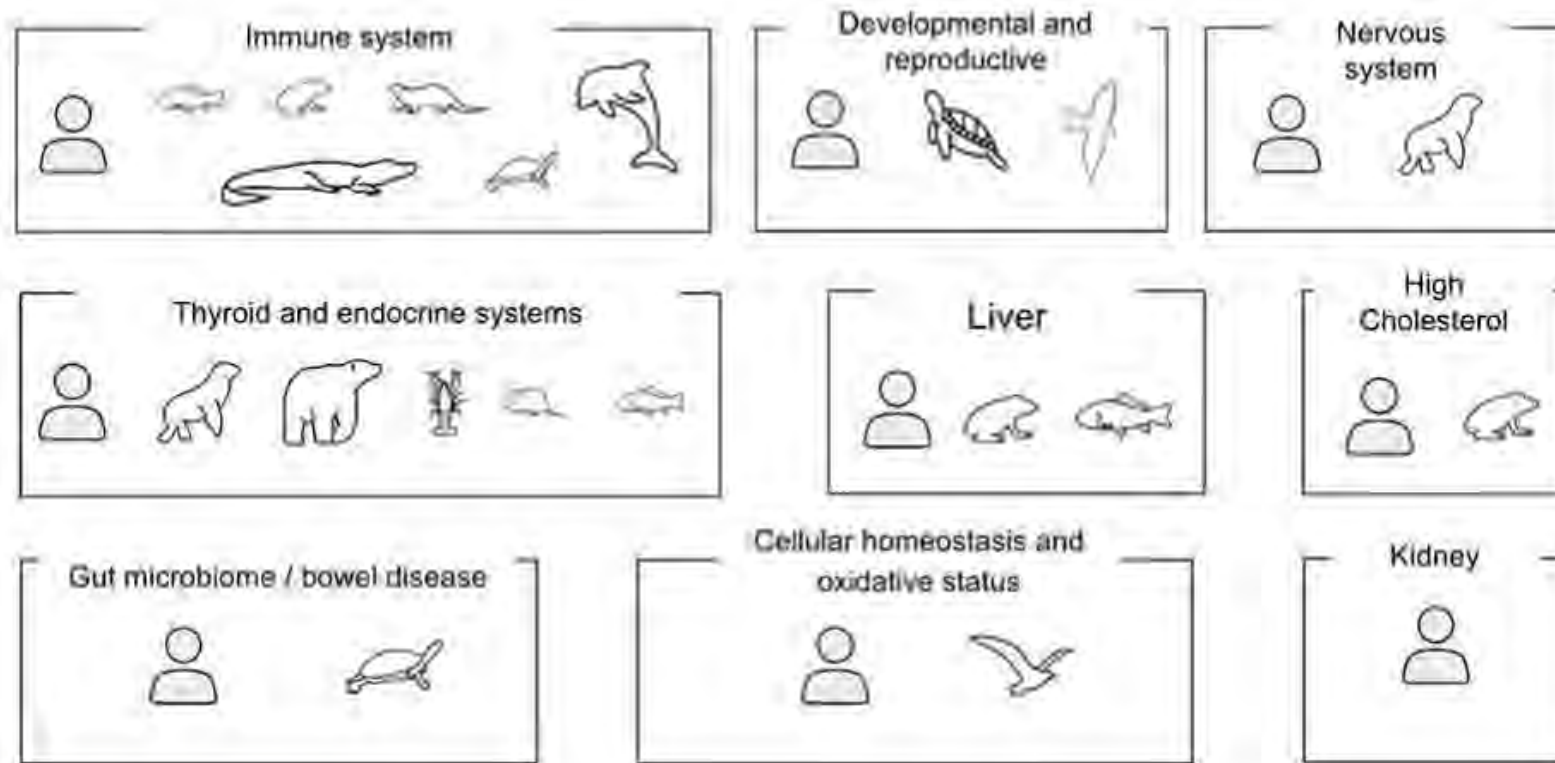
Miscellaneous – thyroid disease, liver damage, and increased cholesterol.

Others are being elucidated via ongoing research.

**FIGURE 1:** Effects of per- and polyfluoroalkyl substances on human health. Used with permission from European Environment Agency (2019). Original sources for this figure: National Toxicology Program (2016), C8 Science Panel (2012), IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (2017), Barry et al. (2013), Fenton et al. (2009), and White et al. (2011b).

From Fenton et al. 2021

# Wildlife suffer the same effects when exposed to PFAS



Andrews et al. (2023) concluded:

- PFAS are detected in wildlife globally.
- There is concordance between findings on PFAS health effects in wildlife and humans.
- Humans can be regarded as a sentinel species for adverse health impacts of PFAS.

So, not only are we putting humans at risk we are putting wildlife and domesticated animals at risk.

## **Plants also bioaccumulate PFAS and exhibit metabolic and phytotoxic responses**

Costello and Lee (2024) found:

- “Land application of PFAS-containing media results in plant uptake of short-chain PFAS into plant components that are consumed by humans, utilized as fodder, or land-applied. Long-chain compounds typically sorb to or are taken up into plant roots and largely remain in the roots while short-chain compounds have a higher propensity to translocate into plant shoots.”
- “Also in lettuce, PFOS and PFOA altered amino acid metabolites, dipeptides, fatty acids, lipids, phytol, purine nucleosides, phenolic antioxidants, and flavonoids, as a result of stress responses to DNA injury, photosynthesis inhibition, and impact to energy metabolism.”
- That plant enzymes were found to convert precursor molecules into more bioavailable PFAS.

Adamopoulos et al. (2025) report:

- Plants take up PFAS from soil and water.
- Elevated PFAS decrease plant productivity (less growth, decrease in photosynthetic productivity) which leads to lower crop yields. Wheat has decreased grain size and protein content.

### Summary:

Plants accumulate PFAS from soil and those PFAS have been shown to disrupt cellular processes – these disruptions can result in reduced crop yields. In addition, plants can convert PFAS into forms that are more disruptive to biological processes putting those that eat them at risk.

## **PFAS for generations to come**

Lin et al. (2024) refer to landfills as “unabating PFAS repositories” and states that LFG may account for more environmental deposition of PFAS than leachate indicating that managing LFG is requisite for preventing long-term, atmospheric transport of PFAS. Coffin Butte Landfill has a substantial fugitive LFG problem.

A landfill expansion –which would remove the cap on the amount of waste hauled to the landfill - would increase our “PFAS repository” making the human health, environmental, and economic burdens much greater.

**PFAS distribution in the atmosphere – is the city testimony providing a warning?**

Given recent findings about PFAS in LFG, I contend that the landfill odor testimony by those in Corvallis is an important indicator of the widespread nature of the LFG problem and that PFAS are being spread over a large area. This means LFG odor is not a nuisance issue, but a public health issue.

The landfill’s history of uncontrolled and insufficiently unmitigated LFG release (as measured by methane emissions) indicates that the distribution of PFAS in the environment will continue at higher levels with an expansion.

To allow the spread of more PFAS would mean the county is not meeting Benton County’s Comprehensive Plan policies 6.1.2, 6.1.4 and 6.3.1. In addition, since studies show plants and animals accumulate PFAS affecting them, and anything that consumes them, the landfill **does seriously interfere with** the ability of farmers on adjacent land to use their properties for their designated purposes and therefore **does not meet BCC 53.215(1)**. For these reasons, I urge the commission to deny the application for expansion of Coffin Butte Landfill.

Respectfully,

Pam Castle

Article

Not peer-reviewed version

# The Impact of PFAS on the Public Health and Safety of Future Food Supply in Europe: Challenges and AI Technologies Solutions of Environmental Sustainability

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Keywords: PFAS contamination; agricultural sustainability; food security; AI technologies; community engagement; environmental health; soil restoration; public health Europe



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*Article*

# The Impact of PFAS on the Public Health and Safety of Future Food Supply in Europe: Challenges and AI Technologies Solutions of Environmental Sustainability

**Abstract:** Per- and polyfluoroalkyl substances (PFAS) are persistent organic pollutants used in everyday products. They pose a significant threat to global agricultural sustainability and food security, particularly in European farmlands. Contamination occurs through industrial discharges, biosolid applications, and contaminated irrigation water. PFAS contamination affects soil fertility, water quality, and food safety, and has broader implications for Europe's food security. This research explores the scale of PFAS contamination, its implications for food security, and innovative remediation solutions. A multi-faceted strategy integrating detection tools, advanced remediation technologies, and policy initiatives is proposed to mitigate PFAS contamination while ensuring sustainable agricultural practices. A significant threat to global agricultural, public health, and food security the AI technologies revolutionizing environmental sustainability by developing machine learning algorithms, predictive statistics, and data analysis tools. Technologies are enhancing ecosystem management, advancing environmental research, providing digital solutions to complex environmental problems, and generative and using AI in Sustainability Environmental Education.

**Keywords:** PFAS contamination; agricultural sustainability; food security; AI technologies; community engagement; environmental health; soil restoration; public health; Europe

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## 1. Introduction

The Per- and polyfluoroalkyl substances (PFAS) are Human-made, persistent organic pollutants that are used in a vast array of everyday products. Research on PFAS (Pollution Prevention and Control Systems) has highlighted the toxicity and contamination of synthetic chemicals in ecosystems through waste outputs, (Winchell et al.2021). PFAS (per- and polyfluoroalkyl substances) have become synonymous with environmental resilience and contamination persistence. Over the past decade, research has shown that PFAS contamination has significant impacts on human health, reproductive performance, and development (Sivagami et al.2023), despite the increasing body of scientific knowledge, PFAS have become ubiquitous and present in various environmental matrices, (Falandysz et al., 2024).

Since their introduction in the mid-20th century, these compounds have been extensively used in industrial and consumer products, including nonstick cookware, firefighting foams, textiles, and food packaging, due to their exceptional heat resistance, chemical stability, and hydrophobic properties. Technological advancements have led to a dramatic increase in understanding and tools for detecting PFAS, leading to increased scientific recognition of their toxicity and environmental impact (Sivagami et al.2023; Said and El, 2024). PFAS contamination, its effects on soil fertility, water quality, and food safety, and the broader implications for Europe's food security, (Lazova & Adamopoulos, 2024). As a result, research is focusing on environmental fate, ecotoxicology (Koulini et al.2024), and source characterization. Historically, PFAS have received little regulatory interest and have not been widely monitored by governments, (Prasad & Elchuri, 2023).

However, as global awareness increases, PFAS contamination is now associated with geopolitical disputes and people's rights to clean food and water (Adamopoulos et al., 2024a; Peritore et al.2023). Research projects are interdisciplinary in nature, addressing complex issues and

addressing knowledge gaps in PFAS impact science and management, (Sivagami et al.2023; Koulini et al.2024). Artificial intelligence is being recognized as a potential solution to sustainability challenges, and can be a powerful tool for sustainability-focused researchers (Mijwil et al., 2024), addressing global PFAS problems and strategic end-of-pipe pollution, (Gerardu et al.2023).The intersection between big tech companies and AI and PFAS research is crucial for both research and policy, (Winchell et al.2022; Bolan et al.2021). Predictive statistics and advanced technologies are revolutionizing the field of environmental sustainability, these tools enable the development of machine learning algorithms (Bibri et al.2024), enabling the management of ecosystems and advancing research in areas such as mine/pan-spectral and hydro-biological sciences, (Ditria et al.2022). Artificial intelligence is increasingly being used in environmental management, particularly in waste management (Chen et al.2023), this involves feature extraction, data reduction, intelligent prediction, classification models, and data visualization, (Shivaprakash et al.2022). PFAS are often referred to as “forever chemicals” because they resist degradation, persist in soil and water, and bioaccumulate in living organisms. The widespread use and improper disposal of PFAS have resulted in contamination hotspots worldwide. These hotspots are particularly pronounced in industrialized regions where manufacturing, waste management, and agriculture intersect.

Studies indicate that PFAS can migrate through soil and water systems, infiltrating crops, livestock, and, ultimately, the food chain. In Europe, PFAS contamination poses a serious threat to agricultural sustainability, particularly in regions with intensive farming practices or proximity to industrial zones, (Adamopoulos et al., 2024a).

### *Aims and Scope*

This study explores the multifaceted challenges posed by PFAS contamination in Europe’s agricultural systems. The primary aim is to assess the scope of PFAS contamination, its effects on soil fertility, water quality, and food safety, and the broader implications for Europe’s food security. By integrating current research and case studies, the paper examines feasible remediation solutions that align with the European Union’s goals under the Green Deal and the Chemical Strategy for Sustainability.

## **2. Methods and Materials**

### *2.1. Literature Current State of PFAS Contamination in Europe*

#### *2.1.1. Sources of Contamination*

Understanding the sources of PFAS contamination is critical for targeted remediation and policy development. In Europe, these sources primarily include:

#### *2.1.2. Industrial Emissions*

The production of textiles, firefighting foams, nonstick cookware, and other PFAS-based products releases these substances into the environment. Factories that manufacture these goods often discharge untreated wastewater containing PFAS directly into local water bodies or soil. Studies have identified elevated PFAS levels in regions with chemical manufacturing plants, such as those in Belgium and Germany. These emissions often lead to persistent contamination of nearby agricultural lands due to surface runoff and atmospheric deposition.

#### *2.1.3. Agricultural Practices*

**Biosolids and Fertilizers:** The application of biosolids (treated sewage sludge) to agricultural lands is a significant contributor. Due to wastewater treatment processes that concentrate these chemicals, biosolids often contain high levels of PFAS. This introduces PFAS into soils, where they can leach into crops and groundwater.

**Contaminated Irrigation Water:** Many European rivers, including the Rhine and Seine, have been identified as carrying PFAS contamination from industrial discharges upstream. When farmers use these water sources for irrigation, PFAS are transferred into the soil and taken up by plants.

#### 2.1.4. Waste Mismanagement

Improper disposal of PFAS-containing products exacerbates the problem. Landfills without adequate lining and leachate collection systems allow PFAS to seep into the ground. Incineration of PFAS products at suboptimal temperatures can release them into the atmosphere, where they return to the soil and water through precipitation.

#### Regulatory Landscape

Europe has taken proactive steps to address PFAS contamination through ambitious policy frameworks like the European Green Deal and the REACH Regulation. While these efforts have laid the groundwork for controlling PFAS use and limiting contamination, significant challenges remain in monitoring, enforcement, and the development of scalable remediation solutions.

#### The European Green Deal

The European Green Deal, adopted in 2019, aims to make the EU climate-neutral by 2050 while addressing pollution and sustainability issues across industries. PFAS contamination, particularly in agricultural and water systems, has been identified as a key priority under its zero-pollution ambition.

##### **Key elements include:**

**Chemical Strategy for Sustainability (CSS):** The CSS within the Green Deal outlines stricter controls on harmful chemicals, including PFAS. The strategy prioritizes eliminating non-essential PFAS uses and reducing their prevalence in consumer and industrial products (European Commission, 2020).

**Circular Economy Action Plan:** This initiative seeks to reduce PFAS in waste streams to prevent reintroduction into the environment, especially in agriculture, where biosolids may contain PFAS.

**Zero Pollution Action Plan:** This plan targets contamination hotspots and includes funding for PFAS research and mitigation technologies, particularly in vulnerable ecosystems like farmland and water sources.

##### **Gaps in Implementation:**

**Insufficient Monitoring:** Existing monitoring networks often fail to capture PFAS hotspots in rural or agricultural regions, which are most affected.

**Lack of Coordination:** Member states implement Green Deal objectives at varying speeds, resulting in inconsistent PFAS mitigation strategies across borders (Goldenman et al., 2019).

#### The REACH Regulation

The Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) Regulation is one of the EU's most comprehensive chemical control policies. Under REACH, several PFAS chemicals, including perfluorooctanoic acid (PFOA) and its salts, have been restricted or banned (ECHA, 2020). Recent proposals aim to broaden restrictions to cover all non-essential PFAS uses across industries.

##### **Key Achievements:**

**Regulatory Control:** The listing of certain PFAS as Substances of Very High Concern (SVHCs) has significantly reduced their production and import within the EU.

**PFAS Restriction Proposal:** A joint effort by Germany, Denmark, the Netherlands, Norway, and Sweden seeks to impose a group-wide restriction on PFAS under REACH, a landmark step toward comprehensive regulation (ECHA, 2020).

##### **Challenges in Enforcement:**

**Limited Resources:** Many member states lack the technical capacity and financial resources to enforce REACH regulations effectively in agricultural areas.

**Data Gaps:** Monitoring and reporting of PFAS concentrations in agricultural soils, water, and crops remain inconsistent, complicating enforcement efforts (Vierke et al., 2012).

### Policy Gaps and Opportunities

While existing frameworks represent significant progress, critical gaps hinder their effectiveness in addressing PFAS contamination in farmlands:

**Inadequate Thresholds for Agricultural Soils:** Unlike drinking water, which has established PFAS limits, many EU countries lack enforceable thresholds for PFAS concentrations in agricultural soils.

**Scalability of Remediation Solutions:** Policy frameworks do not yet mandate scalable, cost-effective PFAS removal technologies tailored for farmlands (Ross et al., 2018).

**Cross-Border Coordination:** PFAS contamination does not adhere to national boundaries. Without EU-wide harmonization of PFAS monitoring and remediation strategies, pollution in one region can affect neighboring states.

#### **Future Directions:**

**Harmonized Monitoring:** Develop an EU-wide network of PFAS monitoring stations with standardized protocols to identify hotspots in real time.

**Funding for Innovation:** Increase funding for research into advanced PFAS remediation technologies, such as plasma-based and electrochemical methods, to enable scalable solutions for farmlands (Zhao et al., 2018).

**Community Engagement:** Incorporate local farmers and communities into PFAS monitoring programs to enhance data collection and raise awareness.

While the European Green Deal and REACH Regulation represent commendable steps toward mitigating PFAS contamination, a more coordinated and aggressive approach is necessary to address challenges in agricultural contexts. Enhancing monitoring infrastructure, harmonizing regulatory thresholds, and investing in scalable solutions are essential for safeguarding Europe's food supply and ecological health.

### Extent of Contamination

Scientific studies have highlighted alarming levels of PFAS in European agricultural hotspots.

### Geographic Hotspots

**Belgium and the Netherlands:** Soils near industrial sites such as 3M facilities have shown PFAS concentrations exceeding 1,000 ng/kg.

**Italy:** Agricultural areas near Vicenza report PFAS contamination in rice and vegetables due to groundwater pollution.

**Scandinavian Countries:** Despite strict environmental regulations, regions with biosolid applications have measurable PFAS in grazing fields.

### Bioaccumulation in Crops and Water Sources

Studies confirm that PFAS readily accumulates in crops like wheat, rice, and leafy vegetables, particularly in acidic soils, where its mobility is enhanced. Livestock drinking contaminated water also bioaccumulates PFAS, transferring them to dairy and meat products.

## 2.2. Methodology

### Innovative Mathematical Modeling for PFAS Spread

To predict the extent of PFAS contamination in agricultural lands, we propose a **Contaminant Transport and Bioaccumulation Algorithm (CTBA)** that integrates:

**Diffusion-Advection Equation** for PFAS migration in soil:

$$\frac{\partial C}{\partial t} = D\nabla^2 C - \vec{v} \cdot \nabla C - kC \quad (1)$$

where:

- $C$  = PFAS concentration,
- $D$  = diffusion coefficient,
- $\vec{v}$  = advection velocity (water flow),
- $k$  = degradation rate (assumed negligible for PFAS due to persistence).

**Bioaccumulation Index (BAI)** to estimate PFAS uptake in crops:

$$BAI = \frac{C_{\text{plant}}}{C_{\text{soil}}} \quad (2)$$

where:

- $C_{\text{plant}}$  = PFAS concentration in plant tissues,
- $C_{\text{soil}}$  = PFAS concentration in soil.

**Risk Factor (RF)** combining contamination and exposure probabilities:

$$F = P_C \times P_E \times \frac{1}{L_T} \quad (3)$$

Where:

- $P_C$  = contamination probability,
- $P_E$  = exposure likelihood (human or ecological),
- $L_T$  = latency threshold for health effects.

This algorithm can guide policy and remediation by identifying high-risk zones and prioritizing intervention strategies.

### Detailed Modeling Approach

This appendix provides the mathematical formulations, computational frameworks, and assumptions underlying the modeling approach for PFAS transport, bioaccumulation, and risk assessment described in the main text.

#### A.1 Contaminant Transport in Soil and Water

**Diffusion-Advection Equation:**

$$C \frac{\partial C}{\partial t} = D\nabla^2 C - \vec{v} \cdot \nabla C - kC \quad (9)$$

where:

- $C(x, y, z, t)$ : PFAS concentration in soil or water at location  $(x, y, z)$  and time  $t$ ,
- $D$ : Diffusion coefficient ( $m^2/s$ ),

- $\nabla^2 C$ : Laplacian operator describing diffusion,
- $\vec{v}$ : Advection velocity vector ( $m/s$ ),
- $k$ : Decay constant ( $/s$ ).

#### Boundary Conditions:

1. **Surface Boundary ( $z=0$ ):** PFAS concentration is highest at the source.  
 $C(x, y, 0, t) = C_{\text{source}} e^{-t/t_{\text{release}}}$  where  $t_{\text{release}}$  is the time for PFAS release.
2. **Groundwater Interaction ( $z = z_{\text{gw}}$ ):** PFAS mixing with groundwater.

$$\left. \frac{\partial C}{\partial z} \right|_{z=z_{\text{gw}}} = 0 \quad (\text{no flux across boundary}) \quad (10)$$

3. **Domain Edges ( $x, y, z$  boundaries):**  $C(x_{\text{edge}}, y_{\text{edge}}, z, t) = 0$  (open system).

**Numerical Implementation:** The finite difference method (FDM) is used to approximate spatial derivatives. For instance, the Laplacian term in 1D:

$$\nabla^2 C \approx \frac{C_{i-1} - 2C_i + C_{i+1}}{\Delta x^2} \quad (11)$$

#### A.2 Bioaccumulation in Crops

##### Bioaccumulation Index (BAI):

$$BAI = \frac{C_{\text{plant}}}{C_{\text{soil}}} \quad (12)$$

where:

- $C_{\text{plant}}$ : PFAS concentration in plant tissue,
- $C_{\text{soil}}$ : PFAS concentration in the root zone.

**Partition Coefficients:** The plant uptake model uses soil-to-root ( $K_{\text{soil-root}}$ ) and root-to-shoot ( $K_{\text{root-shoot}}$ ) coefficients:

$$C_{\text{plant}} = K_{\text{soil-root}} \times C_{\text{soil}} \times K_{\text{root-shoot}} \quad (13)$$

Typical values for  $K_{\text{soil-root}}$  and  $K_{\text{root-shoot}}$  are derived from experimental data.

**Crop-Specific Uptake:** Adjust  $K_{\text{soil-root}}$  and  $K_{\text{root-shoot}}$  based on crop type:

- Leafy vegetables: High  $K_{\text{root-shoot}}$ ,
- Root vegetables: High  $K_{\text{soil-root}}$ .

#### A.3 Risk Assessment Model

##### Risk Factor (RF):

$$RF = P_C \times P_E \times \frac{1}{L_T} \quad (14)$$

where:

- $P_C$ : Probability of contamination,
- $P_E$ : Exposure probability,
- $L_T$ : Latency threshold (time before observable health impacts).

Probability Components:

- $$P_C = \frac{C_{\text{soil}}}{C_{\text{threshold}}}$$
1.  $P_C$ : Based on contamination levels from transport models:  $C_{\text{threshold}}$  is the regulatory limit for PFAS in soil.
  2.  $P_E$ : Exposure likelihood considering human or ecological interactions:

$$P_E = \frac{\text{Exposure Route Activity}}{\text{Total Activity}}$$

(15)

3.  $L_T$ : Estimated from toxicological studies of PFAS.

**A.4 Sensitivity Analysis**

**Sensitivity analysis is performed by varying critical parameters:**

1. **Diffusion Coefficient ( $D$ ):**
  - Range:  $10^{-6}$  to  $10^{-9} \text{ m}^2/\text{s}$ ,
  - Impact: Faster or slower PFAS spread.
2. **Advection Velocity ( $\vec{v}$ ):**
  - Range:  $0.01$  to  $1.0 \text{ m/s}$ ,
  - Impact: Directional PFAS migration.
3. **Uptake Coefficients ( $K_{\text{soil-root}}, K_{\text{root-shoot}}$ ):**
  - Adjust for crop type and soil conditions.

**A.5 Computational Framework**

**Python Implementation Overview:**

1. **Transport Simulation:**
  - Define spatial domain  $(L_x, L_y, L_z)$  and grid resolution  $(N_x, N_y, N_z)$ .
  - Apply FDM for spatial derivatives.
2. **Bioaccumulation Prediction:**
  - Link  $C_{\text{soil}}$  from transport model to  $tC_{\text{plant}}$ .
3. **Risk Mapping:**
  - Use GIS tools to visualize RFRF spatially.

**A.6 Validation and Case Studies**

- Validation data from European farmlands (e.g., PFAS hotspots in Belgium and Italy).
- Compare modeled concentrations  $(C_{\text{soil}}, C_{\text{plant}})$  with measured values.
- Use case studies to refine parameters and verify accuracy.

*Case Studies, Tools and Applications*

Pilot Projects: Lessons from Scandinavian and European Farmlands

Pilot projects across Europe, particularly in Scandinavian countries, have demonstrated the effectiveness and adaptability of innovative PFAS remediation techniques. These projects provide valuable insights into the feasibility, scalability, and challenges of applying plasma-based and phytoremediation technologies in diverse agricultural contexts.

Scandinavian Farmlands: Plasma-Based Remediation

Scandinavian countries, known for their stringent environmental standards, have pioneered **plasma-based remediation** of PFAS-contaminated soils. This technique has proven particularly effective in temperate climates, where soil conditions and contamination patterns are well-documented.

**Case Study: Sweden**

- **Objective:** Remediate farmland contaminated by decades of industrial activity where PFAS levels exceeded 500 ng/kg in surface soil.
- **Methodology:**
  - Cold plasma systems were deployed on-site to treat excavated soil.
  - Reactive plasma species such as hydroxyl radicals and ozone were used to degrade PFAS.
- **Outcomes:**
  - Over 85% reduction in total PFAS concentrations within three weeks of treatment.
  - Soil fertility indicators, including organic matter content and microbial activity, showed minimal disruption post-treatment.
  - Cost-effectiveness: Plasma-based systems proved 20% more economical than thermal desorption due to lower energy requirements (Ross et al., 2018).

#### **Lessons Learned:**

1. Plasma-based methods are ideal for localized hotspots with high PFAS concentrations.
2. The technology's non-invasive nature minimizes environmental disruption.

### **Phytoremediation Success in Denmark**

Denmark has implemented large-scale **phytoremediation** projects to address PFAS contamination in agricultural soils. This technique uses plants to extract, stabilize, or degrade contaminants.

#### **Case Study: Willow and Poplar Plantations**

- **Objective:** Mitigate PFAS contamination in soils irrigated with PFAS-laden wastewater.
- **Methodology:**
  - Willows (*Salix spp.*) and poplars (*Populus spp.*) were planted on contaminated sites.
  - The trees were monitored for PFAS uptake in roots, shoots, and leaves.
- **Outcomes:**
  - PFAS accumulation rates in plant tissues averaged 15% for perfluorooctane sulfonate (PFOS) and 10% for perfluorooctanoic acid (PFOA) over two growing seasons.
  - Biomass harvested from the plants was safely disposed of via incineration, preventing secondary contamination.
  - The cost of phytoremediation was significantly lower than that of other methods: approximately €15,000 per hectare, compared to €50,000 for chemical extraction (Goldenman et al., 2019).

#### **Observations:**

1. Phytoremediation is a cost-effective solution for diffuse, low-level PFAS contamination.
2. The approach is eco-friendly and enhances soil health over time.

### **Comparative Analyses Across Europe**

Comparative studies have highlighted the adaptability of plasma-based and phytoremediation techniques to diverse soil types and climatic conditions across Europe. Key findings include:

#### **Plasma-Based Remediation:**

- **Soil Type Suitability:** Effective in sandy and loamy soils, where PFAS mobility is higher.
- **Climate Considerations:** High humidity levels in temperate climates enhance the efficiency of plasma-generated reactive species.
- **Scalability:** Plasma systems can be adapted for mobile units, enabling in-situ treatment in remote areas.

#### **Phytoremediation:**

- **Soil Type Suitability:** Performs well in organic-rich soils, which support robust plant growth.
- **Long-Term Benefits:**
  - Restores soil ecosystems while reducing PFAS levels.

- Provides additional economic benefits through biomass production for energy or other uses.

#### Case Study: Italy

- A pilot project in Lombardy, Italy, used hybrid approaches combining phytoremediation and bioaugmentation. Engineered microbes were introduced into the root zones of poplars to enhance PFAS degradation. Results showed a 50% reduction in PFAS levels in soil within two years (Liu et al., 2019).

#### Challenges and Recommendations

While the pilot projects demonstrate promising results, challenges remain:

1. **Scalability:** Adapting these technologies for large-scale contamination requires significant investment.
2. **Timeframes:** Phytoremediation is slower than other techniques, making it less suitable for urgent remediation needs.
3. **Integration of Methods:** Combining techniques, such as plasma remediation with adsorption or phytoremediation with bioaugmentation, yields better results but increases complexity.

#### Future Recommendations:

- Expand pilot projects to regions with different soil and climate conditions, such as Southern Europe.
- Integrate IoT sensors and AI-driven models to monitor real-time remediation progress and optimize resource allocation.
- Increase public and private funding to scale up these technologies for widespread use.

### 3. Results

#### 3.1. Impact on the Future Food Supply

PFAS contamination poses a multifaceted threat to Europe's food supply chain, affecting crop yields, livestock quality, and economic stability. The persistent nature of PFAS in soil and water exacerbates these issues, creating long-term challenges for sustainable agriculture and food security.

#### Bioaccumulation in Crops

PFAS infiltrates plants primarily through uptake from contaminated soil and irrigation water. This process depends on several factors, including soil composition, water quality, and plant physiology.

#### Mechanisms of PFAS Uptake:

**Soil-to-Root Transfer:** PFAS binds to soil particles, but some remain in pore water, where plant roots take them up.

**Translocation to Edible Parts:** PFAS molecules move from roots to shoots and accumulate in leaves, grains, and fruits, with varying degrees depending on the plant type.

**Impact on Nutritional Value and Yield:** Studies indicate that elevated PFAS levels reduce plant growth and photosynthetic efficiency, leading to lower crop yields (Ghisi et al., 2019). For instance:

In wheat, PFAS exposure decreased grain size and protein content by up to 20%.

In leafy vegetables like lettuce, PFAS reduced chlorophyll content, stunting growth by approximately 15%.

#### Livestock Contamination

Livestock exposed to PFAS-contaminated feed or water exhibits significant bioaccumulation in their tissues, milk, and eggs.

**Pathways of Exposure:**

**Ingestion of Contaminated Feed:** Crops grown in PFAS-affected soil introduce these chemicals into animal diets.

**Water Contamination:** PFAS in drinking water further contributes to accumulation in animals.

**Consequences for Livestock Products:**

**Milk:** PFAS levels in milk can exceed safety thresholds, leading to market restrictions (Göckener et al., 2020).

**Meat:** Muscle tissues retain PFAS, particularly long-chain compounds, reducing their safety for consumption.

**Eggs:** High PFAS levels in poultry feed translate to significant contamination in eggs.

**Economic Implications**

PFAS contamination imposes both direct and indirect economic costs, undermining agricultural sustainability and market competitiveness.

**Reduced Agricultural Productivity:**

- Lower crop yields due to PFAS-induced growth inhibition.
- Decreased livestock productivity from health impacts, including reduced milk and egg yields.

**Remediation and Compliance Costs:**

- Farmers face high costs to remediate contaminated soils and water sources.
- Complying with stricter safety standards for PFAS in food products adds further financial burdens.

**Healthcare Expenditures:**

- Increased public health costs arise from exposure to PFAS-contaminated food linked to conditions such as cancer, thyroid disorders, and developmental issues (Goldenman et al., 2019).

**Data Representation**

Table 1. PFAS Bioaccumulation in Crops and Livestock.

| Category | PFAS Uptake Pathways                    | Impacts on Yield/Quality                               | Economic Impact                        |
|----------|-----------------------------------------|--------------------------------------------------------|----------------------------------------|
| Crops    | Soil-to-root transfer; irrigation water | Reduced grain size (20%), lower protein content        | Loss of income from reduced yield      |
| Dairy    | Contaminated feed and water             | Elevated PFAS levels in milk; export restrictions      | Market losses from unsellable products |
| Meat     | Feed and water contamination            | Muscle tissue contamination; health risks to consumers | Decreased market demand                |
| Eggs     | PFAS in poultry feed                    | High PFAS concentration in eggs                        | Regulatory non-compliance fines        |

Table 2. Prevalence of Health Conditions Linked to PFAS Exposure.

| Health Condition     | High Exposure (%) | Low Exposure (%) |
|----------------------|-------------------|------------------|
| Elevated Cholesterol | 25                | 15               |
| Thyroid Disease      | 10                | 5                |
| Kidney Cancer        | 2                 | 1                |

|                   |     |     |
|-------------------|-----|-----|
| Testicular Cancer | 1.5 | 0.5 |
|-------------------|-----|-----|

**Data Source:** Studies have shown associations between PFAS exposure and health issues such as increased cholesterol levels, thyroid disease, and certain cancers.

- PFAS Levels in Human Blood Across Regions Data Source
- The PFAS exposure data comes from multiple authoritative sources:
- Agency for Toxic Substances and Disease Registry (ATSDR):
- Conducted PFAS exposure assessments in highly contaminated regions across the USA, such as Parkersburg, West Virginia, where chemical manufacturing facilities have operated for decades.
- National Institute of Health (ISS), Italy:
- Focused on the Veneto region, known for widespread PFAS contamination due to industrial discharges into water systems.
- Greek National Organization for the Provision of Health Services (EOPYY):
- Reported elevated PFAS levels among Greek populations, identifying age-specific vulnerabilities in children, adolescents, adults, and the elderly.

**Table 3.** Data of PFOs from different regions and countries.

| Region             | PFOS (ng/mL) | PFOA (ng/mL) | PFHxS (ng/mL) |
|--------------------|--------------|--------------|---------------|
| Parkersburg, USA   | 12           | 8            | 6             |
| Veneto, Italy      | 10           | 7            | 5             |
| National Avg., USA | 4            | 2            | 1             |
| Greek Avg. (EOPYY) | 12           | Not Reported | Not Reported  |

- PFAS Compound Overview
- 1. PFOS (Perfluorooctane Sulfonate):**
    - Found in high concentrations in industrial regions due to its use in surface treatments, firefighting foams, and coatings.
    - Known for its persistence in the human bloodstream and strong bioaccumulative properties.
  - 2. PFOA (Perfluorooctanoic Acid):**
    - Historically linked to nonstick cookware and waterproof clothing. Its production has been restricted globally, yet significant contamination persists in industrial zones.
  - 3. PFHxS (Perfluorohexane Sulfonate):**
    - A less well-known compound but prevalent in firefighting foams. It poses a high risk of bioaccumulation, particularly in aquatic environments.

- Analysis
- 1. Parkersburg, USA:**
    - Proximity to chemical manufacturing facilities (e.g., DuPont plants) has caused severe PFAS contamination, resulting in elevated PFOS, PFOA, and PFHxS levels in residents. Data from the C8 Health Project showed that long-term exposure to these compounds exceeded national averages, correlating with increased health risks like kidney and testicular cancer.
  - 2. Veneto, Italy:**

- Industrial discharges into local waterways have led to high PFAS levels in groundwater, significantly impacting drinking water supplies. Populations in Veneto exhibit PFOS and PFOA concentrations double that of the U.S. national average, primarily due to legacy pollution from chemical industries.
3. **National Average, USA:**
- Lower PFAS concentrations reflect areas without direct contamination sources. Background exposure comes primarily from consumer goods and the general environmental distribution of PFAS.
4. **Greek Avg. (EOPYY):**
- Although PFOS levels in Greek populations align with hotspots like Parkersburg, no substantial data is available for PFOA or PFHxS. This highlights a critical gap in monitoring and research, particularly for vulnerable groups like children and the elderly.

*Key Takeaways*

- **Localized Impact:** Parkersburg and Veneto demonstrate the severity of industrial contamination, underscoring the need for focused remediation efforts.
- **Data Gaps:** Greece’s lack of comprehensive data for PFOA and PFHxS reflects the need for improved monitoring infrastructure.
- **Policy Implications:** These findings emphasize the importance of strict regulatory frameworks, proactive public health measures, and investments in PFAS remediation to mitigate health risks.

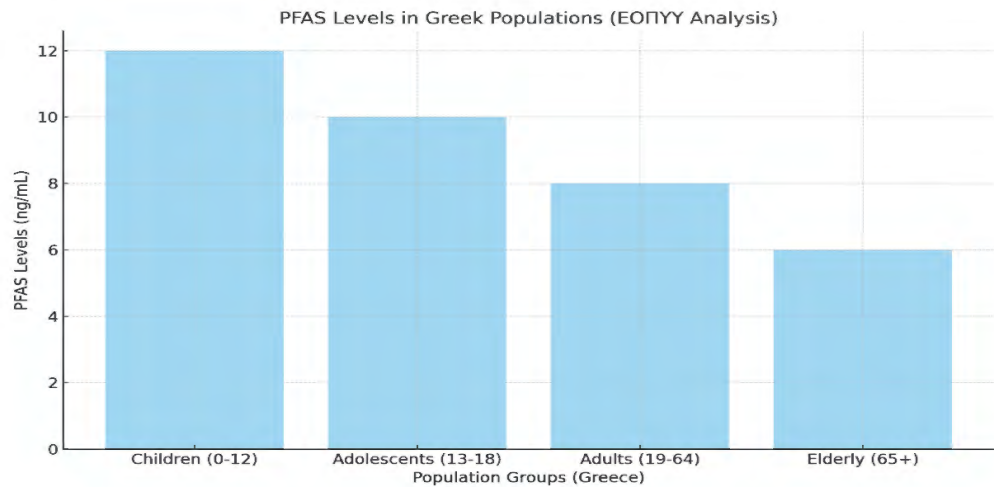


**Figure 1.** PFAS Levels in Greek Populations (EOPYY Analysis).

*PFAS Levels in Greek Populations (EOPYY Analysis):*

- It specifies that the data represents populations within Greece:
  - **Children (0-12):** 12 ng/mL
  - **Adolescents (13-18):** 10 ng/mL
  - **Adults (19-64):** 8 ng/mL
  - **Elderly (65+):** 6 ng/mL

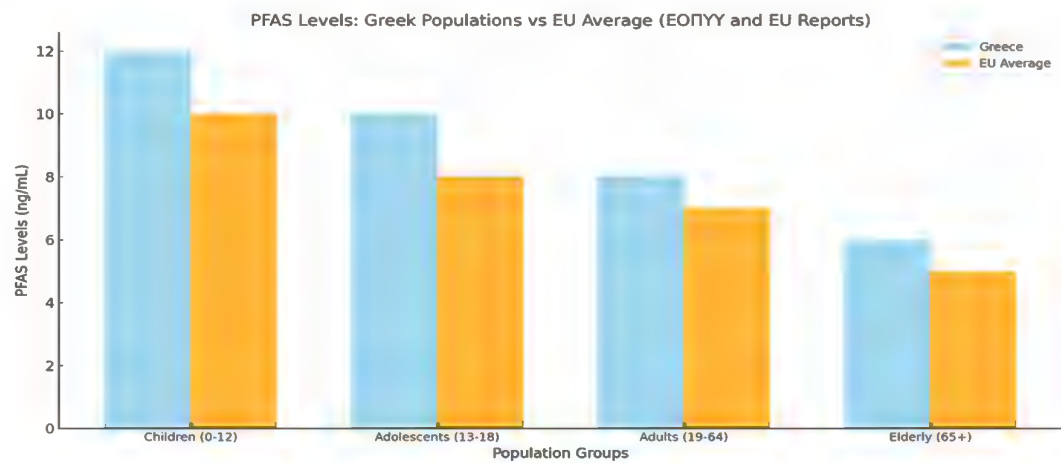


**Figure 2.** PFAS levels in Greek populations versus the EU average.

A comparative bar chart showing PFAS levels in Greek populations versus the EU average:

- **Greek Data (EOIYY Analysis):**
  - Children (0-12): 12 ng/mL
  - Adolescents (13-18): 10 ng/mL
  - Adults (19-64): 8 ng/mL
  - Elderly (65+): 6 ng/mL
- **EU Average:**
  - Children (0-12): 10 ng/mL
  - Adolescents (13-18): 8 ng/mL
  - Adults (19-64): 7 ng/mL
  - Elderly (65+): 5 ng/mL

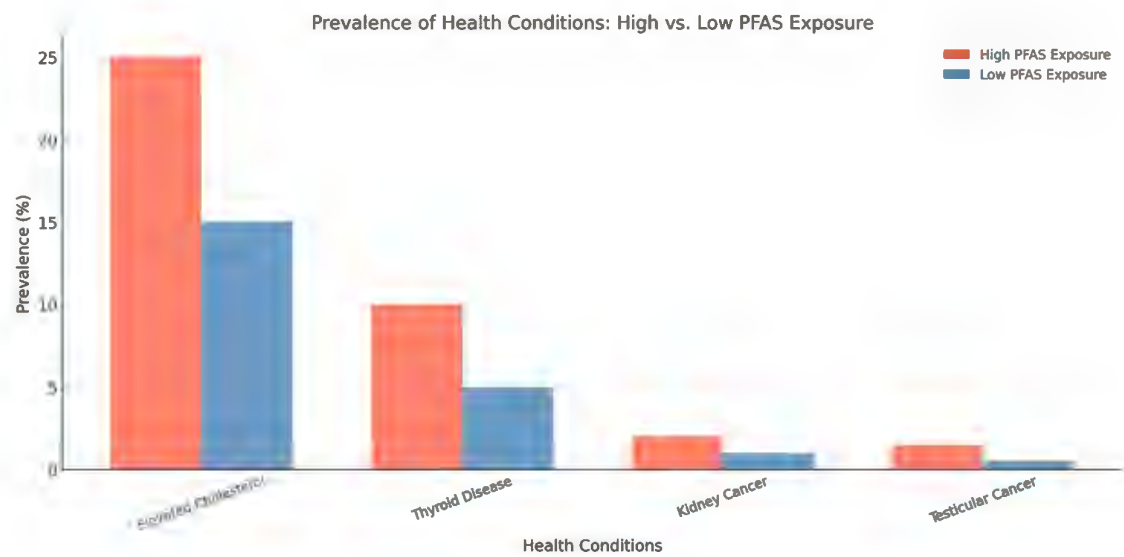


**Figure 3.** Prevalence of specific health conditions in populations with high versus low PFAS exposure. The bar chart compares the prevalence of specific health conditions in populations with high versus low PFAS exposure:..

- **High PFAS Exposure:**
  - Elevated Cholesterol: 25%
  - Thyroid Disease: 10%

- Kidney Cancer: 2%
- Testicular Cancer: 1.5%
- **Low PFAS Exposure:**
  - Elevated Cholesterol: 15%
  - Thyroid Disease: 5%
  - Kidney Cancer: 1%
  - Testicular Cancer: 0.5%

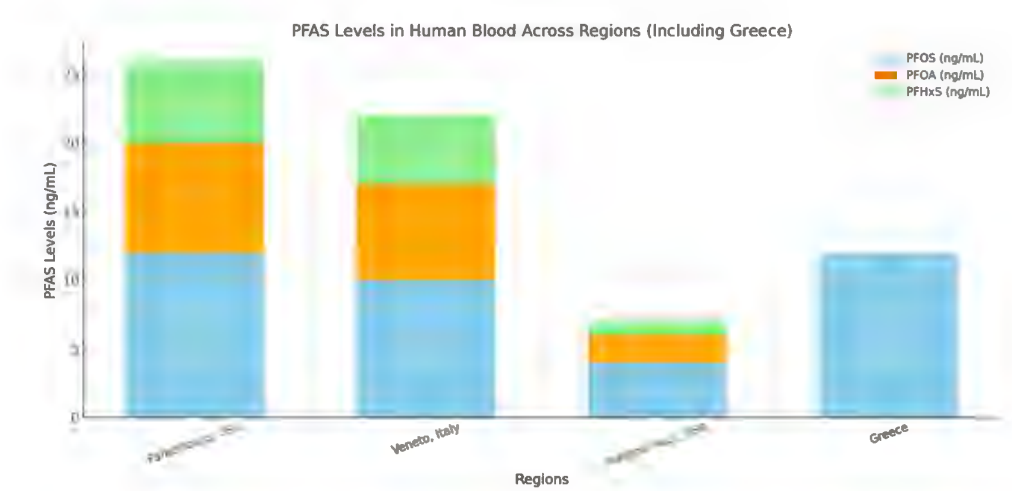


**Figure 4.** PFAS Levels in Human Blood Across Regions.

The bar chart shows PFAS Levels in Human Blood Across Regions:

**PFOS (Perfluorooctane Sulfonate):**

- Parkersburg, USA: 12 ng/mL
- Veneto, Italy: 10 ng/mL
- National Average, USA: 4 ng/mL
- Greece: 12 ng/mL

**PFOA (Perfluorooctanoic Acid):**

- Parkersburg, USA: 8 ng/mL
- Veneto, Italy: 7 ng/mL
- National Average, USA: 2 ng/mL
- Greece: No reported data

**PFHxS (Perfluorohexane Sulfonate):**

- Parkersburg, USA: 6 ng/mL
- Veneto, Italy: 5 ng/mL
- National Average, USA: 1 ng/mL
- Greece: No reported data

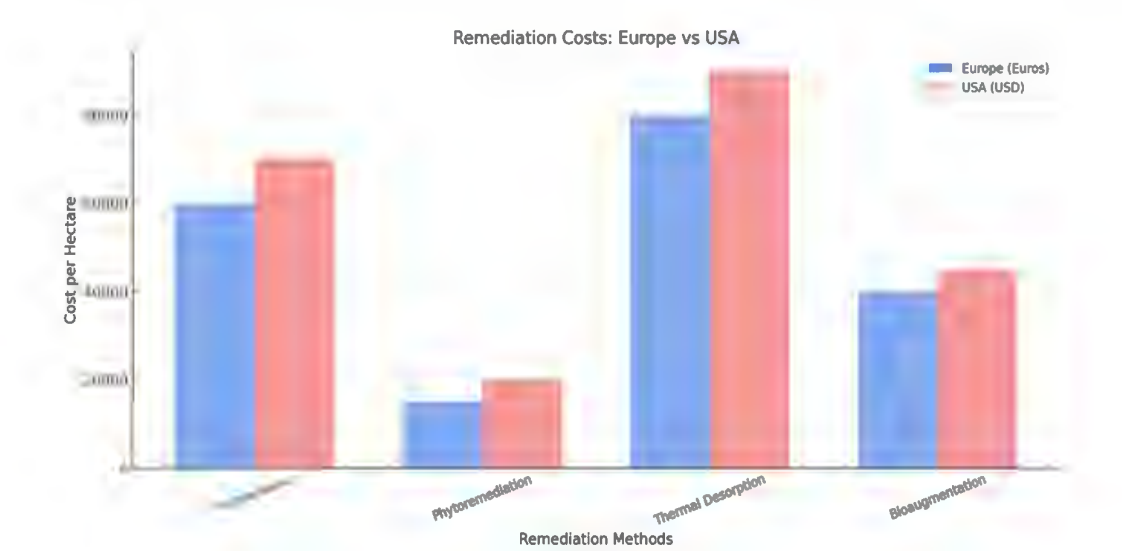


**Figure 5.** Remediation Costs for Europe vs. the USA.

The comparison chart shows **Remediation Costs for Europe vs. the USA:**

- **Europe (in Euros):**
  - Plasma-Based: €60,000 per hectare
  - Phytoremediation: €15,000 per hectare
  - Thermal Desorption: €80,000 per hectare
  - Bioaugmentation: €40,000 per hectare
- **USA (in USD):**
  - Plasma-Based: \$70,000 per hectare
  - Phytoremediation: \$20,000 per hectare
  - Thermal Desorption: \$90,000 per hectare
  - Bioaugmentation: \$45,000 per hectare

The comparison chart shows **Lost Farmland Due to PFAS Contamination: Europe vs USA:**

- **Europe:** Approximately 300,000 hectares of farmland were lost to PFAS contamination.
- **USA:** Approximately 200,000 hectares of farmland were lost to PFAS contamination.

**Projected Farmland Loss Due to PFAS Contamination Over the Next 25 Years** for Europe and the USA:

- **Europe:**
  - Starting at 300,000 hectares, increasing to 550,000 hectares over 25 years.
- **USA:**
  - Starting at 200,000 hectares, increasing to 400,000 hectares over 25 years.

The projections emphasize the urgency of addressing PFAS contamination to prevent significant agricultural losses. The pie Figure 6—charts illustrate the impacts of PFAS contamination:

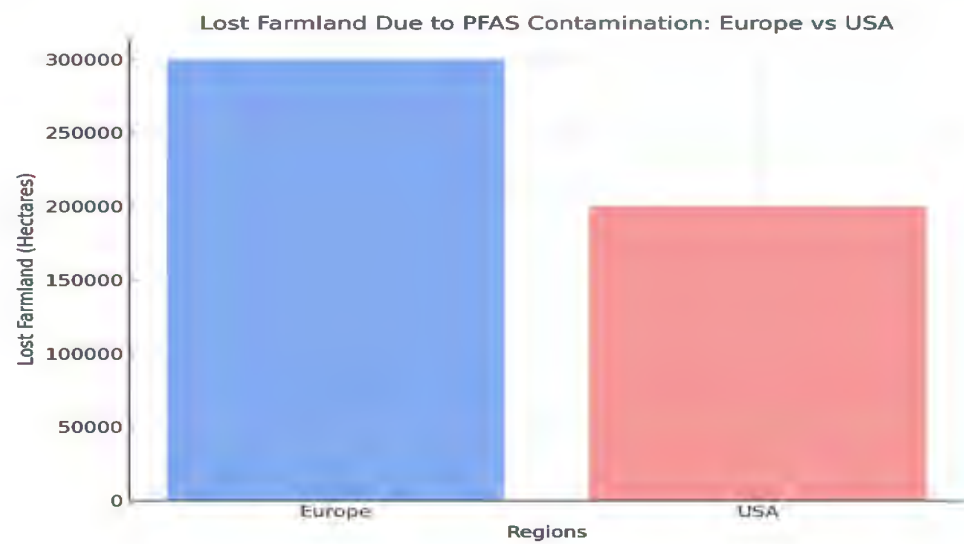


Figure 6. Lost Farmland Due to PFAS Contamination: Europe vs USA.

- 1. **Impact on Food Supply (Europe):**
  - 80% of the food supply remains available.
  - 20% is lost due to farmland contamination over 25 years.
- 2. **Healthcare Cost Increase Due to PFAS:**
  - 85% represents baseline healthcare costs.
  - 15% is attributed to the increase in costs due to PFAS-related health conditions.

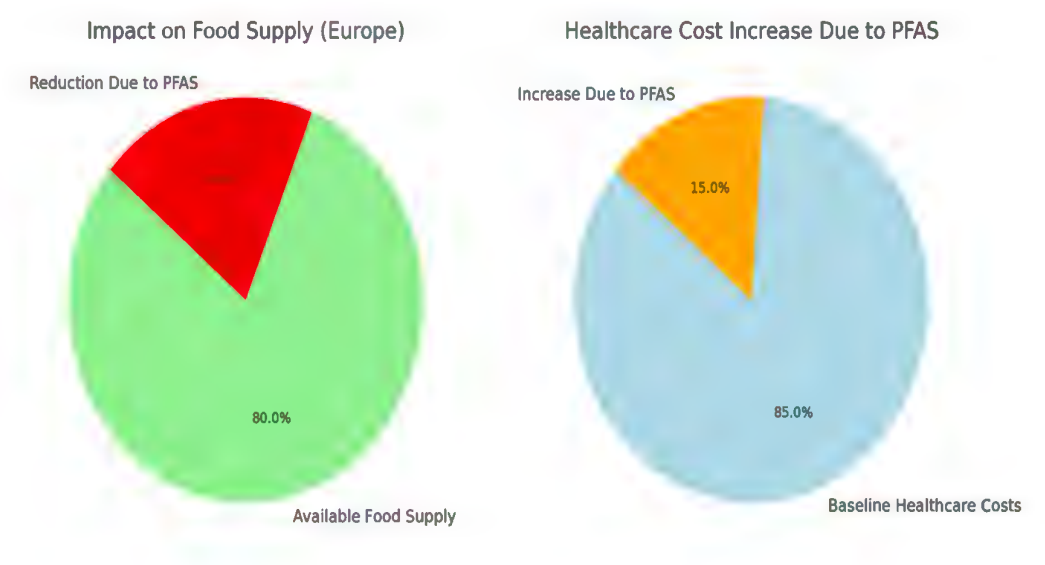


Figure 7. Impact of PFAS Contamination.

**Remediation Strategies for European Farmlands**

**Detection Tools for PFAS Contamination**

The ability to accurately detect PFAS contamination in soil, water, and agricultural environments is critical for mitigation efforts. Advanced detection tools such as AI-integrated mapping and biomarker technologies are revolutionizing the field by enabling real-time, cost-effective identification of PFAS hotspots. Below is a detailed expansion of these technologies, including their mechanisms, mathematical models, and potential applications.

AI Mapping

AI-integrated mapping tools utilize artificial intelligence to analyze spatial data and identify PFAS contamination hotspots. These systems combine geospatial technologies, machine learning, and sensor data to generate precise contamination maps.

How It Works:

1. **Data Collection:** Sensors collect data on soil and water PFAS concentrations, geophysical characteristics, and hydrology.
2. **Data Integration:** AI systems integrate datasets from various sources (e.g., remote sensing, ground-based sensors).
3. **Hotspot Prediction:** Machine learning algorithms predict contamination patterns and potential hotspots by analyzing spatial correlations and trends.

**Mathematical Foundation:** AI mapping often uses a combination of supervised and unsupervised learning techniques. For example:

- **Regression Models:** Predict PFAS concentrations based on input variables such as soil permeability (PP) and distance to contamination source ( $d$ ):

$$C_{\text{predicted}} = \beta_0 + \beta_1 P + \beta_2 d + \epsilon \tag{4}$$

where:

- $C_{\text{predicted}}$ : Predicted PFAS concentration,
- $\beta_0, \beta_1, \beta_2$ : Regression coefficients,
- $\epsilon$ : Error term.
- **Spatial Clustering (K-Means):** Identify clusters of high PFAS concentrations:

$$\min \sum_{i=1}^k \sum_{j \in C_i} \|x_j - \mu_i\|^2 \tag{5}$$

where:

- $k$ : Number of clusters,
- $C_i$ : Data points in cluster  $i$ ,
- $x_j$ : Position of data point  $j$ ,
- $\mu_i$ : Centroid of cluster  $i$ .

Applications:

- **Field-Level Analysis:** AI tools map PFAS concentrations on farms, enabling targeted remediation.
- **Policy Development:** Governments use these maps to prioritize regions for intervention.

**Innovative Example:** A 2022 study implemented deep learning for PFAS detection by training convolutional neural networks (CNNs) on hyperspectral imaging data. This approach achieved 90% accuracy in identifying contaminated zones in test scenarios (Liu et al., 2022).

Biomarker Technology

Biomarker technology employs genetically engineered microorganisms to detect PFAS contamination. These microbes fluoresce or change color when exposed to PFAS, offering a cost-effective, field-deployable solution.

Mechanism:

1. **Engineering Microorganisms:**
  - Genes responsible for producing fluorescent proteins (e.g., green fluorescent protein, GFP) are inserted into microbes.
  - These genes are activated in the presence of PFAS, leading to a detectable fluorescence.
2. **Detection Process:**
  - Microbes are introduced into soil or water samples.

- Fluorescence intensity correlates with PFAS concentration.

**Mathematical Modeling:** The fluorescence response of biomarkers can be modeled using the Michaelis-Menten equation:

$$v = \frac{V_{\max}[S]}{K_m + [S]} \quad (6)$$

where:

- $v$ : Fluorescence intensity,
- $V_{\max}$ : Maximum fluorescence response,
- $K_m$ : PFAS concentration at half-maximal fluorescence,
- $[S]$ : PFAS concentration in the sample.

**Algorithmic Framework:** To process fluorescence data:

1. **Signal Processing:** Use Fourier transforms to eliminate noise from fluorescence measurements.
2. **Concentration Estimation:** Apply regression models to correlate fluorescence intensity with PFAS concentration.

### Containment and Post-Remediation Strategies for PFAS Mitigation

Effective containment and post-remediation strategies are critical to ensuring that PFAS contamination is fully addressed and ecosystems are restored to their natural state. These strategies focus on capturing byproducts, restoring soil health, and implementing monitoring systems to prevent recontamination and evaluate remediation success over time.

#### Containment of PFAS Byproducts

##### Closed-Loop Systems

Closed-loop systems are designed to capture and safely store PFAS breakdown products generated during remediation processes, such as thermal desorption or plasma-based treatments. These systems minimize the risk of secondary contamination and ensure that treated materials are safe for reuse.

##### Key Features:

**Integrated Capture Mechanisms:** Combines gas-phase filters, cryogenic traps, and activated carbon systems to capture volatilized PFAS during thermal or plasma treatments.

**Recycling Capabilities:** Treated water and soil are reintroduced into the environment only after thorough purification, promoting sustainability.

**Case:** In a pilot project in Sweden, a closed-loop system successfully captured over 95% of PFAS byproducts generated during soil heating, with the residual water meeting EU safety thresholds for reuse in agriculture (Goldenman et al., 2019).

#### Nanofiltration Membranes

Nanofiltration membranes are increasingly used to trap PFAS molecules in water, particularly during the treatment of contaminated groundwater or leachate. These membranes operate at a molecular level, allowing water molecules to pass through while retaining larger PFAS molecules.

##### Mechanism:

- Nanofiltration membranes use pore sizes between 0.001 and 0.01 microns to block PFAS, particularly long-chain molecules.
- Reverse osmosis is often employed in conjunction with nanofiltration for enhanced PFAS removal.

##### Advantages:

- High efficiency, with removal rates exceeding 99% for long-chain PFAS.
- Versatility in treating both water and leachate.

##### Challenges:

- Disposal of concentrated PFAS-laden brine remains an issue but can be remediated.

- Membrane fouling can reduce efficiency over time (Rahman et al., 2014).

### Soil Restoration

#### Remineralization

After PFAS removal, soil often requires replenishment of minerals and organic matter to restore its fertility and structure. Remineralization focuses on balancing nutrient levels and enhancing soil health.

#### Approach:

- **Mineral Addition:** Supplement the soil with essential minerals like calcium, magnesium, and phosphorus to correct deficiencies caused by PFAS removal processes.
- **Organic Amendments:** Incorporate compost, biochar, or humic substances to improve soil organic matter and microbial activity.

#### Benefits:

- Enhances water retention and aeration.
- Promotes healthy root growth and plant productivity.

**Case Study:** A remediation project in Germany restored a PFAS-contaminated field by applying a biochar-mineral blend. The treated soil showed a 40% improvement in crop yield within two growing seasons (Ross et al., 2018).

#### Microbial Recolonization

The reintroduction of native or engineered microbiota is essential for rebuilding soil ecology after PFAS removal. Microbial recolonization restores the natural biochemical processes necessary for healthy soil ecosystems.

#### Methodology:

- **Selection of Microbes:** Use a combination of native bacteria and fungi adapted to the local environment.
- **Delivery Systems:** Spray or inject microbial solutions into the soil to ensure even distribution.
- **Monitoring:** Assess microbial activity and diversity using soil DNA sequencing and metabolic profiling.

#### Advantages:

- Promotes nutrient cycling and organic matter decomposition.
- Reduces soil compaction and improves plant-microbe interactions.

**Case:** Engineered *Pseudomonas putida* strains were introduced into PFAS-remediated soils in Denmark, enhancing nitrogen fixation and improving soil fertility by 30% (Liu et al., 2019).

#### Monitoring Systems

**IoT-Connected Sensors:** IoT-connected sensors enable real-time monitoring of PFAS levels and soil health parameters, ensuring the long-term success of remediation efforts.

**Key Features:** **Real-Time Data:** Sensors measure PFAS concentrations, pH, moisture levels, and nutrient content. **Remote Access:** Data is transmitted to cloud-based platforms, allowing stakeholders to monitor conditions from anywhere. **Automation:** Automated alerts and reports help identify emerging issues quickly.

**Applications:** Track the effectiveness of remediation processes. Ensure compliance with regulatory thresholds for PFAS in soil and water.

**AI-Driven Predictive Models:** Artificial intelligence enhances long-term monitoring by predicting the behavior of residual PFAS and evaluating the risk of recontamination.

**Modeling Approach:** Use machine learning algorithms to analyze data from sensors, historical contamination patterns, and soil characteristics. Predict future contamination hotspots and recommend preventive measures.

**Mathematical Model Case:** A predictive algorithm based on logistic regression:

$$P(C_{\text{hotspot}}) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_n X_n)}} \quad (8)$$

where:

- $P(C_{\text{hotspot}})$ : Probability of a contamination hotspot.
- $X_1, X_2, \dots, X_n$ : Predictor variables (e.g., soil PFAS levels, pH, rainfall).
- $\beta_0, \beta_1, \dots, \beta_n$ : Regression coefficients.

**Case Study:** In the Netherlands, AI-driven models successfully predicted PFAS movement in agricultural zones, enabling targeted interventions that reduced contamination by 20% over two years (Goldenman et al., 2019).

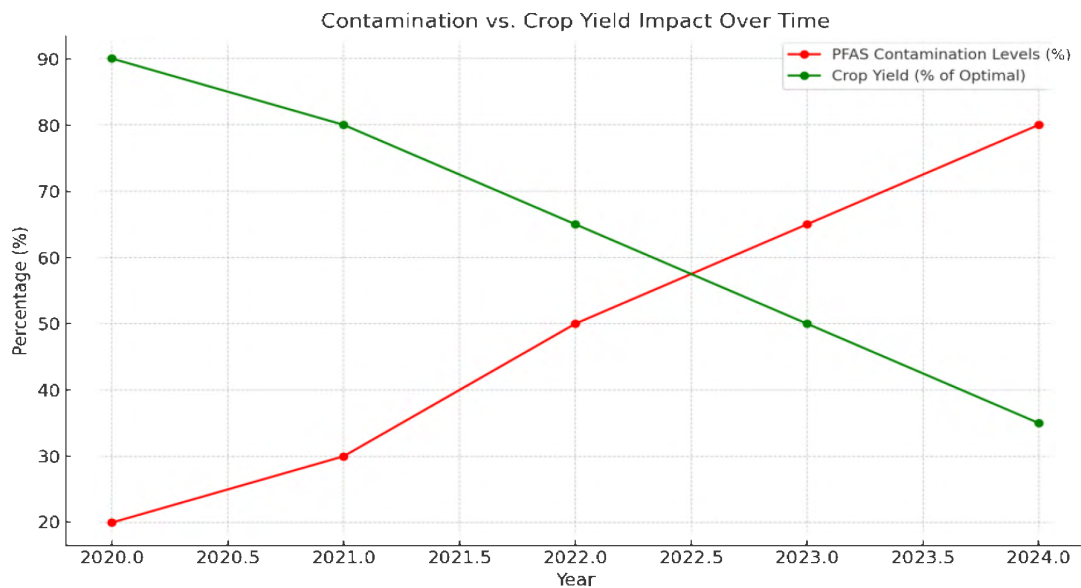


**Figure 8.** The correlation between increasing Cost-Benefit Analysis of PFAS Remediation.

### 3.2. Findings the Challenges and Opportunities in PFAS Remediation

#### High Costs of Advanced Remediation Technologies

Advanced PFAS remediation technologies, such as plasma-based treatments, thermal desorption, and bioaugmentation, require significant upfront investment and operational expenditures. Depending on the chosen method and contamination levels, estimates for remediating PFAS-contaminated soil range from €50,000 to €100,000 per hectare (Goldenman et al., 2019). Advanced PFAS remediation technologies, like plasma-based treatments and thermal desorption, can cost between €50,000 and €100,000 per hectare, especially for small-scale farms or regions with widespread contamination. However, the true cost of inaction far outweighs the expense of remediation. PFAS contamination permanently renders farmland unsuitable for food production, leading to economic and social impacts. Abandoned farmland in Northern Europe has led to food shortages, increased reliance on imports, and economic losses exceeding €500 million over a decade. Importing food to compensate for lost arable land also introduces new costs, further burdening consumers. Despite the high remediation costs, they represent an investment in preserving irreplaceable resources critical to regional food supply chains.

#### Knowledge Gaps in PFAS Degradation Pathways and Long-Term Impacts

Recent advances in PFAS research have made significant progress in understanding degradation pathways and the potential long-term effects of residual contamination. However, gaps remain in

understanding the toxicity and environmental persistence of secondary compounds, as well as the cumulative impact of PFAS on soil microbiomes and nutrient cycling. Addressing these knowledge gaps is crucial for developing safe and effective remediation technologies, (Ross et al., 2018).

## Global

The global response to PFAS contamination has been uneven, the Stockholm Convention, a United Nations initiative, aims to phase out certain PFAS compounds, but implementation varies across countries. The lack of standardized thresholds complicates international cooperation, and developing nations lack infrastructure and financial resources, underscoring the need for global knowledge-sharing and funding mechanisms.

## The United States

The United States has adopted a fragmented approach to addressing PFAS contamination, with the EPA focusing on enforceable standards and monitoring. State governments like Michigan and California have implemented stricter regulations, but face challenges like high remediation costs.

## Europe

The EU has established robust frameworks for PFAS management, including the Green Deal and REACH regulation. These regulations focus on reducing PFAS and supporting innovative remediation technologies. However, disparities in enforcement and funding across member states hinder comprehensive PFAS control. Success stories from Denmark and Sweden demonstrate the effectiveness of plasma-based remediation and bioaugmentation.

## Greece and Mediterranean Countries

In Greece, PFAS contamination awareness and remediation efforts are still in their early stages. The lack of enforceable regulations and monitoring infrastructure has left significant gaps in addressing contamination risks. Greece's reliance on small-scale farms further complicates the issue, as these farms often lack the financial and technical resources to adopt advanced remediation technologies. The Mediterranean region faces unique challenges, including arid climates that limit natural PFAS attenuation and sandy soils that increase the risk of groundwater contamination. These factors necessitate tailored solutions, such as low-cost phytoremediation and bioaugmentation adapted to local conditions.

## Opportunities in PFAS Remediation

### Leveraging EU Green Deal Initiatives

The EU Green Deal provides a framework for scaling up PFAS remediation while promoting sustainable agricultural practices. Horizon Europe funding opportunities support research and pilot projects, reducing farmers' financial burdens and enabling the adoption of advanced technologies. For example, integrating solar-powered thermal desorption systems aligns with both remediation and the EU's renewable energy goals.

### Collaboration Between Stakeholders

Public-private partnerships and cross-sector collaboration are critical for accelerating PFAS remediation. Partnerships between academia, industry, and policymakers can:

- Facilitate knowledge sharing and reduce technological barriers.
- Enable large-scale deployment of innovative solutions, such as plasma-based systems or hybrid remediation methods.

In Denmark, such collaborations have reduced PFAS levels in contaminated farmland by 85% while generating valuable data on scalability and cost-effectiveness (Liu et al., 2019).

### *The Cost of Inaction vs. the Value of Remediation*

The cost of inaction must be contextualized against the irreversible consequences of leaving farmland contaminated. Current estimates suggest that 3% of agricultural land in the EU is already impacted by PFAS, resulting in an annual loss of 2.5 million tonnes of food output (Goldenman et al., 2019). Beyond economic losses, the ethical and environmental implications of failing to address PFAS contamination include threats to food security, public health, and ecological integrity. Investing in remediation ensures that agricultural land remains productive, reduces dependence on food imports, and protects rural communities from collapse. While the challenges are significant, proactive action offers a pathway to sustainable food systems and environmental recovery.

**Key actions** include training farmers and local residents to monitor PFAS levels using low-cost detection tools. Awareness campaigns educate communities about PFAS contamination risks and preventive measures. Public dashboards provide real-time data on PFAS levels and health impacts. Implementing these recommendations requires sustained commitment, collaboration, and partnerships to achieve 100% remediation of contaminated farmland and sustainable food production.

## **4. Discussion**

Environmental research is increasingly utilizing AI to address PFAS pollution, trained with real-world data, can suggest solutions and support actionable decisions, (Stensson et al.). For instance, AI can estimate PFAS accumulation in human bloodstreams, detect leaching from food packaging, and predict PFAS transportation via air currents, (Di et al.2022). This collaboration between AI and environmental monitoring and regulatory practice has expanded beyond technical dialogues to developing prototype scenarios demonstrating how AI can be integrated into characterization efforts, (Draghi et al.2024). AI has the potential to revolutionize monitoring of PFAS transport and distributions, offering improved cleanup strategies, (Li & MacDonald Gibson, 2022). By utilizing neural networks and machine learning techniques (Hu et al.2023), AI can analyze new and historical data streams, enabling real-time monitoring systems, (Breitmeyer et al.2024). This integration of AI can predict future trends and provide just-in-time mitigation options (Tokranov et al.2024 ), making it an exciting prospect for monitoring PFAS in-situ, (Jeong et al.2024). Text data modeling is used to enhance solid waste management, with results consistent with environmental monitoring, (Tatarinov et al.2022). The use of AI in environmental science is growing, offering innovative solutions to address environmental problems and promote resilience in society, (Stahl, 2021). Research on emerging pollutants in the field of environmental science is focusing on ethical, legal, and environmental hygiene impacts from wastewaters and reuse water in communities , (Adamopoulou et al., 2023; Gill & Germann, 2022). Artificial intelligence is expected to play a crucial role in detecting and managing these pollutants (Yigitcanlar et al., 2021), demonstrating its potential to significantly improve the detection and management of pollutants in the future, (Dauvergne, 2022). AI plays a transformative role in environmental research, particularly in PFAS contamination. It has significantly improved modeling of PFAS presence in food and correlations around predicted values in environmental waters and sediments, (Tao et al.2024) . Ensemble regression modeling has shown a 50% decrease in human serum half-lives for six PFASs (Iulini et al.2024) , while artificial neural networks have shown correlations in serum half-life predictions, (Li & MacDonald Gibson, 2022). AI increases the efficiency of research, providing quicker and more accurate reported results, offering new opportunities for environmental scientists, (Lei et al.2023). AI-driven solutions, utilizing machine learning and molecular simulations (Kibbey et al., 2021), are being utilized to predict and prioritize PFAS in various systems (Karbassiyazdi et al.2022), thereby enhancing their environmental relevance and facilitating life cycle assessments and hazard risk assessments, (Zhang & Zhang, 2022; Han et al.2023).The overarching challenge in AI and PFAS studies is the reliance on untrusted sources and statistical tests, (Feinstein et al.2021). This lack of quantitative measurements and comprehensive validation necessitates collaboration among diverse stakeholders to improve data quality, (Su et al.2024). Interdisciplinary approaches, considering both short and long-term goals, are needed to

create less toxic PFAS, shifting the normal logic of isolating variables, (Li & MacDonald Gibson, 2022). Finally, the implications of climate change and extreme weather events (Adamopoulos et al. 2023c; Adamopoulos et al., 2024b), on water supplies and traditional water management in Europe must be emphasized (Adamopoulou et al., 2023), since they have a negative impact on public health, agriculture, and food safety, (Adamopoulos et al., 2022). The discussion above shows that incorporating AI into mitigating PFAS contamination and ecosystem risk is not without challenges, but it also provides enormous opportunities to reveal hidden insights and patterns, generate increasingly reliable predictions, and accelerate the development of sustainable management plans.

### *Recommendations*

Addressing PFAS contamination in Europe's agricultural sector requires strategic investments, robust regulatory frameworks, and active collaboration among stakeholders. The recommendations outlined here focus on creating sustainable, scalable, and inclusive approaches to remediate contaminated farmland and prevent future contamination. The EU is focusing on PFAS remediation and PFAS monitoring to combat contamination in agriculture. Key actions include increasing EU funding for research on cost-effective, scalable remediation technologies, strengthening regulatory frameworks to enforce PFAS monitoring, fostering public-private partnerships for comprehensive remediation, and promoting community involvement in PFAS monitoring and awareness. The EU Green Deal's Chemical Strategy for Sustainability aims to accelerate the development of innovative PFAS remediation technologies, while REACH regulations must be enhanced to include stricter thresholds for PFAS levels in agricultural soils and water sources. Public-private partnerships can mobilize resources and expertise for large-scale PFAS remediation, while promoting community involvement builds trust and promotes sustainable agricultural practices. These actions aim to reduce costs, improve efficiency, and promote sustainable agricultural practices.

### *Future Directions*

The developed world, natural sciences, and social sciences are all interrelated subjects that are critical to comprehending the built environment. By combining data scientists' knowledge with insights from these domains, we can design effective policy initiatives to solve the pressing PFAS issues. It is critical to avoid dismissive rules and laws, instead focusing on cautious principles and dealing with the rebirth of history. The combination of human knowledge and AI capabilities has the potential to solve these complicated problems.

## **5. Conclusions**

The requirement to address PFAS pollution in the environment and in communities is urgent. AI technology hold tremendous promise for environmental research. Implementing cross-disciplinary monitoring frameworks, top-down legislation, and analytical and remedial tools are all necessary for an effective response. Collaboration, democratic engagement, and self-management of affected communities are critical in decision-making processes. The rapid speed of AI advancement highlights the revolutionary potential of these technologies in combating PFAS contamination. Public Health in Europe faces a significant challenge in addressing PFAS contamination, which poses a significant environmental threat to food security and agricultural sustainability. These "forever chemicals" accumulate in soil, water, crops, and livestock, threatening food systems and community health. To combat PFAS contamination, a multi-pronged approach is needed, integrating innovative technologies like plasma-based remediation, bioaugmentation, and nanofiltration with comprehensive regulatory frameworks. Investing in research to develop cost-effective and scalable solutions is crucial, while regulatory reform and public-private partnerships can accelerate the deployment of advanced remediation technologies. Community engagement is also vital, as farmers, local residents, and other stakeholders must be equipped with the knowledge and tools to monitor contamination, participate in remediation efforts, and advocate for sustainable practices. Inaction will

lead to escalating costs in terms of food imports, public health expenditures, and environmental degradation. By combining innovation, regulation, and community empowerment, Europe can lead the way in addressing PFAS contamination and ensuring the well-being of future generations.

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## **References**

1. Adamopoulos, I. P., Frantzana, A. A., & Syrou, N. F. (2023b). Epidemiological surveillance and environmental hygiene, SARS-CoV-2 infection in the community, urban wastewater control in Cyprus, and water reuse. *Journal of Contemporary Studies in Epidemiology and Public Health*, 4(1), ep23003. <https://doi.org/10.29333/jconsep/12948>
2. Adamopoulos, I. P., Lamnisos, D., Syrou, N. F., & Boustras, G. (2022). Public health and work safety pilot study: Inspection of job risks, burn out syndrome and job satisfaction of public health inspectors in Greece. *Safety Science*, 147, Article 105592. <https://doi.org/10.1016/j.ssci.2021.105592>
3. Adamopoulos, I. P., Syrou, N. F., & Adamopoulou, J. P. (2024a). Greece's current water and wastewater regulations and the risks they pose to environmental hygiene and public health, as recommended by the European Union Commission. *European Journal of Sustainable Development Research*, 8(2), em0251. <https://doi.org/10.29333/ejosdr/14301>
4. Adamopoulos, I., & Syrou, N. (2023a). Occupational Hazards Associated with the Quality and Training Needs of Public Health Inspectors in Greece. *Medical Sciences Forum*, 19(1), 2. <https://doi.org/10.3390/msf2023019002>
5. Adamopoulos, I., Frantzana, A., & Syrou, N. (2024b). Climate Crises Associated with Epidemiological, Environmental, and Ecosystem Effects of a Storm: Flooding, Landslides, and Damage to Urban and Rural Areas (Extreme Weather Events of Storm Daniel in Thessaly, Greece). *Medical Sciences Forum*, 25(1), 7. <https://doi.org/10.3390/msf2024025007>
6. Adamopoulos, I., Frantzana, A., Adamopoulou, J., & Syrou, N. (2023c). Climate Change and Adverse Public Health Impacts on Human Health and Water Resources. *Environmental Sciences Proceedings*, 26(1), 178. <https://doi.org/10.3390/envirosciproc2023026178>
7. Adamopoulou, J. P., Frantzana, A. A., & Adamopoulos, I. P. (2023d). Addressing water resource management challenges in the context of climate change and human influence. *European Journal of Sustainable Development Research*, 7(3), em0223. <https://doi.org/10.29333/ejosdr/13297>
8. Agency for Toxic Substances and Disease Registry (ATSDR). (2020). PFAS Exposure Assessments Final Report. Accessed [21-1-2025] Source: <https://www.atsdr.cdc.gov/pfas>

9. Ahrens, L., & Bundschuh, M. (2014). Fate and effects of poly- and perfluoroalkyl substances in the aquatic environment: A review. *Environmental Toxicology and Chemistry*, 33(9), 1921–1929. <https://doi.org/10.1002/etc.2663>
10. Bibri, S. E., Krogstie, J., Kaboli, A., & Alahi, A. (2024). Smarter eco-cities and their leading-edge artificial intelligence of things solutions for environmental sustainability: A comprehensive systematic review. *Environmental Science and Ecotechnology*, 19, 100330. <https://doi.org/10.1016/j.es.2023.100330>
11. Bolan, N., Sarkar, B., Yan, Y., Li, Q., Wijesekara, H., Kannan, K., ... & Rinklebe, J. (2021). Remediation of poly-and perfluoroalkyl substances (PFAS) contaminated soils–to mobilize or to immobilize or to degrade?. *Journal of Hazardous Materials*, 401, 123892. DOI: <https://doi.org/10.1016/j.jhazmat.2020.123892>
12. Breitmeyer, S. E., Williams, A. M., Conlon, M. D., Wertz, T. A., Heflin, B. C., Shull, D. R., & Duris, J. W. (2024). Predicted Potential for Aquatic Exposure Effects of Per-and Polyfluorinated Alkyl Substances (PFAS) in Pennsylvania's Statewide Network of Streams. *Toxics*, 12(12), 921. DOI: <https://doi.org/10.3390/toxics12120921>
13. C8 Health Project. (2013). Community exposure studies in Parkersburg, West Virginia. Accessed [27-1-2025] <https://www.c8sciencepanel.org>
14. Chen, L., Chen, Z., Zhang, Y., Liu, Y., Osman, A. I., Farghali, M., ... & Yap, P. S. (2023). Artificial intelligence-based solutions for climate change: a review. *Environmental Chemistry Letters*, 21(5), 2525–2557. DOI: <https://doi.org/10.1007/s10311-023-01580-0>
15. Cousins, I. T., et al. (2016). The concept of essential use for determining when uses of PFASs can be phased out. *Environmental Science: Processes & Impacts*, 21(11), 1803–1815. <https://doi.org/10.1039/C9EM00163H>
16. Dauvergne, P. (2022). Is artificial intelligence greening global supply chains? Exposing the political economy of environmental costs. *Review of International Political Economy*. DOI: <https://doi.org/10.1080/09692290.2022.2048795>
17. Di Nisio, A., Pannella, M., Vogiatzis, S., Sut, S., Dall'Acqua, S., Santa Rocca, M., ... & Foresta, C. (2022). Impairment of human dopaminergic neurons at different developmental stages by perfluoro-octanoic acid (PFOA) and differential human brain areas accumulation of perfluoroalkyl chemicals. *Environment International*, 158, 106982. DOI: <https://doi.org/10.1016/j.envint.2021.106982>
18. Ditria, E. M., Buelow, C. A., Gonzalez-Rivero, M., & Connolly, R. M. (2022). Artificial intelligence and automated monitoring for assisting conservation of marine ecosystems: A perspective. *Frontiers in Marine Science*, 9, 918104. DOI: <https://doi.org/10.3389/fmars.2022.918104>
19. Draghi, S., Curone, G., Risoluti, R., Materazzi, S., Gullifa, G., Amoresano, A., ... & Arioli, F. (2024). Comparative analysis of PFASs concentrations in fur, muscle, and liver of wild roe deer as biomonitoring matrices. *Frontiers in Veterinary Science*, 11, 1500651. DOI: <https://doi.org/10.3389/fvets.2024.1500651>
20. EPA PFAS Roadmap. (2021). Environmental Protection Agency's strategic plan for addressing PFAS. Accessed [23-1-2025] <https://www.epa.gov/pfas>
21. European Chemicals Agency (ECHA). (2020). Annex XV restriction report: Proposal for a restriction on per- and polyfluoroalkyl substances (PFAS). Accessed [2-1-2025] <https://echa.europa.eu/>
22. European Commission. (2020). Chemicals strategy for sustainability. <https://ec.europa.eu/>
23. European Food Safety Authority (EFSA). (2020). Risk assessment of PFAS in the food chain. Accessed [1-2-2025] <https://www.efsa.europa.eu>
24. Falandysz, J., Liu, G., & Rutkowska, M. (2024). Analytical progress on emerging pollutants in the environment: An overview of the topics. *TrAC Trends in Analytical Chemistry*. DOI: <https://doi.org/10.1016/j.trac.2023.116809>
25. Feinstein, J., Sivaraman, G., Picel, K., Peters, B., Vázquez-Mayagoitia, Á., Ramanathan, A., MacDonell, M., Foster, I., & Yan, E. (2021). Uncertainty-informed deep transfer learning of perfluoroalkyl and polyfluoroalkyl substance toxicity. *Journal of Chemical Information and Modeling*, 61(12), 5793–5803. DOI: <https://doi.org/10.1021/acs.jcim.1c01204>
26. Gerardu, T., Dijkstra, J., Beeltje, H., van Duivenbode, A. V. R., & Griffioen, J. (2023). Accumulation and transport of atmospherically deposited PFOA and PFOS in undisturbed soils downwind from a fluoropolymers factory. *Environmental Advances*, 11, 100332. DOI: <https://doi.org/10.1016/j.envadv.2023.100332>

27. Ghisi, R., Vamerali, T., & Manzetti, S. (2019). Accumulation of perfluorinated alkyl substances (PFAS) in agricultural plants: A review. *Environmental Research*, 169, 326–341. <https://doi.org/10.1016/j.envres.2018.10.023>
28. Giesy, J. P., & Kannan, K. (2001). Global distribution of perfluorooctane sulfonate in wildlife. *Environmental Science & Technology*, 35(7), 1339–1342. <https://doi.org/10.1021/es001834k>
29. Gill, A. S. & Germann, S. (2022). Conceptual and normative approaches to AI governance for a global digital ecosystem supportive of the UN Sustainable Development Goals (SDGs). *AI and Ethics*. DOI: <https://doi.org/10.1007/s43681-022-00160-0>
30. Göckener, B., et al. (2020). Transfer of per- and polyfluoroalkyl substances (PFAS) from feed into milk: Approaching a worst-case scenario. *Chemosphere*, 249, 126111. <https://doi.org/10.1016/j.chemosphere.2020.126111>
31. Goldenman, G., et al. (2019). The cost of inaction: A socioeconomic analysis of environmental and health impacts linked to exposure to PFAS. Nordic Council of Ministers. <https://doi.org/10.6027/TN2019-516>
32. Han, B. C., Liu, J. S., Bizimana, A., Zhang, B. X., Kateryna, S., Zhao, Z., ... & Meng, X. Z. (2023). Identifying priority PBT-like compounds from emerging PFAS by nontargeted analysis and machine learning models. *Environmental Pollution*, 122663. DOI: <https://doi.org/10.1016/j.envpol.2023.122663>
33. Hu, X. C., Dai, M., Sun, J. M., & Sunderland, E. M. (2023). The utility of machine learning models for predicting chemical contaminants in drinking water: Promise, challenges, and opportunities. *Current Environmental Health Reports*, 10(1), 45–60. DOI: <https://doi.org/10.1007/s40572-022-00389-x>
34. Iulini, M., Russo, G., Crispino, E., Paini, A., Fragki, S., Corsini, E., & Pappalardo, F. (2024). Advancing PFAS risk assessment: Integrative approaches using agent-based modelling and physiologically-based kinetic for environmental and health safety. *Computational and Structural Biotechnology Journal*, 23, 2763–2778. DOI: <https://doi.org/10.1016/j.csbj.2024.05.012>
35. Jeong, N., Park, S., Mahajan, S., Zhou, J., Blotvogel, J., Li, Y., ... & Chen, Y. (2024). Elucidating governing factors of PFAS removal by polyamide membranes using machine learning and molecular simulations. *Nature Communications*, 15(1), 10918. DOI: <https://doi.org/10.1038/s41467-024-10918-0>
36. Karbassiyazdi, E., Fattahi, F., Yousefi, N., Tahmassebi, A., Taromi, A. A., Manzari, J. Z., ... & Razmjou, A. (2022). XGBoost model as an efficient machine learning approach for PFAS removal: Effects of material characteristics and operation conditions. *Environmental Research*, 215, 114286. DOI: <https://doi.org/10.1016/j.envres.2022.114286>
37. Kibbey, T. C. G., Jabrzemski, R., & O'Carroll, D. M. (2021). Predicting the relationship between PFAS component signatures in water and non-water phases through mathematical transformation: Application to machine learning. *Chemosphere*, 272, 129870. DOI: <https://doi.org/10.1016/j.chemosphere.2021.129870>
38. Kotthoff, M., Müller, J., Jüriling, H., Schlummer, M., & Fiedler, D. (2015). Perfluoroalkyl and polyfluoroalkyl substances in consumer products. *Environmental Science and Pollution Research*, 22(19), 14546–14559. <https://doi.org/10.1007/s11356-015-4202-7>
39. Koulini, G. V., Vinayagam, V., Nambi, I. M., & Krishna, R. R. (2024). Per-and polyfluoroalkyl substances (PFAS) in Indian environment: Prevalence, impacts and solutions. *Journal of Water Process Engineering*, 66, 105988. DOI: <https://doi.org/10.1016/j.jwpe.2024.105988>
40. Lazova-Borisova, I., & Adamopoulos, I. (2024). COMPLIANCE OF CARMINIC ACID APPLICATION WITH EUROPEAN LEGISLATION FOR FOOD SAFETY AND PUBLIC HEALTH. <https://doi.org/10.5281/zenodo.10727449>
41. Lei, L., Pang, R., Han, Z., Wu, D., Xie, B., & Su, Y. (2023). Current applications and future impact of machine learning in emerging contaminants: A review. *Critical Reviews in Environmental Science and Technology*, 53(20), 1817–1835. DOI: <https://doi.org/10.1080/10643389.2023.2174467>
42. Li, R. & MacDonald Gibson, J. (2022). Predicting the occurrence of short-chain PFAS in groundwater using machine-learned Bayesian networks. *Frontiers in Environmental Science*. DOI: <https://doi.org/10.3389/fenvs.2022.876123>
43. Liu, Y., D'Agostino, L. A., Qu, G., Jiang, G., & Martin, J. W. (2019). High-resolution mass spectrometry (HRMS) methods for nontarget discovery and characterization of poly- and perfluoroalkyl substances

- (PFASs) in environmental and human samples. *Trends in Analytical Chemistry*, 121, 115420. <https://doi.org/10.1016/j.trac.2019.115420>
44. Machine learning Helps in Quickly Diagnosis Cases of “New Corona” (M. M. Mijwil, I. Adamopoulos, & P. Pudasaini , Trans.). (2024). *Mesopotamian Journal of Artificial Intelligence in Healthcare*, 2024, 16-19. <https://doi.org/10.58496/MJAIH/2024/003>
  45. Navidpour, A. H., Hosseinzadeh, A., Huang, Z., Li, D., & Zhou, J. L. (2024). Application of machine learning algorithms in predicting the photocatalytic degradation of perfluorooctanoic acid. *Catalysis Reviews*, 66(2), 687-712. DOI: <https://doi.org/10.1080/01614940.2023.2174467>
  46. OECD. (2021). OECD principles on per- and polyfluoroalkyl substances (PFAS): Towards a framework for global action. Organisation for Economic Co-operation and Development. Accessed [21-12-2024] Retrieved from <https://www.oecd.org/>
  47. Peritore, A. F., Gugliandolo, E., Cuzzocrea, S., Crupi, R., & Britti, D. (2023). Current review of increasing animal health threat of per-and polyfluoroalkyl substances (PFAS): Harms, limitations, and alternatives to manage their toxicity. *International Journal of Molecular Sciences*, 24(14), 11707. DOI: <https://doi.org/10.3390/ijms241411707>
  48. Prasad, M. N. V. & Elchuri, S. V. (2023). Environmental contaminants of emerging concern: occurrence and remediation. *Chemistry-Didactics-Ecology-Metrology*. DOI: <https://doi.org/10.2478/cdem-2023-0005>
  49. Rahman, M. F., Peldszus, S., & Anderson, W. B. (2014). Behaviour and fate of perfluoroalkyl and polyfluoroalkyl substances (PFASs) in drinking water treatment: A review. *Water Research*, 50, 318–340. <https://doi.org/10.1016/j.watres.2013.10.045>
  50. Ross, I., et al. (2018). A review of emerging technologies for remediation of PFASs. *Remediation Journal*, 28(2), 101–126. <https://doi.org/10.1002/rem.21553>
  51. Said, T. O., & El Zokm, G. M. (2024). Fate, Bioaccumulation, Remediation, and Prevention of POPs in Aquatic Systems Regarding Future Orientation. In *Persistent Organic Pollutants in Aquatic Systems: Classification, Toxicity, Remediation and Future* (pp. 115-148). Cham: Springer Nature Switzerland. DOI: [https://doi.org/10.1007/978-3-031-28222-0\\_5](https://doi.org/10.1007/978-3-031-28222-0_5)
  52. Scheringer, M., et al. (2014). Helsingør statement on poly- and perfluorinated alkyl substances (PFASs). *Chemosphere*, 114, 337–339. <https://doi.org/10.1016/j.chemosphere.2014.05.044>
  53. Shivaprakash, K. N., Swami, N., Mysorekar, S., Arora, R., Gangadharan, A., Vohra, K., ... & Kiesecker, J. M. (2022). Potential for artificial intelligence (AI) and machine learning (ML) applications in biodiversity conservation, managing forests, and related services in India. *Sustainability*, 14(12), 7154. DOI: <https://doi.org/10.3390/su14127154>
  54. Sivagami, K., Sharma, P., Karim, A. V., Mohanakrishna, G., Karthika, S., Divyapriya, G., ... & Kumar, A. N. (2023). Electrochemical-based approaches for the treatment of forever chemicals: removal of perfluoroalkyl and polyfluoroalkyl substances (PFAS) from wastewater. *Science of the Total Environment*, 861, 160440. DOI: <https://doi.org/10.1016/j.scitotenv.2022.160440>
  55. Stahl, B. C. (2021). Artificial intelligence for a better future: an ecosystem perspective on the ethics of AI and emerging digital technologies. DOI: <https://doi.org/10.1007/978-3-030-69978-9>
  56. Stensson, N., Lignell, S., Freeman, D., Jordan, F., Helmfriid, I., Karlsson, H., & Ljunggren, S. (2023). PFAS and Lipoproteomics in Swedish Adolescents. SSRN. DOI: <https://doi.org/10.2139/ssrn.5101490>
  57. Su, A., Cheng, Y., Zhang, C., Yang, Y. F., She, Y. B., & Rajan, K. (2024). An artificial intelligence platform for automated PFAS subgroup classification: A discovery tool for PFAS screening. *Science of The Total Environment*, 921, 171229. DOI: <https://doi.org/10.1016/j.scitotenv.2024.171229>
  58. Tao, L., Tang, W., Xia, Z., Wu, B., Liu, H., Fu, J., ... & Huang, Y. (2024). Machine learning predicts the serum PFOA and PFOS levels in pregnant women: Enhancement of fatty acid status on model performance. *Environment International*, 108837. DOI: <https://doi.org/10.1016/j.envint.2024.108837>
  59. Tatarinov, K., Ambos, T. C., & Tschang, F. T. (2022). Scaling digital solutions for wicked problems: Ecosystem versatility. *Journal of International Business Studies*, 54(4), 631. DOI: <https://doi.org/10.1057/s41267-022-00545-0>

60. Tokranov, A. K., Ransom, K. M., Bexfield, L. M., Lindsey, B. D., Watson, E., Dupuy, D. I., ... & Bradley, P. M. (2024). Predictions of groundwater PFAS occurrence at drinking water supply depths in the United States. *Science*, 386(6723), 748-755. DOI: <https://doi.org/10.1126/science.ade6234>
61. Valamontes, A. (2024). Accessible research papers for individuals with dyslexia and autism spectrum disorders. <https://doi.org/10.13140/RG.2.2.34352.37126>
62. Vierke, L., et al. (2012). Perfluorooctanoic acid (PFOA)—A new kid on the block in the EU legislation for chemicals. *Environmental Sciences Europe*, 24(1), 1–11. <https://doi.org/10.1186/2190-4715-24-16>
63. Winchell, L. J., Ross, J. J., Wells, M. J., Fonoll, X., Norton Jr, J. W., & Bell, K. Y. (2021). Per- and polyfluoroalkyl substances thermal destruction at water resource recovery facilities: A state of the science review. *Water Environment Research*, 93(6), 826-843. DOI: <https://doi.org/10.1002/wer.1483>
64. Winchell, L. J., Wells, M. J., Ross, J. J., Fonoll, X., Norton Jr, J. W., Kuplicki, S., ... & Bell, K. Y. (2022). Per- and polyfluoroalkyl substances presence, pathways, and cycling through drinking water and wastewater treatment. *Journal of Environmental Engineering*, 148(1), 03121003. DOI: [https://doi.org/10.1061/\(ASCE\)EE.1943-7870.0001933](https://doi.org/10.1061/(ASCE)EE.1943-7870.0001933)
65. Yigitcanlar, T., Mehmood, R., & Corchado, J. M. (2021). Green artificial intelligence: Towards an efficient, sustainable and equitable technology for smart cities and futures. *Sustainability*. DOI: <https://doi.org/10.3390/su13031318>
66. Zhang, K. & Zhang, H. (2022). Machine learning modeling of environmentally relevant chemical reactions for organic compounds. *ACS ES&T Water*, 2(5), 745-754. DOI: <https://doi.org/10.1021/acsestwater.1c00345>
67. Zhao, L., et al. (2018). Adsorption of perfluoroalkyl substances (PFASs) in water by carbonaceous adsorbents: A review. *Critical Reviews in Environmental Science and Technology*, 48(11), 1042–1083. <https://doi.org/10.1080/10643389.2018.1463388>

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## Discussion

# Discussion. Has the human population become a sentinel for the adverse effects of PFAS contamination on wildlife health and endangered species?

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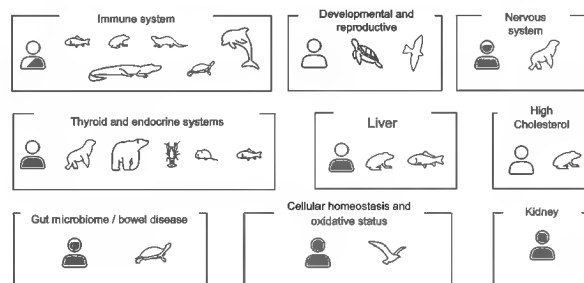
Environmental Working Group, 1250 I Street NW Suite 1000, Washington DC 20005, United States of America

## HIGHLIGHTS

- *Per-* and polyfluoroalkyl substances (PFAS) are global environmental contaminants.
- PFAS are detected in wildlife globally.
- There is concordance between findings on PFAS health effects in wildlife and humans.
- Humans can be regarded as a sentinel species for adverse health impacts of PFAS.
- Wildlife conservation must consider health impacts of chemical contaminants.

## GRAPHICAL ABSTRACT

## Shared health effects of PFAS



## ARTICLE INFO

## Keywords

*Per-* and polyfluoroalkyl substances  
PFAS  
Wildlife health  
Endangered species  
Sentinel species  
Environmental contamination

## ABSTRACT

Global contamination with *per-* and polyfluoroalkyl substances (PFAS) poses a threat to both human health and the environment, with significant implications for ecological conservation policies. A growing list of peer-reviewed publications indicates that PFAS can harm wildlife health and that the adverse effects associated with PFAS exposure in wildlife are in concordance with human epidemiological studies. The correlation of cross-species data supports a unique perspective that humans can be regarded as a sentinel for PFAS effects in other species. The health harms due to PFAS are potentially most concerning for populations of endangered and threatened species that are simultaneously exposed to PFAS and other toxic pollutants, and also face threats to their survival due to habitat loss, degradation of ecosystems, and over-harvesting. Human epidemiological studies on the PFAS doses associated with health harm present a rich source of information about potential impacts on wildlife health due to PFAS. Our analysis suggests that national and international efforts to restrict

**Abbreviations:** DDT, Dichlorodiphenyltrichloroethane; NHANES, National Health and Nutrition Examination Survey; PCB, Polychlorinated biphenyl; PFAS, *Per-* and polyfluoroalkyl substances; PFBS, Perfluorobutane sulfonic acid; PFCA, Perfluoroalkyl carboxylic acid; PFDA, Perfluorodecanoic acid; PFDoDA, Perfluorododecanoic acid; PFHpA, Perfluoroheptanoic acid; PFHxA, Perfluorohexanoic acid; PFHxS, Perfluorohexane sulfonic acid; PFNA, Perfluorononanoic acid; PFOA, Perfluorooctanoic acid; PFOS, Perfluorooctane sulfonate; PFSA, Perfluoroalkyl sulfonic acid; PFTeDA, Perfluorotetradecanoic acid; PFTrDA, Perfluorotridecanoic acid; PFUnDA, Perfluoroundecanoic acid; POP, Persistent organic pollutant; ppt, parts per trillion; U.S. EPA, United States Environmental Protection Agency.

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the discharges of PFAS into the environment and to clean up PFAS-contaminated sites present an opportunity to protect wildlife from chemical pollution and to advance species conservation worldwide.

## 1. Using humans as sentinels to better understand chemical pollution impacts on the biodiversity crisis

In a classic ecotoxicological approach, monitoring of indicator species such as sensitive bird populations has provided information about the health harms due to bioaccumulative pollutants such as PCBs and DDT, including information highly relevant to human health (Bowerman et al., 2002; Solla et al., 2016). As the global wildlife and biodiversity conservation crisis deepens, there is an urgent need to better protect wildlife from the threats of chemical pollution. One such path towards this goal is to shift the perspective so as to understand how what we know from studies in humans applies to wildlife health. The use of animals as toxicity sentinels has been explored and developed for decades as an approach to protect human health. In contrast to this anthropocentric perspective, more recent frameworks emphasize a One Health approach that considers shared health risk for all species, which may provide better opportunities to protect human and wildlife health simultaneously within a global ecosystem (Destoumieux-Garzon et al., 2018). However, adoption of such frameworks has been slow, with examples so far limited to acute high dose chemical exposures or infectious disease risk. Just a handful of publications to-date explored cross-species extrapolation from humans to animals, which may be appropriate when humans are the most extensively studied exposed population (Beasley, 2009; Rabinowitz et al., 2009; Rabinowitz et al., 2008).

Per- and polyfluoroalkyl substances (PFAS) are recognized as pervasive contaminants associated with harmful effects on the global environment and all species that live on the planet (Evich et al., 2022). We use the term “PFAS” in this Discussion to describe this entire broad class of anthropogenic fluorinated chemicals that have been manufactured globally since the 1950s (Kwiatkowski et al., 2020; U.S. Environmental Protection Agency, 2023a; Wang et al., 2021). Research literature presents overwhelming evidence from studies in humans about the health harms of PFAS exposures. Here we explore the idea that humans can be used as sentinels for wildlife health to enable conservation measures for wildlife and endangered species. Loring and co-authors have previously noted “... the versatility of the word ‘sentinel’, which generally describes a sentry or guard, but also can be used to refer to the act of keeping watch, as well as the position from which watch is kept” (Loring et al., 2017). Here we adapt this wider epistemological and policy perspective within which we seek to explore the concept of humans as a sentinel species.

A quickening loss of biodiversity threatens species and ecosystems across the globe with significant negative implications both for food security and human health world-wide (World Health Organization and Secretariat of the Convention on Biological Diversity, 2015). Estimates published in 2023 suggest that 48 % of species globally are experiencing population declines, a feature of population dynamics classified as a symptom of potential extinction (Finn et al., 2023). Anthropogenic influences can impact wildlife health, species diversity, and species survival through alteration of physical, biological and chemical composition of terrestrial and aquatic ecosystems (Rillig et al., 2021). In particular, the chemical contamination of the environment with industrial chemicals, pesticides, and a variety of pollutants discharged by the global economy is both a considerable burden (Persson et al., 2022; Sigmund et al., 2022) and a growing peril (Naidu et al., 2021). Yet, the existing frameworks of industrial chemical regulation in individual countries and globally have not yet given sufficient consideration to the impact of toxic chemicals on wildlife and have not yet developed effective approaches to species conservation and wildlife protection in the face of pervasive anthropogenic pollution.

There is a growing recognition that conservation of biodiversity

plays a fundamental role in sustaining all aspects of society. The need to address global threats to biodiversity, and action steps for doing so, were outlined in the Kunming-Montreal Global Biodiversity Framework adopted in December 2022 at the 15th meeting of the Conference of Parties to the UN Convention on Biological Diversity. One of the eight primary targets includes reducing pollution risks from pesticides and highly hazardous chemicals “to levels that are not harmful to biodiversity and ecosystem functions and services, considering cumulative effects” (Convention on Biological Diversity, 2022). The Framework emphasizes the need for an integrated whole-of-government and civil society approach to reduce threats to biodiversity and calls for urgent actions to protect biodiversity that should be initiated immediately.

## 2. PFAS health effects have been extensively studied in humans

The human health effects of PFAS exposure have been well studied in areas of severe local contamination such as the C8 science panel studies in the mid-Ohio River Valley in the United States (Frisbee et al., 2009) and in human studies evaluating health impacts with exposure differentials across the general population. State, federal, and international human health risk assessments for regulatory action on some PFAS have drawn on the vast literature of likely causal associations between PFAS exposure and adverse health effects in humans to establish health protective exposure limits. The U.S. Environmental Protection Agency 2023 toxicity assessment for the proposed drinking water standard for perfluorooctane sulfonic acid (PFOS) in drinking water included 423 epidemiological studies, 45 animal studies, 89 toxicokinetic studies, 22 physiologically-based pharmacokinetic and pharmacodynamic modeling (PBPK) studies and 301 mechanistic studies (U.S. Environmental Protection Agency, 2023a). A similar number of studies were included in the proposed drinking water standard for perfluorooctanoic acid (PFOA) (U.S. Environmental Protection Agency, 2023b). An effort to catalog the studies on health and toxicological effects for PFAS other than PFOA and PFOS identified 1067 studies (505 in people, 385 in animals) for 29 different PFAS compounds (Pelch et al., 2022).

The well-studied link between PFAS exposure in humans and associated health harms along with widespread contamination of wildlife provide an important opportunity to explore the potential for humans to serve as sentinels for PFAS impacts in other species. In this Discussion, our goal is to bring to the attention of the research community and government decision makers the threat PFAS pollution poses to wildlife health, emphasizing that health impacts of globally significant chemical contaminants must be considered in wildlife conservation strategies.

As a result of uncontrolled discharges into the environment, PFAS now pollute water, soil, air and living organisms, and are found in the blood of people around the world (Evich et al., 2022). In the past two decades, research worldwide revealed that exposure to PFAS can cause numerous health harms, as observed in experimental toxicology studies with laboratory animals and in epidemiological studies of highly exposed human populations in the vicinity of contaminated sites as well as in the general population (Fenton et al., 2021; Sunderland et al., 2019). While initial health studies regarding PFAS exposure focused on two most-studied members of this class, PFOA and PFOS, a growing body of scientific research finds that exposure to numerous types of PFAS can harm health (Pelch et al., 2022; Temkin et al., 2020), acknowledging the importance of considering the health impacts of PFAS mixtures (Goodrich et al., 2023).

## 3. PFAS are detected in wildlife globally

Unlike other classes of industrial chemicals with an identified impact

on wildlife, such as polychlorinated biphenyls (PCBs) that have been phased out from use globally, various types of PFAS continue to be produced, as new fluorochemicals are developed to replace PFOA and PFOS whose use was either phased out or decreased globally. Further, as documented by environmental monitoring studies, there is seemingly no place on the planet untouched by PFAS contamination. A study of the snow on Mount Everest found evidence of PFAS presence, perhaps partially related to PFAS leaching from climbing gear, as well as due to air deposition from the global atmospheric PFAS pollution (Miner et al., 2021).

The manufacturers of PFAS have known for decades that these substances can accumulate in the bodies of living organisms. In 1998, testing by 3M chemical manufacturing company could only find uncontaminated human blood by using archived samples from the Korean War fought in 1950–1953 (3M, 2000). Subsequent testing sponsored by 3M in 2001 documented the ubiquitous presence of PFOS in a global collection of tissue samples for turtles, fish, birds such as bald eagles and albatrosses, and marine mammals such as seals and polar bears (Giesy and Kannan, 2001).

Wildlife are exposed to PFAS through their habitat, such as contaminated waterways (Teunen et al., 2021), as well as their diet (Boisvert et al., 2019). Various PFAS can accumulate in living organisms following exposure to contamination. However, unlike other persistent pollutants, such as organochlorines, PFAS do not tend to accumulate in fat, but rather tend to bind to proteins (Butt et al., 2010). Measurement of PFAS in blood, eggs and other tissues is often limited to a select number of compounds due to analytical capabilities or other limitations in wildlife studies. The set of approximately two dozen PFAS commonly included in various monitoring studies may only account for a fraction of this wide class of chemicals and could underestimate exposure as non-targeted analysis has shown (Barrett et al., 2021; McDonough et al., 2019; Spaan et al., 2020; Wang et al., 2021). Current targeted methods may not be keeping pace with the shifting patterns in global manufacturing of PFAS materials (De Silva et al., 2021).

Hundreds of studies reported the accumulation of various PFAS in animals from a variety of taxa. PFAS are found in wildlife on every continent from manatees in the U.S. state of Florida to fish in Ethiopia and Uganda, flamingos in the Caribbean, whales and dolphins in Hawaii, polar bears across the Arctic, ducks in Australia, sea turtles in Mexico, seafood caught off the coast of Bangladesh and freshwater fish across the United States (Barbo et al., 2023; Vendl et al., 2022; Vendl et al., 2021). For additional resources and visualization of the studies that detected PFAS in the environment, we direct the readers to the U.S. Environmental Protection Agency website (<https://echo.epa.gov/trends/pfas-tools>) as well as the global map of PFAS contamination in wildlife developed by our organization (Environmental Working Group, 2023, [https://www.ewg.org/interactive-maps/pfas\\_in\\_wildlife/map/](https://www.ewg.org/interactive-maps/pfas_in_wildlife/map/)) to view a visualization of a subset of studies documenting this far-reaching contamination.

#### 4. Cross-species extrapolation to assess PFAS toxicity

Current thinking behind traditional toxicity testing is moving towards greatly reducing the use of animals in testing. As alternatives to animal testing, there is now more focus on examining cell-based, computational, and mechanistic approaches to toxicity assessment. Such advanced methods would increase the understanding of biological mechanisms and pathways of adverse effects and their conservation between species and thereby support the research efforts to extrapolate effects across species. For example, the Key Characteristics approach and the Adverse Outcomes Pathways approach (LaLone et al., 2021) offer conceptual frameworks for gathering and utilizing data across species to understand the shared biological linkages that can be used to predict adverse effects (Arzuaga et al., 2019; Germolec et al., 2022; La Merrill et al., 2020; Lind et al., 2021; Rusyn et al., 2021; Smith et al., 2020). Additionally, analytical technologies like transcriptomics and

metabolomics which can assess biomarkers of adverse health effects, such as oxidative stress, DNA damage and changes in hormonal levels, are rapidly being developed in laboratory model species and in humans, and are also applied to investigations of wildlife health. Within this framework, researchers can leverage existing data, with a considerable amount of information from humans, as well as generate data from non-lethal and non-invasive sampling methods to predict potential adverse effects from PFAS exposure to a diversity of species.

PFOA, PFOS, and other compounds in the PFAS chemical family have been linked with a broad array of toxic effects in humans and laboratory animals, including harm to the immune system, harm to reproduction and fetal development, changes in the endocrine balance and increased risk of various cancers (National Academies of Sciences, 2022). Here we briefly review the literature on PFAS toxicity in environmental field studies of wildlife, which indicate similar target organ systems and health impacts in wildlife as humans and model organisms, from PFAS exposure (Acosta-Tlapalamatl et al., 2022; Beaulieu and Costantini, 2014; Bedia, 2022). Importantly, while not covered in this review, PFAS exposure has been also shown to affect the health of domesticated animals, including companion pets and livestock (Rock et al., 2023). Published studies, described in more detail below (Table 1), include reports of the impact of PFAS on hormonal levels in polar bears (Pedersen et al., 2016) and hooded seals (Gronnestad et al., 2018); the immune systems and disease resistance in fish (Guillette et al., 2020), alligators (Guillette et al., 2022) and marine mammals (Ishibashi et al., 2008; Kannan et al., 2006; Soloff et al., 2017); and hatching success in birds and emergence success in turtles (Custer, 2021; Custer et al., 2014) (Wood et al., 2021), as well as metabolic alterations associated with PFAS exposure in turtles (Beale et al., 2022), among other effects. Of note, associations with health parameter changes were reported for several different members of the PFAS family, including the sum of more than 20 PFAS, PFOS and other long chain PFAS, as well as new compounds from PFAS class with regional contamination patterns such as Nafion byproduct 2. Table 1 summarizes the health effects in wildlife associated with summed PFAS exposure and/or individual PFAS, while Table 2 indicates the number of studies where each compound was reported in association with these health effects.

It is important to recognize that reports on PFAS and wildlife health published in peer-reviewed scientific literature to date are likely a significant underestimate of all possible impacts of PFAS on wildlife, due to the practical difficulties of carrying out studies in the field as well as ethical and legal considerations protecting the health and survival of already endangered species. The PFAS-associated health effects described in the studies cited in Table 1 are indicative of chemical stressors that can impact both species fitness and survival and therefore can be considered a factor influencing population dynamics, with a potential connection to overall biodiversity loss (Groh et al., 2022). Impacts on the immune, nervous and endocrine systems, reproduction and development and metabolism are reported consistently by the published studies on different taxa.

##### 4.1. Immune system

The immune system is one of the most sensitive targets of PFAS toxicity, as observed by human studies that examined reduced vaccine response and increased susceptibility to infection and disease (Budtz-Jorgensen and Grandjean, 2018; European Food Safety Authority, 2020). Similarly, studies in reptiles, mammals, fish and birds have shown immune system impacts of PFAS exposure. Researchers studying alligator populations in the industrially contaminated Cape Fear River Basin (North Carolina, United States) observed an association between elevated levels of PFAS and altered biomarkers of innate immune activity related to autoimmune response (Guillette et al., 2022). Additionally, an increased incidence of skin lesions and unhealed wounds was observed, which is uncharacteristic for American alligators, and may be similar to the elevated risk of slow-healing wounds associated

**Table 1**

Recent studies of impacts of PFAS on wildlife health from field studies.

| Species                                                                         | Continent/Region                        | System affected and findings                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------------|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Invertebrate and fish                                                           |                                         |                                                                                                                                                                                                                                                 |
| Crayfish ( <i>Faxonius immunitis</i> , <i>F. rusticus</i> , <i>F. virilis</i> ) | North America, (Northern Michigan, USA) | Behavioral impacts<br><br>Increased exposure to PFAS (sum of 24 compounds) was associated with decreased foraging in crayfish (Coy et al., 2022).                                                                                               |
| Bluegill ( <i>Lepomis macrochirus</i> )                                         | North America, (Northern Michigan, USA) | Behavioral impacts<br><br>Increased exposure to PFAS (sum of 24 compounds) was associated with changes in swim speed (Coy et al., 2022)                                                                                                         |
| Striped bass ( <i>Morone saxatilis</i> )                                        | North America (North Carolina, USA)     | Liver and immune system<br><br>Elevated PFOS and Nafion byproduct 2 concentrations in serum were associated with altered liver biomarkers. Elevated PFOS was associated with alterations in the immune system in fish (Guillette et al., 2020). |
| Amphibians                                                                      |                                         |                                                                                                                                                                                                                                                 |
| Black spotted frog ( <i>Rana nigromaculata</i> )                                | Asia (Zhejiang province, China)         | Liver<br><br>Higher levels of PFAS, particularly PFOA, PFOS, and 6:2 Cl-PFESA, were correlated with liver biomarkers that indicated disrupted lipid metabolism (Lin et al., 2022).                                                              |
| Reptiles                                                                        |                                         |                                                                                                                                                                                                                                                 |
| American alligator ( <i>Alligator mississippiensis</i> )                        | North America (North Carolina, USA)     | Immune system<br><br>Elevated total PFAS (sum of 23) were associated with increased lysozyme activity in serum (an indicator of innate immunity), autoimmune-like traits and increased incidence of skin lesions (Guillette et al., 2022).      |
| Freshwater turtle ( <i>Emydura macquarii macquarii</i> )                        | Australia                               | Immune system<br><br>Changes in the gut microbiome, gut inflammation and gut metabolic changes were observed in turtles exposed to elevated total PFAS concentrations (sum of 47) (Beale et al., 2022).                                         |
| Hawksbill turtle ( <i>Eretmochelys imbricata</i> )                              | North Pacific Ocean                     | Reproduction<br><br>Higher concentrations of PFUnDA and PFTrDA in eggs were correlated with reduced emergence success of the hatchlings (Wood et al., 2021).                                                                                    |
| Birds                                                                           |                                         |                                                                                                                                                                                                                                                 |
| Arctic black-legged kittiwakes ( <i>Rissa tridactyla</i> )                      | Kongsfjorden, Svalbard                  | Cellular homeostasis and oxidative status<br><br>Oxidative status markers were correlated with higher plasma concentrations of PFDoDA, PFTrDA, PFTeDA, PFUnDA, PFOS (Costantini et al., 2019).                                                  |

**Table 1 (continued)**

| Species                                                    | Continent/Region                                    | System affected and findings                                                                                                                                                                                                                                                                                    |
|------------------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Tree swallows ( <i>Tachycineta bicolor</i> )               | North America (Minnesota, Wisconsin, Michigan, USA) | Reproduction<br><br>Decreased hatching success was associated with PFOS concentrations in eggs (Custer et al., 2014).                                                                                                                                                                                           |
| Arctic black-legged kittiwakes ( <i>Rissa tridactyla</i> ) | Kongsfjorden, Svalbard                              | Reproduction and endocrine system<br><br>PFDoDA concentration was related to lower hatching success. PFNA was related to changes in body mass in male kittiwakes and PFTrDA and PFTeDA were related to decreased baseline corticosterone in both sexes (Costantini et al., 2019).                               |
| Mammals                                                    |                                                     |                                                                                                                                                                                                                                                                                                                 |
| Bottlenose dolphin ( <i>Tursiops truncatus</i> )           | North America (South Carolina, USA)                 | Immune system<br><br>PFOS exposure was associated with increased T cell proliferation and proinflammatory cytokine production, a marker of chronic immune activation (Soloff et al., 2017).                                                                                                                     |
| Hooded seals ( <i>Cystophora cristata</i> )                | East Greenland                                      | Endocrine system<br><br>Elevated total PFAS (sum of 8) were associated with changes in both concentrations and ratios of thyroid hormones in mothers and pups (Gronnestad et al., 2018).                                                                                                                        |
| Polar bear ( <i>Ursus maritimus</i> )                      | East Greenland                                      | Nervous system and endocrine system<br><br>Higher concentrations of PFAS (both sum of 10 perfluoroalkyl carboxylic acids and sum of 4 perfluorosulfonic acids) in brain tissue were associated with increased levels of steroid hormones in brain tissue (Pedersen et al., 2016).                               |
| Bank voles ( <i>Myodes glareolus</i> )                     | Europe (Norway)                                     | Nervous system and endocrine system<br><br>Higher PFAS concentrations (sum of 10 perfluoroalkyl carboxylic acids and 5 perfluorosulfonic acids) in the liver were associated with elevated dopamine levels in the brains and lower testosterone levels in muscle of wild bank voles (Gronnestad et al., 2021b). |
| Southern sea otter ( <i>Enhydra lutris nereis</i> )        | North America (California, USA)                     | Immune system<br><br>Higher concentrations of PFOS and PFOA in the liver were associated with higher rates of infectious disease (Kannan et al., 2006).                                                                                                                                                         |

with autoimmune disease in humans (Shanmugam et al., 2017). In marine mammals, increased levels of PFOA and PFOS in the liver were significantly associated with disease mortality in sea otters (Kannan et al., 2006), and environmental exposure to PFOS in bottlenose dolphins was associated with immune system dysregulation (Foguth et al., 2020; Soloff et al., 2017). Exposure to PFAS mixtures as well as exposure

**Table 2**  
Studies where specific PFAS exposure was associated, either as individual compound or as a part of the summed PFAS, with the health outcomes in [Table 1](#). Where total PFAS sum was reported, all PFAS within that summation are listed. PFAS names are provided in footnote.

| PFAS <sup>a</sup> | Beale et al., 2022 | Costantini et al., 2019 | Custer et al., 2014 | Coy et al., 2022 | Gronnestad et al., 2018 | Gronnestad et al., 2021b | Guillette et al., 2020 | Guillette et al., 2022 | Kannan et al., 2006 | Lin et al., 2022 | Pedersen et al., 2016 | Sloff et al., 2017 | Wood et al., 2021 | Number of studies listed in Table 1 |
|-------------------|--------------------|-------------------------|---------------------|------------------|-------------------------|--------------------------|------------------------|------------------------|---------------------|------------------|-----------------------|--------------------|-------------------|-------------------------------------|
| PFOS              | *                  | *                       | *                   | *                | *                       | *                        | *                      | *                      | *                   | *                | *                     | *                  |                   | 12                                  |
| PFOA              | *                  |                         |                     | *                | *                       |                          |                        | *                      | *                   | *                | *                     | *                  |                   | 7                                   |
| PFNA              | *                  | *                       |                     | *                | *                       | *                        |                        | *                      | *                   | *                | *                     |                    | *                 | 7                                   |
| PFTtDA            | *                  | *                       |                     | *                | *                       | *                        |                        |                        |                     |                  | *                     |                    | *                 | 7                                   |
| PFUnDA            | *                  | *                       |                     | *                | *                       | *                        |                        |                        |                     |                  | *                     |                    | *                 | 7                                   |
| PFDA              | *                  |                         |                     | *                | *                       | *                        |                        | *                      |                     |                  | *                     |                    |                   | 6                                   |
| PFDoDA            | *                  | *                       |                     | *                | *                       | *                        |                        |                        |                     |                  | *                     |                    |                   | 6                                   |
| PFHxS             | *                  |                         |                     | *                | *                       | *                        |                        | *                      |                     |                  | *                     |                    |                   | 6                                   |
| PFBS              | *                  |                         |                     | *                | *                       | *                        |                        | *                      |                     |                  | *                     |                    |                   | 5                                   |
| PFHpA             | *                  |                         |                     | *                | *                       | *                        |                        | *                      |                     |                  | *                     |                    |                   | 5                                   |
| PFHxA             | *                  |                         |                     | *                | *                       | *                        |                        | *                      |                     |                  | *                     |                    |                   | 5                                   |
| PFTeDA            | *                  | *                       |                     | *                |                         | *                        |                        |                        |                     |                  | *                     |                    |                   | 5                                   |

\* PFAS reported in 4 studies in [Table 1](#): PFBA (perfluorobutanoic acid), PFAS (perfluoropentanoic acid), PFDS (perfluorodecanoic acid), 6:2 FTS (6:2 fluorotelomer sulfonate). PFAS reported in 2 studies in [Table 1](#): PFPeS (perfluoropentane sulfonic acid), PFNS (perfluorononane sulfonic acid), PFHpS (perfluoroheptane sulfonic acid), Nafion byproduct 2, 7H-Perfluoro-4-methyl-3-(6-sulfonato). PFAS reported in 3 studies in [Table 1](#): PFOSAA (N-Methylperfluorooctane sulfonamidoacetic acid), N-MeFOSA (N-methyl perfluorooctane sulfonamide), N-EtFOSE (N-Ethyl perfluorooctanesulfonic acid), N-EtFOSEA (N-ethyl perfluorooctane sulfonamido ethanol), N-MeFOSAA (N-Methylperfluorooctane sulfonamidoacetic acid), N-MeFOSA (N-methyl perfluorooctane sulfonamide), HFPD-DA (GenX) (Hexafluoropropylene oxide-dimer acid), N-EtFOSEA (N-ethyl perfluorooctane sulfonamido ethanol), N-EtFOSEA (N-ethyl perfluorooctane sulfonamidoacetic acid), PFOS (perfluorooctanesulfonic acid), PFOSAA (perfluorooctanesulfonamide), 8:2 FTS (8:2 fluorotelomer sulfonate), 4:2 FTS (4:2 fluorotelomer sulfonate). PFAS reported in 1 study in [Table 1](#): R-PSDA (Formerly Nafion Byproduct 4) (Perfluoro-4-(2-sulfoethoxy) pentanoic acid), PMPA (Perfluoro-2-methoxypropionic acid), PPPrS (perfluoropropanesulfonic acid), PPPrDA (Perfluoropropanesulfonamide), PFODA (Perfluorooctadecanoic acid), PFODS (Perfluorooctadecanesulfonic acid), PFPeDA (Perfluoropentadecanoic acid), PFPeSA (Perfluoropentanesulfonic acid), PFOA (Perfluorooctanoic acid), PFO3OA (Perfluoro-3,5,7-trioxaoctanoic acid), PFO2HxA (Perfluoro(3,5-dioxahexanoic) acid), PFO4DA (Perfluoro-3,5,7,9-butaoxododecanoic acid), PFO3DA (Perfluoro-3,5,7,9-pentaoxadodecanoic acid), PFO4DoA (TAFNA) (Perfluoro-3,5,7,9,11-pentaaxadodecanoic acid), PFECFS (Perfluoroethylcyclohexene Sulfonate), PFDOdS (Perfluorododecanesulfonic acid), PEPA (perfluoro-2-ethoxypentanoic acid), PFPhxDa (Perfluorohexadecanoic acid).

NVHOS (1,1,2,2-tetrafluoro-2-(1,2,2,2-tetrafluoro-ethoxy)ethane sulfonic acid), Nafion Byproduct 1 (Perfluoro-3,6-dioxo-4-methyl-7-octenesulfonic acid), Hydro-EVE Acid (2,2,3,3-Tetrafluoro-3-([1,1,1,2,3,3-hexafluoro-3-(1,2,2,2-tetrafluoroethoxy)propan-2-yl]oxy)propanoic acid), FPhXSA (perfluorohexane sulfonamide), FBBSA (perfluorobutane sulfonamide).

FASA (perfluoroalkane sulfonamide), ADONA (trade name for 4,8-dioxa-3H-perfluorononanoate), 9Cl-F53B (9-Chloroheicafluoro-3-oxaundecane-1-sulfonic acid), 8Cl-PFOS (Sodium 8-chloroperfluoro-1-octanesulfonate), 8:2 FTCA (8:2 fluorotelomer carboxylic acid), 8:2 DiPAP (8:2 fluorotelomer phosphate diester), 6:6 PFPIA (6:6 perfluorophosphinic acid), 6:2 FTCA (6:2 fluorotelomer carboxylic acid), 6:2 Cl-PFESA (6:2 chlorinated polyfluorinated ether sulfonate), 5:3 FTCA (5:3 fluorotelomer carboxylic acid), 11Cl-F53B (11-Chloroheicafluoro-3-oxaundecane-1-sulfonic acid), 10:2 FTS (10:2 fluorotelomer sulfonate), 10:2 FTCA (10:2 fluorotelomer carboxylic acid).

to PFHxS increased parasite infections in different species of frogs (Brown et al., 2021; Lech et al., 2022). The inability to heal from injury or increased susceptibility to disease may impact both individual survival and overall population of a species.

#### 4.2. Nervous system

Several PFAS have been detected in the brains of laboratory animals, humans, as well as environmentally exposed wild animal populations (Foguth et al., 2020; Shang et al., 2023). While the extent of known PFAS impacts on the human nervous system are somewhat limited, evidence from laboratory animal studies, especially for exposures during development and early life, suggest that PFAS, particularly PFOA and PFOS, can harm the nervous system, causing changes in motor activity and function, and impaired learning and memory (Starnes et al., 2022). In wild bank voles caught in a PFAS-contaminated ski area in Norway, higher PFAS concentrations were associated with higher dopamine levels in the brain compared to voles caught from a reference site (Gronnestad et al., 2021a). The study authors exposed mice in the lab to a mixture of PFAS based on the concentrations at the contaminated site and found disruption of dopamine homeostasis (Gronnestad et al., 2021b). In another study, environmental exposure to PFAS in crustaceans (crayfish) and fish (bluegills) was associated with altered behavioral outcomes, including decreased foraging for crayfish, and altered swim speeds in fish (Coy et al., 2022).

#### 4.3. Endocrine system

Studies suggest that PFAS disrupt levels of thyroid hormones in the body in both humans (Kim et al., 2018) and other species with thyroid-dependent development, like amphibians (Flynn et al., 2022). Additionally, PFAS have been implicated in altering circulating levels of reproductive hormones at different life stages in humans and laboratory animals and endocrine-mediated diseases, effects that may be related to the ability of PFAS to bind directly with sex steroid nuclear hormone receptors (Mokra, 2021). In wild bank voles from a contaminated ski area, some associations were observed between PFAS concentrations and lower testosterone in muscle tissue (Gronnestad et al., 2021b). In a study of hooded seal mothers exposed to complex contaminant mixtures, PFAS contributed to hormone disruption and were the most important predictor of thyroid hormone levels (Gronnestad et al., 2018). Levels of perfluoroalkyl carboxylic acids (PFCAs) and perfluorosulfonic acids (PFSAs) in brain tissue were associated with increased levels of steroid hormones in the brains of polar bears studied in Greenland (Pedersen et al., 2016). Prolonged periods of exposure to elevated levels of steroid hormones could adversely affect reproduction rates and fetal development.

#### 4.4. Reproduction and developmental

In human studies, PFAS impacts on reproduction and development include preeclampsia, low birth weight, altered breastfeeding duration, reduced fertility among others (Blake and Fenton, 2020; Rickard et al., 2022). For wildlife species, reproductive success is critical, especially for a species population that is threatened or endangered. PFAS exposure, happening at the same time with other anthropogenic pressures, may be contributing to decreased reproduction success in wildlife. In hawksbill sea turtles, a critically endangered species, emergent success was negatively correlated with levels of perfluoroundecanoic acid (PFUnDA) and perfluorotridecanoic acid (PFTrDA) in eggs (Wood et al., 2021). Maternal transfer of PFAS to eggs has been observed in both freshwater and sea turtles (Beale et al., 2022; Wood et al., 2021). A negative association with PFOS in tree swallow eggs and hatching success was observed along with total nest failure in nests with eggs that had PFOS concentrations at or above 150 ng/g (Custer et al., 2014). In contrast, a subsequent study by the same team observed no effects of PFAS exposure

on reproduction in tree swallows at another field study site (Custer et al., 2019). It is important to acknowledge that not all published studies detect and report a consistent association of individual PFAS exposures and distinct, measurable adverse outcomes. This diversity of findings could be due to a variety of factors in the population at the site of study, such as site-specific mixtures of PFAS, or the presence of co-occurring contaminants causing or contributing to overall population health effects (Custer, 2021).

#### 4.5. Impacts on metabolism, including liver function and oxidative stress

Blood serum biomarkers can be useful tools indicative of immune and reproductive functions as well as the overall health of populations in wild species where other types of health parameters may be difficult to study. Elevated levels of PFOS were associated with increased activity of blood serum biomarkers indicative of adverse impacts to the liver and immune system in striped bass from the Cape Fear River (North Carolina, United States) (Guillette et al., 2020). In Arctic black-legged kittiwakes, analysis of blood serum biomarkers indicated higher protein oxidative damage and lower plasma antioxidants in birds with higher levels of longer chain PFAS (Costantini et al., 2019). Additionally, freshwater turtle eggs exposed to PFAS contained significantly elevated levels of purine metabolites which may alter eggshell structure and egg physiology and were depleted of lipids needed for growth and development. Overall, higher PFAS exposure may affect egg development and the health of the turtle hatchlings. Analysis of the eggshells showed lower levels of essential calcium and higher levels of lipids and metabolites indicative of weakened physical structure (Beale et al., 2022). In field studies in black spotted frogs, associations were found with PFOS, PFOA and 6:2 Cl-PFESA and lipid metabolism-related indices suggesting that PFAS exposure may disrupt lipid metabolism in frogs collected from a contaminated industrial site (Lin et al., 2022). While changes in lipid metabolism, endocrine system, and immune defense may not be immediately lethal to an individual animal's health, these changes in biomarkers indicate significant alterations in hepatic, endocrine and immune systems, with a potential to contribute to overall population decline (Shi et al., 2023).

### 5. Shared health concept

There is strong concordance between adverse health effects observed in epidemiological research in humans and in wildlife studies in association with PFAS exposure (Fig. 1), supporting an argument that humans can be regarded as a unique sentinel species for the identification of the potential health harms from PFAS to other species. Distinctly, the amount of data available from epidemiological studies as well as humans' large population, geographic spread, and widespread health monitoring make *Homo sapiens* potentially a true global sentinel for the impacts of toxic chemicals on biological organisms. Future research will provide more information on the species differences in sensitivity to individual PFAS and to the overall load of combined exposure to PFAS as a class. Meanwhile, just as wild or domesticated animals have been both regarded and used as early warning sentinels for the impacts of toxic chemicals, humans can also serve in this role, especially for PFAS health harms to other animals, since similar levels of PFAS have been measured, for example, in seals, dolphins, dogs, horses, alligators and humans.

We posit that the mobility of humans does not preclude their potential as a sentinel species. Of note, epidemiological studies that can provide valuable information for cross-species extrapolation about PFAS effects between species were conducted for populations that have stayed in their local area for a long time, such as the C8 health study (Frisbee et al., 2009), the Faroes island study of PFAS effects on the vaccine response (Grandjean et al., 2012), and worker health studies (Olsen et al., 2003). Further, in general population exposures, published data suggest that a significant portion of overall PFAS exposure is due to local

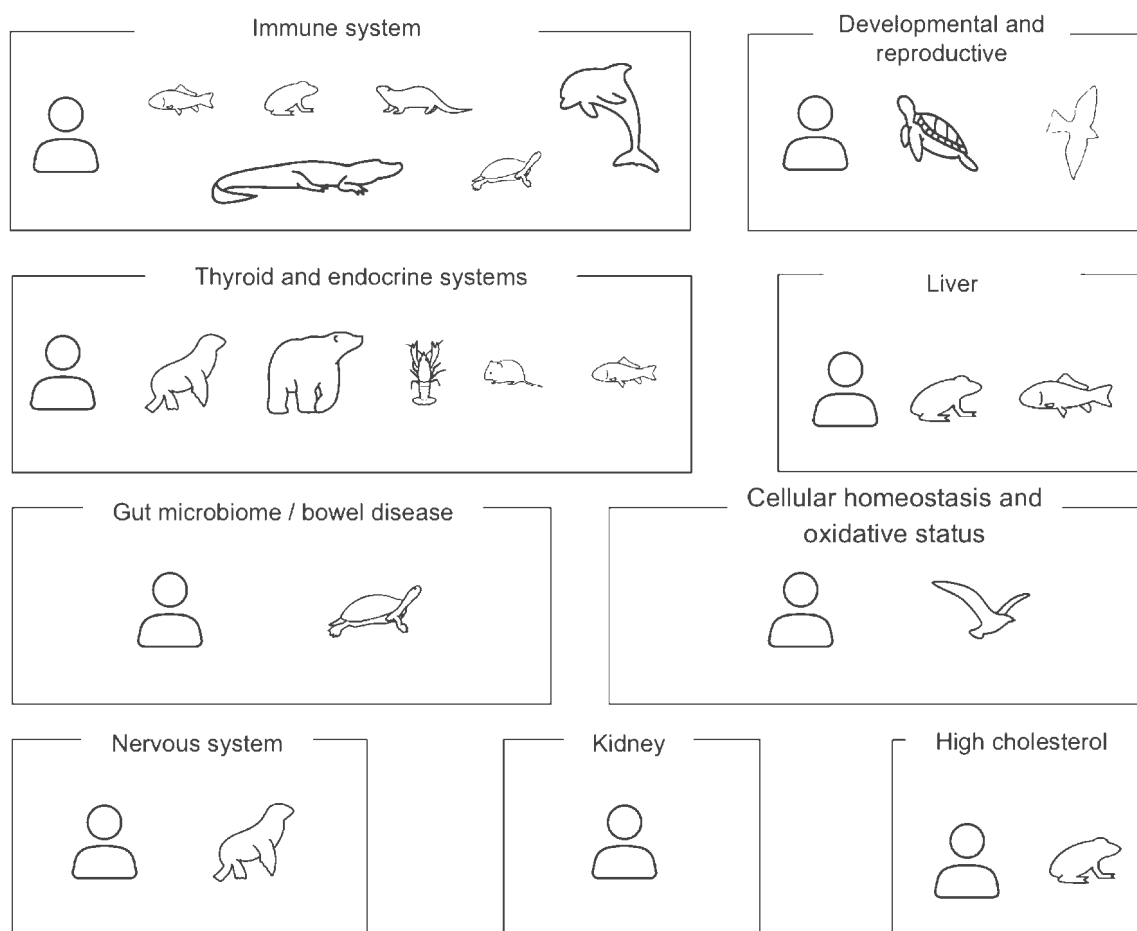


**Fig. 1.** Adverse health effects on organ systems and biomarkers observed in association with PFAS exposure in epidemiological research and wildlife studies. Individual wildlife study references are included in Table 1. Immune system: *Homo sapiens*, Striped bass (*Morone saxatilis*), American alligator (*Alligator mississippiensis*), Black spotted frog (*Rana nigromaculata*), Southern sea otter (*Enhydra lutris nereis*), Freshwater turtle (*Emydura macquarii macquarii*), Bottlenose dolphin (*Tursiops truncatus*). Developmental and reproductive system: *Homo sapiens*, Hawksbill turtle (*Eretmochelys imbricata*), Tree swallows (*Tachycineta bicolor*). Nervous and endocrine systems: *Homo sapiens*, Crayfish (*Faxonius immunis*), Bluegill (*Lepomis macrochirus*), Hooded seals (*Cystophora cristata*), Polar bear (*Ursus maritimus*), Bank voles (*Myodes glareolus*). Liver: *Homo sapiens*, Black spotted frog (*Rana nigromaculata*), Striped bass (*Morone saxatilis*). Gut microbiome/bowel disease: *Homo sapiens*, Freshwater turtle (*Emydura macquarii macquarii*). Cellular homeostasis and oxidative stress: *Homo sapiens*, Arctic black-legged kittiwakes (*Rissa tridactyla*). Thyroid: *Homo sapiens*, Hooded seals (*Cystophora cristata*). Kidney: *Homo sapiens*. High cholesterol: *Homo sapiens*, Black spotted frog (*Rana nigromaculata*).

exposures, through dietary patterns and locally contaminated drinking water supplies (Sunderland et al., 2019). Migratory species of birds, large mammals and reptiles such as aquatic marine turtles can carry out annual journeys of distance, difficulty and diversity of geographic areas that may be well out of range for most humans on the planet. Finally, and irrespectively of whether a “sentinel” or “comparison” populations are localized or mobile, the atmospheric transport of PFAS and global contamination have put all species and populations at risk of PFAS exposures.

Conceptualizing humans as a sentinel species for other animals is supported by the One Environmental Health approach that views human health, wildlife health and ecosystem health as one (Perez et al., 2018). Given the extent of global PFAS contamination (Cousins et al., 2022) and the ubiquitous PFAS exposure of nearly all biota on the planet, this interconnected approach is needed to understand and confront the universal threat to human health and to global biodiversity from PFAS exposure. Further, a translation of the concept “humans as sentinels” to environmental risk assessment points to the value of using human data where available to aid the development of policy measures for protecting wildlife populations.

Examples of the cross-species extrapolation approach comparing human and wildlife health data already exist in the literature. Some of

the highest levels of PFAS reported globally in marine mammals have been measured in bottlenose dolphins from the Charleston, South Carolina (U.S.) urban coast and have been compared to levels in humans that have been exposed occupationally (Fair et al., 2010; Fair et al., 2012). Levels of PFOS ranged from 49 ng/g in plasma from dolphins in Bermuda to 1171 ng/g in dolphins near Charleston, South Carolina from a 2005 study (Houde et al., 2005). Mean PFOS levels in serum in workers at a 3 M facility were reported to be 1.32 ppm, equivalent to 1320 ng/g (Olsen et al., 2003). Comparing human exposure with exposure for bottlenose dolphins may be useful because of dolphin's longevity, top-predator status and high site fidelity in an urban area (Fair et al., 2019). Published studies linked immune system dysregulation in dolphins with exposure to PFOS (De Guise et al., 2019; Fair et al., 2014; Soloff et al., 2017). Nevertheless, a substantial gap in data availability is evident when comparing the number of health studies conducted on wild animal populations to studies in humans. Given the availability of hundreds of studies in humans, epidemiological data could serve as the basis for conservation risk assessments and the development of conservation policies for other mammals or species where such data are lacking.

Available data suggest that the adverse health effects observed in humans due to PFAS exposure are relevant and applicable to all animal

species generally, and across the globe. The health impacts documented in wildlife, as detailed in Table 1, are similar to adverse health endpoints with likely causal associations to PFAS exposure in humans (Agency for Toxic Substances and Disease Registry (ATSDR), 2021) (EPA 2023B). Further, the graphical representations in Fig. 1 and Fig. 2 highlight both reported and anticipated health effects due to PFAS exposure in wildlife and correlate the measured PFAS levels in the blood of wildlife from the studies in Table 1 with the PFAS levels in humans that have documented health impacts.

While the concordance in types of health impacts observed in humans and other species point to the value of cross-species

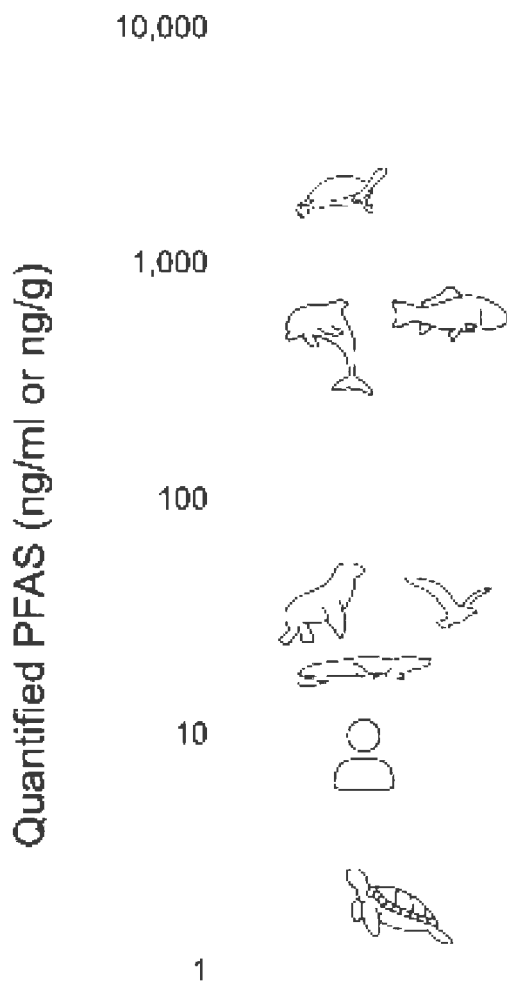


**Fig. 2.** Concentration of PFAS in animals in studies documenting health impacts from exposures, as detailed in Table 1, compared to the median levels in the U.S. population for 2017–2018. PFAS concentrations are cited according to how they were reported in original references. From lowest to highest: Hawksbill turtle (*Eretmochelys imbricata*, 1.74 ng/g median PFAS in plasma with a median of 31 ng/g in eggs), human (*Homo sapiens*, 16.7 ng/ml median PFOS in serum), American alligator (*Alligator mississippiensis*, 18.6 ng/ml median total PFAS in serum), Arctic black-legged kittiwakes (*Rissa tridactyla*, 39.9 ng/g mean PFAS in plasma), Hooded seals (*Cystophora cristata*, 40 ng/g median PFOS in plasma), Striped bass (*Morone saxatilis*, 551 ng/ml median total PFAS in serum), Bottlenose dolphin (*Tursiops truncatus*, 571 ng/g median PFOS in plasma), Freshwater turtle (*Emydera macquarii macquarii*, 1992 ng/ml average total PFAS in plasma). Frequency of associations of different PFAS compounds with reported health effects in different studies is shown in Table 2, with most associations reported for PFOS.

extrapolation for this analysis, the uncertainties associated with dose-response curves for adverse effects in PFAS in different species remain a scientific challenge. In Fig. 2, the circulating concentrations of PFAS do not represent the probability of the frequency of occurrence of specific health effects. Rather, Fig. 2 documents the fact of global PFAS contamination in wildlife at levels that in many circumstances are vastly greater than concentrations shown in epidemiological studies to impact human health parameters. In parallel, Table 2 documents the co-occurrence of different PFAS compounds measured in wildlife health studies, pointing to the relevance and necessity of both assessing and mitigating against the adverse effects of PFAS mixtures.

For practical reasons, the number of studies linking specific health effects in wildlife with PFAS exposure remains limited. Nevertheless, the published literature clearly demonstrates that exposure to PFAS in the environment and elevated levels of PFAS in animals' bodies are associated with changes in key health parameters, such as hormonal levels, immune function, reproduction, and growth of the young, which have also been observed in controlled toxicological studies in laboratory animals as well as human epidemiological cohorts. Changes in these health indicators have significant relevance to individual animal's reproduction and survival and the overall health and stability of wildlife populations and ecosystems.

Available data do not allow a definitive assessment of whether humans are the most susceptible species to the toxic effects of PFAS exposure, or whether other species, including species shown in Fig. 1 and Fig. 2 have a more sensitive population-level dose-response relationship for PFAS. For a read-across or cross-species extrapolation approach, uncertainties remain in the context of exposure of life-histories across species that may vary drastically. Further, exposures may differ, especially for aquatic species that may be exposed simultaneously to numerous contaminants during developmental phases and throughout their life. Yet, given the dramatic and tragic rate of the disappearance of endangered species and shrinking of wildlife populations globally, all measures should be taken to consider pollution reduction as part of the essential framework for protecting threatened and endangered species, and a cross-species extrapolation approach holds, in our view, valuable potential for both research and policy.

It is important to acknowledge the difficulty of conducting wildlife health studies in general, especially in endangered species, as well as the appropriate ethical barriers and legal restrictions on conducting lethal sampling of wildlife. These practical considerations preclude a comprehensive assessment of the full scope of PFAS impacts on wild animals' health. Additionally, given the reality of global PFAS contamination of the environment and wildlife, identifying a true, uncontaminated reference population generally proves impossible, since even samples of animals collected from the geographic sites without known sources of industrial discharges still contain PFAS (Beale et al., 2022). All these factors make it especially urgent and timely to use a read-across or cross-species extrapolation approach so as to draw on all available data to assess potential damage to the ecosystems and specific animals due to PFAS contamination, and to develop and implement measures to prevent such damages.

Scholars and environmental advocates across the world are raising the alarm on the critical state of anthropogenic pollution and its effects on human health globally (Cousins et al., 2022; Groh et al., 2022). As emphasized in previous reports, the planetary boundary for chemical pollution has likely been crossed (Persson et al., 2022). Yet, with the human population continuing to grow, we can anticipate the continued increase of chemical manufacturing and with it, the potential for growing pollution levels in the environment. Given this reality, both regulation and minimization of environmental discharges of industrial chemicals are essential measures for protecting human and wildlife health as well as for wildlife and endangered species conservation on our planet. Protection of a sentinel species from a particular toxic chemical impact would begin the process to protect all species on the planet. In this process, it is especially important to consider the cyclical nature of

PFAS pollution (Stoiber et al., 2020), so as to ensure that remediation policies and practices do not end up shuffling the PFAS pollution load from one site to another. Systematic approaches to tackling the PFAS contamination crisis should be the focus to protect both humans and wildlife.

Summarizing our argument, we posit that the use of human data as a sentinel approach can serve as a foundation for ecological conservation policies that are urgently needed now. While PFAS exposures of humans may be conceptually similar to PFAS in large mammalian carnivorous species such as dolphins and polar bears, the similar health effects in different taxa are documented (Table 1, Fig. 1). Building on this concordance of recorded health effects, future research of the mechanistic basis for toxicological outcomes due to PFAS exposure can provide a framework for extrapolation across species as well as potential explanations of variability (Celander et al., 2011; LaLone et al., 2021). Finally, while human epidemiological data might not provide a full set of information relevant to the environmental impacts of PFAS contamination, this corpus of data is the most extensive dataset on a single species that is currently available and it can shed light on a wide variety of toxic effects elicited by PFAS.

## 6. Research needs

Contamination of living organisms around the globe with anthropogenic environmental pollutants, such as persistent organic pollutants or POPs, has been known for decades. Top predators in terrestrial and aquatic food webs often carry the heaviest body burden of such pollutants, even decades after regulatory action restricting the manufacturing of these persistent substances (Kean et al., 2021; Travis et al., 2020). In co-occurrence with chlorinated and brominated contaminants, PFAS have emerged as ubiquitous pollutants with planetary-wide impact (Cousins et al., 2022). Most species, including species included in the International Union for Conservation of Nature Red List, are exposed to the PFAS family of chemicals that, as human epidemiological evidence indicates, may compromise basic life functions critical to survival of individuals and populations: the ability to reproduce and to resist disease and injury.

Animals in the wild are exposed to PFAS through the water, air, soils and sediments, and the food chain. Those species also face habitat loss, over-harvesting and other anthropogenic threats to their survival. PFAS exposures are potentially most concerning for endangered and threatened species populations that are simultaneously exposed to a mix of toxic pollutants (Routti et al., 2019). With widespread wildlife exposure to mixtures of PFAS and other persistent organic pollutants, additional research on the health impacts of these chemical mixtures is urgently needed. The chemical concentrations of individual pollutants or pollutant mixtures varies in different geographic sites for both people and different wildlife species. It remains to be investigated what might be potential limits on the concordance of adverse health effects of exposure to similar pollutants in humans and in wildlife species. Further studies on characterizing the exposure, dose-response relationship, and toxicological outcomes in various species remain necessary. Yet, such data limitations should not preclude prompt, coherent and comprehensive action on protecting the wildlife species populations that still remain on this planet. A consideration of humans as sentinel species is a promising approach that would be refined with the generation and dissemination of new research studies.

Additional research needs to apply the question of chemical pollutant impacts on population dynamics and trends in population health, which is an under-investigated topic to date. For example, the documented detrimental effects of PFAS exposure on the immune system can make species susceptible to other stressors. Additionally, large aquatic animals that suffer injuries from plastic pollution could potentially face reduced resistance to infections due to their body burden of PFAS. Together, the cumulative pressures of chemical exposures, habitat loss and climate change may act jointly, exacerbating the loss of

biodiversity. As habitat loss increases, species are increasingly living closer and closer to human populations (Simkin et al., 2022). The density of the human population has been observed to correlate with the levels of PFAS measured in wildlife living in close proximity (Guillette et al., 2022; Wood et al., 2021), indicating both elevated PFAS exposure and degraded habitat quality. As documented by numerous studies, the current loss of species and the rate of species loss is unprecedented (IPBES, 2019; Isbell et al., 2022) and understanding the role of chemical exposures in this global extinction will be critical for attempting to conserve biodiversity (Mueller et al., 2023).

We hope that future research will also focus on developing models to characterize specific adverse health effects such as reproductive harm in wildlife, thus facilitating environmental health assessments while avoiding any lethal sampling of wildlife populations (Finn et al., 2023). We look forward to the greater acceptance of the importance of biomarker effects in ecotoxicology studies and the application of the toxicological read-across and cross-species extrapolation concepts for developing effective policies for species conservation. Positively, recent emphasis on reducing animal testing and efforts to focus on cross-species extrapolation and new approach methodologies to leverage existing toxicity data (LaLone et al., 2021) may help to protect all species. These efforts align with the One Health approach and point out the connectedness of all species that share the planetary environment. Methods that focus on examining molecular, cellular and organ-level changes can be more predictive compared to whole-organism endpoints, which reduces animal testing and broadens the possibilities for extrapolating toxicological data across a variety of species.

## 7. Recommendations

Analysis presented in this article supports the call for an integrated government and society approach to reduce threats to biodiversity due to PFAS pollution and for urgent actions to advance species conservation that should be initiated immediately:

1. Biodiversity conservation policymakers need to consider chemical pollution reduction as part of the essential framework for protecting threatened and endangered species.
2. In situations where a direct wildlife health study may be impractical or not appropriate due to endangered species status, a read-across and cross-species extrapolation approach incorporating all available data sets can aid policy measures to protect wildlife populations anthropogenic contaminants.
3. Where available, human epidemiological studies should be included as one of the sources of reference data for developing policies for species conservation. The epidemiological dataset for PFAS presents a compelling case study for such an approach.
4. International measures controlling PFAS pollution and preventing future discharges of PFAS into the environment are essential for protecting both human health and global biodiversity.
5. Protection of wildlife populations from PFAS pollution has the potential to contribute to ecosystem stability and sustainable development goals connected with ecosystem functions and services.
6. Industrial chemical registrations and approvals should be developed and implemented to prevent adverse impacts of PFAS on critical habitats, wildlife populations, and endangered species, by ending ongoing releases to the environment and capturing PFAS in discharges from manufacturing plants, wastewater treatment plants, landfills, and other types of commercial and residential PFAS discharges.
7. More research is needed to develop technologies for assessing and remediating PFAS contamination in the environment and for the cleanup of contaminated sites.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

No data was used for the research described in the article.

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## References

- 3M, 2000. Laboratory Composite Report: Analytical Reports of Data for Fluorochemical Analysis in Human Sera. U.S. EPA Administrative Record AR226-0178.
- Acosta-Tlapalamat, M., Romo-Gomez, C., Anaya-Hernandez, A., Juarez-Santacruz, L., Gaytan-Oyarzun, J.C., Acevedo-Sandoval, O.A., et al., 2022. Metabolomics: a new approach in the evaluation of effects in human beings and wildlife associated with environmental exposition to POPs. *Toxics* 10.
- Agency for Toxic Substances and Disease Registry (ATSDR), 2021. Toxicological Profile for Perfluoroalkyls. US Department of Health and Human Services.
- Arzuaga, X., Smith, M.T., Gibbons, C.F., Skakkebaek, N.E., Yost, E.E., Beverly, B.E.J., et al., 2019. Proposed key characteristics of male reproductive toxicants as an approach for organizing and evaluating mechanistic evidence in human health Hazard assessments. *Environ. Health Perspect.* 127, 65001.
- Barbo, N., Stoiber, T., Naidenko, O.V., Andrews, D.Q., 2023. Locally caught freshwater fish across the United States are likely a significant source of exposure to PFOS and other perfluorinated compounds. *Environ. Res.* 220, 115165.
- Barrett, H., Du, X., Houde, M., Lair, S., Verreault, J., Peng, H., 2021. Suspect and nontarget screening revealed class-specific temporal trends (2000-2017) of poly- and Perfluoroalkyl substances in St. Lawrence Beluga Whales. *Environ. Sci. Technol.* 55, 1659–1671.
- Beale, D.J., Nilsson, S., Bose, U., Bourne, N., Stockwell, S., Broadbent, J.A., et al., 2022. Bioaccumulation and impact of maternal PFAS offloading on egg biochemistry from wild-caught freshwater turtles (*Emydera macquarii macquarii*). *Sci. Total Environ.* 817, 153019.
- Beasley, V., 2009. One toxicology, 'ecosystem health' and 'one health. *Vet. Ital.* 45, 97–110.
- Beaulieu, M., Costantini, D., 2014. Biomarkers of oxidative status: missing tools in conservation physiology. *Conserv. Physiol.* 2, cou014.
- Bedia, C., 2022. Metabolomics in environmental toxicology: applications and challenges. *Trends Environ. Anal. Chem.* 34.
- Blake, B.E., Fenton, S.E., 2020. Early life exposure to per- and polyfluoroalkyl substances (PFAS) and latent health outcomes: a review including the placenta as a target tissue and possible driver of peri- and postnatal effects. *Toxicology* 443, 152565.
- Boisvert, G., Sonne, C., Riget, F.F., Dietz, R., Letcher, R.J., 2019. Bioaccumulation and biomagnification of perfluoroalkyl acids and precursors in East Greenland polar bears and their ringed seal prey. *Environ. Pollut.* 252, 1335–1343.
- Bowerman, W.W., Roe, A.S., Gilbertson, M.J., Best, D.A., Sikarskie, J.G., Mitchell, R.S., et al., 2002. Using bald eagles to indicate the health of the Great Lakes' environment. *Lakes Reserv. Sci. Polic. Manage. Sustain. Use* 7, 183–187.
- Brown, S.R., Flynn, R.W., Hoverman, J.T., 2021. Perfluoroalkyl substances increase susceptibility of northern leopard frog tadpoles to trematode infection. *Environ. Toxicol. Chem.* 40, 689–694.
- Budtz-Jorgensen, E., Grandjean, P., 2018. Application of benchmark analysis for mixed contaminant exposures: mutual adjustment of perfluoroalkylate substances associated with immunotoxicity. *PLoS One* 13, e0205388.
- Butt, C.M., Berger, U., Bossi, R., Tomy, G.T., 2010. Levels and trends of poly- and perfluorinated compounds in the arctic environment. *Sci. Total Environ.* 408, 2936–2965.
- Celander, M.C., Goldstone, J.V., Denslow, N.D., Iguchi, T., Kille, P., Meyerhoff, R.D., et al., 2011. Species extrapolation for the 21st century. *Environ. Toxicol. Chem.* 30, 52–63.
- Convention on Biological Diversity. Kunming-Montreal Global biodiversity framework. 2022.
- Costantini, D., Blevin, P., Herzke, D., Moe, B., Gabrielsen, G.W., Bustnes, J.O., et al., 2019. Higher plasma oxidative damage and lower plasma antioxidant defences in an Arctic seabird exposed to longer perfluoroalkyl acids. *Environ. Res.* 168, 278–285.
- Cousins, I.T., Johansson, J.H., Salter, M.E., Sha, B., Scheringer, M., 2022. Outside the safe operating space of a new planetary boundary for per- and Polyfluoroalkyl substances (PFAS). *Environ. Sci. Technol.* 56, 11172–11179.
- Coy, C.O., Steele, A.N., Abdullelah, S.A., Belanger, R.M., Crile, K.G., Stevenson, L.M., et al., 2022. Differing behavioral changes in crayfish and bluegill under short- and long-chain PFAS exposures: field study in northern Michigan, USA. *Ecotoxicol. Environ. Saf.* 247, 114212.
- Custer, C.M., 2021. Linking field and laboratory studies: reproductive effects of perfluorinated substances on avian populations. *Integr. Environ. Assess. Manag.* 17, 690–696.
- Custer, C.M., Custer, T.W., Dummer, P.M., Etterson, M.A., Thogmartin, W.E., Wu, Q., et al., 2014. Exposure and effects of perfluoroalkyl substances in tree swallows nesting in Minnesota and Wisconsin, USA. *Arch. Environ. Contam. Toxicol.* 66, 120–138.
- Custer, C.M., Custer, T.W., Delaney, R., Dummer, P.M., Schultz, S., Karouna-Renier, N., 2019. Perfluoroalkyl contaminant exposure and effects in tree swallows nesting at Clarks marsh, Oscoda, Michigan, USA. *Arch. Environ. Contam. Toxicol.* 77, 1–13.
- De Guise, S., Levin, M., Jasperse, L., Risatti, G., Wells, R.S., 2019. T helper cell subsets and their functions in common bottlenose dolphins (*Tursiops truncatus*). *Front. Immunol.* 10, 1578.
- De Silva, A.O., Armitage, J.M., Bruton, T.A., Dassuncao, C., Heiger-Bernays, W., Hu, X.C., et al., 2021. PFAS exposure pathways for humans and wildlife: a synthesis of current knowledge and key gaps in understanding. *Environ. Toxicol. Chem.* 40, 631–657.
- Destoumieux-Garzon, D., Mavingui, P., Boetsch, G., Boissier, J., Darriet, F., Duboz, P., et al., 2018. The one health concept: 10 years old and a long road ahead. *Front. Vet. Sci.* 5, 14.
- European Food Safety Authority. Risk to human health related to the presence of perfluoroalkyl substances in food. 18(9):6223. 2020.
- Evich, M.G., Davis, M.J.B., McCord, J.P., Acrey, B., Awkerman, J.A., Knappe, D.R.U., et al., 2022. Per- and polyfluoroalkyl substances in the environment. *Science* 375, eabg9065.
- Fair, P.A., Adams, J., Mitchum, G., Hulsey, T.C., Reif, J.S., Houde, M., et al., 2010. Contaminant blubber burdens in Atlantic bottlenose dolphins (*Tursiops truncatus*) from two southeastern US estuarine areas: concentrations and patterns of PCBs, pesticides, PBDEs, PFCs, and PAHs. *Sci. Total Environ.* 408, 1577–1597.
- Fair, P.A., Houde, M., Hulsey, T.C., Bossart, G.D., Adams, J., Balthis, L., et al., 2012. Assessment of perfluorinated compounds (PFCs) in plasma of bottlenose dolphins from two southeast US estuarine areas: relationship with age, sex and geographic locations. *Mar. Pollut. Bull.* 64, 66–74.
- Fair, P.A., Schaefer, A.M., Romano, T.A., Bossart, G.D., Lamb, S.V., Reif, J.S., 2014. Stress response of wild bottlenose dolphins (*Tursiops truncatus*) during capture-release health assessment studies. *Gen. Comp. Endocrinol.* 206, 203–212.
- Fair, P.A., Wolf, B., White, N.D., Arnott, S.A., Kannan, K., Karthikraj, R., et al., 2019. Perfluoroalkyl substances (PFASs) in edible fish species from Charleston Harbor and tributaries, South Carolina, United States: exposure and risk assessment. *Environ. Res.* 171, 266–277.
- Fenton, S.E., Ducatman, A., Boobis, A., DeWitt, J.C., Lau, C., Ng, C., et al., 2021. Per- and polyfluoroalkyl substance toxicity and human health review: current state of knowledge and strategies for informing future research. *Environ. Toxicol. Chem.* 40, 606–630.
- Finn, C., Grattarola, F., Pincheira-Donoso, D., 2023. More losers than winners: investigating Anthropocene defaunation through the diversity of population trends. *Biol. Rev. Camb. Philos. Soc.*
- Flynn, R.W., Hoover, G., Iacchetta, M., Guffey, S., de Perre, C., Huerta, B., et al., 2022. Comparative toxicity of aquatic per- and polyfluoroalkyl substance exposure in three species of amphibians. *Environ. Toxicol. Chem.* 41, 1407–1415.
- Foguth, R., Sepulveda, M.S., Cannon, J., 2020. Per- and Polyfluoroalkyl substances (PFAS) neurotoxicity in sentinel and non-traditional laboratory model systems: potential utility in predicting adverse outcomes in human health. *Toxics* 8.
- Frisbee, S.J., Brooks Jr., A.P., Maher, A., Flensburg, P., Arnold, S., Fletcher, T., et al., 2009. The C8 health project: design, methods, and participants. *Environ. Health Perspect.* 117, 1873–1882.
- Germolec, D.R., Lebre, H., Anderson, S.E., Burleson, G.R., Cardenas, A., Corsini, E., et al., 2022. Consensus on the key characteristics of immunotoxic agents as a basis for hazard identification. *Environ. Health Perspect.* 130, 105001.
- Giesy, J.P., Kannan, K., 2001. Global distribution of perfluorooctane sulfonate in wildlife. *Environ. Sci. Technol.* 35, 1339–1342.
- Goodrich, J.A., Walker, D.L., He, J., Lin, X., Baumert, B.O., Hu, X., et al., 2023. Metabolic signatures of youth exposure to mixtures of per- and Polyfluoroalkyl substances: a multi-cohort study. *Environ. Health Perspect.* 131, 27005.
- Grandjean, P., Andersen, E.W., Budtz-Jorgensen, E., Nielsen, F., Molbak, K., Weihe, P., et al., 2012. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. *JAMA* 307, 391–397.
- Groh, K., Vom Berg, C., Schirmer, K., Tili, A., 2022. Anthropogenic chemicals as underestimated drivers of biodiversity loss: scientific and societal implications. *Environ. Sci. Technol.* 56, 707–710.
- Gronnestad, R., Villanger, G.D., Polder, A., Kovacs, K.M., Lydersen, C., Jenssen, B.M., et al., 2018. Effects of a complex contaminant mixture on thyroid hormones in breeding hooded seal mothers and their pups. *Environ. Pollut.* 240, 10–16.
- Gronnestad, R., Johanson, S.M., Muller, M.H.B., Schlenk, D., Tanabe, P., Krokje, A., et al., 2021a. Effects of an environmentally relevant PFAS mixture on dopamine and steroid hormone levels in exposed mice. *Toxicol. Appl. Pharmacol.* 428, 115670.

- Gronnestad, R., Schlenk, D., Krokje, A., Jaspers, V.L.B., Jenssen, B.M., Coffin, S., et al., 2021b. Alteration of neuro-dopamine and steroid hormone homeostasis in wild Bank voles in relation to tissue concentrations of PFAS at a Nordic skiing area. *Sci. Total Environ.* 756, 143745.
- Guillette, T.C., McCord, J., Guillette, M., Polera, M.E., Rachels, K.T., Morgeson, C., et al., 2020. Elevated levels of per- and polyfluoroalkyl substances in cape fear river striped bass (*Morone saxatilis*) are associated with biomarkers of altered immune and liver function. *Environ. Int.* 136, 105358.
- Guillette, T.C., Jackson, T.W., Guillette, M., McCord, J., Belcher, S.M., 2022. Blood concentrations of per- and polyfluoroalkyl substances are associated with autoimmune-like effects in American alligators from Wilmington, North Carolina. *Front. Toxicol.* 4, 1010185.
- Houde, M., Wells, R.S., Fair, P.A., Bossart, G.D., Hohn, A.A., Rowles, T.K., et al., 2005. Polyfluoroalkyl compounds in free-ranging bottlenose dolphins (*Tursiops truncatus*) from the Gulf of Mexico and the Atlantic Ocean. *Environ. Sci. Technol.* 39, 6591–6598.
- IPBES, 2019. In: Brondizio, E.S., Settle, J., Díaz, S., Ngo, H.T. (Eds.), *Global Assessment Report on Biodiversity and Ecosystem Services of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services*. IPBES secretariat, Bonn, Germany. <https://doi.org/10.5281/zenodo.3831673>, 1148 pages.
- Isbell, F., Balvanera, P., Mori, A.S., He, J.S., Bullock, J.M., Regmi, G.R., et al., 2022. Expert perspectives on global biodiversity loss and its drivers and impacts on people. *Front. Ecol. Environ.* 21, 94–103.
- Ishibashi, H., Iwata, H., Kim, E.Y., Tao, L., Kannan, K., Tanabe, S., et al., 2008. Contamination and effects of perfluorinated chemicals in Baikal seal (*Pusa sibirica*). 2. Molecular characterization, expression level, and transcriptional activation of peroxisome proliferator-activated receptor alpha. *Environ. Sci. Technol.* 42, 2302–2308.
- Kannan, K., Perrotta, E., Thomas, N.J., 2006. Association between perfluorinated compounds and pathological conditions in southern sea otters. *Environ. Sci. Technol.* 40, 4943–4948.
- Kean, E.F., Shore, R.F., Scholey, G., Strachan, R., Chadwick, E.A., 2021. Persistent pollutants exceed toxic thresholds in a freshwater top predator decades after legislative control. *Environ. Pollut.* 272, 116415.
- Kim, M.J., Moon, S., Oh, B.C., Jung, D., Ji, K., Choi, K., et al., 2018. Association between perfluoroalkyl substances exposure and thyroid function in adults: a meta-analysis. *PLoS One* 13, e0197244.
- Kwiatkowski, C.F., Andrews, D.Q., Birnbaum, L.S., Bruton, T.A., DeWitt, J.C., Knappe, D. R.U., Maffini, M.V., Miller, M.F., Pelch, K.E., Reade, A., Soehl, A., Trier, X., Venier, M., Wagner, C.C., Wang, Z., Blum, A., 2020. Scientific basis for managing PFAS as a chemical class. *Environ. Sci. Technol. Lett.* 7, 532–543. <https://doi.org/10.1021/acs.estlett.0c00255>.
- La Merrill, M.A., Vandenberg, L.N., Smith, M.T., Goodson, W., Browne, P., Patisaul, H.B., et al., 2020. Consensus on the key characteristics of endocrine-disrupting chemicals as a basis for hazard identification. *Nat. Rev. Endocrinol.* 16, 45–57.
- LaLone, C.A., Basu, N., Browne, P., Edwards, S.W., Embry, M., Sewell, F., et al., 2021. International consortium to advance cross-species extrapolation of the effects of chemicals in regulatory toxicology. *Environ. Toxicol. Chem.* 40, 3226–3233.
- Lech, M.E., Choi, Y.J., Lee, L.S., Sepulveda, M.S., Hoverman, J.T., 2022. Effects of per- and Polyfluoroalkyl substance mixtures on the susceptibility of larval American bullfrogs to parasites. *Environ. Sci. Technol.* 56, 15953–15959.
- Lin, H., Liu, Z., Yang, H., Lu, L., Chen, R., Zhang, X., et al., 2022. Per- and Polyfluoroalkyl substances (PFASs) impair lipid metabolism in *Rana nigromaculata*: a field investigation and laboratory study. *Environ. Sci. Technol.* 56, 13222–13232.
- Lind, L., Araujo, J.A., Barchowsky, A., Belcher, S., Berridge, B.R., Chiamvimonvat, N., et al., 2021. Key characteristics of cardiovascular toxicants. *Environ. Health Perspect.* 129, 95001.
- Loring, P.A., Hinzman, M.S., Neufeld, H., Favaro, B., 2017. Can people be sentinels of sustainability? Identifying the linkages among ecosystem health and human well-being. *Facets* 1, 148–162.
- McDonough, C.A., Guelfo, J.L., Higgins, C.P., 2019. Measuring total PFASs in water: the tradeoff between selectivity and inclusivity. *Curr. Opin. Environ. Sci. Health* 7, 13–18.
- Miner, K.R., Clifford, H., Taruscio, T., Potocki, M., Solomon, G., Ritari, M., et al., 2021. Deposition of PFAS ‘forever chemicals’ on Mt. Everest. *Sci. Total Environ.* 759, 144421.
- Mokra, K., 2021. Endocrine disruptor potential of short- and long-chain Perfluoroalkyl substances (PFASs)-a synthesis of current knowledge with proposal of molecular mechanism. *Int. J. Mol. Sci.* 22.
- Mueller, L.K., Ågerstrand, M., Backhaus, T., Diamond, M., Erdelen, W.R., Evers, D., et al., 2023. Policy options to account for multiple chemical pollutants threatening biodiversity. *Environ. Sci. Adv.* 2, 151–161.
- Naidu, R., Biswas, B., Willett, I.R., Cribb, J., Kumar Singh, B., Paul Nathanail, C., et al., 2021. Chemical pollution: a growing peril and potential catastrophic risk to humanity. *Environ. Int.* 156, 106616.
- “National Academies of Sciences E, and Medicine”, *Guidance on PFAS Exposure, Testing, and Clinical Follow-Up*, 2022.
- Olsen, G.W., Burris, J.M., Burlew, M.M., Mandel, J.H., 2003. Epidemiologic assessment of worker serum perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) concentrations and medical surveillance examinations. *J. Occup. Environ. Med.* 45, 260–270.
- Pedersen, K.E., Letcher, R.J., Sonne, C., Dietz, R., Styrishave, B., 2016. Per- and polyfluoroalkyl substances (PFASs) - new endocrine disruptors in polar bears (*Ursus maritimus*)? *Environ. Int.* 96, 180–189.
- Pelch, K.E., Reade, A., Kwiatkowski, C.F., Merced-Nieves, F.M., Cavalier, H., Schultz, K., et al., 2022. The PFAS-Tox database: a systematic evidence map of health studies on 29 per- and polyfluoroalkyl substances. *Environ. Int.* 167, 107408.
- Perez A, Pierce Wise J, Sr. *One environmental health: an emerging perspective in toxicology*. F1000Res 2018; 7.
- Persson, L., Carney Almroth, B.M., Collins, C.D., Cornell, S., de Wit, C.A., Diamond, M.L., et al., 2022. Outside the safe operating space of the planetary boundary for novel entities. *Environ. Sci. Technol.* 56, 1510–1521.
- Rabinowitz, P.M., Odofin, L., Dein, F.J., 2008. From “us vs. them” to “shared risk”: can animals help link environmental factors to human health? *Ecohealth* 5, 224–229.
- Rabinowitz, P., Scotch, M., Conti, L., 2009. Human and animal sentinels for shared health risks. *Vet. Ital.* 45, 23–24.
- Rickard, B.P., Rizvi, I., Fenton, S.E., 2022. Per- and poly-fluoroalkyl substances (PFAS) and female reproductive outcomes: PFAS elimination, endocrine-mediated effects, and disease. *Toxicology* 465, 153031.
- Rillig, M.C., Ryo, M., Lehmann, A., 2021. Classifying human influences on terrestrial ecosystems. *Glob. Chang. Biol.* 27, 2273–2278.
- Rock, K.D., Polera, M.E., Guillette, T.C., Starnes, H.M., Dean, K., Watters, M., et al., 2023. Domestic dogs and horses as sentinels of per- and Polyfluoroalkyl substance exposure and associated health biomarkers in Gray’s creek North Carolina. *Environ. Sci. Technol.* 57, 9567–9579.
- Routti, H., Atwood, T.C., Bechshoft, T., Boltunov, A., Ciesielski, T.M., Desforges, J.P., et al., 2019. State of knowledge on current exposure, fate and potential health effects of contaminants in polar bears from the circumpolar Arctic. *Sci. Total Environ.* 664, 1063–1083.
- Rusyn, I., Arzuaga, X., Cattley, R.C., Corton, J.C., Ferguson, S.S., Godoy, P., et al., 2021. Key characteristics of human Hepatotoxicants as a basis for identification and characterization of the causes of liver toxicity. *Hepatology* 74, 3486–3496.
- Shang, J., Gao, K., Chi, B., Piao, Y., Ma, Q., Lu, L., et al., 2023. Automated and fast online method for simultaneously determining a broad spectrum of per- and polyfluoroalkyl substances in a small volume of cerebrospinal fluid. *Anal. Bioanal. Chem.* 415, 1221–1233.
- Shanmugam, V.K., Angra, D., Rahimi, H., McNish, S., 2017. Vasculitic and autoimmune wounds. *J. Vasc. Surg. Venous Lymphat. Disord.* 5, 280–292.
- Shi, C., Yang, H., Xu, M., Hua, T., He, M., Yang, Y., et al., 2023. PFOS induces Lipometabolism change, immune defense, and endocrine disorders in black-spotted frogs: application of transcriptome profiling. *Diversity* 15.
- Sigmund, G., Ågerstrand, M., Brodin, T., Diamond, M.L., Erdelen, W.R., Evers, D.C., et al., 2022. Broad chemicals scope in biodiversity targets. *Science* 376, 1280.
- Simkin, R.D., Seto, K.C., McDonald, R.I., Jetz, W., 2022. Biodiversity impacts and conservation implications of urban land expansion projected to 2050. *Proc. Natl. Acad. Sci. U. S. A.* 119, e2117297119.
- Smith, M.T., Guyton, K.Z., Kleinstreuer, N., Borrel, A., Cardenas, A., Chiu, W.A., et al., 2020. The key characteristics of carcinogens: relationship to the hallmarks of Cancer, relevant biomarkers, and assays to measure them. *Cancer Epidemiol. Biomark. Prev.* 29, 1887–1903.
- Solla, Srd, Weseloh, D.V.C., Hughes, K.D., Forty-Year, Moore D.J., 2016. Decline of Organic Contaminants in Eggs of Herring Gulls (*Larus argentatus*) from the Great Lakes, 1974 to 2013. *Waterbirds* (39), 166–179.
- Soloff, A.C., Wolf, B.J., White, N.D., Muir, D., Courtney, S., Hardiman, G., et al., 2017. Environmental perfluorooctane sulfonate exposure drives T cell activation in bottlenose dolphins. *J. Appl. Toxicol.* 37, 1108–1116.
- Spaan, K.M., van Noordenburg, C., Plassmann, M.M., Schultes, L., Shaw, S., Berger, M., et al., 2020. Fluorine mass balance and suspect screening in marine mammals from the northern hemisphere. *Environ. Sci. Technol.* 54, 4046–4058.
- Starnes, H.M., Rock, K.D., Jackson, T.W., Belcher, S.M., 2022. A critical review and Meta-analysis of impacts of per- and Polyfluorinated substances on the brain and behavior. *Front. Toxicol.* 4, 881584.
- Stoiber, T., Evans, S., Naidenko, O.V., 2020. Disposal of products and materials containing per- and polyfluoroalkyl substances (PFAS): a cyclical problem. *Chemosphere* 260, 127659.
- Sunderland, E.M., Hu, X.C., Dassuncao, C., Tokranov, A.K., Wagner, C.C., Allen, J.G., 2019. A review of the pathways of human exposure to poly- and perfluoroalkyl substances (PFASs) and present understanding of health effects. *J. Expo. Sci. Environ. Epidemiol.* 29, 131–147.
- Temkin, A.M., Hovevar, B.A., Andrews, D.Q., Naidenko, O.V., Kamendulis, L.M., 2020. Application of the key characteristics of carcinogens to per and Polyfluoroalkyl substances. *Int. J. Environ. Res. Public Health* 17.
- Teunen, L., Bervoets, L., Belpaire, C., De Jonge, M., Groffen, T., 2021. PFAS accumulation in indigenous and translocated aquatic organisms from Belgium, with translation to human and ecological health risk. *Environ. Sci. Eur.* 33.
- Travis, S.C., Perez-Fuentetaja, A., Aga, D.S., 2020. Evidence of continued exposure to legacy persistent organic pollutants in threatened migratory common terns nesting in the Great Lakes. *Environ. Int.* 144, 106065.
- U.S. Environmental Protection Agency. *PUBLIC COMMENT DRAFT Toxicity Assessment and Proposed Maximum Contaminant Level Goal for Perfluorooctane Sulfonic Acid (PFOS) in Drinking Water*, 2023a.

- U.S. Environmental Protection Agency. PUBLIC COMMENT DRAFT Toxicity Assessment and Proposed Maximum Contaminant Level Goal for Perfluorooctanoic Acid (PFOA) in Drinking Water. 2023b.
- Vendl, C., Taylor, M.D., Bräunig, J., Gibson, M.J., Hesselson, D., Neely, G.G., et al., 2021. Profiling research on PFAS in wildlife: protocol of a systematic evidence map and bibliometric analysis. *Ecol. Sol. Evid.* 2.
- Vendl, C., Taylor, M.D., Bräunig, J., Gibson, M.J., Hesselson, D., Gregory Neely, G., et al., 2022. PFAS exposure of humans, animals and the environment: protocol of an evidence review map and bibliometric analysis. *Environ. Int.* 158.
- Wang, Q., Ruan, Y., Jin, L., Zhang, X., Li, J., He, Y., et al., 2021. Target, nontarget, and suspect screening and temporal trends of per- and Polyfluoroalkyl substances in marine mammals from the South China Sea. *Environ. Sci. Technol.* 55, 1045–1056.
- Wood, C., Balazs, G.H., Rice, M., Work, T.M., Jones, T.T., Sterling, E., et al., 2021. Sea turtles across the North Pacific are exposed to perfluoroalkyl substances. *Environ. Pollut.* 279, 116875.
- World Health Organization and Secretariat of the Convention on Biological Diversity. Connecting global priorities: biodiversity and human health: a state of knowledge review. [https://apps.who.int/iris/bitstream/handle/10665/174012/9789241508537\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/174012/9789241508537_eng.pdf), 2015.



# Sources, Fate, and Plant Uptake in Agricultural Systems of Per- and Polyfluoroalkyl Substances

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## Abstract

**Purpose of Review** Per- and polyfluoroalkyl substances (PFAS) are a family of > 4700 recalcitrant compounds, many of which are ubiquitous in the environment. This review aims to (1) identify PFAS sources and fate processes relevant to agricultural systems and (2) expand on plant uptake mechanisms and plant responses to PFAS.

**Recent Findings** The number of PFAS being quantified in studies involving soil, water, and plants is increasing. Transformation of precursors that tend to stay in the rhizosphere can lead to long-term PFAS reservoir to plants. Some PFAS are readily taken up, particularly the shorter-chain PFAS, and can evoke metabolic responses and phytotoxic effects at high concentrations. PFAS translocation from roots to shoots occurs through both active and passive transport mechanisms. Both PFAS uptake and effects vary between and within species.

**Summary** As new PFAS emerge, it will be necessary to continue expanding the list of PFAS quantified in land-applied media and assessing their accumulation potential in plants. While controlled laboratory or greenhouse studies have merit, comprehensive field studies are needed to provide clarity on PFAS fate and their relative risk in agricultural systems. Field studies should include identifying site-specific PFAS sources, quantifying a broader suite of PFAS and identifying potential precursors, evaluating plant uptake of replacement PFAS, reporting of soil properties and climatic conditions, and assessing risk of impacts to source and irrigation waters. This information can be utilized to inform future studies towards evaluating and mitigating risks to our food chain associated with PFAS in agricultural systems.

**Keywords** PFAS · PFOS · PFOA · Soil amendments · Phytotoxicity · Crops · Vegetables

## Introduction

Per- and polyfluorinated alkyl substances (PFAS) are a widely utilized chemical family [1–3] now referred to as forever chemicals due to their high thermal and chemical stability as well as minimal biodegradability [4]. The perfluoroalkyl chain length ( $C_nF_{2n+1}$ ), the functional head group (e.g., carboxylic acid, sulfonate, alcohol, phosphate, amino, or other groups), which may be attached to a nonfluorinated hydrocarbon entity, and structural differences in the fluoroalkyl chain itself

(e.g., branching, ether moiety) govern their behavior, sub-classification, and nomenclature [5]. Some PFAS are highly bioaccumulative and have been reported in blood serum and breast milk of humans throughout the globe [6–8] and have been associated with adverse health effects [9]. Two classes within the PFAS family that have received the most attention are the perfluoroalkyl sulfonic acids (PFASAs) and the perfluoroalkyl carboxylic acids (PFCAs) [10•] of which perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA), respectively, are the most researched to date. Due to their highly bioaccumulative nature, PFOS and PFOA have been voluntarily phased out and are on the Stockholm Convention persistent organic pollutant lists Annex B (restricted) and Annex A (eliminated), and perfluorohexane sulfonic acid (PFHxS) is under review [11]. A range of less studied and often more mobile PFAS that are substitutes for PFOS and PFOA [12] have been found to be equally persistent and often with similar adverse effects, albeit often at higher concentrations [9], thus leading to additional management and regulatory challenges.

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The primary PFAS exposure routes researched to date are drinking water, meat, fish, milk, food packaged in PFAS-containing materials, and indoor dust inhalation [13–16]. More recently, research has included evaluating PFAS exposure from commonly consumed agricultural products (grains, cereals, vegetables, fruits); therefore, it is crucial to understand PFAS sources to plants and the processes controlling how much of each PFAS is taken up by various plant types. Sources of PFAS to agricultural field crops consist of atmospheric deposition via precipitation or particle-bound PFAS, and absorption from the gaseous phase [17, 18], irrigation with contaminated well water or treated wastewater effluent [19–23], pesticides [24, 25], aqueous film-forming foams (AFFFs) used to extinguish fires [26], and land-applied sewage sludge or biosolids [27, 28–32, 33], as well as industrial or municipal compost [34, 35]. Likewise, food grown in hydroponic and greenhouse systems can be impacted by contaminated water as well as other sources. Relative PFAS contributions from different sources will vary depending on location-specific activities and facilities. For example, PFAS contributions from atmospheric deposition have been especially concerning for crops grown near fluorochemical manufacturing facilities [36, 37]. AFFFs are typically the major PFAS source of highly contaminated water near fire training areas; however, impacts to agriculture are generally limited to irrigation with AFFF-contaminated water [26] which could significantly increase exposure risks [38]. Much less is known about the relative PFAS contribution to crops from land-applied biosolids and composts, which serve as both a valuable resource for improving crop yields and a waste management strategy. Also, factors and mechanisms controlling PFAS uptake by plants are not well understood. A critical understanding of these sources and mechanisms is necessary to determine the associated risks, trade-offs, and need for regulatory action [39–41].

## Aim and Scope

This review will address PFAS in agricultural systems with an emphasis on land application scenarios, PFAS reservoirs in the rhizosphere, soil–plant transfer, and plant health. A recent review by Ghisi et al. [42] summarized research on PFAS uptake and occurrence in grains, vegetables, and fruit prior to 2018 with an emphasis on comparing bioaccumulation trends between plants and impacts of environmental factors with a primary focus on C4 and C8 PFCAs and PFSA. Studies after 2018 have addressed an expanded list of PFAS and began to address precursor contributions to plant uptake. Precursors are PFAS that can degrade to PFCAs or PFSA, which are the terminal metabolites and collectively referred to as perfluoroalkyl acids (PFAAs). Precursors are often less mobile than PFAAs, thus they can serve as a PFAA reservoir in the rhizosphere. The previous review did not include

several field studies that provide valuable information on soil–plant transfer of PFAS under field conditions. In addition, insight into uptake mechanisms and effects to plant health were not specifically addressed. Therefore, this review expands upon the work by Ghisi et al. [42] accordingly. In addition, hydroponic, pot, and field studies will be compared and contextualized to inform future studies. Recent studies on uptake of PFAS in different agricultural plants are synthesized and discussed in light of previously hypothesized uptake mechanisms and trends. Furthermore, studies on plant responses to PFAS contamination are discussed. Immediate data gaps are highlighted to guide future plant uptake studies, clarify potential PFAS sources in agricultural systems, and better inform relative risk of PFAS exposure through our food chain.

## The Expanding List of PFAS

At least 4700 PFAS have been used in industrial and commercial processes and thus potentially released to the environment [3, 43]. PFAS include anionic, cationic, zwitterionic, and neutral compound groups with a range of functional groups (e.g., carboxylic acid, sulfonic acid, ether sulfonate, sulfonamide, sulfonamido acetic acid, phosphate diester, acrylate, amido ammonium salt, amido betaine, and others) [44, 45]. In addition, for a given PFAS, there can be multiple isomers depending on the manufacturing process, e.g., PFOS produced from an electrochemical fluorination process yields multiple branched isomers in addition to the linear isomer [5]. Initial PFAS occurrence studies targeted only PFOS and/or PFOA, and without isomer delineation. Research involving additional PFAS has increased as awareness of the numbers of PFAS in the environment, analytical method development, and analytical standard availability have increased. Table 1 provides a classification and acronym summary for the PFAS that have been included in the plant uptake studies reviewed. PFAS in these studies were quantified using liquid chromatography (LC) paired with mass spectrometry (MS), tandem mass spectrometry (MS/MS), high-resolution mass spectrometry (HRMS), or quadrupole time of flight MS (QToF-MS) [46, 47]. Targeted quantification is limited to availability of standards, which currently includes approximately 60 PFAS. Suspect and nontarget screening with advanced MS instrumentation (e.g., QToF-MS) may be used to identify other PFAS including precursors and intermediates in the pathways to PFAAs. Precursor transformation to PFAAs typically involves multiple transformation steps with different degradation rates and some quite stable intermediates. Degradation rates, metabolites, and metabolite yields vary with each PFAS class as well as environmental factors commonly known to affect microbial degradation [48]. For example, aerobic half-lives of fluorotelomer alcohols are < 1 week with yields to PFOA as high as 40% whereas aerobic soil

**Table 1** PFAS included in analytical methods used in plant uptake studies along with acronyms and chemical formulas

| Class                                                     | PFAS                                             | Acronym      | Formula                                                                                                                                 |
|-----------------------------------------------------------|--------------------------------------------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| Carboxylic Acid<br>(PFCA)                                 | Trifluoroacetic acid                             | TFA          | CF <sub>3</sub> COOH                                                                                                                    |
|                                                           | Perfluoropropanoic acid                          | PFPtA        | CF <sub>3</sub> CF <sub>2</sub> COOH                                                                                                    |
|                                                           | Perfluoro-butanoic acid                          | PFBA         | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>2</sub> COOH                                                                                    |
|                                                           | Perfluoropentanoic acid                          | PFPtA        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>3</sub> COOH                                                                                    |
|                                                           | Perfluorohexanoic acid                           | PFHxA        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>4</sub> COOH                                                                                    |
|                                                           | Perfluoroheptanoic acid                          | PFHpA        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>5</sub> COOH                                                                                    |
|                                                           | Perfluorooctanoic acid                           | PFOA         | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>6</sub> COOH                                                                                    |
|                                                           | Perfluorononanoic acid                           | PFNA         | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> COOH                                                                                    |
|                                                           | Perfluorodecanoic acid                           | PFDA         | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>8</sub> COOH                                                                                    |
|                                                           | Perfluoroundecanoic acid                         | PFUnDA       | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>9</sub> COOH                                                                                    |
|                                                           | Perfluorododecanoic acid                         | PFDoA        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>10</sub> COOH                                                                                   |
|                                                           | Perfluorotridecanoic acid                        | PFTtDA       | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>11</sub> COOH                                                                                   |
|                                                           | Perfluorotetradecanoic acid                      | PFTtDA       | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>12</sub> COOH                                                                                   |
|                                                           | Perfluorohexadecanoic acid                       | PFHxDA       | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>14</sub> COOH                                                                                   |
|                                                           | Perfluorooctadecanoic acid                       | PFODA        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>16</sub> COOH                                                                                   |
|                                                           | Perfluoroethane sulfonate                        | PFEtS        | CF <sub>3</sub> CF <sub>2</sub> SO <sub>3</sub>                                                                                         |
|                                                           | Perfluoropropane sulfonate                       | PFPtS        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>2</sub> SO <sub>3</sub>                                                                         |
|                                                           | Perfluorobutanesulfonate                         | PFBS         | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>3</sub> SO <sub>3</sub>                                                                         |
|                                                           | Perfluoropentanesulfonate                        | PFPtS        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>4</sub> SO <sub>3</sub>                                                                         |
|                                                           | Perfluorohexanesulfonate                         | PFHxS        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>5</sub> SO <sub>3</sub>                                                                         |
| Sulfonic Acid<br>(PFSA)                                   | Perfluoroheptanesulfonate                        | PFHpS        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>6</sub> SO <sub>3</sub>                                                                         |
|                                                           | Perfluorooctanesulfonate                         | PFOS         | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> SO <sub>3</sub>                                                                         |
|                                                           | Perfluorodecane sulfonate                        | PFUdA        | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>9</sub> SO <sub>3</sub>                                                                         |
|                                                           | Perfluorooctane sulfonamide                      | FOSA, PFOSA  | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> SO <sub>2</sub> NH <sub>2</sub>                                                         |
|                                                           | N-methylperfluorooctane sulfonamide              | N-MeFOSA     | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> SO <sub>2</sub> NHCH <sub>3</sub>                                                       |
|                                                           | N-ethylperfluorooctane sulfonamide               | N-EtFOSA     | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> SO <sub>2</sub> NHCH <sub>2</sub> CH <sub>3</sub>                                       |
|                                                           | N-Methylperfluorooctanesulfonamidoethanol        | N-MeFOSE     | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> SO <sub>2</sub> N(CH <sub>3</sub> )(CH <sub>2</sub> CH <sub>2</sub> OH)                 |
|                                                           | N-ethylperfluorooctanesulfonamidoethanol         | N-EtFOSE     | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> SO <sub>2</sub> N(CH <sub>2</sub> CH <sub>3</sub> )(CH <sub>2</sub> CH <sub>2</sub> OH) |
|                                                           | 6:2 chlorinated polyfluoroalkyl ether sulfonate  | 6:2 Cl-PFAES | Cl(CF <sub>2</sub> ) <sub>6</sub> O(CF <sub>2</sub> ) <sub>2</sub> SO <sub>3</sub>                                                      |
|                                                           | 8:2 chlorinated polyfluoroalkyl ether sulfonate  | 8:2 Cl-PFAES | Cl(CF <sub>2</sub> ) <sub>8</sub> O(CF <sub>2</sub> ) <sub>2</sub> SO <sub>3</sub>                                                      |
| Perfluoroalkane Sulfonamide<br>(FASA)                     | N-methyl perfluorooctane sulfonamido acetic acid | N-MeFOSAA    | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> SO <sub>2</sub> N(CH <sub>3</sub> )(CH <sub>2</sub> CO <sub>2</sub> )                   |
|                                                           | N-ethyl perfluorooctane sulfonamido acetic acid  | N-EtFOSAA    | CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> SO <sub>2</sub> N(CH <sub>2</sub> CH <sub>3</sub> )(CH <sub>2</sub> CO <sub>2</sub> )   |
|                                                           | 6:2 fluorotelomer phosphate diester              | 6:2 DiPAP    | [CF <sub>3</sub> (CF <sub>2</sub> ) <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub> O] <sub>2</sub> PO <sub>2</sub>                        |
|                                                           | 8:2 fluorotelomer phosphate diester              | 8:2 DiPAP    | [CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> (CH <sub>2</sub> ) <sub>2</sub> O] <sub>2</sub> PO <sub>2</sub>                        |
| Perfluoroalkane Sulfonamido Ethanol<br>(FASE)             | 10:2 fluorotelomer phosphate diester             | 10:2 DiPAP   | [CF <sub>3</sub> (CF <sub>2</sub> ) <sub>9</sub> (CH <sub>2</sub> ) <sub>2</sub> O] <sub>2</sub> PO <sub>2</sub>                        |
| Chlorinated Polyfluoroalkyl Ether Sulfonate<br>(Cl-PFAES) |                                                  |              |                                                                                                                                         |
| Perfluoroalkane Sulfonamido Acetic Acid<br>(FASAA)        |                                                  |              |                                                                                                                                         |
| Fluorotelomer Phosphate Diester<br>(DiPAP)                |                                                  |              |                                                                                                                                         |

Table 1 (continued)

| Class                                                                  | PFAS                                      | Acronym   | Formula                                                       |
|------------------------------------------------------------------------|-------------------------------------------|-----------|---------------------------------------------------------------|
| Fluorotelomer Sulfonic Acid (FTSA)<br>Fluorotelomer Carboxylate (FTCA) | 6:2 fluorotelomer sulfonic acid           | 6:2 FTSA  | $\text{CF}_3(\text{CF}_2)_5(\text{CH}_2)_2\text{SO}_3$        |
|                                                                        | 3:3 fluorotelomer carboxylic acid         | 3:3 FTCA  | $\text{CF}_3(\text{CF}_2)_2\text{CH}_2\text{CH}_2\text{COOH}$ |
|                                                                        | 5:3 fluorotelomer carboxylic acid         | 5:3 FTCA  | $\text{CF}_3(\text{CF}_2)_4\text{CH}_2\text{CH}_2\text{COOH}$ |
|                                                                        | 7:3 fluorotelomer carboxylic acid         | 7:3 FTCA  | $\text{CF}_3(\text{CF}_2)_6\text{CH}_2\text{CH}_2\text{COOH}$ |
|                                                                        | 6:2 fluorotelomer carboxylic acid         | 6:2 FTCA  | $\text{CF}_3(\text{CF}_2)_5\text{CH}_2\text{COOH}$            |
|                                                                        | 6:2 fluorotelomer carboxylic acid         | 8:2 FTCA  | $\text{CF}_3(\text{CF}_2)_7\text{CH}_2\text{COOH}$            |
|                                                                        | 6:2 unsaturated fluorotelomer carboxylate | 6:2 FTUCA | $\text{CF}_3(\text{CF}_2)_4\text{CF}=\text{CHCOOH}$           |
|                                                                        | 8:2 unsaturated fluorotelomer carboxylate | 8:2 FTUCA | $\text{CF}_3(\text{CF}_2)_6\text{CF}=\text{CHCOOH}$           |
|                                                                        | 6:2 fluorotelomer alcohol                 | 6:2 FTOH  | $\text{CF}_3(\text{CF}_2)_5(\text{CH}_2)_2\text{OH}$          |
| Fluorotelomer Alcohol (FTOH)                                           | 8:2 fluorotelomer alcohol                 | 8:2 FTOH  | $\text{CF}_3(\text{CF}_2)_7(\text{CH}_2)_2\text{OH}$          |
|                                                                        | 10:2 fluorotelomer alcohol                | 10:2 FTOH | $\text{CF}_3(\text{CF}_2)_9(\text{CH}_2)_2\text{OH}$          |

degradation of fluorotelomer sulfonates, which is both a precursor and an intermediate of some larger S-containing PFAS, is much slower with desulfonation being the rate-limiting step [49].

Other approaches for estimating the contribution of unknown PFAS loads include conducting a fluorine mole balance using bulk organofluorine measurements or chemical assays such as the total oxidizable precursor (TOP) assay, particle-induced gamma-ray emission (PIGE) method, and adsorbable organic fluorine (AOF) or extractable organic fluorine (EOF) paired with combustion ion chromatography (CIC) methods [50]. Understanding the contribution of the unknown PFAS is helpful when making cross-study comparisons between  $\Sigma$ PFAS,  $\Sigma$ PFASs, and  $\Sigma$ PFCAs in targeted studies, due to variations between media and precursor degradation in temporal studies. For example, the PFOS precursor sulfluramid (active ingredient EtFOSA), which is a pesticide used in the region to control leaf-cutting ants, was proposed as the most likely source of measured PFOS in Brazilian soils (0.020–3.77 ng/g) [24•]. In a carrot uptake study using soil fortified with EtFOSA, temporal generation of FOSAA and FOSA (intermediates to PFOS) and PFOS with yields up to 34% was attributed to EtFOSA degradation [25]. Likewise, in a wheat uptake study using FOSA-fortified soil, degradation to PFOS was observed in both the soil and the earthworms [51]. A small subset of these now known precursors is starting to be routinely quantified; however, currently, there are still many known precursors that are often not quantified. In addition, there are likely still many unknown and difficult to quantify precursors that may be a significant fraction of the total PFAS present and could serve as a continual source of PFAAs depending on degradation potential and degradation rates. For example, a recent study looking at several Canadian biosolids found two side-chain fluorinated polymer surfactants used in consumer products at higher concentrations than the total for targeted PFAAs [33•]. Therefore, although the list of PFAS typically quantified is likely to expand rapidly over the next few years, PFAS occurrence and potential PFAA reservoir are likely underestimated, especially in, but not limited to, earlier studies.

PFAS Sources and Presence in Soils and Growing Media

To provide a foundation to discuss PFAS availability to plants in different growing media, typical PFAS types including precursors and concentration ranges are briefly detailed in this section. PFAS have become so ubiquitous in the environment that finding pristine soils is rare. A recent review by Vedagiri et al. [52] of soils in North America with no known PFAS

point sources found background levels of PFOS and PFOA ranged from 0.018 to 2.55 ng/g ( $n = 38$  studies) and 0.059 to 1.84 ng/g ( $n = 40$ ), respectively. A global survey of 32 PFAS in soils taken from 62 locations with limited to no anthropogenic impact revealed PFAS presence in every sample; long-range transport was identified as the source [53]. Of the data reviewed, 33 samples from North America only reported PFOS and PFOA values. Globally,  $\Sigma$ PFCA (C6–C14) ranged from 0.03 to 14.3 ng/g, and  $\Sigma$ PFSA (C6–C10) ranged from < LOD to 3.27 ng/g. Other PFAS quantified are intermediates and precursors in the PFAA degradation pathway including a series of ten FTUCAs and ten FTCAs, which ranged from < LOD to 0.106 ng/g and < LOD to 0.048 ng/g in soils, respectfully. Comparison across the globe indicated that the northern hemisphere (especially Asia and North America) had higher PFAS concentrations than the southern hemisphere, which is consistent with results from previous atmospheric distribution studies and oceanic studies [53].

Biosolids and irrigation waters are the most prominently studied sources of PFAS in agricultural soils. PFAS are found in multiple water resources around the world [52], which when utilized as an irrigation source can lead to higher PFAS loads in soils than global background concentrations. Irrigation with well water, treated wastewater effluent, and surface water is essential to agriculture in many regions, and thus is a source of PFAS to plants that is difficult to avoid. Of 13 PFAS tested in agricultural soils from a Ugandan wetland irrigated with surface water receiving effluent discharged by wastewater treatment plants (WWTPs), PFOS was the most abundant (36–50% of  $\Sigma$ PFAS, 0.6–3.0 ng/g dw) > PFOA (6.2–15%, 0.48–0.91 ng/g dw) > PFHxA (4.7–18% dw, 0.2–0.5 ng/g dw) [23]. In a South Korean rice paddy irrigated with surface water impacted by effluent from WWTP receiving textile industry waste, the soil contained  $\Sigma$ PFAS ranging from 0.12 to 13.9 ng/g dw [54]. Zhang et al. [55] reported  $\Sigma$ PFAAs in irrigated agricultural fields in China ranging from 0.29 to 4.28 ng/g (mean 1.62 ng/g) with PFOA (39% of  $\Sigma$ PFAAs) > PFDA (16%) > PFBA (9%) > PFHxA (7%) = PFNA (7%). In home gardens in the USA irrigated with landfill leachate-contaminated groundwater, several PFAAs, including PFOA (0.11–3.0 ng/g), PFOS (0.57–12.0 ng/g), PFBA (0.04–13.0 ng/g), PFPeA (ND–0.57 ng/g), PFHxS (ND–0.24 ng/g), and PFHxA (ND–0.66 ng/g), were detected in over 70% of the soil samples from 20 home gardens [22]. Comparatively lower concentrations were found in 3 irrigated gardens outside the contaminated zone: PFOS (0.93–2.1 ng/g), PFOA (0.29–0.54 ng/g), and PFBA (0.073–0.49 ng/g).

Waste-derived soil amendments and fertilizers, including biosolids and composts made from biodegradable solid wastes, are frequently land-applied as an organic matter source that improves soil structure and water-holding capacity as well as a slow-release source of nitrogen and other micro- and macronutrients [56–58]. Concerns that these waste-

derived soil amendments are significant sources of PFAS to the environment have been increasing over the past decade [27, 30, 33, 35, 59, 60]. Biosolids, which are prepared from the sludge produced in the wastewater treatment process, inherently contain higher concentrations of the more sorptive longer perfluoroalkyl chains and larger precursors than the corresponding wastewater effluent. Longer-chain PFAS refer to those that have six or more perfluoroalkyl carbons. Degradation of these precursors throughout the sludge treatment process and after land application can lead to increased concentrations of the shorter-chain PFAAs [61]. PFAS loads to soil from biosolid application depend on the PFAS sources to WWTPs, the PFAS concentrations in the biosolids, and biosolid application rates [33, 62, 63]. Furthermore, given the persistence of PFAS, multiple biosolids applications may result in higher PFAS concentrations [63, 64]. Sepulvado et al. [64] investigated PFAS at a site in Illinois where biosolids were applied over a 3-year period. Various loading rates and soil types were utilized, along with 6 different biosolids that contained a mean  $\Sigma$ PFAS concentration of 433 ng/g. PFOS (80–219 ng/g), MeFOSAA (63–143 ng/g), EtFOSAA (42–72 ng/g), and PFOA (8–68 ng/g) were detected most frequently in biosolid samples [64]. PFAS leaching at the site increased with decreasing carbon chain length, thus greater leaching of short-chain PFAS was observed [64]. While Sepulvado et al. [64] did include known PFAA precursors MeFOSAA and EtFOSAA in their study, other precursors yet to be identified may have been present. For example, in soils from a biosolid-amended field in Ontario, Chu and Letcher [30] found, for the first time, two side-chain fluorinated polymer surfactants (S1 and its shorter-chain replacement S2) from Scotchgard™ fabric protectors totaling ~240 ng/g dw, which was one hundred times higher than the total sum of 22 other more typically targeted PFAS [30]. Later, they found these same PFAS in biosolids from numerous wastewater treatment plants in Canada [33]. While studies have yet to be conducted to quantify the degradation of these larger PFAS, PFAS used in textiles and leather for stain and water resistance may be a long-term source in domestic wastewater with potential to generate PFAAs.

Most commercially available waste-derived products sold in local or major store chains, which are typically purchased for use in urban and sub-urban gardens, golf courses, and public and homeowner lawns, have been found to contain PFAS. Kim Lazcano et al. [59] found 9.0–181 ng/g of total PFAAs in commercially available municipal biosolid-based products. PFAS are also present in non-biosolid urban waste-derived composts made from compostable paper products, food wastes, and tree and grass clippings. Total PFAAs in organic waste composts ranged from 31 to 75 ng/g for those containing food packaging with PFAS concentrations being lower in composts of only food and yard wastes ( $\leq 18.89$  ng/g) [35, 59]. All these biosolid and non-biosolid waste-derived

composts contained PFOA and PFOS even though phase out was several years earlier than when these materials were produced. Several PFAS precursors were also detected with the most common being the 6:2 diPAP and 6:2 FTS [35, 59]. Likewise, total PFAAs up to 80 ng/g dw were found in biowaste from biogas production [31]. Overall shorter-chain PFAAs were higher in municipal solid waste- and biowaste-derived amendments compared to biosolid-based products [31, 35, 59]. Other waste-derived materials used as soil amendments that have not been studied for PFAS occurrence include paper mill wastes [65] which are expected to contain PFAS associated with PFAS-based paper coatings. Other PFAS sources applied to agricultural soils include PFAS-based pesticides, e.g., sulfluramid as exemplified already, or pesticides that may contain PFAS in their formulations as an ingredient in the surfactant carrier of which little is known.

PFAS production or use in manufacturing can lead to PFAS additions to agricultural soils through atmospheric deposition and/or contaminating water used for irrigation. Soil samples in agricultural fields located in five cities near fluorochemical manufacturing sites were commonly found to contain PFAS with detection frequency of PFBA (18.2%) > PFOA (31.8%), > PFDA (11.4%) > PFNA (12.6%) [66]. Liu et al. [36] reported total PFAS concentrations in agricultural soils of 79.9 to 200 ng/g and 2.09 to 3.75 ng/g within 0.3 km and 10 km, respectively, of a fluorochemical plant. PFOA made up the greatest portion (83.4%, up to 181 ng/g) of the total quantified with the remainder being primarily the shorter-chain PFCAs [36].

Use of AFFFs has led to release of a wide range of both PFAS types and concentrations to the environment. For example, in Australia, 60 different PFAS were detected in AFFF-impacted soil, including novel PFAS identified with nontarget techniques [26]. Several PFSAs, PFCAs, chlorinated perfluoroalkyl sulfonate (Cl-PFSAs), ketone perfluoroalkyl sulfonates, FASA, perfluoroalkyl sulfinates, perfluoroalkyl sulfonamidoethanols, fluorotelomer sulfonates, and perfluoroalkyl sulfoamido amines as well as one fluorotelomer thioamido sulfonate were detected. This exemplifies the need to include nontarget screening in future studies, particularly at, but not limited to, AFFF-impacted sites. High total PFAS concentrations are often observed at fire training sites, e.g., Dauchy et al. [67] reported up to 710,126 ng/g in surface soils and 300 to 8300 ng/L in groundwater.

## PFAS Sorption and Mobility Characteristics

PFAS interactions with soil moderate PFAS mobility and plant availability, thus the long-term dynamics of PFAS in agricultural systems. Within a class of PFAS (e.g., PFCAs, PFSAs), PFAS sorption to soils increases with increasing

perfluoroalkyl chain length [68]; therefore, leaching and bio-availability increase with decreasing chain length [64, 69]. For a given chain length, sorption tends to be higher for PFSAs compared to PFCAs [68]. Cationic and some zwitterionic PFAS tend to have a high affinity to agricultural soils, since healthy soils typically contain a significant cation exchange capacity [45, 70]. Although soil organic carbon (OC) generally increases sorption of organic contaminants, in a review by Li et al. [60], no consistent trend was apparent between OC and PFAS sorption by soils across the globe. Although parameters that may affect sorption were not provided in all papers, Li et al. [60] were able to evaluate trends between sorption, pH, and cation concentrations. They found pH to be significantly correlated to sorption for only EtFOSAA ( $n = 10$ ), MeFOSAA ( $n = 10$ ), and PFDS ( $n = 10$ ), while a general trend of increasing PFAA sorption with increasing cation concentration and overall salinity was evident [60]. Correlations to other soil properties such as exchange capacities were constrained because property information was most often not reported [60]. Using PFAA sorption data obtained for a single soil and a single concentration but with different solution pH and cation presence (Al, Ca, and Na), Campos Pereira et al. [68] generally observed inverse correlations between OC-normalized sorption coefficients and pH. Both PFAAs and acid functional groups in soil organic matter (SOM) become more anionic with increasing pH, thus lower sorption with higher pH may be expected for anionic PFAAs. Cation effects were more varied and complicated since their addition can invoke pH changes as well. Overall, the authors attributed the effects observed to changes in the net charge of organic matter, which can be impacted by pH as well as cation charge and concentration. They also hypothesized that longer-chain PFAAs preferentially sorb to the humin SOM fraction whereas sorption of the shorter chain was more to humic and fulvic acid domains [68]. Although data were limited, results indicated that different OM sources (e.g., OM arising from different crop and management strategies including land-applied waste-derived amendments) may alter PFAS retention, thus mobility and plant uptake potential. Factors not considered by Campos Pereira et al. [68] include nonlinear sorption behavior [71] and the effect of cation charge and concentration on PFAA clustering [72].

Inorganic anions can also impact PFAA sorption. Addition of phosphate decreased sorption of PFOS due to site-specific competition with the greatest impact being in soils with low OM content and high ferric oxide content [71]. Given the importance of phosphorus as a nutrient in agricultural systems, further studies on the effect of phosphorus speciation and concentration on sorption of additional PFAS are warranted. Lastly, other sorption mechanisms unique to PFAS as surfactants include the potential for enhanced retention at the air–water interface in the vadose zone [73, 74] (the unsaturated zone of soil above the water table including the root zone).

In unsaturated soils, air–water partitioning of PFOS [74] and PFOA [73] at higher concentrations typical of AFFF-impacted sites accounted for 32% and up to 75% of the retention by soil, respectively. This indicates that rain events that lead to saturation may temporarily mobilize sorbed PFAS. The role of interfacial tension at PFAS concentrations that may be released from typical waste-derived soil amendments versus AFFFs is yet to be determined.

## Uptake into Agricultural Plants

The plant uptake studies reviewed include hydroponic studies ( $n = 17$ ), pot studies ( $n = 19$ ), and field studies ( $n = 14$ ) (Table S1). Table 2 provides a summary of the plant species studied, reported uptake and comparisons between study types for the most commonly studied PFAAs, and the range in number of PFAS that have been included in at least one study for the given species organized by classification. A total of 63 field crops and produce types have been studied with the most studied reported in Table 2. Grains, leaf vegetables, and root vegetables were the most studied plants, with sweet fruits being the least studied. Generally, vegetables and vegetative plant components had higher PFAS concentrations than grains and fruits. In home gardens, floret vegetables had higher concentrations of PFAS than other plant categories [22]. Studies indicate that long-chain PFAAs will be less susceptible to leaching and less likely to transfer from soils to plants or be translocated compared to the shorter-chain replacements which are more water soluble [12, 35, 75•]. Likewise, precursors can serve as a reservoir of smaller more mobile and bioavailable PFAS (intermediate metabolites and subsequent terminal PFAAs) [51]. The source strength of the precursor reservoir will depend on degradation rates and PFAA yield potential [48], which has not been determined for many precursors especially those more recently identified.

Synthesizing data from plant uptake studies can be challenging due to reported differences between plant species, within plant species (different cultivars), and within the different plant components (root, shoot, leaves, fruit) [42•, 82, 92•], as well if data are reported on a wet or dry weight basis. To compare between treatments and different systems, several ratios have been utilized including the root concentration factor (RCF, ratio of root to soil concentration), translocation factor (TF, ratio of shoot to root concentration) or sometimes called the foliage to root concentration ratios (FRCFs), shoot concentration factor (SCF, ratio of shoot to the growing media), and bioconcentration factor (BCF, ratio of the plant to growing media). In addition, a transpiration stream concentration factor (TSCF) can be used to describe translocation of PFAS via the transpiration stream; however, TSCF is not highly reported and is better suited to hydroponic studies; plants grown in soil require a porewater analysis to calculate TSCF [102•].

In studies using different ratios of PFAS between compartments in various plant systems, the PFAS characteristic appears to be the single most consistent factor affecting TFs and RCFs [20, 36, 62, 75•, 74–76, 77•, 79–81, 102•, 103, 104], which allots some insight into uptake mechanism. RCFs generally increased with increasing chain length and were greater for PFASs compared to PFCAs of similar chain length [76, 80, 102•, 104], whereas TFs generally increased with decreasing chain length [20, 36, 62, 75•, 76, 79, 80]. However, there are exceptions to these general trends attributed to plant-specific mechanisms to be discussed in the mechanism section [91, 105•]. For a given PFAS, there are also notable trends with PFAS concentrations in the growing media. Current trends described in the literature indicate that root uptake concentrations increase with increasing PFAS concentrations [82, 91, 96]. This leads to relatively constant RCF values for given PFAS unless sorption to tissues reaches a maximum (e.g., nonlinear sorption to tissues) in which case the RCFs may decrease [91]. Across many species, short-chain PFAAs readily uptake and translocate throughout the plants [36, 42•, 75•, 79, 104], thus they tend to have higher TFs than longer chain. Short-chain PFAAs translocated to edible portions of crops more often than long-chain PFAAs [66], partially because short-chain PFAS sorb less to soils [106] and thus are more bioavailable [22•, 104, 107]. Also, it is plausible that with smaller size PFAS, plant root barriers may have a reduced impact on restricting their translocation [75•] as will be discussed in regard to plant uptake mechanisms.

Study type and design will affect PFAS bioavailability, the contact period during which the plant can uptake PFAS and/or PFAS effects on the plant. In hydroponic systems, overall PFAS availability is high compared to soil since it is not moderated by sorption; however, the root surface area where uptake occurs can be reduced in a hydroponic system. For example, red chicory root development in hydroponic systems was reduced; thus, uptake surface area decreased compared to chicory grown in soil [102•]. Most studies, particularly in pot and hydroponic studies, invoke PFAS treatments to seedlings (germination occurs in a different environment); thus, potential effects on germination and early growth are missed. Field studies often include impacts on germination since seeds are planted rather than seedlings and have additional variables that can impact PFAS availability for plant uptake such as potential for compounds to leach out of the root zone and climate variability. Also in most pot studies, leaching is minimized or prevented; thus, short-chain PFAS remain in the root zone unlike what is likely to occur in the field. For example, decreases were reported in short-chain PFAS concentrations in the soil profile throughout a growing season due to leaching [64, 106], whereas in a pot study short-chain PFAS became enriched in the bottom layers of the pot compared to the longer-chain PFAS and remained accessible for

**Table 2** Comparison between three study types (A = hydroponic, B = pot studies, C = field studies) conducted on agricultural plants for PFBA (C4), PFHxA (C6), PFOA (C8), PFBS (C4), PFHxS (C6), and PFOS (C8) with parenthetical indicating total carbon chain length

| Plant    | Study type (# of studies)                                        |   |   | Results     | References                        |            |              |             |          |           |            |         |         |                                                                 |   |
|----------|------------------------------------------------------------------|---|---|-------------|-----------------------------------|------------|--------------|-------------|----------|-----------|------------|---------|---------|-----------------------------------------------------------------|---|
|          | PFAS class<br>(range studied within the class for a given study) |   |   |             | Concentration ranges<br>(ng/g dw) |            |              | RCF (range) |          |           | TF (range) |         |         | Hydroponic <sup>a</sup> , pot <sup>b</sup> , field <sup>c</sup> |   |
|          | A                                                                | B | C |             |                                   | A          | B            | C           | A        | B         | C          | A       | B       |                                                                 | C |
| Wheat    | 5                                                                | 4 | 2 |             | PFCA (1–9)                        | 200–1400   | 3170–406,080 | 1–1100      | 18–19    | 2.7–43.91 | 0.7–2.5    | 1.2–2.3 | 0.6–1.4 | [20, 75–78] <sup>a</sup>                                        |   |
|          |                                                                  |   |   |             | PFHxA                             | 500–2000   | 810–8060     | 0.3–135     | 0.2–6.8  | 2.8–4.3   | –          | 1.1–1.9 | 0.3–1.0 | [79–82] <sup>b</sup>                                            |   |
|          |                                                                  |   |   |             | PFSA                              | 100–10,800 | 30–341,000   | 1–809       | 0.05–2   | 1.3–4.9   | 0.02–0.3   | 0.1–1.1 | 0.2–0.5 | [36, 62] <sup>c</sup>                                           |   |
|          |                                                                  |   |   |             | PFBS (0–3)                        | –          | 310–15,280   | <LOQ–60     | 0.4–1.6  | NA–1.8    | –          | 0.1–1.3 | NA–0.4  |                                                                 |   |
|          |                                                                  |   |   |             | Cl-PFAES (0–2)                    | –          | 150–7240     | <LOQ–68     | 0.1–2    | NA–2.8    | –          | 0.2–1.2 | NA–0.2  |                                                                 |   |
| Ryegrass | 3                                                                |   |   |             | PFOS                              | 500–28,600 | 100–76,900   | 0.2–12,500  | 0.02–1.4 | 0.8–6     | 0.018      | 0.1–1   | 0.2–1   | [82–84] <sup>b</sup>                                            |   |
|          |                                                                  |   |   |             | PFBA                              | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | PFHxA                             | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | PFOA                              | –          | 1–100,300    | –           | 2.35     | –         | –          | 0.6     | –       |                                                                 |   |
|          |                                                                  |   |   |             | PFBS                              | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
| Maize    |                                                                  |   |   |             | PFHxS                             | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | PFOS                              | –          | 1–42,000     | –           | 1.4–1.5  | –         | –          | 0.1–2.1 | –       |                                                                 |   |
|          | 5                                                                | 5 |   |             | PFCA                              | –          | 30–35,200    | <LOQ–1449   | –        | 11–25.5   | –          | –       | 0.7–1.3 | [28, 82–85] <sup>a</sup>                                        |   |
|          |                                                                  |   |   |             | PFHxA                             | –          | 30–2800      | <LOQ–116    | –        | 1.9–11.3  | –          | –       | 0.6–0.7 | [22, 23, 36, 63, 86] <sup>c</sup>                               |   |
|          |                                                                  |   |   |             | PFSA                              | –          | <LOQ–640     | <LOQ–2478   | –        | 1.1–2.4   | –          | –       | 0.1–0.3 |                                                                 |   |
|          |                                                                  |   |   |             | PFBS (1–4)                        | –          | 2–1800       | <LOQ–100    | 5        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | FASA                              | –          | <LOQ–7980    | <LOQ–0.05   | 2.6      | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | PFHxS (0–2)                       | –          | <LOQ–23100   | <LOQ–0.2    | 8.8      | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | FASE (0–2)                        | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | FASAA (0–2)                       | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
| Rice     |                                                                  |   |   |             | FTSA (0–1)                        | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | FTCA (0–7)                        | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | FTOH (0–3)                        | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | DiPAP (0–3)                       | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | Cl-PFESA (0–2)                    | –          | –            | –           | –        | –         | –          | –       | –       |                                                                 |   |
|          | 1                                                                | 1 |   |             | PFBA                              | –          | ND           | 0.01–2.4    | –        | –         | –          | 2.2–60  | –       | [19] <sup>b</sup>                                               |   |
|          |                                                                  |   |   |             | PFHxA (10–13)                     | –          | ND           | 0.02–1      | –        | –         | –          | 4.3–6.2 | –       | [54] <sup>c</sup>                                               |   |
|          |                                                                  |   |   |             | PFSA (4–5)                        | –          | ND–1.73      | <LOQ–1.9    | –        | –         | –          | 0.1–1.6 | –       |                                                                 |   |
|          |                                                                  |   |   |             | PFBS (0–2)                        | –          | ND           | <LOQ–0.03   | –        | –         | –          | –       | –       |                                                                 |   |
|          |                                                                  |   |   |             | FASA (0–2)                        | –          | ND           | <LOQ–3.8    | –        | –         | –          | 0.1–0.5 | –       |                                                                 |   |
|          |                                                                  |   |   | FASAA (0–1) | –                                 | ND         | <LOQ–55.5    | –           | –        | –         | 0.1–0.2    | –       |         |                                                                 |   |

**Table 2** (continued)

| Plant   | Study type (# of studies) |   |       | Results        | PFAS class<br>(range studied within the class for a given study) | Concentration ranges<br>(ng/g dw) |               |           | RCF (range) |         |      | TF (range) |       |     | References                               |  |
|---------|---------------------------|---|-------|----------------|------------------------------------------------------------------|-----------------------------------|---------------|-----------|-------------|---------|------|------------|-------|-----|------------------------------------------|--|
|         | A                         | B | C     |                |                                                                  | Concentration ranges<br>(ng/g dw) |               |           | RCF (range) |         |      | TF (range) |       |     |                                          |  |
|         |                           |   |       |                |                                                                  | A                                 | B             | C         | A           | B       | C    | A          | B     | C   |                                          |  |
| Soybean | 1                         | 2 | 1     | PFCA<br>(0–9)  | PFBA                                                             | –                                 | –             | 223–2378  | –           | 69.5    | –    | –          | –     | 0.7 | [87] <sup>a</sup>                        |  |
|         |                           |   |       | PFSA           | PFHxA                                                            | –                                 | –             | 5.5–212   | –           | 6.4     | –    | –          | –     | 0.6 | [83, 84] <sup>b</sup>                    |  |
|         |                           |   |       | (0–3)          | PFOA                                                             | ND                                | 120–1340      | 0.3–3967  | –           | 1.7     | –    | 0.1        | 0.002 | –   | [36] <sup>c</sup>                        |  |
|         |                           |   |       | PFSA           | PFBS                                                             | 0.02–0.15                         | –             | <LOQ      | –           | –       | –    | –          | –     | –   | –                                        |  |
|         |                           |   |       | FASA           | PFHxS                                                            | 0.02–0.2                          | –             | <LOQ      | –           | –       | –    | –          | –     | –   | –                                        |  |
|         |                           |   |       | (0–2)          | PFOS                                                             | 0.3–15                            | 20–720        | 0.12.3    | 2.3–4.7     | 5.6     | 0.02 | 0.1–1.2    | 0.8   | –   | –                                        |  |
| Alfalfa |                           | 3 | 1     | FASAA<br>(0–2) |                                                                  |                                   |               |           |             |         |      |            |       |     |                                          |  |
|         |                           |   |       | PFCA           | PFBA                                                             | –                                 | –             | ND        | –           | –       | –    | –          | –     | –   | [83, 84, 88] <sup>b</sup>                |  |
|         |                           |   |       | (0–11)         | PFHxA                                                            | –                                 | –             | ND        | –           | –       | –    | –          | –     | –   | [89] <sup>c</sup>                        |  |
|         |                           |   |       | PFSA           | PFOA                                                             | –                                 | 1311.5–4310.3 | ND        | 10.3        | –       | –    | 0.304      | –     | –   | –                                        |  |
|         |                           |   |       | (1–4)          | PFBS                                                             | –                                 | –             | ND        | –           | –       | –    | –          | –     | –   | –                                        |  |
|         |                           |   |       | FASA           | PFHxS                                                            | –                                 | –             | ND        | –           | –       | –    | –          | –     | –   | –                                        |  |
| Lettuce |                           | 3 | 8     | (0–3)          | PFOS                                                             | –                                 | 10–481.4      | ND        | 2.3–3.12    | –       | –    | 0.131–1.1  | –     | –   | –                                        |  |
|         |                           |   |       | FASAA<br>(0–2) |                                                                  |                                   |               |           |             |         |      |            |       |     |                                          |  |
|         |                           |   |       | PFCA           | PFBA                                                             | <LOQ–84                           | <LOQ–25,100   | <LOQ–2365 | –           | –       | 2.7  | –          | –     | –   | [21, 90, 91] <sup>a</sup>                |  |
|         |                           |   |       | (1–11)         | PFHxA                                                            | <LOQ–14.4                         | <LOQ–9460     | <LOQ–72   | –           | –       | 0.7  | –          | –     | –   | [34, 63, 83, 84, 88, 92–94] <sup>b</sup> |  |
|         |                           |   |       | PFSA           | PFOA                                                             | 0.02–135                          | <LOQ–2523     | <LOQ–1038 | –           | 6       | 0.3  | 0.2        | –     | –   | [22, 36, 63] <sup>c</sup>                |  |
|         |                           |   |       | (0–5)          | PFBS                                                             | <LOQ–17                           | <LOQ–3670     | <LOQ–1.6  | –           | –       | 0.3  | –          | –     | –   | –                                        |  |
| Spinach |                           | 1 | 4     | FASA           | PFHxS                                                            | <LOQ–30                           | <LOQ–1250     | <LOQ–0.5  | –           | –       | 0.2  | 0.1–1.6    | –     | –   | –                                        |  |
|         |                           |   |       | (0–2)          | PFOS                                                             | <OQ–205                           | <LOQ–279      | <LOQ–3.5  | 0.2–14.6    | 3.8–3.9 | 0.1  | 0.02–0.4   | –     | –   | –                                        |  |
|         |                           |   |       | FASAA<br>(0–2) |                                                                  |                                   |               |           |             |         |      |            |       |     |                                          |  |
|         |                           |   |       | DIPAP<br>(0–1) |                                                                  |                                   |               |           |             |         |      |            |       |     |                                          |  |
|         |                           |   |       | PFCA           | PFBA                                                             | –                                 | ND            | ND–6.7    | –           | –       | –    | –          | –     | –   | [28] <sup>b</sup>                        |  |
|         |                           |   |       | (9–13)         | PFHxA                                                            | –                                 | ND            | ND–1.2    | –           | –       | –    | –          | –     | –   | [22, 55, 66, 95] <sup>c</sup>            |  |
| Cabbage |                           |   |       | PFSA           | PFOA                                                             | –                                 | ND–2.4        | ND–6.7    | –           | –       | –    | –          | –     | –   | –                                        |  |
|         |                           |   |       | (2–8)          | PFBS                                                             | –                                 | ND            | ND–1.7    | –           | –       | –    | –          | –     | –   | –                                        |  |
|         |                           |   |       | FASA           | PFHxS                                                            | –                                 | –             | ND–0.1    | –           | –       | –    | –          | –     | –   | –                                        |  |
|         |                           |   |       | (0–3)          | PFOS                                                             | –                                 | 1–1.6         | ND–0.1    | –           | –       | –    | –          | –     | –   | –                                        |  |
|         |                           |   |       | FASAA<br>(0–2) |                                                                  |                                   |               |           |             |         |      |            |       |     |                                          |  |
|         |                           |   |       | FTCA<br>(0–1)  |                                                                  |                                   |               |           |             |         |      |            |       |     |                                          |  |
| Cabbage | 1                         |   | 2     | PFCA<br>(9–11) | PFBA                                                             | <LOQ–10.9                         | –             | 2.5–17.8  | –           | –       | 1.5  | –          | –     | –   | [96] <sup>a</sup>                        |  |
|         |                           |   |       | PFSA           | PFHxA                                                            | 0.1–14.4                          | –             | 0.2–1.4   | –           | –       | 0.6  | –          | –     | –   | [22, 55] <sup>c</sup>                    |  |
|         |                           |   |       | (3)            | PFOA                                                             | 0.1–10.9                          | –             | 1.3–4.0   | –           | –       | 0.4  | –          | –     | –   | –                                        |  |
|         |                           |   |       | PFBS           | PFBS                                                             | 0.2–31.5                          | –             | ND–0.1    | –           | –       | 0.7  | –          | –     | –   | –                                        |  |
|         |                           |   | PFHxS | PFHxS          | 0.1–31.2                                                         | –                                 | ND–0.1        | –         | –           | 0.4     | –    | –          | –     | –   | –                                        |  |

Table 2 (continued)

| Plant    | Study type (# of studies) |   |                                                                                                                                   | Results                                                | PFAS class<br>(range studied within the class for a given study)       | Concentration ranges<br>(ng/g dw)                                            |                                                                                          |                                            | RCF (range)                                |                                                    |                                             | TF (range)                                  |                                                                |   | References |
|----------|---------------------------|---|-----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|--------------------------------------------|--------------------------------------------|----------------------------------------------------|---------------------------------------------|---------------------------------------------|----------------------------------------------------------------|---|------------|
|          | A                         | B | C                                                                                                                                 |                                                        |                                                                        | A                                                                            | B                                                                                        | C                                          | A                                          | B                                                  | C                                           | A                                           | B                                                              | C |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
| Celery   | 1                         | 2 | PFCA<br>(7–9)<br>PFSA<br>(3–5)                                                                                                    | PFOS<br>PFBA<br>PFHxA<br>PFOA<br>PFBS<br>PFHxS<br>PFOS | 0.1–90.1<br>–<br>–<br>–<br>–<br>–<br>–                                 | –<br><LOQ–80.8<br>7.2–137.1<br>2–111.3<br>4.5–122.6<br>0.4–3.9<br>17.2–209.8 | ND–0.08<br>433.2–517.8<br>18.4–19.9<br>75.4–218.2<br>0.05–0.07<br>0.05–0.09<br>0.07–0.11 | –<br>17.3<br>4.8<br>1.4<br>2.5<br>5<br>4.2 | –<br>133.5<br>16.2<br>2.7<br>–<br>–<br>1.8 | 0.2<br>–<br>–<br>–<br>–<br>–<br>–                  | –<br>1.4<br>1.3<br>0.3<br>0.5<br>0.5<br>0.2 | –<br>0.8<br>1.1<br>0.3<br>0.7<br>0.6<br>0.6 | [97] <sup>b</sup><br>[22, 36] <sup>c</sup>                     |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
| Cucumber | 3                         | 5 | PFCA<br>(1–13)<br>PFSA<br>(1–8)<br>FASA<br>(0–3)<br>FASAA<br>(0–2)<br>FTCA<br>(0–1)                                               | PFBA<br>PFHxA<br>PFOA<br>PFBS<br>PFHxS<br>PFOS         | –<br>–<br>–<br>–<br>–<br>–                                             | 17–63<br>ND–0.3<br>0.5–797<br>3.8–15<br>0.2–0.3<br>ND–119                    | 0.1–13.6<br>ND–1.4<br>0.005–1.4<br>ND–0.06<br>ND–0.004<br>ND–0.06                        | –<br>–<br>–<br>–<br>–<br>–                 | –<br>–<br>–<br>–<br>–<br>–                 | –<br>–<br>–<br>–<br>–<br>–                         | –<br>–<br>–<br>–<br>–<br>–                  | –<br>–<br>–<br>–<br>–<br>–                  | [88, 98, 99] <sup>b</sup><br>[22, 37, 55, 66, 95] <sup>c</sup> |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
| Zucchini | 1                         | 2 | PFCA<br>(9–13)<br>PFSA<br>(3–5)<br>FASA<br>(0–3)<br>FASAA<br>(0–2)<br>FTCA<br>(0–1)                                               | PFBA<br>PFHxA<br>PFOA<br>PFBS<br>PFHxS<br>PFOS         | <LOQ–2.6<br><LOQ–9.6<br><LOQ–28.9<br><LOQ–19.0<br><LOQ–19.8<br><LOQ–81 | –<br>–<br>–<br>–<br>–<br>–                                                   | 1.5–2<br>0.03–0.1<br>ND–0.64<br>ND<br>ND<br>ND                                           | –<br>–<br>–<br>–<br>–<br>–                 | –<br>–<br>–<br>–<br>–<br>–                 | 0.6<br>1<br>0.4<br>0.1<br>0.2<br>0.1               | –<br>–<br>–<br>–<br>–<br>–                  | –<br>–<br>–<br>–<br>–<br>–                  | [96] <sup>a</sup><br>[55, 95] <sup>c</sup>                     |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
| Pumpkin  | 2                         | 2 | PFCA<br>(2–13)<br>PFSA<br>(3–8)<br>FASA (0–1)<br>FTSA (0–1)<br>PFCA<br>(5–13)<br>PFSA<br>(3–5)<br>FASA<br>(0–3)<br>FASAA<br>(0–3) | PFBA<br>PFHxA<br>PFOA<br>PFBS<br>PFHxS<br>PFOS         | <LOQ–0.6<br><LOQ–0.2<br><LOQ<br><LOQ–0.05<br><LOQ–0.2<br><LOQ–15       | –<br>–<br>–<br>–<br>–<br>–                                                   | <LOQ–638.1<br><LOQ–11.7<br>0.05–15.1<br><LOQ<br><LOQ<br><LOQ–0.09                        | –<br>–<br>–<br>–<br>–<br>–                 | –<br>–<br>–<br>–<br>–<br>–                 | 0.6<br>0.5<br>0.2<br>0.4–0.5<br>0.2–0.4<br>0.2–0.3 | –<br>–<br>–<br>–<br>–<br>–                  | –<br>–<br>–<br>–<br>–<br>–                  | [87, 100] <sup>a</sup><br>[36, 66] <sup>c</sup>                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
| Pepper   | 5                         | 5 | PFCA<br>(5–13)<br>PFSA<br>(3–5)<br>FASA<br>(0–3)<br>FASAA<br>(0–3)                                                                | PFBA<br>PFHxA<br>PFOA<br>PFBS<br>PFHxS<br>PFOS         | –<br>–<br>–<br>–<br>–<br>–                                             | 0.1–946.5<br>0.2–74.4<br>0.007–39.3<br>ND–0.2<br>ND–0.005<br>ND–0.2          | –<br>–<br>–<br>–<br>–<br>–                                                               | –<br>–<br>–<br>–<br>–<br>–                 | –<br>–<br>–<br>–<br>–<br>–                 | –<br>–<br>–<br>–<br>–<br>–                         | –<br>–<br>–<br>–<br>–<br>–                  | –<br>–<br>–<br>–<br>–<br>–                  | [22, 36, 37, 55, 95] <sup>c</sup>                              |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |
|          |                           |   |                                                                                                                                   |                                                        |                                                                        |                                                                              |                                                                                          |                                            |                                            |                                                    |                                             |                                             |                                                                |   |            |

**Table 2** (continued)

| Plant      | Study type (# of studies)                                        |   |   | Results      | References |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|------------|------------------------------------------------------------------|---|---|--------------|------------|-------------|-------------|---------|-----------|---|-----|-----------|----------|---|---|---|---|---|-----------------------------------|---------------------------------------|
|            | PFAS class<br>(range studied within the class for a given study) |   |   |              |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            | Concentration ranges<br>(ng/g dw)                                |   |   |              |            | TF (range)  |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
| A          | B                                                                | C | A | B            | C          |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
| Eggplant   | 5                                                                |   |   | FTCA (1)     |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            |                                                                  |   |   | PFCA (9-13)  | –          | –           | 0.5–4.5     | –       | –         | – | –   | –         | –        | – | – | – | – | – | [22, 37, 55, 66, 95] <sup>c</sup> |                                       |
|            |                                                                  |   |   | PFHxA        | –          | –           | ND-0.4      | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 |                                       |
|            |                                                                  |   |   | PFOA         | –          | –           | 0.2–0.8     | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 |                                       |
|            |                                                                  |   |   | PFBS (3-8)   | –          | –           | ND          | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 |                                       |
|            |                                                                  |   |   | PFHxS        | –          | –           | ND-0.001    | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 | –                                     |
|            |                                                                  |   |   | PFOS (0-3)   | –          | –           | ND          | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 | –                                     |
| Tomato     | 6                                                                |   |   | FASAA (0-2)  |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            |                                                                  |   |   | FTCA (1)     |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            |                                                                  |   |   | PFCA (9-13)  | <LOQ-48    | ND-121.9    | <LOQ-3.3    | 5       | –         | – | 2.1 | 5.2–15.35 | –        | – | – | – | – | – | –                                 | [96] <sup>a</sup>                     |
|            |                                                                  |   |   | PFHxA        | <LOQ-39.3  | ND-102.8    | ND-1.4      | 1-1.4   | –         | – | 1.8 | 1.77–6.2  | –        | – | – | – | – | – | –                                 | [28, 63, 88, 94, 97, 99] <sup>b</sup> |
|            |                                                                  |   |   | PFOA         | <LOQ-82.1  | ND-190.2    | ND-0.5      | 1-4.4   | –         | – | 1.3 | 0.5–2.5   | –        | – | – | – | – | – | –                                 | [22, 37, 55, 63, 66, 95] <sup>c</sup> |
|            |                                                                  |   |   | PFBS (3-8)   | <LOQ-78.7  | ND-177.1    | ND-0.3      | 0.7     | –         | – | 0.5 | 5.1       | –        | – | – | – | – | – | –                                 | –                                     |
|            |                                                                  |   |   | PFHxS        | <LOQ-84.4  | ND-7.7      | ND-0.004    | 1.8     | –         | – | 0.4 | 1.8       | –        | – | – | – | – | – | –                                 | –                                     |
| Strawberry | 2                                                                |   |   | PFOS (0-3)   | <LOQ-490   | ND-225.1    | ND-0.2      | 0.2–4.5 | –         | – | –   | –         | –        | – | – | – | – | – |                                   |                                       |
|            |                                                                  |   |   | FASAA (0-2)  |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            |                                                                  |   |   | FTCA         |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            |                                                                  |   |   | PFCA (0-1)   | –          | <LOQ-11,200 | <LOQ        | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 | [88, 93] <sup>b</sup>                 |
|            |                                                                  |   |   | PFHxA (2-13) | –          | <LOQ-1380   | <LOQ        | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 | [22, 101] <sup>c</sup>                |
|            |                                                                  |   |   | PFOA         | –          | <LOQ-302    | <LOQ        | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 | –                                     |
|            |                                                                  |   |   | PFBS (2-4)   | –          | <LOQ-373    | <LOQ        | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 | –                                     |
| Radish     | 3                                                                |   |   | FASA         | –          | <LOQ-150    | <LOQ-0.14   | –       | –         | – | –   | –         | –        | – | – | – | – | – |                                   |                                       |
|            |                                                                  |   |   | PFHxS (0-2)  | –          | <LOQ-132    | <LOQ        | –       | –         | – | –   | –         | –        | – | – | – | – | – | –                                 | –                                     |
|            |                                                                  |   |   | FASAA (0-3)  |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            |                                                                  |   |   | FASE (0-2)   |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            |                                                                  |   |   | FTSA (0-1)   |            |             |             |         |           |   |     |           |          |   |   |   |   |   |                                   |                                       |
|            |                                                                  |   |   | PFCA (7-9)   | –          | <LOQ-13.7   | 1-1167.5    | 2.9     | 10.8-15.2 | – | –   | 9.5       | 2.1-13.9 | – | – | – | – | – | –                                 | [83, 84, 88, 97] <sup>b</sup>         |
|            |                                                                  |   |   | PFHxA (3-5)  | –          | 7.3-44.5    | 0.1-103.3   | 1.2     | 3.1-14.2  | – | –   | 4.3       | 2.2-4.9  | – | – | – | – | – | –                                 | [22, 36, 55] <sup>c</sup>             |
| Carrot     | 4                                                                |   |   | PFOA         | –          | 0.08-1879.8 | 8-3.0       | –       | –         | – | –   | –         | –        | – | – | – | – | – |                                   |                                       |
|            |                                                                  |   |   | PFBS         | –          | 23.9-164.2  | <LOQ-0.5    | 1.3     | NA        | – | –   | –         | –        | – | – | – | – | – | –                                 |                                       |
|            |                                                                  |   |   | PFHxS        | –          | 2.8-10.3    | ND-0.1      | 2       | NA        | – | –   | –         | –        | – | – | – | – | – | –                                 |                                       |
|            |                                                                  |   |   | PFOS         | –          | 17-1250.3   | ND-1.8      | 0.7-2.6 | NA-0.9    | – | –   | –         | –        | – | – | – | – | – | –                                 | –                                     |
|            |                                                                  |   |   | PFHxA (1-13) | –          | 36-130      | 0.02-865.8  | 4.74    | 7.6-38.9  | – | –   | 13.7      | 2.2-3.1  | – | – | – | – | – | –                                 | [25, 34, 94, 98] <sup>b</sup>         |
|            |                                                                  |   |   | PFOA         | –          | ND-32.4     | ND-32.4     | 0.86    | 1.6-4.2   | – | –   | 9.6-15.8  | 3.2-4.3  | – | – | – | – | – | –                                 | [22, 36, 55, 95] <sup>c</sup>         |
|            |                                                                  |   |   | PFSA         | –          | ND-3567     | 0.005-138.6 | 0.5-0.6 | 0.3-0.6   | – | –   | 2.8-9.6   | 2.7-4.0  | – | – | – | – | – | –                                 | –                                     |

**Table 2** (continued)

| Plant  | Study type (# of studies) |   |   | Results | References                                                       |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|--------|---------------------------|---|---|---------|------------------------------------------------------------------|-----------------------------------|---------------------|---------|-------------|---|---|------------|---------|---|-----------------------------------------------------------------|------------------------------------------------|
|        | A                         | B | C |         | PFAS class<br>(range studied within the class for a given study) | Concentration ranges<br>(ng/g dw) |                     |         | RCF (range) |   |   | TF (range) |         |   | Hydroponic <sup>a</sup> , pot <sup>b</sup> , field <sup>c</sup> |                                                |
|        |                           |   |   |         |                                                                  | A                                 | B                   | C       | B           | C | A | B          | C       |   |                                                                 |                                                |
| Potato | 2                         | 2 |   | (1–5)   | –                                                                | –                                 | –                   | –       | –           | – | – | –          | –       | – | –                                                               | [82, 98] <sup>b</sup><br>[22, 95] <sup>c</sup> |
|        |                           |   |   | FASA    | –                                                                | –                                 | ND–1.0              | –       | NA–3        | – | – | –          | NA–10.9 |   |                                                                 |                                                |
|        |                           |   |   | PFHxS   | –                                                                | –                                 | ND–0.07             | –       | NA–0.07     | – | – | –          | NA–1.4  |   |                                                                 |                                                |
|        |                           |   |   | PFOS    | –                                                                | 0.5–782                           | ND–1.73             | 0.1–1.3 | NA          | – | – | –          | NA–2.2  |   |                                                                 |                                                |
|        |                           |   |   | FASAA   |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|        |                           |   |   | (0–2)   |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|        |                           |   |   | FTCA    |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|        |                           |   |   | (0–2)   |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|        |                           |   |   | DiPAP   |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|        |                           |   |   | (0–1)   |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|        |                           |   |   | PFCA    | –                                                                | –                                 | 0.8 <sup>d</sup>    | –       | –           | – | – | –          | –       | – |                                                                 |                                                |
|        |                           |   |   | (1–13)  | –                                                                | –                                 | 0.006 <sup>d</sup>  | –       | –           | – | – | –          | –       | – |                                                                 |                                                |
|        |                           |   |   | PFSA    | –                                                                | ND–234                            | 0.01 <sup>d</sup>   | –       | –           | – | – | –          | –       | – |                                                                 |                                                |
|        |                           |   |   | (1–5)   | –                                                                | –                                 | ND <sup>d</sup>     | –       | –           | – | – | –          | –       | – |                                                                 |                                                |
|        |                           |   |   | FASA    | –                                                                | –                                 | 0.0008 <sup>d</sup> | –       | –           | – | – | –          | –       | – |                                                                 |                                                |
|        |                           |   |   | (0–3)   | –                                                                | ND–590                            | ND <sup>d</sup>     | –       | –           | – | – | –          | –       | – |                                                                 |                                                |
|        |                           |   |   | FASAA   |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|        |                           |   |   | (0–2)   |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
|        |                           |   |   | FTCA    |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |
| (0–1)  |                           |   |   |         |                                                                  |                                   |                     |         |             |   |   |            |         |   |                                                                 |                                                |

Additional PFAS classes studied for each plant type are reported PFAS class column. Plant species with only one study, or one study and studies by Bao et al. [37] or Scher et al. [22] which reported collective values by plant types are not listed. Spiked and biosolid amended pot studies are combined in category B. The PFAS class column indicates additional PFAS studied in reported plants; however, sufficient data were not available for comparisons across study types and within a given species for these additional PFAS

Variables reported include concentration ranges, root concentration factors (RCF), and translocation factors (TF)

< LOQ below method limit of quantitation, ND not detected, NA not applicable, <sup>d</sup> value estimate

plant uptake [104]. Thus, study design must be considered when interpreting plant uptake magnitudes and mechanisms.

Field studies on plant uptake of PFAS and the number of different PFAS analyzed have increased in recent years; eleven field studies are summarized here that were not previously reviewed [42•]. Two field studies noted a correlation between the level of short-chain PFAS taken up by crops and the volume of PFAS-contaminated irrigation water used [22•, 55]. For example, 60% of the variability in PFBA concentrations in home garden-grown produce was accounted for by differences in the volume of PFAS-contaminated water used to irrigate the gardens [22•]. For a variety of lab and greenhouse designed studies, PFCAs have been shown to translocate from plant roots to shoots more readily than PFSA. However, field-scale translocation and soil-root transfer data are sparse; sampling rarely includes harvest of non-edible crop components. In cases where soil-root transfer was evaluated, PFAS contributions from atmospheric deposition confounded accurate TF and BCF comparisons, especially in plants grown near fluorochemical manufacturing. For example, field-grown lettuce at a site 0.3 km from fluorochemical manufacturing had up to 2370 ng/g PFBA and 1040 ng/g PFOA in lettuce and only 5 ng/g PFBA and 90 ng/g PFOA in soil [36], whereas lower concentrations in lettuce (no more than 270 ng/g PFBA and 200 ng/g PFOA) were observed in pot studies grown at similar soil PFAS concentrations (6 ng/g PFBA and 80 ng/g PFOA in soil at the time of harvest) [63]. Though costly, future field study designs should target inclusion of data that will enable estimations of BCFs and TFs to different plant domains to better ascertain uptake mechanisms and predict risks associated with accumulation in both human and animal edible components.

Studies that include additional PFAS classes as well as precursor and precursor degradation intermediates in plant studies are limited. A single study that included Cl-PFAESs found that the TF in wheat of 6:2 Cl-PFAES (a PFOS replacement) was similar to that of PFOS, while 8:2 Cl-PFAES had a lower TF, indicating that chain length effects occur within other PFAS classes similar to those observed for PFCAs and PFSA [77•]. A single study addressed uptake of ultra-short-chain PFCAs (C2 and C3) [75•]. This study was with hydroponically cultivated wheat in which they found high uptake of C2 and C3 PFCAs into the roots and shoots due to multiple uptake mechanisms [75•]. As previously noted, EtFOSA-fortified soils produced a series of degradation products (FOSAA, FOSA, and PFOS) which increased when growing carrots [25]. Both the intermediate FOSA and terminal metabolite PFOS were found on the carrot peel as well as transported into the leaves along with small amounts into the carrot core whereas the precursor EtFOSA remained in the soil with only small amounts found on the peel [25]. Zhao et al. [108] exposed hydroponically cultivated wheat, soybean, and pumpkin to EtFOSA (1 mmol/mL) and proposed

in vivo transformation of EtFOSA to FOSAA, FOSA, and PFOS in solution by microbes and further metabolic degradation in plant tissue to PFOS, PFHxS, and PFBS. Impurities in the EtFOSA standard lead to initial PFOS concentrations in the incubation solution; however, PFOS concentrations significantly increased in the presence of plant roots and associated microbes [108]. Similar results were observed for wheat with FOSA-fortified soils [51] and hydroponically grown soybeans and pumpkin [87] except that additional shorter-chain PFSA (PFHxS and PFBS) were observed, particularly in the roots with some in the shoots, albeit at much lower concentrations than PFOS. PFOS is a known microbial degradation product of FOSA while PFBS and PFHxS are not [34]. The authors attributed the formation of short-chain PFSA to a unique metabolic pathway. However, there are several noteworthy points to consider. First, the FOSA used was a technical grade (90–92% purity) with 8 mol% PFOS. Analysis targeted only FOSA, PFOS, and shorter-chain PFSA and PFCAs; therefore, other impurities would have been missed such as shorter perfluoroalkyl chain sulfonamides, which would lead to PFSA degradation products of the corresponding chain length. In addition, in the case of wheat grown in both systems, higher levels of these short chains were found when grown in soils where microbial degradation would be higher [51]. Also in the hydroponic systems for soybean and pumpkin, small amounts of both PFBS and PFHxS were found in the plant controls (no FOSA added) [87]. Lastly, in order to form PFBS and PFHxS from FOSA, cleavage to produce a shorter fluorinated alkyl chain with reattachment of either a fluorine atom (if C-C cleavage occurred) or a sulfonate group (if C-S cleavage occurred) would have had to happen, which seems thermodynamically unlikely. Therefore, although the authors propose that production of PFBS and PFHxS from FOSA indicates a unique plant-mediated metabolism, it is much more plausible that these results are due to impurities in the technical FOSA used, for which additional support using oxidative stress measures was provided [87]. Enhanced degradation in the presence of plants and formation of additional metabolites relative to what is known to occur in microbially active soils have also been shown for 6:2 FTSA [87] and 8:2 diPAP [34]. Carrots enhanced 8:2 diPAP degradation and yielded additional PFCAs compared to what occurred in soil-only controls as well as what was observed with lettuce [34]. Whereas acid metabolites translocated, 8:2 diPAP remained primarily in plant portions in contact with the soil (e.g., carrot, lettuce heart) [34]. Therefore, plant-mediated degradation of 8:2 diPAP was likely due to carrot exudates rather than degradation within the plant. In 6:2 FTSA exposure to hydroponically grown pumpkin, series of PFCAs (C2–C7) were produced with the C2 and C3 acids not present in root exudates controls; therefore, the authors concluded some 6:2 FTSA biotransformation was occurring within the plant. Such complexities can complicate interpretation of PFAS-specific uptake.

## Plant Uptake Mechanisms

Plant mechanisms involved in chemical uptake are plant-specific, but must first involve initial transfer to the root and adsorption to apoplastic plant tissue followed by translocation through the xylem in the central vasculature to the shoot and remainder of the plant. It is widely accepted that the Casparian strip, which is located in the root endodermis and made up of lignified structures that regulate water and mineral uptake by the roots, also serves to constrain translocation of contaminants from roots to the central vasculature, thus the rest of the plant [109]. The Casparian strip prevents passive transport of compounds across the endodermis, by sealing the nonliving spaces between cells and cell membranes (apoplast) [110]. The suberin lamella is an additional selective barrier that is formed in some plants by covering the endodermal cells with the hydrophobic polymer suberin [109].

Trends discussed in PFAS plant uptake studies are consistent with this hypothesis that the Casparian strip constrains translocation of long-chain PFCAs, PFSA, FOSA, and Cl-PFAEs, thus resulting in  $TF < 1$  for these PFAS. Felizeter et al. [91] hypothesized that transfer of long-chain PFAS was inhibited by the Casparian strip while the more soluble shorter chains were transported with water into the foliage by comparing RCF, FRCF, and TSCF values for C4–C14 PFCAs and C4–C8 PFSA in hydroponic studies with lettuce and in light of sorption to root isotherms. They showed that both RCFs and TSCFs had U-shaped curves with the minimum occurring with C7 PFCA while FRCFs consistently decreased with increasing chain length. They also showed that sorption to root isotherms were only linear for C4–C6 PFCAs and PFBS while all longer-chain PFAS exhibited nonlinear isotherms. Findings from hydroponic studies may not transfer well to studies with soils due to the strong chain-length-dependent interactions of PFAS with soils, thus affecting RCFs and subsequent translocation. Müller et al. [105•] further investigated this U-shaped curve phenomenon by measuring uptake, depuration, and translocation kinetics for C4–C10 PFAAs in hydroponically cultivated *Arabidopsis thaliana* in which they evaluated uptake kinetics to root and shoot independently. They also evaluated sorption to dead roots which they used to calculate sorption normalized concentration factors (SNCFs) to better differentiate between physical adsorption and active uptake. They observed preferential uptake of PFBA followed by slow and incomplete depuration. Thus, they proposed a 2-compartment uptake process occurs in which PFBA uptake by the root symplast is reversible whereas uptake by one or more compartments is not reversible, which may involve the central vasculature and/or organelles and be influenced by active transport from the roots [105•]. Other hydroponic studies with wheat also saw enhanced translocation of shorter-chain PFBA compared to the longer-chain PFAAs [75•, 78]. Different transport inhibitors were used to

elucidate active transport mechanisms in hydroponically grown wheat exposed to C2–C8 PFAAs [75•] and in an Asian wetland plant (*Alisma orientale*) exposed to PFOA and PFOS [111]. Both studies observed Michaelis-Menten type uptake behavior and when coupled to the effects of inhibitors concluded that PFAA uptake is an energy-dependent active uptake process mediated by carrier proteins. Depending on the specific PFAA and plant species, transport of these carriers could involve anion channels and/or aquaporin channels [75•, 111]. For chicory grown hydroponically, Gredelj et al. [102•] did not observe a pronounced U-shape trend in PFAA (C4–C10) uptake behavior, which was attributed to using higher PFAA exposure concentrations than comparable studies [91, 105•]. Gredelj et al. [102•, 104] also exemplified that chain-length-dependent uptake patterns observed hydroponically may not compare directly to soils grown in soils due to PFAS-soil interactions.

Several studies indicate that root proteins and lipids may influence uptake and bioaccumulation of PFAS in plant tissues [76, 83, 84, 108, 111]. Wen et al. [83, 84] found positive correlations between PFOS and PFOA RCFs and root protein content [83] as well as between TFs and shoot to root protein ratios [84] across seven plant species (alfalfa, lettuce, maize, mung bean, radish, ryegrass, and soybean). Likewise for the same plants, Wen et al. [83] found that although root protein content could account for 55% of the variations in N-EtFOSAA plant concentrations, when combined with lipid content, 85% of the variation across species was predicted. This was in contrast to PFOS and PFOA in which RCFs were negatively correlated to lipid content. In hydroponic studies, H. Zhao et al. [76] attributed increasing root accumulation with increasing PFCA chain length to sorption to root lipids or membrane proteins resulting in lower translocation of the longer-chain PFCAs (e.g., PFDoA) compared to the shorter-chain PFCAs. Zhao et al. [108] found that RCFs for N-EtFOSA increased with increasing root lipid content of hydroponically grown pumpkin, wheat, and soybean. Wang et al. [111] demonstrated that PFOS and PFOA partitioned differently into the subcellular plant components of the hydroponically grown wetland plant *Alisma orientale*, with PFOA residing primarily in the water-soluble fractions of stems, roots, and leaves and PFOS residing primarily in cell walls of roots and leaves and the water-soluble fraction of stems. PFOA and PFOS increased in the cell walls (anionic) and organelles (15–30% lipid) of roots, stems, and leaves with time, and reached an approximate equilibrium after 8 days of exposure [111]. When plants were transplanted into new PFAS-free culture solutions, approximately 80% of PFAS originally taken up was released [111]. These results exemplify that PFAS properties impact uptake to various plant components as well as differences in the subcellular distribution within a plant component.

Contaminants other than PFAS can invoke responses by the Casparian strip and suberin lamellae. For example, maize

roots responded to Cd exposure by developing suberin lamella, which along with the Casparian strip can inhibit the translocation of Cd and other contaminants to the xylem and the remainder of the plant [112]. Co-contamination of PFOS or PFOA with Cd decreased the bioaccumulation of these PFAAs in both wheat and rapeseed; however, the PFAA TFs decreased in wheat only and increased in rapeseed. Interestingly, both the bioaccumulation and TFs of Cd were increased in both plant types in the presence of these PFAAs [81]. Although the authors hypothesized that the cause of co-contamination effects was due to impacts on sorption to soil, thus soil solution concentrations, this is not well supported given the inconsistent data trends. It is more likely that Cd invoked changes in the plant. Wang et al. [113] observed an increased presence of suberin lamella or inactivation of aquaporin channels in response to Cd, which may also decrease PFAS translocation [81]. Additionally, potential PFAS-induced damage to the barriers in root structure at high concentrations (200 mg/L) [78] may allow for increased uptake. Therefore, future studies should consider plant properties that may impact PFAS uptake in addition to sorption dynamics.

Identifying and differentiating PFAS source contributions especially in field studies can be difficult as previously noted. PFAS in irrigation water are readily bioavailable for plant uptake, as demonstrated by Gredelj et al. [104] who showed chicory irrigated with PFAA-containing water having an increased uptake of long-chain PFAAs into the edible heads whereas PFAA soil concentration had a stronger impact on PFAA root concentrations. Seo et al. [114] attributed higher concentrations in plants than expected from soil transfer alone to atmospheric deposition [36]. Seo et al. [114] showed that PFCAs, neutral PFAS, and PFBS commonly partition to the gas phase, while PFOS tends to partition onto airborne particles. Gaseous uptake by tree bark from multiple species in China was identified as the main uptake mechanism for short-chain PFAS, which associated well with high lipid content [115]. In contrast, the presence of long-chain PFAS was attributed to airborne particles being trapped in bark fissures given the lower concentrations in the smooth bark species [115]. The influence of particles and surface texture on PFAS concentrations may also be responsible for higher PFAS concentrations in potato peel than flesh [42]. For example, recent work showed the presence of PFAS-containing soil mineral derived micron-sized particles on the surface of potatoes even after washing [95]. Therefore, while field studies are critical to bounding PFAS occurrence levels in plants, the multiple variables and variations that exist in field-scale studies confound data interpretation targeted at understanding uptake mechanisms.

## Metabolic Responses and Phytotoxicity

PFAS presence and uptake can elicit a metabolic response in plants [21, 75, 100, 116] which may include chemical modification, conjugation, and compartmentation. Superoxide dismutase (SOD), peroxidase (POD), catalase (CAT), glutathione (GSH), glutathione-S-transferase (GST), cytochromes P450 (CYP450), and malondialdehyde (MDA) are enzymes and metabolites that collectively serve as a defense against damage from superoxide radicals and reactive oxygen species (ROS) by preventing their formation or destroying those formed. PFAS exposure induces plant responses including enzymatic activity [78, 81, 87, 100, 103, 116] and metabolite production [21, 90] that may play a role in reducing phytotoxic impacts of PFAS within plants and/or promote in vivo degradation [87, 100].

Metabolic and phytotoxic responses were reported in crops and produce. Co-exposure of PFOS and PFOA caused several inorganic plant elements (Na, Mg, Cu, Fe, Ca, Mo, and K) to decrease in lettuce leaves while Zn increased, which may be due to ROS-induced ion channel leakage [21]. Also in lettuce, PFOS and PFOA altered amino acid metabolites, dipeptides, fatty acids, lipids, phytol, purine nucleosides, phenolic antioxidants, and flavonoids, as a result of stress responses to DNA injury, photosynthesis inhibition, and impact to energy metabolism [90]. PFAS exposure significantly increased chlorophyll, MDA, and POD, but slightly decreased SOD in rapeseed [81]. Co-contamination with Cd led to PFAS stress responses including decreased urease activity, POD activity, and biomass in rapeseed. In wheat, chlorophyll and MDA inhibition occurred [81]. Also, wheat shoot and root biomass decreased at higher PFAA exposure concentrations (2000 ng/g) while root biomass increased at lower exposure concentrations (200 ng/g) [79]. Additionally in wheat, exposures of PFOS at higher concentrations (100–200,000 µg/L) invoked changes in chlorophyll, protein synthesis, growth, SOD, and POD [78]. Chlorophyll *a* and chlorophyll *b* increased with exposure to long-chain PFAAs while exposure to short-chain PFAAs led to decreases in chlorophyll *a* [79]. Pumpkin and soybean exposure to FOSA increased SOD (soybean 19.2–30.8%, pumpkin 39.2–92.8%) and POD (soybean 19.2–20.7%, pumpkin 21.1–37.6%), likely in response to increased production of ROS [87]. GST and CYP450 also increased with FOSA exposure. Both enzymes are known to play a role in detoxification of contaminants, and thus may have also played a role in plant-mediated FOSA degradation [87]. CYP450 activity increased in pumpkin exposed to 6:2 FTSA and when CYP450 activity was reduced by addition of a CYP450 oxidation inhibitor (1-aminobenzotriazole), PFCA metabolites from 6:2 FTSA degradation decreased, supporting plant-mediated biotransformation [100]. Thus, metabolic responses may lead to some oxidative degradation of PFAS, which will be plant and PFAS dependent. However, stress

responses at the field-scale when irrigating fields or land applying waste-derived fertilizers have not been reported or observed. This is likely due to environmental concentrations typically being lower than those used in lab-based studies, the positive attributes of the amendments to the plants, and their ability to compensate for chemical-induced stress.

## Conclusions and Data Gaps

The PFAS list previously considered to be of interest in soil-plant transfer studies has expanded from select PFAAs (mainly PFOS, PFOA, PFBA, and PFBS) to include PFAS precursors, additional PFAAs, and additional PFAS classes (FASAs, Cl-PFAESs, FASAAAs, diPAPs, FTSAs, and FTCAs). Of the PFAS discussed, side-chain fluorinated polymer surfactants, diPAPs, FASAAAs, and FTSAs, were identified in waste-derived fertilizers or fields treated with waste-derived fertilizers. Cl-PFAESs should also be considered, especially in China [12, 77]. Future field studies on plant accumulation would benefit from including either nontarget PFAS screening and/or utilizing non-specific tests to better evaluate the level of precursors present that may serve as a PFAA reservoir. Degradation rates and pathways (intermediates on the way to PFAAs) in agriculturally relevant soils and conditions are lacking for many precursors and those for recently identified are completely unknown [30, 33]. Such studies are needed to elucidate the true potential for these precursors to contribute to PFAS intermediates and PFAAs becoming available in the root zone for uptake during the life of the plant. Field studies should also expand upon the number of PFAS quantified as increasingly more standards are becoming available. Future studies on PFAS in agricultural soils in both greenhouse and field studies should include sufficient details on soil and soil amendment properties that can influence PFAS mobility, and thus plant availability [60].

Land application of PFAS-containing media results in plant uptake of short-chain PFAS into plant components that are consumed by humans, utilized as fodder, or land-applied. Long-chain compounds typically sorb to or are taken up into plant roots and largely remain in the roots while short-chain compounds have a higher propensity to translocate into plant shoots. Uptake varied between species and within species and was associated with different plant properties including root lipids and proteins. However, more research is needed to make further inferences on the effects of plant characteristics on uptake. Uptake was shown to be an active carrier protein-mediated process in wheat, which contrasts with frequently cited passive transport processes that are constrained by the Casparian strip. Plant uptake depends on how long PFAS reside in the root zone and on PFAS concentrations. Therefore, the use of high concentrations and growing conditions that minimize leaching could explain why plants grown

in pot studies generally have higher concentrations of short-chain PFAS than have been observed in field studies. However, when plants are grown in fields close to fluorochemical manufacturing plants, higher concentrations than predicted from PFAS concentrations in soils may be observed due to atmospheric deposition or irrigation with PFAS-contaminated water. Likewise, comparisons made between hydroponic and soil-based studies must take into consideration the impacts of soil-based sorption, air–water interface sorption variability, porewater available compounds in soil, and morphological growth differences (root structure and surface area). Lastly, in some cases, plant enzymes were found to enhance degradation rates of precursors and increase the yields of the more bioavailable PFAAs.

Knowledge on mechanisms of soil–plant transfer, phytotoxicity, and PFAS metabolism in plants is growing and can inform future decision-making regarding cultivation on PFAS-laden soils. Similar to how lower PFAS levels are found in agricultural fields than pot studies, phytotoxic effects were observed at exposure concentrations that are generally considerably much higher than those observed in field studies. Risk of PFAS exposure from plant uptake is multifaceted [38] and encompasses not only plants that are directly consumed, but also through the food web (e.g., bioaccumulation in livestock feeding on PFAS contaminated water, forage, and feed) [117]. Field studies that demonstrate plant uptake, fate of PFAS, and risks associated with land-applied media containing PFAS are needed to inform farmers, landowners, and policymakers on how farming practices will impact the food supply chain.

Future studies should aim to:

- Investigate paper mill waste, industrial byproducts, recycled water, and pesticides as potential sources of PFAS in agricultural systems and their impact on source water in agricultural operations
- Conduct additional field studies, particularly those involving land application of typical waste-derived fertilizers or treated effluent
- Include a larger suite of PFAS for quantification consistent with current knowledge as well as analytical approaches that identify allow insight into additional PFAS including precursors that may serve as a long-term release reservoir of more mobile PFAS
- Investigate soil–plant transfer of replacements compounds, e.g., GenX, ADONA, and others as they become known
- Include more realistic PFAS concentrations in studies designed to improve our understanding of plant-specific uptake mechanisms and plant responses to PFAS exposure
- Include studies that improve our ability to quantify the role of plant enzymes on enhanced precursor degradation in the rhizosphere and within the plant

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## Compliance with Ethical Standards

**Conflict of Interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors. **Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s40726-020-00168-y>.

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## References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Bečanová J, Melymuk L, Vojta Š, Komprdová K, Klánová J. Screening for perfluoroalkyl acids in consumer products, building materials and wastes. *Chemosphere*. 2016;164:322–9. <https://doi.org/10.1016/j.chemosphere.2016.08.112>.
2. Schaidler LA, Balan SA, Blum A, Andrews DQ, Strynar MJ, Dickinson ME, et al. Fluorinated compounds in U.S. fast food packaging. *Environ Sci Technol Lett*. 2017;4:105–11. <https://doi.org/10.1021/acs.estlett.6b00435>.
3. Johnson MS, Buck RC, Cousins IT, et al. Estimating environmental hazard and risks from exposure to per- and polyfluoroalkyl substances (PFASs): outcome of a SETAC focused topic meeting. *Environ Toxicol Chem* 00:etc. 2020;4784. <https://doi.org/10.1002/etc.4784>.
4. Gibbens S. Toxic ‘ forever chemicals ’ more common in tap water than thought , report says. *Natl Geogr Mag*. 2020.
5. Buck RC, Franklin J, Berger JM, Conder JM, Cousins IT, de Voogt P, et al. Perfluoroalkyl and polyfluoroalkyl substances in the environment: terminology, classification, and origins. *Integr Environ Assess Manag*. 2011;7:513–41. <https://doi.org/10.1002/ieam.258>.
6. Poonthong S, Papadopoulou E, Padilla-Sánchez JA, Thomsen C, Haug LS. Multiple pathways of human exposure to poly- and perfluoroalkyl substances (PFASs): from external exposure to human blood. *Environ Int*. 2020;134:105244. <https://doi.org/10.1016/j.envint.2019.105244>.
7. Jian JM, Chen D, Han FJ, Guo Y, Zeng L, Lu X, et al. A short review on human exposure to and tissue distribution of per- and polyfluoroalkyl substances (PFASs). *Sci Total Environ*. 2018;636:1058–69. <https://doi.org/10.1016/j.scitotenv.2018.04.380>.
8. Liu Y, D’Agostino LA, Qu G, et al. High-resolution mass spectrometry (HRMS) methods for nontarget discovery and characterization of poly- and per-fluoroalkyl substances (PFASs) in environmental and human samples. *TrAC - Trends Anal Chem*. 2019;121:115420. <https://doi.org/10.1016/j.trac.2019.02.021>.
9. Liu W, Wu J, He W, Xu F. A review on perfluoroalkyl acids studies: environmental behaviors, toxic effects, and ecological and health risks. *Ecosyst Heal Sustain*. 2019;5:1–19. <https://doi.org/10.1080/20964129.2018.1558031>.
10. • Atea M, Maroli A, Tharayil N, Karanfil T. The overlooked short- and ultrashort-chain poly- and perfluorinated substances: a review. *Chemosphere*. 2019;220:866–82. <https://doi.org/10.1016/j.chemosphere.2018.12.186>. **Review of the research completed on short-chain PFAS in the environment and water. Continues to describe analytical methods and removal techniques.**
11. UNEP SC (2020) Alternatives to POPs.
12. Munoz G, Liu J, Vo Duy S, Sauv   S. Analysis of F-53B, Gen-X, ADONA, and emerging fluoroalkylether substances in environmental and biomonitoring samples: a review. *Trends Environ Anal Chem*. 2019;23:e00066. <https://doi.org/10.1016/j.teac.2019.e00066>.
13. Sunderland EM, Hu XC, Dassuncao C, Tokranov AK, Wagner CC, Allen JG. A review of the pathways of human exposure to poly- and perfluoroalkyl substances (PFASs) and present understanding of health effects. *J Expo Sci Environ Epidemiol*. 2018;29:131–47. <https://doi.org/10.1038/s41370-018-0094-1>.
14. Sungur Ş, K  ro  lu M, Turgut F. Determination of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) in food and beverages. *Int J Environ Anal Chem*. 2018;98:360–8. <https://doi.org/10.1080/03067319.2018.1468440>.
15. Sznajder-Katarzy  ska K, Surma M, Cie  lik I. A review of perfluoroalkyl acids (PFAAs) in terms of sources, applications, human exposure, dietary intake, toxicity, legal regulation, and methods of determination. *J Chem* 2019. 2019;2019:1–20. <https://doi.org/10.1155/2019/2717528>.
16. Jian JM, Guo Y, Zeng L, Liang-Ying L, Lu X, Wang F, et al. Global distribution of perfluorochemicals (PFCs) in potential human exposure source—a review. *Environ Int*. 2017;108:51–62. <https://doi.org/10.1016/j.envint.2017.07.024>.
17. Dreyer A, Kirchgeorg T, Weinberg I, Matthias V. Particle-size distribution of airborne poly- and perfluorinated alkyl substances. *Chemosphere*. 2015;129:142–9. <https://doi.org/10.1016/j.chemosphere.2014.06.069>.
18. Han D, Ma Y, Huang C, Zhang X, Xu H, Zhou Y, et al. Occurrence and source apportionment of perfluoroalkyl acids (PFAAs) in the atmosphere in China. *Atmos Chem Phys*. 2019;19:14107–17. <https://doi.org/10.5194/acp-19-14107-2019>.
19. Yamazaki E, Taniyasu S, Noborio K, Eun H, Thaker P, Kumar NJI, et al. Accumulation of perfluoroalkyl substances in lysimeter-grown rice in Japan using tap water and simulated contaminated water. *Chemosphere*. 2019;231:502–9. <https://doi.org/10.1016/j.chemosphere.2019.05.022>.
20. Zhao H, Qu B, Guan Y, et al. Influence of salinity and temperature on uptake of perfluorinated carboxylic acids (PFCAs) by

- hydroponically grown wheat (*Triticum aestivum* L.). Springerplus 5. 2016. <https://doi.org/10.1186/s40064-016-2016-9>.
21. Li P, Oyang X, Xie X, Li Z, Yang H, Xi J, et al. Phytotoxicity induced by perfluorooctanoic acid and perfluorooctane sulfonate via metabolomics. *J Hazard Mater*. 2019;389:121852. <https://doi.org/10.1016/j.jhazmat.2019.121852>.
  22. Scher DP, Kelly JE, Huset CA, et al. Occurrence of perfluoroalkyl substances (PFAS) in garden produce at homes with a history of PFAS-contaminated drinking water. *Chemosphere*. 2018;196:548–55. <https://doi.org/10.1016/j.chemosphere.2017.12.179>. **Edible portions of plants were collected from gardens at 20 homes within a water district, along with water samples and soil samples. Water concentrations for homes in the district were reported to have PFAS detected in all unfiltered samples. PFBA was found in water samples (85%) at high concentrations along with PFPeA (40%). Related concentration of PFBA in floret, leaves, and seeds to water or irrigation or watering events. Indicated that (a) PFCAs preferred to PFASs, (2) short-chain PFAAs bioaccumulated more, (3) species have uptake differences, and (4) plant-uptake differences between plant components.**
  23. Dalahmeh S, Tirgani S, Komakech AJ, Niwagaba CB, Ahrens L. Per- and polyfluoroalkyl substances (PFASs) in water, soil and plants in wetlands and agricultural areas in Kampala, Uganda. *Sci Total Environ*. 2018;631–632:660–7. <https://doi.org/10.1016/j.scitotenv.2018.03.024>.
  24. Nascimento RA, DBO N, Bizkarguenaga E, et al. Sulfuramid use in Brazilian agriculture: a source of per- and polyfluoroalkyl substances (PFASs) to the environment. *Environ Pollut*. 2018;242:1436–43. <https://doi.org/10.1016/j.envpol.2018.07.122>. **Sulfuramid (EtFOSA) is a precursor to PFOS, FOSAA, FOSA, and PFOA. Half-life of EtFOSA in the soil is short, so detection of FOSA and PFOS degradation products indicates use of sulfuramid contributes to PFAS contamination in Brazil. Soil samples reported PFAS, linear and branched PFOS detected at concentrations < 20 up to 3770 pg/g (1490 pg/g mean). PFAS were also found in river water, coastal water, and coastal sediments.**
  25. Zabaleta I, Bizkarguenaga E, Nunoo DBO, Schultes L, Leonel J, Prieto A, et al. Biodegradation and uptake of the pesticide sulfuramid in a soil-carrot mesocosm. *Environ Sci Technol*. 2018;52:2603–11. <https://doi.org/10.1021/acs.est.7b03876>.
  26. Baduel C, Mueller JF, Rotander A, Corfield J, Gomez-Ramos MJ. Discovery of novel per- and polyfluoroalkyl substances (PFASs) at a fire fighting training ground and preliminary investigation of their fate and mobility. *Chemosphere*. 2017;185:1030–8. <https://doi.org/10.1016/j.chemosphere.2017.06.096>.
  27. Gallen C, Drage D, Kaserzon S, et al. Occurrence and distribution of brominated flame retardants and perfluoroalkyl substances in Australian landfill leachate and biosolids. *J Hazard Mater*. 2016;312:55–64. <https://doi.org/10.1016/j.jhazmat.2016.03.031>. **Biosolids from 16 Australian water treatment plants were tested in addition to landfill leachate for PFAS, PBDEs, and HBCDDs (hexabromocyclodecane). BDE-209 and PFOS were detected at the highest concentrations in biosolids.**
  28. Navarro I, de la Torre A, Sanz P, Porcel MÁ, Pro J, Carbonell G, et al. Uptake of perfluoroalkyl substances and halogenated flame retardants by crop plants grown in biosolids-amended soils. *Environ Res*. 2017;152:199–206. <https://doi.org/10.1016/j.envres.2016.10.018>.
  29. Navarro I, de la Torre A, Sanz P, Porcel MÁ, Carbonell G, Martínez MÁ. Transfer of perfluorooctanesulfonate (PFOS), decabrominated diphenyl ether (BDE-209) and Dechlorane Plus (DP) from biosolid-amended soils to leachate and runoff water. *Environ Chem*. 2018;15:195. <https://doi.org/10.1071/EN18032>.
  30. Chu S, Letcher RJ. Side-chain fluorinated polymer surfactants in aquatic sediment and biosolid-augmented agricultural soil from the Great Lakes basin of North America. *Sci Total Environ*. 2017;607–608:262–70. <https://doi.org/10.1016/j.scitotenv.2017.06.252>.
  31. Stahl T, Gassmann M, Falk S, Brunn H. Concentrations and distribution patterns of perfluoroalkyl acids in sewage sludge and in biowaste in Hesse, Germany. *J Agric Food Chem*. 2018;66:10147–53. <https://doi.org/10.1021/acs.jafc.8b03063>.
  32. Armstrong DL, Lozano N, Rice CP, Ramirez M, Torrents A. Temporal trends of perfluoroalkyl substances in limed biosolids from a large municipal water resource recovery facility. *J Environ Manag*. 2016;165:88–95. <https://doi.org/10.1016/j.jenvman.2015.09.023>.
  33. Letcher RJ, Chu S, Smyth SA. Side-chain fluorinated polymer surfactants in biosolids from wastewater treatment plants. *J Hazard Mater*. 2020;388:122044. <https://doi.org/10.1016/j.jhazmat.2020.122044>. **Reported side-chain fluorinated polymer surfactants from Scotchgard™ fabric protectors, commonly quantified PFAS, and total fluorine in biosolids from Canadian WWTPs. Concentrations from two polymers utilized prior to and after 2002 ranged from 1.1 to 105 ng/g dw and 37.5 to 2051 ng/g dw, respectively, and were 30 times higher than that of 22  $\Sigma$ PFAS tested. Demonstrates how underestimation of PFAS in biosolids occurs without additional PFAS to be included in analytical methods and nontarget monitoring of PFAS.**
  34. Bizkarguenaga E, Zabaleta I, Prieto A, Fernández LA, Zuloaga O. Uptake of 8:2 perfluoroalkyl phosphate diester and its degradation products by carrot and lettuce from compost-amended soil. *Chemosphere*. 2016;152:309–17. <https://doi.org/10.1016/j.chemosphere.2016.02.130>.
  35. Choi YJ, Kim Lazcano R, Yousefi P, Trim H, Lee LS. Perfluoroalkyl acid characterization in U.S. municipal organic solid waste composts. *Environ Sci Technol Lett*. 2019;6:372–7. <https://doi.org/10.1021/acs.estlett.9b00280>.
  36. Liu Z, Lu Y, Song X, Jones K, Sweetman AJ, Johnson AC, et al. Multiple crop bioaccumulation and human exposure of perfluoroalkyl substances around a mega fluorochemical industrial park, China: implication for planting optimization and food safety. *Environ Int*. 2019;127:671–84. <https://doi.org/10.1016/j.envint.2019.04.008>.
  37. Bao J, Yu WJ, Liu Y, Wang X, Jin YH, Dong GH. Perfluoroalkyl substances in groundwater and home-produced vegetables and eggs around a fluorochemical industrial park in China. *Ecotoxicol Environ Saf*. 2019;171:199–205. <https://doi.org/10.1016/j.ecoenv.2018.12.086>.
  38. Brown JB, Conder JM, Arblaster JA, Higgins CP. Assessing human health risks from per- and polyfluoroalkyl substance (PFAS)-impacted vegetable consumption: a tiered modeling approach. *Environ Sci Technol*. 2020. <https://doi.org/10.1021/acs.est.0c03411>.
  39. Collivignarelli MC, Abbà A, Frattarola A, Carnevale Miino M, Padovani S, Katsoyiannis I, et al. Legislation for the reuse of biosolids on agricultural land in Europe: overview. *Sustain*. 2019;11:1–22. <https://doi.org/10.3390/su11216015>.
  40. Navarro I, de la Torre A, Sanz P, Fernández C, Carbonell G, Martínez MÁ. Environmental risk assessment of perfluoroalkyl substances and halogenated flame retardants released from biosolids-amended soils. *Chemosphere*. 2018;210:147–55. <https://doi.org/10.1016/j.chemosphere.2018.07.007>.
  41. Weber R, Bell L, Watson A, Petrlik J, Paun MC, Vijgen J. Assessment of pops contaminated sites and the need for stringent soil standards for food safety for the protection of human health. *Environ Pollut*. 2019;249:703–15. <https://doi.org/10.1016/j.envpol.2019.03.066>.

42. Ghisi R, Vamerali T, Manzetti S. Accumulation of perfluorinated alkyl substances (PFAS) in agricultural plants: a review. *Environ Res.* 2019;169:326–41. <https://doi.org/10.1016/j.envres.2018.10.023>. **The first review to outline PFAS in agriculture. Discussed sources from irrigation, land-applied biosolids, and atmospheric depositions. Uptake from studies reviewed included plant protein contribution, root surface area and biomass, water evapotranspiration (transpiration factor), and PFAS chain length dynamics.**
43. OECD. Toward a new comprehensive global database of per- and polyfluoroalkyl substances (PFASs): summary report on updating the OECD 2007 list of per- and polyfluoroalkyl substances (PFASs). *Ser Risk Manag.* 2018;39:1–24.
44. Zhi Y, Liu J. Sorption and desorption of anionic, cationic and zwitterionic polyfluoroalkyl substances by soil organic matter and pyrogenic carbonaceous materials. *Chem Eng J.* 2018;346:682–91. <https://doi.org/10.1016/j.cej.2018.04.042>.
45. Xiao F, Jin B, Golovko SA, Golovko MY, Xing B. Sorption and desorption mechanisms of cationic and zwitterionic per- and polyfluoroalkyl substances in natural soils: thermodynamics and hysteresis. *Environ Sci Technol.* 2019;53:11818–27. <https://doi.org/10.1021/acs.est.9b05379>.
46. Nakayama SF, Yoshikane M, Onoda Y, Nishihama Y, Iwai-Shimada M, Takagi M, et al. Worldwide trends in tracing poly- and perfluoroalkyl substances (PFAS) in the environment. *TrAC - Trends Anal Chem.* 2019;121:115410. <https://doi.org/10.1016/j.trac.2019.02.011>.
47. Martínez-Bueno MJ, Gómez Ramos MJ, Bauer A, Fernández-Alba AR. An overview of non-targeted screening strategies based on high resolution accurate mass spectrometry for the identification of migrants coming from plastic food packaging materials. *Trends Anal Chem.* 2019;110:191–203. <https://doi.org/10.1016/j.trac.2018.10.035>.
48. Liu J, Mejia Avendaño S. Microbial degradation of polyfluoroalkyl chemicals in the environment: a review. *Environ Int.* 2013;61:98–114. <https://doi.org/10.1016/j.envint.2013.08.022>.
49. Zhang S, Lu X, Wang N, Buck RC. Biotransformation potential of 6:2 fluorotelomer sulfonate (6:2 FTSA) in aerobic and anaerobic sediment. *Chemosphere.* 2016;154:224–30. <https://doi.org/10.1016/j.chemosphere.2016.03.062>.
50. Koch A, Aro R, Wang T, Yeung LWY. Towards a comprehensive analytical workflow for the chemical characterisation of organofluorine in consumer products and environmental samples. *TrAC - Trends Anal Chem.* 2020;123:115423. <https://doi.org/10.1016/j.trac.2019.02.024>.
51. Zhao S, Zhou T, Wang B, Zhu L, Chen M, Li D, et al. Different biotransformation behaviors of perfluorooctane sulfonamide in wheat (*Triticum aestivum* L.) from earthworms (*Eisenia fetida*). *J Hazard Mater.* 2018;346:191–8. <https://doi.org/10.1016/j.jhazmat.2017.12.018>.
52. Vedagiri UK, Anderson RH, Loso HM, Schwach CM. Ambient levels of PFOS and PFOA in multiple environmental media. *Remediat J.* 2018;28:9–51. <https://doi.org/10.1002/rem.21548>.
53. Rankin K, Mabury SA, Jenkins TM, Washington JW. A North American and global survey of perfluoroalkyl substances in surface soils: distribution patterns and mode of occurrence. *Chemosphere.* 2016;161:333–41. <https://doi.org/10.1016/j.chemosphere.2016.06.109>.
54. Kim H, Ekpe OD, Lee JH, Kim DH, Oh JE. Field-scale evaluation of the uptake of perfluoroalkyl substances from soil by rice in paddy fields in South Korea. *Sci Total Environ.* 2019;671:714–21. <https://doi.org/10.1016/j.scitotenv.2019.03.240>.
55. Zhang M, Wang P, Lu Y, Lu X, Zhang A, Liu Z, et al. Bioaccumulation and human exposure of perfluoroalkyl acids (PFAAs) in vegetables from the largest vegetable production base of China. *Environ Int.* 2020;135:105347. <https://doi.org/10.1016/j.envint.2019.105347>.
56. Riaz U, Murtaza G, Saifullah FM. Influence of different sewage sludges and composts on growth, yield, and trace elements accumulation in rice and wheat. *L Degrad Dev.* 2018;29:1343–52. <https://doi.org/10.1002/ldr.2925>.
57. Klavivko EJ, Nelson DW. Changes in soil properties from application of anaerobic sludge. *J Water Pollut Control Fed.* 1979;51:325–32.
58. Lu Q, He ZL, Stoffella PJ. Land application of biosolids in the USA: a review. *Appl Environ Soil Sci* 2012. 2012;2012:1–11. <https://doi.org/10.1155/2012/201462>.
59. Kim Lazcano R, Choi YJ, Mashtare ML, Lee LS. Characterizing and comparing per- and polyfluoroalkyl substances in commercially available biosolid and organic non-biosolid-based products. *Environ Sci Technol.* 2020;54:8640–8. <https://doi.org/10.1021/acs.est.9b07281>.
60. Li Y, Oliver DP, Kookana RS. A critical analysis of published data to discern the role of soil and sediment properties in determining sorption of per and polyfluoroalkyl substances (PFASs). *Sci Total Environ.* 2018;(628–629):110–20. <https://doi.org/10.1016/j.scitotenv.2018.01.167>.
61. Eriksson U, Haglund P, Kärman A. Contribution of precursor compounds to the release of per- and polyfluoroalkyl substances (PFASs) from waste water treatment plants (WWTPs). *J Environ Sci.* 2017;61:80–90. <https://doi.org/10.1016/j.jes.2017.05.004>.
62. Wen B, Li L, Zhang H, Ma Y, Shan XQ, Zhang S. Field study on the uptake and translocation of perfluoroalkyl acids (PFAAs) by wheat (*Triticum aestivum* L.) grown in biosolids-amended soils. *Environ Pollut.* 2014;184:547–54. <https://doi.org/10.1016/j.envpol.2013.09.040>.
63. Blaine AC, Rich CD, Hundal LS, Lau C, Mills MA, Harris KM, et al. Uptake of perfluoroalkyl acids into edible crops via land applied biosolids: field and greenhouse studies. *Environ Sci Technol.* 2013;47:14062–9. <https://doi.org/10.1021/es403094q>.
64. Sepulvado JG, Blaine AC, Hundal LS, Higgins CP. Occurrence and fate of perfluorochemicals in soil following the land application of municipal biosolids. *Environ Sci Technol.* 2011;45:8106–12. <https://doi.org/10.1021/es103903d>.
65. Faubert P, Bélisle CL, Bertrand N, Bouchard S, Chantigny MH, Paré MC, et al. Land application of pulp and paper mill sludge may reduce greenhouse gas emissions compared to landfilling. *Resour Conserv Recycl.* 2019;150:104415. <https://doi.org/10.1016/j.resconrec.2019.104415>.
66. Li P, Oyang X, Zhao Y, Tu T, Tian X, Li L, et al. Occurrence of perfluorinated compounds in agricultural environment, vegetables, and fruits in regions influenced by a fluorine-chemical industrial park in China. *Chemosphere.* 2019;225:659–67. <https://doi.org/10.1016/j.chemosphere.2019.03.045>.
67. Dauchy X, Boiteux V, Colin A, Hémard J, Bach C, Rosin C, et al. Deep seepage of per- and polyfluoroalkyl substances through the soil of a firefighter training site and subsequent groundwater contamination. *Chemosphere.* 2019;214:729–37. <https://doi.org/10.1016/j.chemosphere.2018.10.003>.
68. Campos Pereira H, Ullberg M, Kleja DB, Gustafsson JP, Ahrens L. Sorption of perfluoroalkyl substances (PFASs) to an organic soil horizon – effect of cation composition and pH. *Chemosphere.* 2018;207:183–91. <https://doi.org/10.1016/j.chemosphere.2018.05.012>.
69. McLachlan MS, Felizeter S, Klein M, et al. Fate of a perfluoroalkyl acid mixture in an agricultural soil studied in lysimeters. *Chemosphere.* 2019;223:180–7. <https://doi.org/10.1016/j.chemosphere.2019.02.012>.
70. Barzen-Hanson KA, Davis SE, Kleber M, Field JA. Sorption of fluorotelomer sulfonates, fluorotelomer sulfonamido betaines, and a fluorotelomer sulfonamido amine in national foam aqueous film-

- forming foam to soil. *Environ Sci Technol*. 2017;51:12394–404. <https://doi.org/10.1021/acs.est.7b03452>.
71. Qian J, Shen M, Wang P, Wang C, Hou J, Ao Y, et al. Adsorption of perfluorooctane sulfonate on soils: effects of soil characteristics and phosphate competition. *Chemosphere*. 2017;168:1383–8. <https://doi.org/10.1016/j.chemosphere.2016.11.114>.
  72. Park S, Lee LS, Ross I, Hurst J. Evaluating perfluorooctanesulfonate oxidation in permanganate systems. *Environ Sci Pollut Res*. 2020;27:13976–84. <https://doi.org/10.1007/s11356-020-07803-7>.
  73. Lyu Y, Brusseau ML, Chen W, Yan N, Fu X, Lin X. Adsorption of PFOA at the air–water interface during transport in unsaturated porous media. *Environ Sci Technol*. 2018;52:7745–53. <https://doi.org/10.1021/acs.est.8b02348>.
  74. Brusseau ML, Yan N, Van Glubt S, et al. Comprehensive retention model for PFAS transport in subsurface systems. *Water Res*. 2019;148:41–50. <https://doi.org/10.1016/j.watres.2018.10.035>.
  74. Zhang L, Sun H, Wang Q, et al. Uptake mechanisms of perfluoroalkyl acids with different carbon chain lengths (C2–C8) by wheat (*Triticum aestivum* L.). *Sci Total Environ*. 2019;654:19–27. <https://doi.org/10.1016/j.scitotenv.2018.10.443>. **Determined that PFCA uptake is an active process (carrier protein mediated), and aquaporins and the anion channel are additional uptake routes for C2 and C3 compounds. Ultra-short-chain PFAS had rapid uptake into the wheat roots that did not reach steady state compared to longer-chain PFAS where uptake slowed, and C8 PFAS where uptake reached steady state within 32 h.**
  76. Zhao H, Guan Y, Qu B. PFCA uptake and translocation in dominant wheat species (*Triticum aestivum* L.). *Int J Phytoremediation*. 2018;20:68–74. <https://doi.org/10.1080/15226514.2017.1337066>.
  76. Lin Q, Zhou C, Chen L, et al. Accumulation and associated phytotoxicity of novel chlorinated polyfluorinated ether sulfonate in wheat seedlings. *Chemosphere*. 2020;249:126447. <https://doi.org/10.1016/j.chemosphere.2020.126447>. **F-53B is an electroplating alternative to PFOS in China. Uptake and phytotoxicity were observed in the presence of Cl-PFAES. Uptake was observed mainly in roots, though 6:2 Cl-PFAES was comparable to PFOS uptake, and phytotoxic effects were greater than those of PFOS.**
  78. Qu B, Zhao H, Zhou J. Toxic effects of perfluorooctane sulfonate (PFOS) on wheat (*Triticum aestivum* L.) plant. *Chemosphere*. 2010;79:555–60. <https://doi.org/10.1016/j.chemosphere.2010.02.012>.
  79. Lan Z, Zhou M, Yao Y, Sun H. Plant uptake and translocation of perfluoroalkyl acids in a wheat–soil system. *Environ Sci Pollut Res*. 2018;25:30907–16. <https://doi.org/10.1007/s11356-018-3070-3>.
  80. Zhao S, Fang S, Zhu L, Liu L, Liu Z, Zhang Y. Mutual impacts of wheat (*Triticum aestivum* L.) and earthworms (*Eisenia fetida*) on the bioavailability of perfluoroalkyl substances (PFASs) in soil. *Environ Pollut*. 2014;184:495–501. <https://doi.org/10.1016/j.envpol.2013.09.032>.
  81. Zhao S, Fan Z, Sun L, Zhou T, Xing Y, Liu L. Interaction effects on uptake and toxicity of perfluoroalkyl substances and cadmium in wheat (*Triticum aestivum* L.) and rapeseed (*Brassica campestris* L.) from co-contaminated soil. *Ecotoxicol Environ Saf*. 2017;137:194–201. <https://doi.org/10.1016/j.ecoenv.2016.12.007>.
  82. Stahl T, Heyn J, Thiele H, Hüther J, Failing K, Georgii S, et al. Carryover of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) from soil to plants. *Arch Environ Contam Toxicol*. 2009;57:289–98. <https://doi.org/10.1007/s00244-008-9272-9>.
  83. Wen B, Pan Y, Shi X, Zhang H, Hu X, Huang H, et al. Behavior of N-ethyl perfluorooctane sulfonamido acetic acid (N-EFOSAA) in biosolids amended soil-plant microcosms of seven plant species: accumulation and degradation. *Sci Total Environ*. 2018;642:366–73. <https://doi.org/10.1016/j.scitotenv.2018.06.073>.
  84. Wen B, Wu Y, Zhang H, Liu Y, Hu X, Huang H, et al. The roles of protein and lipid in the accumulation and distribution of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in plants grown in biosolids-amended soils. *Environ Pollut*. 2016;216:682–8. <https://doi.org/10.1016/j.envpol.2016.06.032>.
  85. Krippner J, Falk S, Brunn H, Georgii S, Schubert S, Stahl T. Accumulation potentials of perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkyl sulfonic acids (PFASs) in maize (*Zea mays*). *J Agric Food Chem*. 2015;63:3646–53. <https://doi.org/10.1021/acs.jafc.5b00012>.
  86. Lan Z, Yao Y, Xu J, Chen H, Ren C, Fang X, et al. Novel and legacy per- and polyfluoroalkyl substances (PFASs) in a farmland environment: soil distribution and biomonitoring with plant leaves and locusts. *Environ Pollut*. 2020;263:114487. <https://doi.org/10.1016/j.envpol.2020.114487>.
  87. Zhao S, Liang T, Zhou T, Li D, Wang B, Zhan J, et al. Biotransformation and responses of antioxidant enzymes in hydroponically cultured soybean and pumpkin exposed to perfluorooctane sulfonamide (FOSA). *Ecotoxicol Environ Saf*. 2018;161:669–75. <https://doi.org/10.1016/j.ecoenv.2018.06.048>.
  88. Defence AGD of (2017) PFAS in plants – 2017 Study findings Army Aviation Centre Oakey Stage 2C Environmental Investigation Background to the Plant Study.
  89. Shigei M, Ahren L, Hazaymeh A, Dalahmeh S. Per- and polyfluoroalkyl substances in water and soil in wastewater-irrigated farmland in Jordan. *Sci Total Environ*. 2020;716:137057. <https://doi.org/10.1016/j.scitotenv.2020.137057>.
  90. Li P, Oyang X, Xie X, Guo Y, Li Z, Xi J, et al. Perfluorooctanoic acid and perfluorooctane sulfonate co-exposure induced changes of metabolites and defense pathways in lettuce leaves. *Environ Pollut*. 2019;256:113512. <https://doi.org/10.1016/j.envpol.2019.113512>.
  91. Felizeter S, McLachlan MS, de Voogt P. Uptake of perfluorinated alkyl acids by hydroponically grown lettuce (*Lactuca sativa*). *Environ Sci Technol*. 2012;46:11735–43. <https://doi.org/10.1021/es302398u>.
  91. Yu P-F, Xiang L, Li X-H, et al (2018) Cultivar-dependent accumulation and translocation of perfluorooctanesulfonate among lettuce (*Lactuca sativa* L.) cultivars grown on perfluorooctanesulfonate-contaminated soil. *J Agric Food Chem* 66:13096–13106. <https://doi.org/10.1021/acs.jafc.8b04548>. **Accumulation comparisons between 3 lettuce subtypes (14 romaine lettuce cultivars, 7 leaf lettuce cultivars, and 5 head cultivars). Leaf lettuce subtypes had the lowest PFOS accumulations, but all subtypes had differences in accumulation between treatments and cultivars. PFOS did not influence transpiration or protein content (no toxicity determined by the values measured). Infers that contaminated fields should be planted with cultivars that take up less PFOS including leaf lettuce subtype with low protein content, low stomatal conductance, and low transpiration. These subtypes have lower protein-mediated transpiration and it is suggested that proteins in shoots and roots may be carriers (uptake and translocation mechanism), so carrier or channel proteins should be evaluated to determine which proteins are present in low PFOS accumulating cultivars.**
  93. Blaine AC, Rich CD, Sedlacko EM, Hyland KC, Stushnoff C, Dickenson ERV, et al. Perfluoroalkyl acid uptake in lettuce (*Lactuca sativa*) and strawberry (*Fragaria ananassa*) irrigated with

- reclaimed water. Environ Sci Technol. 2014;48:14361–8. <https://doi.org/10.1021/es504150h>.
94. Lal MS, Megharaj M, Naidu R, Bahar MM. Uptake of perfluorooctane sulfonate (PFOS) by common home-grown vegetable plants and potential risks to human health. Environ Technol Innov. 2020;19:100863. <https://doi.org/10.1016/j.eti.2020.100863>.
  95. Eun H, Yamazaki E, Taniyasu S, Miecznikowska A, Falandysz J, Yamashita N. Evaluation of perfluoroalkyl substances in field-cultivated vegetables. Chemosphere. 2020;239:124750. <https://doi.org/10.1016/j.chemosphere.2019.124750>.
  96. Felizeter S, McLachlan MS, De Voogt P. Root uptake and translocation of perfluorinated alkyl acids by three hydroponically grown crops. J Agric Food Chem. 2014;62:3334–42. <https://doi.org/10.1021/jf500674j>.
  97. Blaine AC, Rich CD, Sedlacko EM, Hundal LS, Kumar K, Lau C, et al. Perfluoroalkyl acid distribution in various plant compartments of edible crops grown in biosolids-amended soils. Environ Sci Technol. 2014;48:7858–65. <https://doi.org/10.1021/es500016s>.
  98. Lechner M, Knapp H. Carryover of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) from soil to plant and distribution to the different plant compartments studied in cultures of carrots (*Daucus carota* ssp. *Sativus*), potatoes (*Solanum tuberosum*), and cucu. J Agric Food Chem. 2011;59:11011–8. <https://doi.org/10.1021/jf201355y>.
  99. Bao J, Li CL, Liu Y, Wang X, Yu WJ, Liu ZQ, et al. Bioaccumulation of perfluoroalkyl substances in greenhouse vegetables with long-term groundwater irrigation near fluorochemical plants in Fuxin, China. Environ Res. 2020;188:109751. <https://doi.org/10.1016/j.envres.2020.109751>.
  100. Zhao S, Liang T, Zhu L, Yang L, Liu T, Fu J, et al. Fate of 6:2 fluorotelomer sulfonic acid in pumpkin (*Cucurbita maxima* L.) based on hydroponic culture: uptake, translocation and biotransformation. Environ Pollut. 2019;252:804–12. <https://doi.org/10.1016/j.envpol.2019.06.020>.
  101. Gobelius L, Lewis J, Ahrens L. Plant uptake of per- and polyfluoroalkyl substances at a contaminated fire training facility to evaluate the phytoremediation potential of various plant species. Environ Sci Technol. 2017;51:12602–10. <https://doi.org/10.1021/acs.est.7b02926>.
  101. Gredelj A, Nicoletto C, Polesello S, et al. Uptake and translocation of perfluoroalkyl acids (PFAAs) in hydroponically grown red chicory (*Cichorium intybus* L.): growth and developmental toxicity, comparison with growth in soil and bioavailability implications. Sci Total Environ. 2020;720:137333. <https://doi.org/10.1016/j.scitotenv.2020.137333> **Plant uptake model built on prior experiments in soil. Creates comparisons between soil and hydroponically grown chicory. Contributed high accumulation of perfluoroalkyl acids in crops to root to xylem partition coefficients. Describes a dynamic system with no rapid uptake, but with chemical mass increasing continuously with transpiration.**
  103. Sharma N, Barion G, Shrestha I, Ebinezer LB, Trentin AR, Vamerali T, et al. Accumulation and effects of perfluoroalkyl substances in three hydroponically grown *Salix* L. species. Ecotoxicol Environ Saf. 2020;191:110150. <https://doi.org/10.1016/j.ecoenv.2019.110150>.
  104. Gredelj A, Nicoletto C, Valsecchi S, et al (2020) Uptake and translocation of perfluoroalkyl acids (PFAA) in red chicory (*Cichorium intybus* L.) under various treatments with pre-contaminated soil and irrigation water. Sci Total Environ 708: 134766. <https://doi.org/10.1016/j.scitotenv.2019.134766>.
  104. Müller CE, GH LF, Timofte AE, et al. Competing mechanisms for perfluoroalkyl acid accumulation in plants revealed using an *Arabidopsis* model system. Environ Toxicol Chem. 2016;35:1138–47. <https://doi.org/10.1002/etc.3251> **Established uptake models for PFAAs in hydroponically grown thale cress (*Arabidopsis thaliana*) by examining uptake and depuration in plant roots and shoots as well as sorption to dead root tissue. Root concentrations increased via adsorption to apoplast and symplast and quickly reached a steady state for 9 PFAAs; however, PFBA saturation kinetics were reduced and indicated increased transport. Depuration occurred completely in roots for 9 PFAAs excluding PFBA but not for PFAAs translocated to shoots. Thus, proposing a 2-compartment uptake model for PFBA and a 1-compartment model for the other PFAAs examined.**
  106. McLachlan MS, Felizeter S, Klein M, et al. Fate of a perfluoroalkyl acid mixture in an agricultural soil studied in lysimeters. Chemosphere. 2019;223:180–7. <https://doi.org/10.1016/j.chemosphere.2019.02.012>.
  107. Bräunig J, Baduel C, Barnes CM, Mueller JF. Leaching and bio-availability of selected perfluoroalkyl acids (PFAAs) from soil contaminated by firefighting activities. Sci Total Environ. 2019;646:471–9. <https://doi.org/10.1016/j.scitotenv.2018.07.231>.
  108. Zhao S, Zhou T, Zhu L, Wang B, Li Z, Yang L, et al. Uptake, translocation and biotransformation of N-ethyl perfluorooctanesulfonamide (N-EtFOSA) by hydroponically grown plants. Environ Pollut. 2018;235:404–10. <https://doi.org/10.1016/j.envpol.2017.12.053>.
  109. Barberon M. The endodermis as a checkpoint for nutrients. New Phytol. 2017;213:1604–10. <https://doi.org/10.1111/nph.14140>.
  110. Doblas VG, Geldner N, Barberon M. The endodermis, a tightly controlled barrier for nutrients. Curr Opin Plant Biol. 2017;39:136–43. <https://doi.org/10.1016/j.pbi.2017.06.010>.
  111. Wang TT, Ying GG, He LY, Liu YS, Zhao JL. Uptake mechanism, subcellular distribution, and uptake process of perfluorooctanoic acid and perfluorooctane sulfonic acid by wetland plant *Alisma orientale*. Sci Total Environ. 2020;733:139383. <https://doi.org/10.1016/j.scitotenv.2020.139383>.
  112. Liska D, Martinka M, Kohanova J, Lux A. Asymmetrical development of root endodermis and exodermis in reaction to abiotic stresses. Ann Bot. 2016;118:667–74. <https://doi.org/10.1093/aob/mcw047>.
  113. Wang P, Calvo-Polanco M, Rey G, Barberon M, Champeyroux C, Santoni V, et al. Surveillance of cell wall diffusion barrier integrity modulates water and solute transport in plants. Sci Rep. 2019;9:1–11. <https://doi.org/10.1038/s41598-019-40588-5>.
  114. Seo SH, Son MH, Shin ES, Choi SD, Chang YS. Matrix-specific distribution and compositional profiles of perfluoroalkyl substances (PFASs) in multimedia environments. J Hazard Mater. 2019;364:19–27. <https://doi.org/10.1016/j.jhazmat.2018.10.012>.
  115. Liu Y, Hou X, Chen W, Kong W, Wang D, Liu J, et al. Occurrences of perfluoroalkyl and polyfluoroalkyl substances in tree bark: interspecies variability related to chain length. Sci Total Environ. 2019;689:1388–95. <https://doi.org/10.1016/j.scitotenv.2019.06.454>.
  116. Zhang W, Zhang D, Zagorevski DV, Liang Y. Exposure of *Juncus effusus* to seven perfluoroalkyl acids: uptake, accumulation and phytotoxicity. Chemosphere. 2019;233:300–8. <https://doi.org/10.1016/j.chemosphere.2019.05.258>.
  117. Brambilla G, D'Hollander W, Oliaei F, et al. Pathways and factors for food safety and food security at PFOS contaminated sites with a problem based learning approach. Chemosphere. 2015;129:192–202. <https://doi.org/10.1016/j.chemosphere.2014.09.050>.

## Critical Review

# Per- and Polyfluoroalkyl Substance Toxicity and Human Health Review: Current State of Knowledge and Strategies for Informing Future Research

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**Abstract:** Reports of environmental and human health impacts of per- and polyfluoroalkyl substances (PFAS) have greatly increased in the peer-reviewed literature. The goals of the present review are to assess the state of the science regarding toxicological effects of PFAS and to develop strategies for advancing knowledge on the health effects of this large family of chemicals. Currently, much of the toxicity data available for PFAS are for a handful of chemicals, primarily legacy PFAS such as perfluorooctanoic acid and perfluorooctane sulfonate. Epidemiological studies have revealed associations between exposure to specific PFAS and a variety of health effects, including altered immune and thyroid function, liver disease, lipid and insulin dysregulation, kidney disease, adverse reproductive and developmental outcomes, and cancer. Concordance with experimental animal data exists for many of these effects. However, information on modes of action and adverse outcome pathways must be expanded, and profound differences in PFAS toxicokinetic properties must be considered in understanding differences in responses between the sexes and among species and life stages. With many health effects noted for a relatively few example compounds and hundreds of other PFAS in commerce lacking toxicity data, more contemporary and high-throughput approaches such as read-across, molecular dynamics, and protein modeling are proposed to accelerate the development of toxicity information on emerging and legacy PFAS, individually and as mixtures. In addition, an appropriate degree of precaution, given what is already known from the PFAS examples noted, may be needed to protect human health. *Environ Toxicol Chem* 2021;40:606–630. © 2020 SETAC

**Keywords:** Per- and polyfluoroalkyl substances; Perfluorooctane sulfonate; Perfluorooctanoic acid; Persistent compounds; Contaminants of emerging concern

## INTRODUCTION

Per- and polyfluoroalkyl substances (PFAS) are ubiquitous in environmental media because of their prolific use in a variety of industrial and consumer products and processes (Jian et al. 2018; Sunderland et al. 2019). Widespread human

exposure to PFAS in water, food, and air coupled with the lengthy environmental persistence and biological half-lives of some PFAS have led to measurable PFAS in the blood of nearly the entire population in developed countries, with health effects reported globally (Kato et al. 2011; Khalil et al. 2016; Stableski et al. 2016; Jian et al. 2018). Information needed to evaluate the potential risk of harm from PFAS includes the types of adverse health effects that might occur at environmentally relevant exposures, especially in sensitive life stages. Information is also needed regarding the mode(s) of action for

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PFAS toxicity, PFAS toxicokinetics in both humans and laboratory animal models, and dose–response relationships. Risk estimates can be used to inform public health exposure limits that will determine the need for exposure mitigation and environmental cleanup.

There are several challenges in obtaining the information needed to assess human health risk from the large number of PFAS with a wide range of structures and chemical properties (Buck et al. 2011; Wang Z et al. 2017; Organisation for Economic Co-operation Development 2018). Data on the identity, composition, and quantity of PFAS used in products and processes are often treated as confidential business information, hampering efforts to estimate exposure sources and routes. The Organisation for Economic Co-operation and Development's (OECD's) chemical inventory reports over 4000 substances that contain at least one perfluoroalkyl (–CnF2n–) moiety (Organisation for Economic Co-operation Development 2018), and the US Environmental Protection Agency (USEPA) has a curated list of over 8000 PFAS included, based on structure (US Environmental Protection Agency 2018) from the CompTox Chemicals Dashboard (Williams et al. 2017). The USEPA estimates that more than 600 PFAS are currently in commercial use (US Environmental Protection Agency 2019). Experimental studies of PFAS have been limited by funding and the availability of analytical standards, confounded by the prevalence of background contamination in laboratory materials, and challenged by physicochemical properties such as high surface activity that can interfere with and complicate measurements. Consequently, sufficient information to conduct quantitative risk assessment is currently available for only a relative few PFAS (Post 2020). Further, although typical human exposures involve various combinations of PFAS (Centers for Disease Control and Prevention 2017), only a few efforts address interactions of PFAS mixtures; and a well-founded, scientific basis on which to evaluate their combined toxic potential does not yet exist (Carr et al. 2013; Wolf et al. 2014; Zhou et al. 2017; Hoover et al. 2019; US Environmental Protection Agency 2020).

The Society of Environmental Toxicology and Chemistry (SETAC) North America held the focused topic meeting and workshop “Environmental Risk Assessment of PFAS” on 12 to 15 August 2019, covering a wide range of topics related to the characterization of health risks posed by PFAS. The overarching purpose of the meeting was to begin a scientific discussion on how best to approach studying, grouping, and regulating the large number of PFAS to which people and other species are potentially exposed (for charge questions and other details, see Johnson et al. 2020). We refer to these PFAS as “legacy” (those perfluoroalkyl acids for which there are accumulating health data but that may be phased out or decreased in use) and “emerging” (those which are being used as replacements, often with minimal health effects data). The objectives of the Human Health Toxicity section were to provide an assessment of the state of the science in understanding toxicological effects of PFAS and to explore and discuss strategies for advancing knowledge on the toxicity of individual and groups of PFAS.

## CURRENT KNOWLEDGE OF PFAS TOXICITY IN HUMANS

Like other chemicals, PFAS are potentially capable of producing a wide range of adverse health effects depending on the circumstances of exposure (magnitude, duration, and route of exposures, etc.) and factors associated with the individuals exposed (e.g., age, sex, ethnicity, health status, and genetic predisposition). Aspects to consider when establishing the health effects of greatest concern are 1) effects for which evidence is the strongest (strength of evidence can come from consistency of effect across studies, strength of effect associations in epidemiological studies, and species concordance, as examples), and 2) effects for which potential impact is greatest (factors contributing to impact can include severity of effect, functional impairment, persistence, and specific age groups that are susceptible, as examples). Brief summaries of candidate PFAS health effects from human and experimental reports are provided in this section (Figure 1).

### Immune function

Epidemiological studies have explored relationships between PFAS exposure and laboratory biomarkers of immunomodulation, such as vaccine responses. A doubling of perfluorooctane sulfonate (PFOS) in maternal serum was associated with a 39% ( $p < 0.001$ ) reduction in diphtheria antibody concentration in children (age 5 yr), with increased odds of falling below clinically protective values against diphtheria and tetanus at age 7 yr. The authors noted that a “2-fold greater concentration of major PFCs [perfluorinated compounds] in child serum was associated with a difference of –49% (95% CI, –67% to –23%) in the overall antibody concentration” (Grandjean et al. 2012). Decreased immunological response persisted at age 13 yr (Grandjean et al. 2017). Adverse associations were also noted for responses to rubella, mumps, and *Hemophilus influenza* vaccinations in children and to vaccinations in adults (Granum et al. 2013; Looker et al. 2014; Stein et al. 2016; Abraham et al. 2020). In a single study, modest down-regulation of C-reactive protein response, a marker of human systemic inflammation, was also reported to be associated with perfluorooctanoic acid (PFOA) blood levels (Genser et al. 2015).

Disease outcomes linked with immunosuppression such as clinician-recorded diagnoses of childhood infections have also been associated with prenatal exposures to PFOS and perfluorohexane sulfonate (PFHxS) (Goudarzi et al. 2017). A pregnancy cohort study prospectively detected increased risk of airway and throat infections and diarrhea in children through age 10 yr, correlated with cord-blood PFAS measurements (Impinen et al. 2018, 2019). A recent review concluded that exposure to PFAS in infancy and childhood resulted in an immunosuppressive effect characterized by an increased incidence of atopic dermatitis and lower respiratory tract infections (Kvalem et al. 2020). Some of the immunological effects were sex-specific, but the authors cautioned that there were inconsistencies across studies (Kvalem et al. 2020).

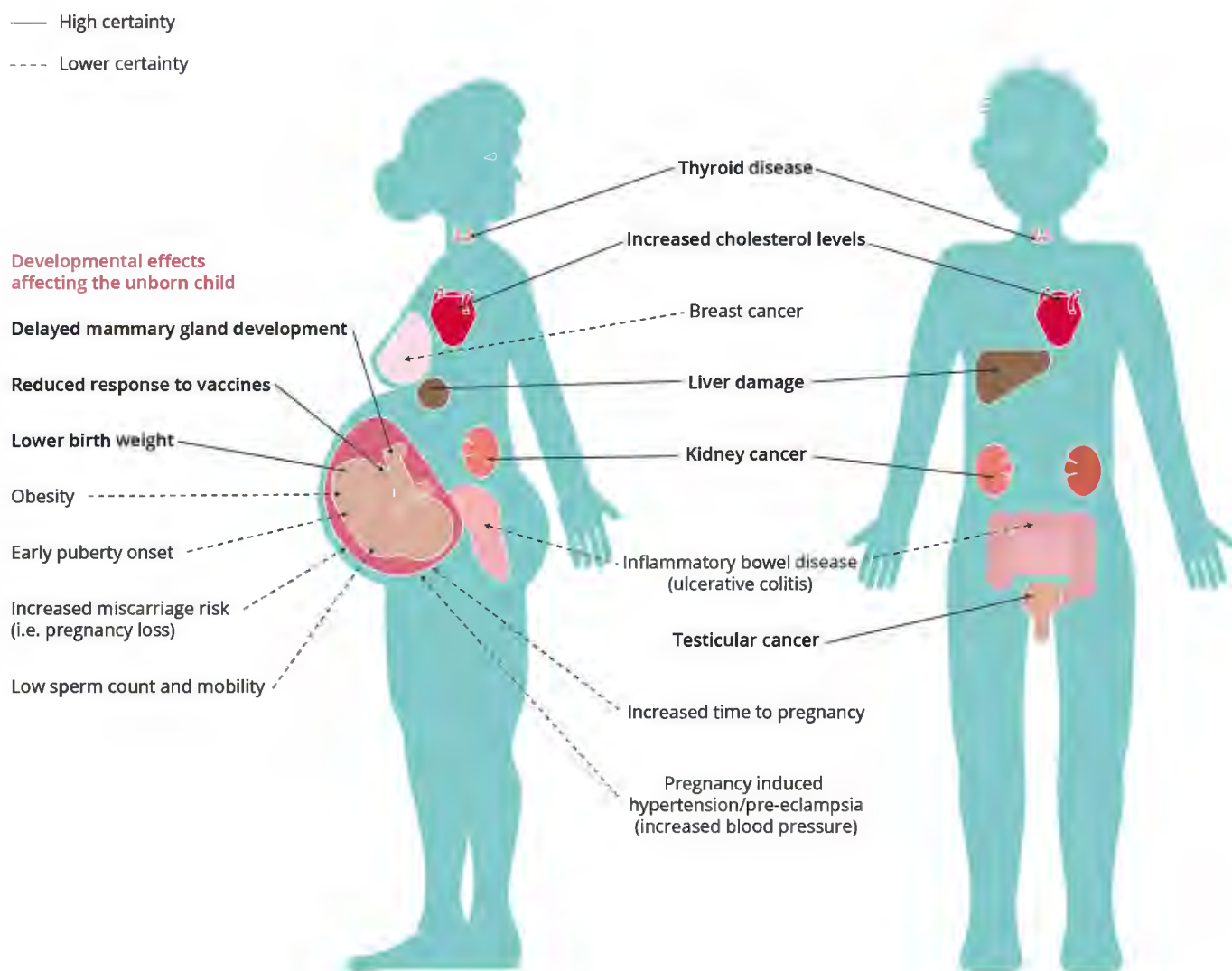


**FIGURE 1:** Effects of per- and polyfluoroalkyl substances on human health. Used with permission from European Environment Agency (2019). Original sources for this figure: National Toxicology Program (2016), C8 Science Panel (2012), IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (2017), Barry et al. (2013), Fenton et al. (2009), and White et al. (2011b).

Overall, available data provide strong evidence that PFAS exposure can suppress the human immune response.

Population studies of immune hyperreactive diseases have resulted in mixed findings. Studies on childhood allergy and asthma outcomes have shown no association with PFAS (Impinen et al. 2018, 2019), whereas others have found substantial effects, including provocative evidence that subgroups of individuals not adequately immunized may be at an increased risk for disease a priori (Qin et al. 2017; Timmermann et al. 2017a). For example, a case-control study of Taiwanese children compared the first and fourth quartiles of serum measurements for 11 PFAS with asthma and other immune markers and reported confidence intervals well above 1.0 for PFOA and others (Qin et al. 2017). However, review articles concerning PFAS and childhood allergy and asthma offer nuanced, age- and sex-specific interpretations and advise against firm conclusions (Kvalem et al. 2020).

Chronic autoimmune outcomes, including thyroid disease (see section *Thyroid function*) and inflammatory bowel disease

(IBD), have also been considered. A study in contaminated communities ( $n=32\,254$ ) detected an association between both prevalence and incidence of ulcerative colitis (UC) and PFOA exposure (linear trend  $p=0.0001$  [Steenland et al. 2013]). A worker study ( $n=3\,713$ ) found a higher prevalence ( $p=0.01$ ) and incidence ( $p<0.05$ ) of UC with increasing log PFOA serum concentrations (Steenland et al. 2015). A case-control study of children and young adults from a background exposure community in Atlanta, Georgia, USA, also found higher serum PFOA levels in patients with UC (Steenland et al. 2018b). In contrast to PFOA-related associations in US populations, a study of a contaminated community in Sweden ( $n=63\,074$ ) did not show a consistent association of IBD with any PFAS exposure (Xu et al. 2020b).

Recent, thorough reviews (National Toxicology Program 2016; DeWitt et al. 2019; Pachkowski et al. 2019) emphasize some key concepts: 1) there is concordance between animal studies and human epidemiological observations that PFAS modify the immune response, and 2) there are noted

complexities in assuming dose–response continuums, including possible differences in life-stage vulnerability. Authors of these reviews note uncertainty about which outcome will be of most importance but agree that immunotoxicity should be included among sensitive human PFAS toxicity endpoints.

### Thyroid function

The C8 Science Panelists concluded that there is a “probable link” of PFOA exposure to thyroid disease, with sex-specific outcomes in women (for hyperthyroid disease) versus men (hypothyroid disease) (C8 Science Panel 2012). Subsequent reviews drew attention to hypothyroid outcomes in women and children and to the possibility that populations with a priori circulating antithyroid peroxidase antibodies may be at additional risk (Coperchini et al. 2017). A broad childhood disease review noted “some evidence” that PFAS cause childhood hypothyroidism and characterized the number of studies as “limited” for childhood disease conclusions (Rappazzo et al. 2017). A meta-analysis of 12 child and adult studies that excluded populations with higher exposures noted that PFAS exposure is negatively associated with serum total thyroxine levels and that “PFAS could induce thyroid dysfunction and disease” (Lee and Choi 2017).

Human thyroid disease is mostly the result of an autoimmune response and is 5 to 10 times more prevalent in women than men (Tadic et al. 2018). Concerning PFAS and clinically diagnosed outcomes, women in the highest quartile of PFOA exposure ( $>5.7$  ng/mL) reported clinical hypothyroid disease (odds ratio 2.2, 95% confidence interval [CI] 1.4–3.7) over 3 cycles of National Health and Nutrition Examination Survey (NHANES) data (1999–2006,  $n = 3974$  adults), with similar findings in men (Melzer et al. 2010). The C8 Science Panel studies (median serum PFOA 26.1 ng/mL) found thyroid disease hazard ratios of 1.00, 1.24, 1.27, 1.36, and 1.37 across cumulative exposure quintiles in women (log-linear trend  $p = 0.03$  [Winqvist and Steenland 2014b]), with parallel hypothyroid findings in children aged 1 to 17 yr (Lopez-Espinosa et al. 2012). The Ronneby, Sweden, population experienced excess risk of thyroid disease in a discrete time period (1984–2005) among women (hazard ratio 1.29, 95% CI 1.05–1.57) that did not persist over time despite higher cumulative PFAS exposure (Andersson et al. 2019). The authors did not link exposure to hypothyroid outcome, noting a nonmonotonic dose–response relationship (Andersson et al. 2019).

Human population studies augment experimental data that PFAS interact with thyroid hormone binding proteins (Berg et al. 2015; Ren et al. 2016; Zhang J et al. 2016), one of several mechanisms by which PFAS can perturb feedback relationships between free thyroid hormone and the hypothalamic–pituitary–thyroid axis. Exposures to PFAS also interfere with thyroid peroxidase (TPO) enzyme activity in vitro (Song et al. 2012). Several PFAS studies have pursued this putative mechanism, finding that maternal and neonatal thyroid hormone outcomes were more readily detected in those with a priori abnormally high circulating anti-TPO antibodies (Webster

et al. 2014, 2016). One case–control study investigated congenital hypothyroidism, a rare condition. Serum concentrations of PFOA (5.40 vs 2.12 ng/mL;  $p < 0.01$ ), perfluorononanoic acid (PFNA; 1.93 vs 0.63 ng/mL;  $p < 0.001$ ), perfluorodecanoic acid (PFDA; 0.52 vs 0.30 ng/mL;  $p < 0.005$ ), and perfluoroundecanoic acid (0.98 vs 0.44 ng/mL;  $p < 0.005$ ) were higher in the diagnosed newborns; and levels of several PFAS, including PFOA and PFHxS, were correlated with thyroid autoantibodies (Kim et al. 2016).

Thyroid disease is not the only concern. Clinicians are concerned about subclinically elevated thyroid-stimulating hormone (TSH) in early pregnancy because it may be associated with several possible adverse maternal and fetal outcomes (Forhead and Fowden 2014). This general concern has prompted numerous PFAS-exposure evaluations of corresponding TSH in maternal serum, cord blood, and newborns. A review of maternal and child biomarkers with PFAS exposure noted that higher TSH has been reported in 4 second-trimester studies (Ballesteros et al. 2017), but there are also conflicting findings. Studies measuring PFAS in the first trimester have also found associations between PFAS exposure and altered TSH levels in newborns, including nonmonotonic patterns of dose response that mirror the marked alterations of thyroid hormone levels during pregnancy (Inoue et al. 2019).

From the available studies, PFAS definitively alter human thyroid hormones and potentially contribute to thyroid autoimmunity but do not so far appear to be a cause of thyroid cancer (Barry et al. 2013; Vieira et al. 2013). Also, thyroid cancer is usually survived; thus, morbidity rather than mortality studies are useful.

### Liver disease and cancer

The liver is a primary target organ for long-chain PFAS storage, and accompanying experimental evidence of toxicity includes hepatocyte fat infiltration, specific P450 (CYP) pathway induction, apoptosis, hepatocellular adenomas and carcinomas, and disrupted fatty acid trafficking that can be peroxisome proliferator-activated receptor alpha (PPAR $\alpha$ )-dependent or -independent and present across species (Maestri et al. 2006; Cui et al. 2009; Wan et al. 2012; Huang et al. 2013; Perez et al. 2013; Filgo et al. 2015; Xu et al. 2016, 2020a; Yao et al. 2016; Zhang L et al. 2016b; Hui et al. 2017; Li et al. 2017a; Guillette et al. 2020; National Toxicology Program 2020a).

Population studies demonstrate significant associations of long-chain PFAS ( $>6$  fluorinated carbons) exposure to higher liver enzymes, such as alanine aminotransferase in adults and adolescents (Sakr et al. 2007a; Gallo et al. 2012; Yamaguchi et al. 2013; Gleason et al. 2015; Attanasio 2019; Nian et al. 2019), including in longitudinal studies (Sakr et al. 2007b; Darrow et al. 2016). Following low-dose exposures, these associations may be more evident in obese participants (Lin et al. 2010; Gallo et al. 2012; Jain and Ducatman 2019e).

Based on experimental data (Martin et al. 2007; Wan et al. 2012; Wang et al. 2013; Das et al. 2017), nonalcoholic

fatty liver disease (NAFLD) has been investigated as a clinical outcome of PFAS exposure mediating consistent population PFAS-altered liver enzyme findings. Studies with NAFLD cytokeratin C18 biomarkers have provided supportive evidence for PFAS inducing steatosis (Bassler et al. 2019). Metabolomic studies have been directed at potentially explanatory human glycerophosphocholine and fatty acid profiles (Kingsley et al. 2019; Salihovic et al. 2019; Wahlang et al. 2019). Processes which favor steatosis promote advanced liver disease including liver cancer in humans (Massoud and Charlton 2018; National Toxicology Program 2020a). Associations of PFAS with advanced human liver disease and liver cancer are technically hard to study for reasons including (and not limited to) lethality, selection of comparison populations, and alterations of excretion mechanics associated with disease states. In a clinic-based study, mostly obese (85%) children aged 7 to 19 yr with biopsy-proven NAFLD had more advanced disease associated with PFOS and PFHxS exposure as well as associations with lipid and amino acid pathways linked to NAFLD pathogenesis (Jin et al. 2020). However, an adult study reported that serum PFHxS was inversely associated with hepatic lobular inflammation in morbidly obese bariatric surgery patients (Rantakokko et al. 2015). A study of heavily exposed workers ( $n=462$ , geometric mean serum PFOA of 4048 ng/mL) detected significantly increased incident mortality for cirrhosis (relative risk = 3.87, 95% CI 1.18–12.7) and liver cancer (relative risk = 6.69, 95% CI 1.71–26.2) compared to a regional population (Girardi and Merler 2019), whereas no PFAS association to cancer or advanced liver disease was reported in a 3M worker cohort or in the C8 Health study population (Lundin et al. 2009; Barry et al. 2013; Vieira et al. 2013).

Emerging animal toxicology and histology and human population data provide mechanistic clues that PFAS disrupt hepatic metabolism, leading to increased bile acid reuptake and lipid accumulation in liver (Salihovic et al. 2020; Schlezinger et al. 2020). A review of NAFLD and toxicant exposure concluded that PFAS are associated with early steatosis (“fatty liver”), the preclinical stage of NAFLD (Armstrong and Guo 2019).

### Lipid and insulin dysregulation

Cross-sectional and longitudinal investigations indicate that PFAS increase serum total and low-density lipoprotein cholesterol in adults and children (Steenland et al. 2009; Frisbee et al. 2010; Nelson et al. 2010; Eriksen et al. 2013; Fisher et al. 2013; Fitz-Simon et al. 2013; Geiger et al. 2013; Fu et al. 2014; Starling et al. 2014; Winkquist and Steenland 2014a; Skuladottir et al. 2015; Zeng et al. 2015; Koshy et al. 2017; Convertino et al. 2018; He et al. 2018; Seo et al. 2018; Dong et al. 2019; Lin et al. 2019; Li et al. 2020; Liu G et al. 2020), including clinically defined high cholesterol (Steenland et al. 2009; Winkquist and Steenland 2014a; Lin et al. 2019). Studies of large populations, featuring wide exposure ranges, demonstrate that serum lipids rapidly increase beginning at background (1–10 ng/mL) serum concentration and then are followed by attenuating (“plateaued”) cholesterol measurements as (log-transformed)

exposures to long-chain PFAS increase (Steenland et al. 2009; Frisbee et al. 2010; Li et al. 2020). These findings suggest partially saturable mechanisms; thus, the cholesterol dose response at pharmacologic or acutely toxic doses should be viewed with caution; associations can be missed or may be misleading when an environmental range of exposure is absent. At background exposure levels, residual associations may be more detectable in obese participants (Timmermann et al. 2014; Jain and Ducatman 2019d), a finding congruent with experimental PFAS outcomes in rodents fed “Western” or high-fat diets (Tan et al. 2013; Quist et al. 2015; Rebholz et al. 2016). Human gene expression pathways provide support for an interaction of obesity and PFAS exposures and suggest possible sex differences (Fletcher et al. 2013). A pharmacokinetic model predicts that approximately half of the PFOS-exposed population would experience a >20% rise in serum cholesterol (Chou and Lin 2020). Risk-assessment implications for low-PFAS dose increases in cholesterol have been noted (New Jersey Drinking Water Quality Institute Health Effects Subcommittee 2017; Li et al. 2020), and a review of population and toxicity data concluded that dyslipidemia is the strongest metabolic outcome of PFAS exposure (Sunderland et al. 2019).

Human PFAS lipid findings may be related to experimental findings of induced adipogenesis, impaired bile acid metabolism/synthesis, strongly decreased CYP7A1 enzyme activity, altered fatty acid transport, and intracellular lipid accumulation with steatosis, including in PPAR- $\alpha$ -null or PPAR- $\alpha$ -humanized animals (Guruge et al. 2006; Lau et al. 2007; Bijland et al. 2011; Bjork et al. 2011; Wang et al. 2014; Filgo et al. 2015; Das et al. 2017; Salihovic et al. 2019; Zhang et al. 2019; Behr et al. 2020a; Liu S et al. 2020b; Schlezinger et al. 2020). Independent of PFAS exposure, similar alterations in metabolic pathways have been related to disrupted fatty acid beta-oxidation and increased free cholesterol in toxicology studies (Perla et al. 2017).

Cross-sectional studies of diabetes outcomes can be misleading for reasons discussed in the renal section (see section *Kidney disease, uric acid, and kidney cancer*). Emerging longitudinal and diabetes clinical trial data indicate that PFAS may increase human insulin resistance, associated with dysregulated lipogenesis activity (Alderete et al. 2019; Lin et al. 2019). Longitudinal studies of clinically diagnosed diabetes patients have sometimes associated PFAS exposures with diabetes (Sun et al. 2018) or with small changes in glycemic markers (Cardenas et al. 2017); however, diabetes associations to date are not consistent (Karnes et al. 2014; Cardenas et al. 2017; Donat-Vargas et al. 2019). Future studies should consider whether PFAS may instigate autoimmune diabetic outcomes in humans, as shown in experimental studies (Bodin et al. 2016). Experimental data reveal that PFAS activate G protein-coupled receptor 40, a free fatty acid-regulated membrane receptor on islet  $\beta$  cells, stimulating insulin secretion (Qin et al. 2020; Zhang L et al. 2020).

### Kidney disease, uric acid, and kidney cancer

Extended human half-lives of long-chain PFAS are attributed to active renal tubular reabsorption. Of concern, legacy PFAS

such as PFOA and PFOS are concentrated in renal tissues, and histopathologic, molecular, oxidative stress, and epigenetic studies provide evidence of potential nephrotoxicity (Wen et al. 2016; Stanifer et al. 2018; Sakuma et al. 2019; Rashid et al. 2020). In addition, the strong influence of kidney reabsorption on the extended half-lives of long-chain PFAS is consistent with both human protein binding and experimental PFAS excretion data.

Human studies have associated legacy PFAS exposure to diminished glomerular filtration and/or defined chronic kidney disease in adults and children (Shankar et al. 2011; Watkins et al. 2013; Kataria et al. 2015; Blake et al. 2018). However, this outcome may be due to reverse causation (Watkins et al. 2013; Dhingra et al. 2017). Some reviews of the available epidemiologic and toxicologic evidence suggest causative links between PFAS and diminished kidney function and chronic kidney disease (Stanifer et al. 2018; Ferrari et al. 2019); these authors also note several knowledge gaps and uncertainty about which proposed mechanisms of action are most important. A propensity score approach to NHANES data (Jain and Ducatman 2019c; Zhao et al. 2020) and a study with repeated PFAS and health measures over an 18-yr period (Blake et al. 2018) recently concluded that PFAS exposure likely causes diminished renal glomerular filtration.

Uric acid, a biomarker of increased risk for renal disease (Obermayr et al. 2008), is also consistently associated with PFAS exposure in adults and children (Steenland et al. 2010; Geiger et al. 2013; Gleason et al. 2015; Kataria et al. 2015; Qin et al. 2016; Zeng et al. 2019), including a visible dose–response curve that begins at or near historic background levels in human populations (Steenland et al. 2010; Zeng et al. 2019). Serum PFAS concentrations exhibit an inverted U-shaped pattern related to glomerular filtration, initially exhibiting a modest accumulation as glomerular filtration begins to decrease and then decreasing in advancing renal disease, likely due to failure of normal strong reabsorption mechanisms in moderate to severe kidney disease (Jain and Ducatman 2019c). This finding is more dramatic across stages of glomerular filtration when there is also albuminuria (Jain and Ducatman 2019b). Studies suggest that the association of PFAS to uric acid is not due to reverse causation and is underestimated because the failing kidney excretes long-chain PFAS but retains uric acid. An implication is that population outcomes that occur in the presence of either albuminuria or moderate to severe renal disease such as hypertension (Jain 2020) increasing presence of and uric acid (a biomarker of renal disease; Jain and Ducatman 2019a; Zeng et al. 2019) can be underestimated in cross-sectional studies; in other words, the link between these health outcomes and PFAS exposure is obscured in these studies because of enhanced PFAS excretion patterns in the presence of either albuminuria or moderate to severe kidney disease. Furthermore, the strong influence of renal reabsorption on the long half-lives of long chain PFAS is consistent with both human protein binding of PFAS and experimental PFAS excretion rates in high-dose rodent studies (Cheng and Ng 2017).

Kidney cancer diagnoses have been increasing since 1975, a finding that is partially independent of improved detection, with

5-yr cancer-specific survival of approximately 80% (Gandaglia et al. 2014). The C8 Health studies noted longitudinal ( $n = 32\,254$ ) increases of kidney cancer (hazard ratio = 1.10, 95% CI 0.98–1.24) and kidney cancer mortality (Steenland and Woskie 2012; Barry et al. 2013; Vieira et al. 2013). A review of 6 published studies found long-chain PFAS exposure associated with kidney cancer or kidney cancer mortality, with risks ranging from 1.07 to 12.8 (Stanifer et al. 2018). Subsequent preliminary data from the heavily exposed Veneto, Italy, population also suggest a significant increase in kidney cancer mortality with PFAS exposure (Mastrantonio et al. 2018). Evidence is accumulating for PFAS as a cause of chronic disease and kidney cancer. Study designs must consider the peculiar PFAS excretion mechanics involved in and associated with kidney disease.

### Reproductive and developmental outcomes

Exposure to PFOA impairs human sperm motility and sperm penetration into viscous media (Sabovic et al. 2020; Yuan et al. 2020) and is longitudinally associated with lower sperm concentration and count and higher adjusted levels of luteinizing and follicle-stimulating hormones in young men (Joensen et al. 2009; Vested et al. 2013; Song et al. 2018). Serum concentrations of PFAS are also cross-sectionally associated with deleterious markers of semen quality (Louis et al. 2015; Pan et al. 2019).

Legacy and emerging PFAS have been found in follicular fluid (Kang et al. 2020). They appear to alter endometrial regulation such as progesterone activity in young women (Di Nisio et al. 2020b) and possibly menstrual cycle length (Lum et al. 2017). Associations with menarche and menopause may be substantially due to reverse causation because menstruation is a route by which women eliminate PFAS (Dhingra et al. 2017), partially explaining why men have higher PFAS levels than women in the same communities. Women on birth control and who do not menstruate or with poor cyclicity because of age, activity level, or disease may have elevated PFAS levels in comparison with menstruating women. Exposure to PFAS has been associated with endometriosis in the United States and in China (Louis et al. 2012; Campbell et al. 2016; Wang B et al. 2017a), but the specific PFAS associated with this effect vary among studies.

Time-to-pregnancy (fecundity) studies provide indirect evidence of changes in fertility. Methodologic considerations include maternal and paternal age, parity (which in turn affects serum PFAS), and health status. Among 1240 women in the Danish National Birth Cohort, PFOS exposure was associated with decreased fecundity (median serum PFOS 35.5 ng/mL; Fei et al. 2009). Reverse causation may explain this finding because it is duplicated in parous, but not among nonparous, women (Whitworth et al. 2012; Bach et al. 2015). Prospective odds of actual infertility in the Maternal–Infant Research on Environmental Chemicals cohort ( $n = 1743$ ) at low-dose exposures were associated with PFOA (geometric mean 1.66 ng/mL; odds ratio = 1.31, 95% CI 1.11–1.53) and PFHxS

(odds ratio = 1.27, 95% CI 1.09–1.48; Velez et al. 2015). The reported fertility rate improved following water filtration in a PFAS-contaminated community (incidence rate ratio 0.73, 95% CI 0.69–0.77 prior to filtration) along with measures of birth weight (Waterfield et al. 2020).

Per- and polyfluoroalkyl substances reliably move across the placenta and enter breast milk (Gyllenhammar et al. 2018; VanNoy et al. 2018); serum PFAS levels in young children generally exceed maternal serum concentrations (Fromme et al. 2010; Papadopoulou et al. 2016; Eryasa et al. 2019). Population studies provide evidence that breastfeeding duration and milk quantity are adversely affected by PFAS exposure (Romano et al. 2016; Timmermann et al. 2017b; Rosen et al. 2018).

A systematic review reported that PFOA exposure was associated with a small decrease in infant birth weight; the meta-analysis estimated that a 1-ng/mL increase in PFOA was associated with an approximately 19-g reduction (95% CI –29.8 to –7.9 g) in birth weight (Lam et al. 2014). The authors noted similarities in experimental studies (Johnson et al. 2014; Koustas et al. 2014) and concluded that there was “sufficient” human and corroborative toxicology evidence of a detrimental effect of PFOA on birth weight (Johnson et al. 2014; Koustas et al. 2014; Lam et al. 2014). However, another meta-subpopulation analysis, focused on early pregnancy or the time shortly before conception, detected only a small and nonsignificant association, which was less subject to bias (Steenland et al. 2018a). Different approaches to the possible confounding role of shifting glomerular filtration rates in pregnancy can affect interpretations; evidence suggests this consideration can, at most, only partially explain associations of PFAS exposure to decreased birth weight (Interstate Technology and Regulatory Council 2020; Wikstrom et al. 2020). A recent review of mostly prospective cohort studies ( $n = 24$  studies) noted PFAS associated with altered fetal and postnatal growth measures, such as lower birth weight. Many ( $n = 22$ ) of the relevant studies suggest developmental and childhood immunomodulatory effects, whereas 21 studies concerning neurodevelopment were inconclusive (Liew et al. 2018). The authors of the review noted methodologic challenges of developmental and newborn epidemiology, including consideration of critical exposure windows for developmental effects, the effects of breastfeeding and parity on maternal PFAS levels, and the variety of possible mechanistic explanations for growth outcomes, such as disruption of glucocorticoid and thyroid hormone metabolism in utero (Liew et al. 2018). Recent Faroe Island studies report that prenatal PFAS effects on thyroid hormone status do not support a causal relationship (Xiao et al. 2020).

Review articles suggest that prenatal exposure to PFOA may increase risk of subsequent childhood adiposity, noting that steroid hormones, retinoid X receptor, and other pathways may be contributing to this effect (Halldorsson et al. 2012; Hall and Greco 2019). Prospective evidence supports this relationship in adults with a high risk of diabetes (Cardenas et al. 2017). However, some well-performed community studies do not support this outcome in adults or children (Barry et al. 2014; Martinsson et al. 2020).

Based on several preliminary findings, supported by longitudinal follow-up studies (Stein et al. 2009; Savitz et al. 2012; Darrow et al. 2013; Avanasani et al. 2016a, 2016b), the C8 Science Panel concluded that PFOA is probably linked to pregnancy-induced hypertension or preeclampsia. Population-level evidence implicating additional PFAS having this effect has included studies with longitudinal designs (Huang et al. 2019; Wikstrom et al. 2019; Borghese et al. 2020). Experimental support includes PFAS effects on human trophoblast migration in vitro (Szilagyi et al. 2020) and recent evidence of PFOA and GenX (or hexafluoropropylene oxide dimer acid) effects on mouse placenta, as well as excessive gestational weight gain (Blake et al. 2020). However, a recent longitudinal study did not find an association of PFAS with pregnancy-associated hypertension (Huo et al. 2020).

The possibility that circulating PFAS may reduce bone mineral density has been investigated. Cross-sectional and practical trial associations have been found in adults (Lin et al. 2014; Hu et al. 2019; Di Nisio et al. 2020a), and there is emerging longitudinal evidence from a mother and child pair study indicating that children may also be affected (Cluett et al. 2019).

Testicular cancer diagnoses are increasing steadily, a trend unrelated to improved detection (Cheng et al. 2018; Park et al. 2018). Most patients diagnosed (>90%) will be cured and die of other causes; mortality studies therefore provide little help in understanding disease risk factors. The C8 Science Panel detected longitudinal evidence for increased testicular cancer risk (1.35, 95% CI 1.00–1.79) for cumulative PFOA exposure (Barry et al. 2013). There are ample supportive data of testicular damage following PFAS exposure, including strong evidence of endocrine disruption; but the cell-specific associations are different in humans (germ cell) than the outcomes in rodents (stromal).

Per- and polyfluoroalkyl substances have deleterious effects on conception, pregnancy, and infant development. The underlying birth weight data are mostly supportive, although the subsequent growth and adiposity literature is mixed. The most sensitive reproductive and developmental outcomes are a topic of ongoing discussion.

Outcomes replicated across populations, such as perfluorocarboxylate (PFCA) and perfluorosulfonate (PFSA) exposures associated with down-regulation of immune response; increases in cholesterol, liver enzymes, and uric acid; alterations in thyroid hormone binding proteins; growth deficits; and effects on breast milk and lactation, indicate priority areas for understanding mechanisms and health implications.

## CURRENT KNOWLEDGE OF PFAS TOXICITY IN EXPERIMENTAL MODELS

Animal studies have focused most intensely on PFOA and PFOS, using laboratory rodents and, more recently, zebrafish as models. Perfluoroalkyl acids of varied carbon-chain lengths as well as a few replacement chemicals with ether linkages in the carbon backbone (such as GenX and 3H-perfluoro-3-[(3-methoxy-propoxy)propanoic acid], or ADONA) have also

been examined, with outcome profiles thus far generally consistent with legacy chemicals. The varying extent of responses is likely related to toxicokinetic disposition (excretion or half-life) and relative potency and affinity of the individual chemical for binding to receptor proteins. Some PFAS (i.e., PFHxS, PFOA, and PFNA) have longer half-lives in mice than rats and typically much longer half-lives in humans (Table 1). These differences in elimination kinetics complicate the cross-species evaluation of toxicity. In addition, some PFAS (such as PFOA and PFNA) exhibit a profound sex difference in the rate of chemical elimination and bioaccumulation in the rat: females eliminate them much faster than males (Table 1). Sex differences in half-lives, although important, are much smaller in humans and have a different explanation. The mouse also typically has more limited sex-based PFAS elimination differences, making this species more amenable for extrapolation to humans, especially for mechanistic and toxicity evaluations.

In general, human health effects associated with PFOA and PFOS exposure (described in section *Current Knowledge of PFAS Toxicity in Humans*) have also been reported in animal models: hepatic/lipid metabolic toxicity, developmental toxicity, immune suppression, tumor induction, endocrine disruption, and obesity. These findings are often derived from well-controlled laboratory experiments in more than one species using wide dose ranges that are often orders of magnitude higher than typical human exposure, to account for differences in half-life across species. Some of the phenotypic findings are supported by in vitro mechanistic investigation and/or molecular queries on target tissues. Our understanding of the toxicologic properties of PFAS other than PFOA and PFOS is notably less advanced and, in the case of emerging replacements and by-products, completely unexplored.

### Hepatic and metabolic toxicity

In rodent studies, dose-dependent increases in liver weight, in hepatocellular hypertrophy associated with vacuole formation, and with or without increased peroxisome proliferation have been observed with a significant body burden of PFAS, especially for the most persistent and potent long-chain homologs. Hepatocyte proliferation, necrosis, and apoptosis are outcomes occurring at relatively low doses. This is also true for a new replacement chemical, GenX, which altered liver histopathology and function and increased apoptosis in mice and fish (Blake et al. 2020; Guillette et al. 2020). Correspondingly, transcriptional activation of mouse and, to a lesser extent, human PPAR $\alpha$ -related genes in liver was detected in adult-exposed models; activation of other nuclear receptors such as PPAR $\gamma$ , constitutive androstane receptor (CAR), and pregnane X-receptor (PXR) has also been reported. These nuclear receptors, metabolic sensors that regulate lipid and glucose metabolism and transport and inflammation, tend to be more responsive in tissues of rodents than in humans (Wolf et al. 2012; Rosen et al. 2017). Recent work using developmental models reports that

**TABLE 1:** Per- and polyfluoroalkyl substances serum half-life estimates in rat, mouse, monkey, and humans

|            | PFBS (C4) |           | PFHxS (C6) |        | PFOS (C8)  |         | PFBA (C4) |       | PFHxA (C6) |           | PFHpA (C7) |       | PFOA (C8)  |       | PFNA (C9)  |         | PFDA (C10) |         | F-53B |   | GenX    |      |
|------------|-----------|-----------|------------|--------|------------|---------|-----------|-------|------------|-----------|------------|-------|------------|-------|------------|---------|------------|---------|-------|---|---------|------|
|            | F         | M         | F          | M      | F          | M       | F         | M     | F          | M         | F          | M     | F          | M     | F          | M       | F          | M       | F     | M | F       | M    |
| Rat        | 0.6–4.0 h | 2.1–4.5 h | 1.8 d      | 6.8 d  | 62–71 d    | 38–41 d | 1.0–1.8 h | 6–9 h | 0.4–0.6 h  | 1.0–1.7 h | 1.2 h      | 2.4 h | 2–4 h      | 4–6 d | 1.4–6.4 d  | 31–55 d | 59–75 d    | 40–80 d |       |   | 8 h     | 3 h  |
| Mouse      | 4.5 h     | 5.8 h     | 25–2 d     | 28–3 d | 31–3 d     | 36–4 d  | 3 h       | 12 h  | ~1.2 h     | ~1.6 h    |            |       | 16 d       | 22 d  | 26–6 d     | 34–6 d  |            |         |       |   | 18 h    | 20 h |
| Cynomolgus | 3.5 d     | 4.0 d     | 87 d       | 141 d  | 110 d      | 132 d   | 1.7 d     |       | 2.4 h      | 5.3 h     |            |       | 30 d       | 21 d  |            |         |            |         |       |   |         |      |
| Monkey     |           |           |            |        |            |         |           |       |            |           |            |       |            |       |            |         |            |         |       |   |         |      |
| Human      | 28 d      |           | 5.3–8.5 yr |        | 3.4–5.0 yr |         | 3 d       |       | 32 d       |           | 1.2–2.5 yr |       | 2.1–3.8 yr |       | 2.5–4.3 yr |         |            |         |       |   | 15.3 yr |      |

GenX = hexafluoropropylene oxide dimer acid; PFBA = perfluorobutanoic acid; PFBS = perfluorobutanesulfonic acid; PFDA = perfluorodecanoic acid; PFHpA = perfluoroheptanoic acid; PFHxA = perfluorohexanoic acid; PFHxS = perfluorohexane sulfonate; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonate.

mitochondrial dysfunction is associated with hepatocellular hypertrophy in young adult mice (Quist et al., 2015) and that other fatty acid metabolism pathways are activated (Jones et al. 2003; Shabalina et al. 2016). Steatosis is also a common feature of PFAS chronic exposure in rodents. Exposure in rodent models typically decreases serum cholesterol, whereas elevations of circulating cholesterol levels have been reported in humans. The mode of action concerning serum cholesterol is debatable. For example, PFOA exposure increased liver weight, increased liver enzymes, and led to persistent histopathological changes (particularly damage to the bile duct) in livers of wild-type and PPAR $\alpha$ -null rodent strains (reviewed in Division of Science and Research, New Jersey Department of Environmental Protection 2019). Many of these effects are reversible on cessation of PFAS exposure, and this observation has been interpreted by some as evidence of “adaptive” responses to exposure. However, this reversibility is irrelevant to ongoing environmental PFAS exposure (for instance, from drinking water) because exposure will persist until contamination is remediated. In summary, there is a strong confluence of animal toxicology and histology and human population data that PFAS disrupt hepatic metabolism and lead to lipid accumulation in liver, although the mechanism(s) is unclear. Effects on bile acid metabolism, mitochondrial perturbation, and cholestatic mechanisms deserve further investigation at human-relevant exposures.

### Reproductive and developmental toxicity

Only a few reproductive toxicity studies of males and females are available, primarily focusing on long-chain PFAS. Profound developmental toxicity has been described following gestational and lactational exposure to PFOS, PFOA, and PFNA in mice (Thibodeaux et al. 2003; Lau et al. 2006; Das et al. 2015) and in mice and rats gestationally exposed to GenX (Conley et al. 2019; Blake et al. 2020). Neonatal morbidity and mortality were seen with exposure to high doses of legacy PFAS; growth deficits and developmental delays were noted in offspring exposed to lower doses. Evidence of lactation impairment was seen in mice at doses of 5 mg PFOA/kg body weight (White et al. 2007), leading to increased offspring mortality (Lau et al. 2006); recent studies have indicated a role of placental dysfunction in these adverse developmental outcomes (Blake et al. 2020). Deficits of mammary gland development were also observed in mice exposed to PFOA (doses of 1 mg/kg body wt and lower) during gestation, which persisted into adulthood, although these exposure levels did not alter body weight, lactational function, or neonatal growth of offspring (F1 or F2 mice; Macon et al. 2011; White et al. 2011b; Tucker et al. 2015). Systematic reviews support a relationship between in utero exposure to PFOA and PFOS and reduced fetal growth in animals and humans, and the relationship between PFOA and reduced fetal growth in mice was recently validated (Koustas et al. 2014; Blake et al. 2020). Also, PFAS are reported to have reproductive effects such as ovulation failure in mice (Zhang Y et al. 2020).

### Immunotoxicity

A few long-chain PFAS (PFOS, PFOA, PFNA, and PFDA) have been shown to alter immune status in rodents and non-human primates. Effects are predominantly immunosuppressive and include reductions in thymus and spleen weights and associated immune cell populations, in numbers of circulating immune cells, in certain aspects of innate immunity (i.e., natural killer cell cytotoxicity), in infectious disease resistance, and in antibodies produced in response to an antigen (i.e., analogous to the vaccine response in humans). In their 2018 draft *Toxicological Profile for Perfluoroalkyls*, the US Agency for Toxic Substances and Disease Registry (ATSDR) noted changes to the aforementioned immune parameters observed in experimental rodents exposed to PFOA, PFOS, PFNA, PFHxS, PFDA, perfluorobutanesulfonic acid (PFBS), or perfluorobutanoic acid (PFBA; Agency for Toxic Substances and Disease Registry 2018). The US National Toxicology Program conducted a systematic review of the immunotoxicological literature for PFOA and PFOS and concluded that PFOA and PFOS were presumed to be immune hazards to humans based on a high level of evidence for suppression of antibody responses in experimental animals and a moderate level of evidence for suppression of antibody responses in humans (National Toxicology Program 2016). The ATSDR (Agency for Toxic Substances and Disease Registry 2018) also included a decreased antibody response to vaccines (PFOA, PFOS, PFHxS, and PFDA) and increased risk of asthma diagnosis (PFOA) among the list of adverse health effects in PFAS-exposed humans. Reduction in the antibody response to a vaccine, an adaptive immune function, is a well-accepted measure of immunotoxicity, is consistent with the mode of action for the effects of fatty acids on immune system function (Fritsche 2006), and is compelling evidence that the immune system is a sensitive target of PFAS.

### Tumor induction

Per- and polyfluoroalkyl substances are not known to be directly mutagenic; PFOA, PFOS, and other tested PFAS show little or no evidence for induction of gene mutation, clastogenicity, or aneuploidy in vitro or in vivo by a direct mode of action (see EFSA Panel on Contaminants in the Food Chain [2020] for details). There is evidence that PFAS can induce DNA damage, such as strand breaks, and other genotoxic effects, secondary to oxidative stress (EFSA Panel on Contaminants in the Food Chain 2020). This occurs at concentrations or doses that are high relative to human environmental exposures to PFAS, and the mechanism is such that their dose–response will be sublinear. Hence, PFAS are unlikely to be of mutagenic concern in exposed populations.

In adult-exposed rodents and fish, PFOA and PFOS have been shown to induce tumors. Liver adenomas, pancreatic acinar cell tumors, and testicular Leydig cell adenomas have been detected in rats treated chronically with PFOA (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans 2017) as well as its replacement, GenX (Caverly Rae et al. 2015). Following

gestational and chronic exposure to PFOA, 58% of male rats demonstrated pancreatic tumors at the lowest dose administered (National Toxicology Program 2020b). This finding has spurred Minnesota and California policymakers to consider cancer as an endpoint in risk assessment, whereas the European Food Safety Authority (EFSA Panel on Contaminants in the Food Chain 2020) has the opinion that there is not adequate evidence for a link between exposure to PFAS and cancer risk in humans. This “tumor triad” profile has been associated with the PPAR $\alpha$ -mediated molecular signaling pathway in rats exposed to high doses of PFAS. Consequently, liver tumors involving this mode of action are not considered relevant to humans at equivalent PFAS exposures (Post et al. 2017). The human relevance of PPAR $\alpha$ -mediated pancreatic tumors in rodents remains to be determined. Liver lesions evident in PPAR $\alpha$ -null mice exposed to PFOA during pregnancy and lactation (Filgo et al. 2015) suggest a non-PPAR $\alpha$ -mediated liver response. Induction of liver tumors mediated by estrogen receptor (ER) activation has also been reported in fish (Tilton et al. 2008), and several non-PPAR $\alpha$ -mediated hypotheses, including increased reactive oxygen species formation, oxidative stress, and mitochondrial dysfunction; decreased tumor cell surveillance by the immune system; and diminished gap junction cellular communication, are documented (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans 2017; New Jersey Drinking Water Quality Institute Health Effects Subcommittee 2017).

## Endocrine disruption

The primary evidence for the endocrine-disrupting potential of PFAS involves induction of hypothyroxinemia and reduction of serum testosterone in rats. An early review of PFAS endocrine-disrupting properties in humans concluded that the “thyroid may be one axis significantly affected by PFOA exposure while the animal toxicology literature is less certain due to technical issues” (White et al. 2011a).

The effects of PFAS on thyroid hormone status detected in animal studies differ from classical hypothyroidism, in that reduction of circulating total thyroxine is not accompanied by a compensatory increase of TSH. A possible mechanism for these effects may be related to the propensity of protein binding of legacy PFAS, which could lead to displaced total thyroxine binding to its carrier proteins (transthyretin and thyroxine-binding globulin). Human population studies augment animal data showing that PFAS interact with thyroid hormone binding proteins (Berg et al. 2015; Ren et al. 2016; Zhang J et al. 2016a), one of several mechanisms by which PFAS can perturb feedback relationships between free thyroid hormone available to cells (free total thyroxine) and the hypothalamic–pituitary axis. Some estrogenic effects of PFAS have also been illustrated by *in vitro* studies, although there is no evidence of direct trans-activation of estrogen, androgen, or glucocorticoid receptors (Behr et al. 2018, 2020b).

The evidence for PFAS affecting ER signaling in humans and animals is mixed. Although studies have identified some PFAS as being without estrogenic activity (Behr et al. 2018; Borghoff

et al. 2018; Gogola et al. 2019), others suggest an ability of PFAS to modulate or even activate ER-mediated effects (Benninghoff et al. 2010; Kjeldsen and Bonefeld-Jørgensen 2013; Wang et al. 2018; Bjerregaard-Olesen et al. 2019; Qiu et al. 2020), with some effects only observed in aquatic organisms (Wei et al. 2009; Chen et al. 2016, 2018). Microarray analyses of human primary hepatocytes confirmed that PFOA activated the ER pathway (Buhrke et al. 2015).

## Neurotoxicity

Potential adverse effects of PFAS on the nervous system and functions have not been widely investigated. A few studies reported neurotoxicity of PFOS, PFHxS, and PFOA in cell culture systems (Slotkin et al. 2008), as well as altered behavioral responses (Goulding et al. 2017) and deficits in learning and memory ability in rodents (Viberg et al. 2013). In contrast, no significant developmental neurotoxic effects were seen from prenatal exposure to PFOS in USEPA guideline-based studies with rats (Butenhoff et al. 2009).

## Obesity

Numerous cell-based assays in human and mouse pre-adipocytes and animal studies with and without high-fat diets have consistently shown that some PFAS have the potential to increase lipid production by adipocytes and fat pads (van Esterik et al. 2016). Exposure of pregnant mice to low doses of PFOA produced obesity in young adult female offspring (Hines et al. 2009; van Esterik et al. 2016), a finding that was recapitulated in Danish women exposed *in utero* to PFOA (Halldorsson et al. 2012). Both PFOA and GenX increased weight gain of pregnant mice (Blake et al. 2020), an effect also seen in women during pregnancy (Ashley-Martin et al. 2016), although discordant results have been reported in other studies (Barry et al. 2014; Ngo et al. 2014). These apparently disparate findings in experimental models may be associated with differences among mouse strains examined, exposure periods, statistical methodology, and/or the rodent diets used.

There are specific differences in human and rodent health outcomes that deserve further investigation: 1) cholesterol metabolism, 2) thyroid effects, 3) mode of action for liver effects (different or same), and 4) kidney transporter or other mode of action leading to large differences in half-life. However, species concordance in the 6 human health effects discussed in the present review supports a weight of evidence for these effects for the handful of extensively studied PFAS.

Human health advisory and guidance values for a few PFAS have been issued to date by the USEPA, the ATSDR, several individual state environmental agencies or health departments, as well as regulatory agencies in Canada and Europe that are largely (but not exclusively) based on toxicological findings in animal models. However, risk-assessment scientists have not reached consensus in selecting a singular apical endpoint as the basis for a point of departure for assessments. Three

toxicological features of PFAS that have been commonly highlighted, based on their sensitivity (low dose effect), strength of evidence (robust corroborating studies with mechanistic support for human relevance), and corresponding findings noted in epidemiological investigation, are hepatotoxicity (and alterations in lipid metabolism), developmental toxicity, and immunotoxicity. It should be noted that apical endpoints that drive risk assessments often differ among individual PFAS, perhaps highlighting the complexity of these chemicals and the family of PFAS, in general.

## IMPORTANCE OF TOXICOKINETICS IN UNDERSTANDING PFAS TOXICITY

### *Species and sex differences*

Few of the substantial number of structurally diverse PFAS have been tested for toxicological effects. Some available toxicological information has come from studies in animals, where marked species and (in rat) sex differences in half-life for some PFAS (Table 1) have been observed and the relevance to humans is uncertain. These differences are due to toxicokinetic and toxicodynamic factors. There are also differences in mean PFAS serum levels between men and women in the same communities. Children may have elevated serum levels compared to parents, even with the same exposures (Emmett et al. 2006; Daly et al. 2018; Graber et al. 2019), for reasons relating to transplacental transfer, breastfeeding, and body mass (Emmett et al. 2006; Daly et al. 2018; Graber et al. 2019; Blake et al. 2020). Transplacental transfer of PFAS confers a substantial burden to the newborn infant. Because the infant has a smaller overall mass and blood volume, PFAS are concentrated, increasing PFAS per volume (Koponen et al. 2018). In addition, transfer of PFAS is common through lactation, and the longer a child breastfeeds, the higher the body burden (Gyllenhammar et al. 2018; VanNoy et al. 2018).

### *Effects of comorbidity on PFAS toxicokinetics*

Factors affecting renal function can influence PFAS toxicokinetics. As discussed, opposing types of causation should be considered. Human toxicokinetics appear to vary bidirectionally with changing renal function, leading to nonmonotonic dose–response relationships and, depending on the study goal, possibly to errors in estimating disease associations. As progress is made in the field of PFAS toxicokinetics, new chemistries may have different clearance factors and nuances that vary by PFAS group or structures, and that will need to be investigated to accurately model half-lives in different exposure subgroups.

### *Sources of information on toxicokinetics in humans: strengths and limitations of studies*

Some PFAS half-life data in humans were obtained from retired industry workers, particularly those who worked with PFOS, PFOA, and PFHxS (Olsen et al. 2007). Since then, these

estimates have been modified slightly or confirmed with longitudinal data and modeling from contaminated communities once uncontaminated water options were provided (Bartell et al. 2010; Li et al. 2018). Other contemporary PFAS estimates are derived from biomonitoring studies of production workers, blood donors, study participants, and/or occupationally exposed cohorts (Olsen et al. 2009, 2017; Russell et al. 2013; Zhang et al. 2013). Some caution must be taken in using these data because variables affecting PFAS clearance may not be taken into consideration (age, sex, menstruation, disease, and medication status) and may contribute to confounding.

The challenge in determining a reliable human half-life in these types of studies is that exposure does not end with a clean water source, retirement, or a change of job and that continued exposures vary over potential depuration periods. Model components may also vary in subclasses. Children (small blood volumes and a large fraction of exposures comes from drinking), pregnant women (large increase in blood volume and water intake), parous women (transfer to fetus and breast milk), and athletes (water intake elevated) are examples of subpopulations with expected variation in half-life compared to adult men (Post et al. 2017). There will be more human estimates of PFAS forthcoming that involve variations in half-life (Post et al. 2017). Realistic computational modeling can help, so long as it clearly characterizes exposures and applicable populations. The continued goal should be to provide predictive values for those PFAS lacking actual measurements, based on chemical structures and trusted physiological parameters.

### *Physiologically based pharmacokinetic/toxicokinetic modeling in different-aged populations*

In the blood and other tissues, PFAS toxicokinetics are influenced by their interactions with proteins (Andersen et al. 2006; Katakura et al. 2007; Nakagawa et al. 2008; Weaver et al. 2009; Figure 2). Certain toxicokinetic features are saturable, and thus dosing in toxicokinetic studies is of profound importance. Studies of renal reabsorption mechanisms in mammals show that reduced activity of transporters such as organic anion transporting polypeptide 1a1, through inactivation (e.g., genetic manipulation, castration, treatment with estrogen) or by saturation at increasing doses, leads to substantial reductions in half-lives of PFOA and PFOS (Andersen et al. 2006; Nakagawa et al. 2008; Weaver et al. 2009; Yang et al. 2009).

These protein-associated toxicokinetic processes were recently incorporated into a model for PFOA in the male Sprague-Dawley rat (Cheng and Ng 2017), which provides a useful platform to explore how changes in protein interactions might affect estimates of PFAS half-life (Figure 3). At high doses, it is typical to see clear biphasic behavior with rapid initial clearance, during which the serum half-life appears to be shorter especially at high enough doses that processes such as renal reabsorption are saturated, followed by a much longer tail

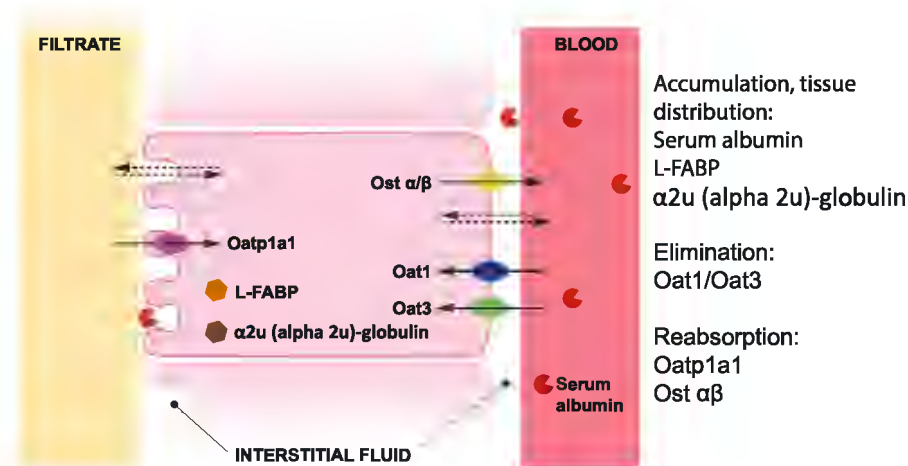


**FIGURE 2:** Example of proteins that are known to influence per- and polyfluoroalkyl substance toxicokinetics through binding (which affects tissue distribution and accumulation) and facilitation of membrane transport (which affects clearance and reabsorption). Illustrated for kidney and blood. L-FABP = liver fatty acid binding protein; Oat1 = organic anion transporting 1; Oatp1a1 = organic anion transporting polypeptide 1a1; Ost = organic solute transporter.

(Figure 3A). In a similar fashion, the magnitude of internal dose and rate of serum clearance can be profoundly influenced by proteins known to bind PFAS, such as serum albumin (Figure 3B). Increasing and decreasing the extent of reabsorption in the kidney increases and decreases the serum half-life, respectively (Figure 3C). Finally, the effect of saturating reabsorption is magnified when the half-life is longer because

of increased serum binding (Figure 3D). In this case, taking an initial slope to calculate the serum half-life at high doses would lead to a profound underestimation.

Differences in protein expression, circulating levels, and even protein type across populations, sex, and species could lead to important species and sex differences in PFAS biological half-lives (Han et al. 2012); such differences should be

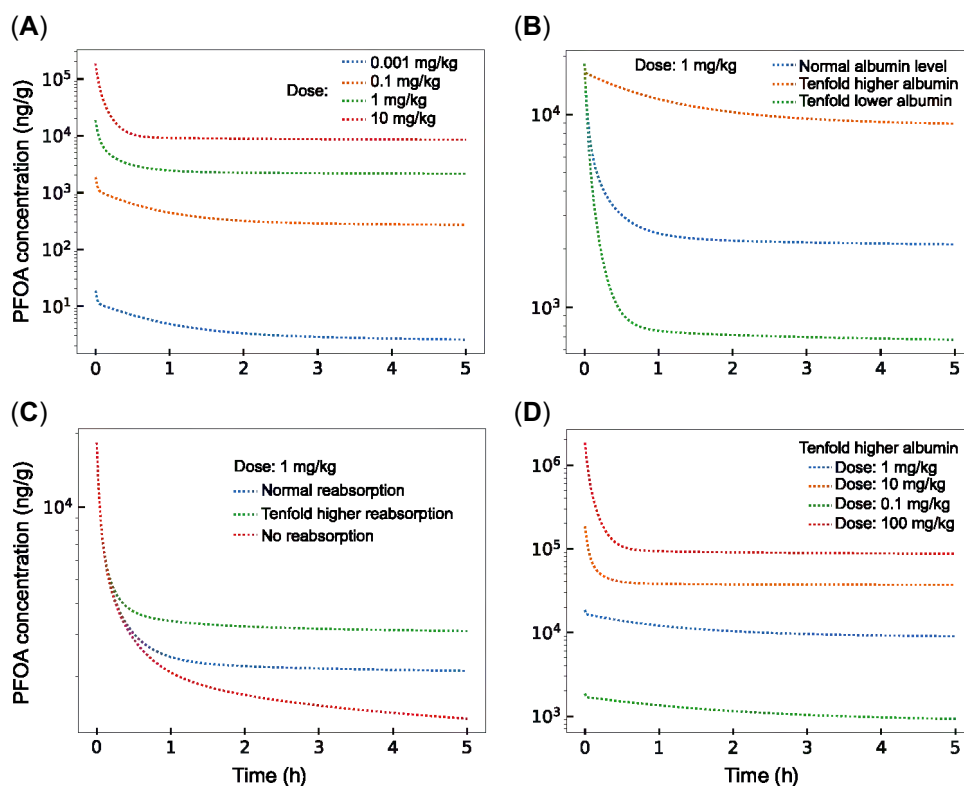


**FIGURE 3:** Simulations based on Cheng and Ng (2017), perfluorooctanoic acid (PFOA) toxicokinetic model for Sprague-Dawley rats. (A) Effect of dose on initial half-life. (B) Effect of higher and lower levels of serum albumin, which binds to PFOA, on serum clearance dynamics. (C) Effect of extent of reabsorption in kidney on serum half-life, based on organic anion transporting polypeptide 1a1 activity. (D) Effect of dose on elimination kinetics when half-life is longer because of higher albumin binding. Oat1 = organic anion transporting 1; Oat3 = organic anion transporting 3; Ost = organic solute transporter.

investigated and taken into account in the extrapolation to human equivalent doses. Because expression of proteins may change at different life stages, clearance factors and toxicokinetics may also change.

Given the large number of species-, sex-, and age-specific differences that have been observed, coupled with the lack of data for many PFAS, the parameterization of complex physiologically based toxicokinetic models remains a persistent challenge. Therefore, lower-resolution models (e.g., one-compartment or few-compartment models) may be more appropriate for species and settings where insufficient data are available for reasonably accurate parameterization. Alternatively, *in silico* and *in vitro* methods are under development that could aid in parameterization in the absence of *in vivo* data, as discussed in the section *New approaches for developing PFAS toxicity information*.

## SO MANY PFAS, SO LITTLE TIME: ACCELERATING THE PACE OF DISCOVERY

### *Importance of determining mode of action and adverse outcome pathways*

Information on modes of action and/or adverse outcome pathways (AOPs) is invaluable in 1) establishing human relevance of experimental evidence, 2) assessing causality in epidemiological studies, 3) applying “read-across” to PFAS for which there is little toxicological information, 4) assessing risks from mixtures, 5) guiding development and interpretation of new approach methodologies, 6) informing the development of biomarkers in epidemiologic investigation, and 7) identifying potentially vulnerable subpopulations and life stage-specific effects (Meek et al. 2014; LaLone et al. 2017). Verified modes of action and AOPs can inform risk assessment based on intermediate effects and enable development of new methodology-based approaches to assess PFAS safety (Meek et al. 2014).

### *Postulated modes of action/AOPs for PFAS*

Mechanistic studies have been performed on only a few PFAS. These have been shown to activate a range of putative molecular initiating targets, among which are the nuclear receptors PPAR $\alpha$ , PPAR $\gamma$ , PPAR $\beta/\delta$ , CAR, PXR, liver X receptor  $\alpha$ , and ER $\alpha$  (Bijland et al. 2011; Bjork et al. 2011; Rosen et al. 2017; Li et al. 2019). However, modes of action verified by agreed procedures (World Health Organization 2020) have been established for few reported effects of PFAS, and those that have been interrogated involve activation of PPAR $\alpha$  and, at higher doses, CAR as molecular initiating events (Klaunig et al. 2012; Rosen et al. 2017). Several AOPs involving these molecular targets are in various stages of development (Organisation for Economic Co-operation Development 2020), but few have been endorsed by the OECD following its agreed procedures (Organisation for Economic Co-operation Development 2017). Demonstration of receptor activation alone is insufficient to establish involvement of a mode of action or AOP in an

observed effect, for which an overall weight-of-evidence approach is necessary (World Health Organization 2020).

Andersen et al. (2007) provide a useful, albeit dated, review of possible PFAS modes of action. Established modes of action are restricted largely to the liver and include species-specific hepatic hyperplasia and liver tumors (Butenhoff et al. 2012; Elcombe et al. 2012; Corton et al. 2018). Available studies on PFBS, PFHxS, perfluorohexanoic acid, PFNA and PFDA suggest that they share molecular targets with similar consequences, albeit with differences in potency, in part due to differences in their excretion and protein-interaction kinetics (Zeilmaker et al. 2018). However, studies *in vitro* have established intrinsic differences in potency among PFAS analogues. Potency in activating PPAR $\alpha$  showed some relationship with PFAS chain length (Wolf et al. 2008). A mode of action or AOP provides a causal chain of key events between chemical exposure and outcome. The established modes of action for PFOS and PFOA provide a causal explanation for development of liver tumors observed in rodents on exposure to these compounds, through activation of PPAR $\alpha$ , and the possible relevance to humans. However, this does not mean that other effects of PFAS are due to activation of PPAR $\alpha$  or that other pathways might not lead to liver tumors in humans, such as secondary to the primary effect of steatosis.

Until recently, there has been little study of modes of action/AOPs for effects of PFAS other than hepatic outcomes in rodents, particularly for critical effects, such as immunosuppression and developmental toxicity, and from PFAS other than PFOS and PFOA (EFSA Panel on Contaminants in the Food Chain 2020; Temkin et al. 2020). The ability of various PFAS to interact with and modify lipid metabolism is, however, an intriguing hypothesis (Xu et al. 1999; Jones et al. 2003; Andersen et al. 2007; Tan et al. 2013; Pouwer et al. 2019). Other putative molecular initiating/key events for PFAS, in addition to nuclear receptor activation, include gap junctional inhibition to disrupt cell–cell communication, mitochondrial dysfunction, interference of protein binding, partitioning into lipid bilayers, oxidative stress, altered calcium homeostasis, and inappropriate activation of molecular signals controlling cell functions. Many of these effects are consistent with a nonspecific action of PFAS on the cellular lipid membrane (Spector and Yorek 1985; Bourre et al. 1989; Dodes Traian et al. 2012; Casares et al. 2019). However, these alternative events lack robust evidence to support a specific pathophysiological role in the multifaceted effects of PFAS. A better characterization of the modes of action/AOPs for PFAS toxicities remains an important area of future investigation, necessary to improve our understanding of PFAS impacts on human health.

At present, there is insufficient evidence to determine which of, and to what extent, these molecular interactions play a pathophysiological role in observed adverse outcomes of PFAS (Michigan PFAS Science Advisory Panel 2018). Hence, there is a need to integrate such mechanistic information into a weight-of-evidence framework, first by establishing the mode of action or AOP linking a proposed chain of key events to an adverse outcome and then by demonstrating that at human exposure levels of PFAS the established AOP or mode of action is causal in the adverse outcome observed. The substantial advantage

offered by such an approach is the ability to read across from representative members of appropriate PFAS groupings, based on quantitative information from new approach methodologies and exposure estimates. Hence, better characterization of the modes of action/AOPs for PFAS toxicities remains a critical area of future investigation and will allow us to understand which adversely PFAS-modified pathways must be interrogated prior to new chemicals joining this class. Predicting PFAS activity in the body should be the goal prior to approving novel PFAS for use.

### New approaches for developing PFAS toxicity information

When it comes to determining which PFAS should be prioritized for further testing, there are too many chemicals, even in one subclass, for traditional approaches. Numerous creative and high-throughput methodologies are being developed and tested to provide valuable data on PFAS with no toxicity data.

**Collaborative approaches.** Problem formulation and approach must be guided by available equipment, funds, and technical staff, and important principles: 1) What biological activity and toxicology information can be generated in a *responsive time frame*? 2) Can this information be used to make public health decisions? 3) What are appropriate tools to bring to this problem (platforms, species/sex of cells used, metabolic competency of the model system, and data analysis)? 4) How do we organize, and what are the best mechanisms to report useful biological activity/toxicological information?

Developing “how” to evaluate potential health effects of new PFAS requires some thought to PFAS heterogeneity. Although subclass names have been suggested by several investigators (Buck et al. 2011; Wang Z et al. 2017; Sha et al. 2019), there is still disagreement on those groupings. In addition, half-lives and biological persistence are not predictable based on structure, and exposure routes may be complex. Given that traditional approaches to generate toxicity information are resource-intensive, new approach methodologies, which may include in vitro high-throughput toxicity screening and toxicokinetic testing, will be needed to inform further (in vivo) testing of PFAS.

One example of how agencies/institutes are collaborating to prioritize a list of PFAS needing further study is the REACT Program (Responsive Evaluation and Assessment of Chemical Toxicity). Scientists from the USEPA and the National Institute of Environmental Health Sciences (NIEHS) National Toxicology Program have joined forces to determine if read-across approaches would work. Essentially, they will use existing data for a data-rich substance (the source, e.g., PFOA or PFOS) as an anchor for a data-poor substance (the target, a novel PFAS), which is considered similar enough to the source substance to use the same data as a basis for the safety assessment. For example, the US National Toxicology Program 28-d PFAS or chronic PFOA data set (National Toxicology Program 2020c) could be used as an anchor. The goal is to group PFAS by biological activities and then use in vitro to in vivo extrapolation data and models to estimate oral equivalent exposures for PFAS. For example, multiple biological endpoints (Table 2) were chosen to generate data on 150 PFAS (Patlewicz et al. 2019), representing several structural subclasses for use in read-across.

Selecting assays shown in Table 2 based on PFOA and PFOS health effects covers a broad range of biology. However, because of the structural diversity of PFAS, biological activity of subclasses of PFAS may be missed; but this can be addressed in 2 ways. First, using transcriptomics as a screen, similar and unique pathways altered by different PFAS can be identified. Second, structure–activity relationships may predict potentially missing biological activities. As an example, Leadscape model predictions conducted at the NIEHS predicted biology that was covered in assays already chosen for evaluation, which increased confidence in the approaches chosen. Because model predictions are only as robust as data sets from which they are generated, these outputs should be used to identify assays for screening efforts and not as synonymous with toxicities induced by PFAS. Ultimately, the REACT program aims to prioritize PFAS for additional targeted testing and follow-up with in vivo studies as needed.

**Molecular dynamics and protein interactions.** Advances in computational tools, many developed for drug discovery, allow environmental and public health researchers to better anticipate some impacts of emerging contaminants even in the absence of substantial experimental data (Rabinowitz et al. 2008). For example, molecular docking and molecular dynamics to predict strengths of interactions between biomolecules and

**TABLE 2:** Fit-for purpose assays proposed in the REACT program

| Endpoint of interest            | Assay proposed                                                                   |
|---------------------------------|----------------------------------------------------------------------------------|
| High-throughput transcriptomics | Metabolically competent human liver cells/MCF-7 (Tempo-Seq <sup>®</sup> )        |
| Hepatotoxicity                  | 2D HepaRG <sup>®</sup> cells                                                     |
| Developmental toxicity          | Zebrafish embryo assay                                                           |
| Developmental neurotoxicity     | Multielectrode array in neonatal cortical cells and neurite outgrowth            |
| Immunotoxicity                  | Cytokine alterations in human vascular endothelial cells (BioSeek <sup>®</sup> ) |
| Hepatic clearance               | Metabolic clearance in 50 donor-pooled hepatocyte suspensions                    |
| Plasma protein binding          | Serum protein binding assay using human serum                                    |
| Enterohepatic recirculation     | Qualyst B-CLEAR <sup>®</sup> hepatocyte transporter assay                        |
| In vitro disposition            | In vitro disposition in cell lines under study                                   |

REACT = Responsive Evaluation and Assessment of Chemical Toxicity.

contaminants can be an *in vitro* screening tool for assessing legacy and emerging PFAS for bioaccumulation potential, to identify potential sites of toxic action (Salvalaglio et al. 2010; Ng and Hungerbuehler 2015; Cheng and Ng 2018; Li et al. 2019) and to gain insights into toxic mechanisms (Sheng et al. 2018). Relatively strong binding with particular proteins (e.g., serum albumin, liver fatty acid binding protein) has already proven useful in correlating PFAS structure with potential for bioaccumulation (Ng and Hungerbuehler 2014; Cheng and Ng 2017). Tools including molecular docking and molecular dynamics can correlate relative binding affinities of emerging PFAS with these target proteins and subsequently compare with affinities of legacy chemicals with known bioaccumulation potentials, thus providing a first-tier rapid screening mechanism (Luebker et al. 2002; Cheng and Ng 2018).

The use of fluorinated substances in pharmaceutical products has led to an unexpected data source for discovery of structural features in PFAS associated with various types of bioactivity. These data were recently used to train machine learning models to predict potential bioactivity for thousands of untested PFAS (Cheng and Ng 2019). Classification approaches such as these serve as preliminary screening tools for identifying PFAS as a first step in a tiered assessment when detailed mechanistic information is not available.

**Addressing mixtures.** Based on their potential for complex exposure patterns, PFAS are a mixtures issue. Communities with water-monitoring programs reporting PFAS concentrations demonstrated that they are exposed to mixtures of PFAS. This mixture may be from one or more point sources releasing multiple PFAS and/or PFAS by-products into the air and water, such as a Chemours plant in North Carolina, and suggest that exposures may be substantial (McCord and Strynar 2019). However, numerous other PFAS sources are known to impact community exposure to PFAS mixtures, such as landfill leachate, biosolids recycling, and aqueous film-forming foam contamination of drinking water sources, among others (Sunderland et al. 2019; Solo-Gabriele et al. 2020). Aqueous film-forming foam and other mixtures evident in drinking water, food packaging, health and beauty products, and food-based sources are often poorly characterized (Sunderland et al. 2019; Susmann et al. 2019).

Discussions on whether PFAS may be addressed using a relative potency framework or toxic equivalency factor approach are ongoing. Substances could be grouped by bioaccumulation and persistence (toxicokinetics), function (biology), molecular initiating events, with potency factors derived from several assays, or subclass (structural similarity).

## SPECIAL CONSIDERATIONS IN FUTURE STUDY DESIGNS

### *Future epidemiological studies*

Future human studies need to characterize immune outcomes including (and not limited to) immune effects from exposure in early pregnancy and possible roles of PFAS in

initiating allergic and autoimmune processes, conditions for which a dose response is hard to predict. Interactions of immune pathways with liver and lipid toxicity deserve additional consideration.

Liver and lipid studies have reasonably characterized associations between PFAS and effects and should now address why and what to do about it. Characterization of possible *a priori* susceptibility, such as in the obese, is important. Human and animal lipid data suggest that future experimental studies should focus on mitochondrial toxicity, alterations in bile acid metabolism, cholestasis, and resultant steatosis. These outcomes are already known to be associated with altered serum lipids, liver enzymes, and uric acid in the human population regardless of PFAS (Cohen and Fisher 2013; Sattar et al. 2014; Arguello et al. 2015; Jensen et al. 2018).

Studies of human kidney markers related to PFAS exposures illustrate the importance of understanding physiology to inform study design choices and reasonable interpretations. These substances have complex excretion mechanics that vary with dose, state of the healthy or progressively diseased kidney, as well as a potentially additional causative effect on kidney disease outcome(s). Appropriate definition of biological and mechanistic targets and more precise investigation of PFAS subclasses will better inform study designs and research questions. For example, consistent reports of disrupted cholesterol metabolism should prompt mechanistic studies evaluating effects on steroid hormones that may influence cancer, fecundity, lactation, and developmental signals seen in human population data. More attention could be given to effects of PFAS on the hypothalamic–pituitary–gonadal axis and then reconsidered based on life stages.

The history of long-chain PFAS studies indicates that collaborative team approaches featuring clinical, epidemiologic, computational modeling, and laboratory toxicological expertise are needed. Future population designs and more sensitive analytical methodologies should address replacement chemicals, typically found as mixtures; study designs must account for shorter PFAS half-lives and unpredictable PFAS detection in exposed individuals/communities. Innovative use of biomarkers in specifically designated risk subpopulations (obesity, immune) will likely be important.

### *Sex differences, nonmonotonic dose responses, sensitive subpopulations*

Although serum-level differences exist between men and women similarly exposed to individual PFAS, sex-dependent differences in half-life have not been reported in human populations for short-chain (PFBS, PFBA) or long-chain perfluoroalkyl acids thus far (Li et al. 2017b). Perhaps the half-life differences between the sexes is similar to interindividual variability and cannot be detected above background, or studies deriving data sets used to model half-lives were not designed to detect sex differences (convenience sampling or workers were mostly male, etc.). However, sex-specific elimination half-lives are defined (Table 1) for some PFAS in rodent models.

In addition, developmental exposure studies in experimental models have consistently shown effects at lower doses than adult-only exposures and should be given priority in testing replacement chemicals. In vitro and alternative models that capture developmental susceptibility are encouraged. In summary, care should be taken in testing replacement PFAS in rodent or alternative (cell-based or zebrafish, for example) models to consider 1) the possibilities of sex-based differences in elimination half-lives, 2) dose range used (to include human relevant exposures), 3) life stage represented in the model system, and 4) variability of the response to enable the use of data generated for risk assessment.

### Future experimental model studies

Experimental rodent studies have been essential in confirming PFAS health effects (liver and thyroid disease, lipid homeostasis), even when effects were not identical to those in humans; in some cases, novel targets (mammary and immune changes) were identified in animals. Future animal, cell-based, and high-throughput toxicity screening should enhance transparency in reporting to include blinded dose allocation, reporting of all data, adherence to Animal Research Reporting In Vivo Experiments (ARRIVE) guidelines (Kilkenny et al. 2010), and dose ranges that approach human relevance (adjusted to reflect the differences in elimination between species and potentially chronic exposures) so that they suitably inform systematic reviews that may be used in chemical regulation.

Model selection for health effects evaluation is critical. An appropriate model should be sensitive, be susceptible to the outcome(s) of interest (obesity, immune), and produce outcomes that will inform human health effects. Alternative research models, such as transgenic mice, zebrafish, developmental models for most affected target tissues, and diet-challenged designs in susceptible rodent strains, will strengthen our knowledge of PFAS-related health effects. Validation of fish neurobehavior models to inform mammalian, including human, developmental responses is needed.

Finally, advanced human cell-based platforms—that have been validated for relevant outcomes in humans—will facilitate concurrent screening of larger numbers of PFAS, but bioavailability of PFAS in the culture system needs to be understood because binding to media proteins or labware, the instability of some PFAS in some vehicles, and altered metabolism may exist in some cases (Gaballah et al. 2020; Liberatore et al. 2020).

### Future alternative approaches

One way to determine the toxicity of the large number of PFAS compounds currently used in commerce is to develop quantitative structure–activity relationships (QSAR). Such QSAR attempt to define relationships between a PFAS compound structure with a specific biological activity or response that identifies or is a biomarker for toxicity. Few data are available for receptor binding of PFAS, mainly limited to a few

PFACAs and PFASAs; and even between carboxylates and sulfonates of similar chain length substantial differences have been observed (Cheng and Ng 2017, 2018). If there are substantial differences between perfluoroalkyl carboxylic and sulfonic acids, which differ only in their acid head group, construction of successful QSAR for the large and diverse class of all PFAS will be particularly challenging. Several QSAR may be developed, each predictive of toxicity of a distinct class or subclass of PFAS, based on a unique functional moiety or other feature. Although this brings additional challenges in finding sufficient data for QSAR training and validation, big data approaches, such as the recently developed machine learning models to predict PFAS bioactivity (Cheng and Ng 2019), show promise for advancing these computational approaches at the screening level.

For example, it may be determined by affinity for receptor-specific binding and nonspecific interactions with cellular membranes that the specific toxic effect exhibits a multiphasic dose response reflecting 2 potential modes of action. In addition, the critical effect may change with levels of PFAS exposure. Add to this that people are typically exposed to PFAS mixtures, each of which may have a different affinity for a binding site and ability to impact cellular membrane fluidity, and the potential to predict PFAS toxicity becomes extremely complicated. In the foreseeable future, we may be limited to assessing PFAS toxicity using high-throughput assays designed to inform regulators as to the relative toxicity of PFAS mixtures or compounds. Such approaches are suited to the use of artificial intelligence (i.e., machine learning approaches) that integrate data from multiple sources to identify bioaccumulation potential, relevant pathways triggered, protein binding affinities, and modes of action involved in the development of individual and mixture toxicity of PFAS.

The utility of any future approach to determining PFAS toxicity must consider tissue-specific modes of action. Such an approach may rely on molecular interactions with specific binding sites on enzymes/storage/transport proteins or the nonspecific ability to alter cell membrane fluidity by which membrane-bound protein activities are altered within a particular organ/system. Regardless of the mode of action, model, and/or simulation, the predictive result should be biologically plausible and represent dose–effect responses across species.

## CONCLUSION

Future research on the health effects of replacement PFAS and mechanistic studies on legacy PFAS must apply “lessons learned” such as those highlighted in the present review. There are only a handful of PFAS with enough health effects data for use in decision-making, as evidenced by state-led standard setting. There are numerous health effects reported for those PFAS tested, which sets this family of chemicals apart from many others and elevates the need for precautionary action. With hundreds of PFAS lacking health effects data, translational research teams using innovative methodologies and carefully designed studies will be critical to our state of knowledge on

PFAS-related health effects and our enhanced strategies for informing risk assessment of this large family of chemicals.

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## REFERENCES

- Abraham K, Mielke H, Fromme H, Volkel W, Menzel J, Peiser M, Zepp F, Willich SN, Weikert C. 2020. Internal exposure to perfluoroalkyl substances (PFASs) and biological markers in 101 healthy 1-year-old children: Associations between levels of perfluorooctanoic acid (PFOA) and vaccine response. *Arch Toxicol* 94:2131–2147.
- Agency for Toxic Substances and Disease Registry. 2018. Toxicological profile for perfluoroalkyls. US Department of Health and Human Services, Washington, DC. [cited 2020 July 13]. Available from: <https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf>
- Alderete TL, Jin R, Walker DI, Valvi D, Chen Z, Jones DP, Peng C, Gilliland FD, Berhane K, Conti DV, Goran MI, Chatzi L. 2019. Perfluoroalkyl substances, metabolomic profiling, and alterations in glucose homeostasis among overweight and obese Hispanic children: A proof-of-concept analysis. *Environ Int* 126:445–453.
- Andersen ME, Butenhoff JL, Chang S-C, Farrar DG, Kennedy GL Jr, Lau C, Olsen GW, Seed J, Wallace KB. 2007. Perfluoroalkyl acids and related chemistries—Toxicokinetics and modes of action. *Toxicol Sci* 102:3–14.
- Andersen ME, Clewell HJ, Tan Y-M, Butenhoff JL, Olsen GW. 2006. Pharmacokinetic modeling of saturable, renal resorption of perfluoroalkylacids in monkeys—Probing the determinants of long plasma half-lives. *Toxicology* 227:156–164.
- Andersson EM, Scott K, Xu Y, Li Y, Olsson DS, Fletcher T, Jakobsson K. 2019. High exposure to perfluorinated compounds in drinking water and thyroid disease. A cohort study from Ronneby, Sweden. *Environ Res* 176:108540.
- Arguello G, Balboa E, Arrese M, Zanlungo S. 2015. Recent insights on the role of cholesterol in non-alcoholic fatty liver disease. *Biochim Biophys Acta* 1852:1765–1778.
- Armstrong LE, Guo GL. 2019. Understanding environmental contaminants' direct effects on non-alcoholic fatty liver disease progression. *Curr Environ Health Rep* 6:95–104.
- Ashley-Martin J, Dodds L, Arbuckle TE, Morisset AS, Fisher M, Bouchard MF, Shapiro GD, Ettinger AS, Monnier P, Dallaire R, Taback S, Fraser W. 2016. Maternal and neonatal levels of perfluoroalkyl substances in relation to gestational weight gain. *Int J Environ Res Public Health* 13:146.
- Attanasio R. 2019. Sex differences in the association between perfluoroalkyl acids and liver function in US adolescents: Analyses of NHANES 2013–2016. *Environ Pollut* 254:113061.
- Avanasi R, Shin HM, Vieira VM, Bartell SM. 2016a. Variability and epistemic uncertainty in water ingestion rates and pharmacokinetic parameters, and impact on the association between perfluorooctanoate and preeclampsia in the C8 Health Project population. *Environ Res* 146:299–307.
- Avanasi R, Shin HM, Vieira VM, Savitz DA, Bartell SM. 2016b. Impact of exposure uncertainty on the association between perfluorooctanoate and preeclampsia in the C8 Health Project population. *Environ Health Perspect* 124:126–132.
- Bach CC, Liew Z, Bech BH, Nohr EA, Fei C, Bonefeld-Jorgensen EC, Henriksen TB, Olsen J. 2015. Perfluoroalkyl acids and time to pregnancy revisited: An update from the Danish National Birth Cohort. *Environ Health* 14:59.
- Ballesteros V, Costa O, Iniguez C, Fletcher T, Ballester F, Lopez-Espinosa MJ. 2017. Exposure to perfluoroalkyl substances and thyroid function in pregnant women and children: A systematic review of epidemiologic studies. *Environ Int* 99:15–28.
- Barry V, Darrow LA, Klein M, Winquist A, Steenland K. 2014. Early life perfluorooctanoic acid (PFOA) exposure and overweight and obesity risk in adulthood in a community with elevated exposure. *Environ Res* 132:62–69.
- Barry V, Winquist A, Steenland K. 2013. Perfluorooctanoic acid (PFOA) exposures and incident cancers among adults living near a chemical plant. *Environ Health Perspect* 121:1313–1318.
- Bartell SM, Calafat AM, Lyu C, Kato K, Ryan PB, Steenland K. 2010. Rate of decline in serum PFOA concentrations after granular activated carbon filtration at two public water systems in Ohio and West Virginia. *Environ Health Perspect* 118:222–228.
- Bassler J, Ducatman A, Elliott M, Wen S, Wahlang B, Barnett J, Cave MC. 2019. Environmental perfluoroalkyl acid exposures are associated with liver disease characterized by apoptosis and altered serum adipocytokines. *Environ Pollut* 247:1055–1063.
- Behr AC, Kwiatkowski A, Stahlman M, Schmidt FF, Luckert C, Braeuning A, Buhrke T. 2020a. Impairment of bile acid metabolism by perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) in human HepaRG hepatoma cells. *Arch Toxicol* 94:1673–1686.
- Behr A-C, Lichtenstein D, Braeuning A, Lampen A, Buhrke T. 2018. Perfluoroalkylated substances (PFAS) affect neither estrogen and androgen receptor activity nor steroidogenesis in human cells in vitro. *Toxicol Lett* 291:51–60.
- Behr A-C, Plinsch C, Braeuning A, Buhrke T. 2020b. Activation of human nuclear receptors by perfluoroalkylated substances (PFAS). *Toxicol In Vitro* 62:104700.
- Benninghoff AD, Bisson WH, Koch DC, Ehresman DJ, Kolluri SK, Williams DE. 2010. Estrogen-like activity of perfluoroalkyl acids in vivo and interaction with human and rainbow trout estrogen receptors in vitro. *Toxicol Sci* 120:42–58.
- Berg V, Nost TH, Hansen S, Elverland A, Veyhe AS, Jorde R, Odland JO, Sandanger TM. 2015. Assessing the relationship between perfluoroalkyl substances, thyroid hormones and binding proteins in pregnant women; a longitudinal mixed effects approach. *Environ Int* 77:63–69.
- Bijland S, Rensen PC, Pieterman EJ, Maas AC, van der Hoorn JW, van Erk MJ, Havekes LM, Willems van Dijk K, Chang SC, Ehresman DJ, Butenhoff JL, Princen HMG. 2011. Perfluoroalkyl sulfonates cause alkyl

- chain length-dependent hepatic steatosis and hypolipidemia mainly by impairing lipoprotein production in APOE\*3-Leiden CETP mice. *Toxicol Sci* 123:290–303.
- Bjerregaard-Olesen C, Bach CC, Long M, Wielsøe M, Bech BH, Henriksen TB, Olsen J, Bonefeld-Jørgensen EC. 2019. Associations of fetal growth outcomes with measures of the combined xenoestrogenic activity of maternal serum perfluorinated alkyl acids in Danish pregnant women. *Environ Health Perspect* 127:017006.
- Bjork JA, Butenhoff JL, Wallace KB. 2011. Multiplicity of nuclear receptor activation by PFOA and PFOS in primary human and rodent hepatocytes. *Toxicology* 288:8–17.
- Blake BE, Cope HA, Hall SM, Keys RD, Mahler BW, McCord J, Scott B, Stapleton HM, Strynar MJ, Elmore SA, Fenton SE. 2020. Evaluation of maternal, embryo, and placental effects in CD-1 mice following gestational exposure to perfluorooctanoic acid (PFOA) or hexafluoropropylene oxide dimer acid (HFPO-DA or GenX). *Environ Health Perspect* 128:27006.
- Blake BE, Pinney SM, Hines EP, Fenton SE, Ferguson KK. 2018. Associations between longitudinal serum perfluoroalkyl substance (PFAS) levels and measures of thyroid hormone, kidney function, and body mass index in the Fernald Community Cohort. *Environ Pollut* 242:894–904.
- Bodin J, Groeng EC, Andreassen M, Dirven H, Nygaard UC. 2016. Exposure to perfluoroundecanoic acid (PFUnDA) accelerates insulin development in a mouse model of type 1 diabetes. *Toxicol Rep* 3:664–672.
- Borghese MM, Walker M, Helewa ME, Fraser WD, Arbuckle TE. 2020. Association of perfluoroalkyl substances with gestational hypertension and preeclampsia in the MIREC study. *Environ Int* 141:105789.
- Borghoff SJ, Fitch S, Rager JE, Huggett D. 2018. A hypothesis-driven weight-of-evidence analysis to evaluate potential endocrine activity of perfluorohexanoic acid. *Regul Toxicol Pharmacol* 99:168–181.
- Bourre J-M, Francois M, Youyou A, Dumont O, Piciotti M, Pascal G, Durand G. 1989. The Effects of dietary  $\alpha$ -linolenic acid on the composition of nerve membranes, enzymatic activity, amplitude of electrophysiological parameters, resistance to poisons and performance of learning tasks in rats. *J Nutr* 119:1880–1892.
- Buck RC, Franklin J, Berger U, Conder JM, Cousins IT, de Voogt P, Jensen AA, Kannan K, Mabury SA, van Leeuwen SP. 2011. Perfluoroalkyl and polyfluoroalkyl substances in the environment: Terminology, classification, and origins. *Integr Environ Assess Manag* 7:513–541.
- Buhrke T, Kruger E, Pevny S, Rossler M, Bitter K, Lampen A. 2015. Perfluorooctanoic acid (PFOA) affects distinct molecular signalling pathways in human primary hepatocytes. *Toxicology* 333:53–62.
- Butenhoff JL, Chang SC, Olsen GW, Thomford PJ. 2012. Chronic dietary toxicity and carcinogenicity study with potassium perfluorooctanesulfonate in Sprague Dawley rats. *Toxicology* 293:1–15.
- Butenhoff JL, Ehresman DJ, Chang SC, Parker GA, Stump DG. 2009. Gestational and lactational exposure to potassium perfluorooctanesulfonate (K+PFOS) in rats: Developmental neurotoxicity. *Reprod Toxicol* 27:319–330.
- C8 Science Panel. 2012. Probable Link Evaluation of Thyroid disease. [cited 2020 July 13]. Available from: [http://www.c8sciencepanel.org/pdfs/Probable\\_Link\\_C8\\_Thyroid\\_30Jul2012.pdf](http://www.c8sciencepanel.org/pdfs/Probable_Link_C8_Thyroid_30Jul2012.pdf)
- Campbell S, Raza M, Pollack AZ. 2016. Perfluoroalkyl substances and endometriosis in US women in NHANES 2003–2006. *Reprod Toxicol* 65:230–235.
- Cardenas A, Gold DR, Hauser R, Kleinman KP, Hivert MF, Calafat AM, Ye X, Webster TF, Horton ES, Oken E. 2017. Plasma concentrations of per- and polyfluoroalkyl substances at baseline and associations with glycemic indicators and diabetes incidence among high-risk adults in the Diabetes Prevention Program Trial. *Environ Health Perspect* 125:107001.
- Carr CK, Watkins AM, Wolf CJ, Abbott BD, Lau C, Gennings C. 2013. Testing for departures from additivity in mixtures of perfluoroalkyl acids (PFAAs). *Toxicology* 306:169–175.
- Casares D, Escribá PV, Rosselló CA. 2019. Membrane lipid composition: Effect on membrane and organelle structure, function and compartmentalization and therapeutic avenues. *Int J Mol Sci* 20:2167.
- Caverly Rae JM, Craig L, Buxton TW, Frame SR, Kennedy GL. 2015. Evaluation of chronic toxicity and carcinogenicity of ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoate in Sprague–Dawley rats. *Toxicol Rep* 2:939–949.
- Centers for Disease Control and Prevention. 2017. Per- and polyfluorinated substances (PFAS) factsheet. [cited 2020 May 19]. Available from: [https://www.cdc.gov/biomonitoring/PFAS\\_FactSheet.html](https://www.cdc.gov/biomonitoring/PFAS_FactSheet.html)
- Chen J, Wang X, Ge X, Wang D, Wang T, Zhang L, Tanguay RL, Simonich M, Huang C, Dong Q. 2016. Chronic perfluorooctanesulphonic acid (PFOS) exposure produces estrogenic effects in zebrafish. *Environ Pollut* 218:702–708.
- Chen P, Wang Q, Chen M, Yang J, Wang R, Zhong W, Zhu L, Yang L. 2018. Antagonistic estrogenic effects displayed by bisphenol AF and perfluorooctanoic acid on zebrafish (*Danio rerio*) at an early developmental stage. *Environ Sci Technol Lett* 5:655–661.
- Cheng L, Albers P, Berney DM, Feldman DR, Dugaard G, Gilligan T, Looijenga LHJ. 2018. Testicular cancer. *Nat Rev Dis Primers* 4:29.
- Cheng W, Ng CA. 2017. A permeability-limited physiologically based pharmacokinetic (PBPK) model for perfluorooctanoic acid (PFOA) in male rats. *Environ Sci Technol* 51:9930–9939.
- Cheng W, Ng CA. 2018. Predicting relative protein affinity of novel per- and polyfluoroalkyl substances (PFASs) by an efficient molecular dynamics approach. *Environ Sci Technol* 52:7972–7980.
- Cheng W, Ng CA. 2019. Using machine learning to classify bioactivity for 3486 per- and polyfluoroalkyl substances (PFASs) from the OECD list. *Environ Sci Technol* 53:13970–13980.
- Chou WC, Lin Z. 2020. Probabilistic human health risk assessment of perfluorooctane sulfonate (PFOS) by integrating in vitro, in vivo toxicity, and human epidemiological studies using a Bayesian-based dose–response assessment coupled with physiologically based pharmacokinetic (PBPK) modeling approach. *Environ Int* 137:105581.
- Cluett R, Seshasayee SM, Rokoff LB, Rifas-Shiman SL, Ye X, Calafat AM, Gold DR, Coull B, Gordon CM, Rosen CJ, Oken E, Sagiv SK, Fleisch AF. 2019. Per- and polyfluoroalkyl substance plasma concentrations and bone mineral density in midchildhood: A cross-sectional study (Project Viva, United States). *Environ Health Perspect* 127:87006.
- Cohen DE, Fisher EA. 2013. Lipoprotein metabolism, dyslipidemia, and nonalcoholic fatty liver disease. *Semin Liver Dis* 33:380–388.
- Conley JM, Lambright CS, Evans N, Strynar MJ, McCord J, McIntyre BS, Travlos GS, Cardon MC, Medlock-Kakaley E, Hartig PC, Wilson VS, Gray LE Jr. 2019. Adverse maternal, fetal, and postnatal effects of hexafluoropropylene oxide dimer acid (GenX) from oral gestational exposure in Sprague-Dawley rats. *Environ Health Perspect* 127:37008.
- Convertino M, Church TR, Olsen GW, Liu Y, Doyle E, Elcombe CR, Barnett AL, Samuel LM, MacPherson IR, Evans TRJ. 2018. Stochastic pharmacokinetic-pharmacodynamic modeling for assessing the systemic health risk of perfluorooctanoate (PFOA). *Toxicol Sci* 163:293–306.
- Coperchini F, Awwad O, Rotondi M, Santini F, Imbriani M, Chiovato L. 2017. Thyroid disruption by perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA). *J Endocrinol Invest* 40:105–121.
- Corton JC, Peters JM, Klaunig JE. 2018. The PPAR $\alpha$ -dependent rodent liver tumor response is not relevant to humans: Addressing misconceptions. *Arch Toxicol* 92:83–119.
- Cui L, Zhou QF, Liao CY, Fu JJ, Jiang GB. 2009. Studies on the toxicological effects of PFOA and PFOS on rats using histological observation and chemical analysis. *Arch Environ Contam Toxicol* 56:338–349.
- Daly ER, Chan BP, Talbot EA, Nassif J, Bean C, Cavallo SJ, Metcalf E, Simone K, Woolf AD. 2018. Per- and polyfluoroalkyl substance (PFAS) exposure assessment in a community exposed to contaminated drinking water, New Hampshire, 2015. *Int J Hyg Environ Health* 221:569–577.
- Darrow LA, Groth AC, Winquist A, Shin HM, Bartell SM, Steenland K. 2016. Modeled perfluorooctanoic acid (PFOA) exposure and liver function in a mid-Ohio Valley community. *Environ Health Perspect* 124:1227–1233.
- Darrow LA, Stein CR, Steenland K. 2013. Serum perfluorooctanoic acid and perfluorooctane sulfonate concentrations in relation to birth outcomes in the mid-Ohio Valley, 2005–2010. *Environ Health Perspect* 121:1207–1213.
- Das KP, Grey BE, Rosen MB, Wood CR, Tatum-Gibbs KR, Zehr RD, Strynar MJ, Lindstrom AB, Lau C. 2015. Developmental toxicity of perfluorononanoic acid in mice. *Reprod Toxicol* 51:133–144.
- Das KP, Wood CR, Lin MT, Starkov AA, Lau C, Wallace KB, Corton JC, Abbott BD. 2017. Perfluoroalkyl acids-induced liver steatosis: Effects on genes controlling lipid homeostasis. *Toxicology* 378:37–52.
- DeWitt JC, Blossom SJ, Schaidler LA. 2019. Exposure to per-fluoroalkyl and polyfluoroalkyl substances leads to immunotoxicity: Epidemiological and toxicological evidence. *J Expo Sci Environ Epidemiol* 29:148–156.
- Dhingra R, Winquist A, Darrow LA, Klein M, Steenland K. 2017. A study of reverse causation: Examining the associations of perfluorooctanoic acid serum levels with two outcomes. *Environ Health Perspect* 125:416–421.

- Di Nisio A, De Rocco Ponce M, Giadone A, Rocca MS, Guidolin D, Foresta C. 2020a. Perfluoroalkyl substances and bone health in young men: A pilot study. *Endocrine* 67:678–684.
- Di Nisio A, Rocca MS, Sabovic I, De Rocco Ponce M, Corsini C, Guidolin D, Zanon C, Acquasaliente L, Carosso AR, De Toni L, Foresta C. 2020b. Perfluorooctanoic acid alters progesterone activity in human endometrial cells and induces reproductive alterations in young women. *Chemosphere* 242:125208.
- Division of Science and Research, New Jersey Department of Environmental Protection. 2019. Interim specific ground water criterion for perfluorooctanoic acid (PFOA, C8) (CAS #: 335-67-1; chemical structure:  $\text{CF}_3(\text{CF}_2)_6\text{COOH}$ )\*. Trenton, NJ, USA. [cited 2020 July 13]. Available from: [https://www.nj.gov/dep/dsr/supportdocs/PFOA\\_TSD.pdf](https://www.nj.gov/dep/dsr/supportdocs/PFOA_TSD.pdf)
- Dodes Traian MM, Cattoni DI, Levi V, Gonzalez Flecha FL. 2012. A two-stage model for lipid modulation of the activity of integral membrane proteins. *PLoS One* 7:e39255.
- Donat-Vargas C, Bergdahl IA, Tornevi A, Wennberg M, Sommar J, Kiviranta H, Koponen J, Rolandsson O, Akesson A. 2019. Perfluoroalkyl substances and risk of type II diabetes: A prospective nested case-control study. *Environ Int* 123:390–398.
- Dong Z, Wang H, Yu YY, Li YB, Naidu R, Liu Y. 2019. Using 2003–2014 U.S. NHANES data to determine the associations between per- and polyfluoroalkyl substances and cholesterol: Trend and implications. *Ecotoxicol Environ Saf* 173:461–468.
- EFSA Panel on Contaminants in the Food Chain. 2020. Public consultation on the draft scientific opinion on the risks to human health related to the presence of perfluoroalkyl substances in food. European Food Safety Authority, Parma, Italy. [cited 2020 September 15]. Available from: <https://www.efsa.europa.eu/en/consultations/call/public-consultation-draft-scientific-opinion-risks-human-health>
- Elcombe CR, Elcombe BM, Foster JR, Chang SC, Ehresman DJ, Butenhoff JL. 2012. Hepatocellular hypertrophy and cell proliferation in Sprague-Dawley rats from dietary exposure to potassium perfluorooctanesulfonate results from increased expression of xenosensor nuclear receptors PPAR $\alpha$  and CAR/PXR. *Toxicology* 293:16–29.
- Emmett EA, Shofer FS, Zhang H, Freeman D, Desai C, Shaw LM. 2006. Community exposure to perfluorooctanoate: Relationships between serum concentrations and exposure sources. *J Occup Environ Med* 48:759–770.
- Eriksen KT, Raaschou-Nielsen O, McLaughlin JK, Lipworth L, Tjonneland A, Overvad K, Sorensen M. 2013. Association between plasma PFOA and PFOS levels and total cholesterol in a middle-aged Danish population. *PLoS One* 8:e56969.
- Eryasa B, Grandjean P, Nielsen F, Valvi D, Zmirou-Navier D, Sunderland E, Weihe P, Oulhote Y. 2019. Physico-chemical properties and gestational diabetes predict transplacental transfer and partitioning of perfluoroalkyl substances. *Environ Int* 130:104874.
- European Environment Agency. 2019. Emerging chemical risks in Europe—“PFAS.” Copenhagen, Denmark. [cited 2020 July 13]. Available from: <https://www.eea.europa.eu/themes/human/chemicals/emerging-chemical-risks-in-europe>
- Fei C, McLaughlin JK, Lipworth L, Olsen J. 2009. Maternal levels of perfluorinated chemicals and subfecundity. *Hum Reprod* 24:1200–1205.
- Fenton SE, Reiner JL, Nakayama SF, Delinsky AD, Stanko JP, Hines EP, White SS, Lindstrom AB, Strynar MJ, Petropoulou SE. 2009. Analysis of PFOA in dosed CD-1 mice. Part 2. Disposition of PFOA in tissues and fluids from pregnant and lactating mice and their pups. *Reprod Toxicol* 27:365–372.
- Ferrari F, Orlando A, Ricci Z, Ronco C. 2019. Persistent pollutants: Focus on perfluorinated compounds and kidney. *Curr Opin Crit Care* 25:539–549.
- Filgo AJ, Quist EM, Hoenerhoff MJ, Brix AE, Kissling GE, Fenton SE. 2015. Perfluorooctanoic acid (PFOA)-induced liver lesions in two strains of mice following developmental exposures: PPAR $\alpha$  is not required. *Toxicol Pathol* 43:558–568.
- Fisher M, Arbuckle TE, Wade M, Haines DA. 2013. Do perfluoroalkyl substances affect metabolic function and plasma lipids? Analysis of the 2007–2009, Canadian Health Measures Survey (CHMS) cycle 1. *Environ Res* 121:95–103.
- Fitz-Simon N, Fletcher T, Luster MI, Steenland K, Calafat AM, Kato K, Armstrong B. 2013. Reductions in serum lipids with a 4-year decline in serum perfluorooctanoic acid and perfluorooctanesulfonic acid. *Epidemiology* 24:569–576.
- Fletcher T, Galloway TS, Melzer D, Holcroft P, Cipelli R, Pilling LC, Mondal D, Luster M, Harries LW. 2013. Associations between PFOA, PFOS and changes in the expression of genes involved in cholesterol metabolism in humans. *Environ Int* 57–58:2–10.
- Forhead AJ, Fowden AL. 2014. Thyroid hormones in fetal growth and prepartum maturation. *J Endocrinol* 221:R87–R103.
- Frisbee SJ, Shankar A, Knox SS, Steenland K, Savitz DA, Fletcher T, Ducatman AM. 2010. Perfluorooctanoic acid, perfluorooctanesulfonate, and serum lipids in children and adolescents: Results from the C8 Health Project. *Arch Pediatr Adolesc Med* 164:860–869.
- Fritsche K. 2006. Fatty acids as modulators of the immune response. *Annu Rev Nutr* 26:45–73.
- Fromme H, Mosch C, Morovitz M, Alba-Alejandre I, Boehmer S, Kiranoglu M, Faber F, Hannibal I, Genzel-Boroviczeny O, Koletzko B, Volkel W. 2010. Pre- and postnatal exposure to perfluorinated compounds (PFCs). *Environ Sci Technol* 44:7123–7129.
- Fu Y, Wang T, Fu Q, Wang P, Lu Y. 2014. Associations between serum concentrations of perfluoroalkyl acids and serum lipid levels in a Chinese population. *Ecotoxicol Environ Saf* 106:246–252.
- Gaballah S, Swank A, Sobus JR, Howey XM, Schmid J, Catron T, McCord J, Hines E, Strynar M, Tal T. 2020. Evaluation of developmental toxicity, developmental neurotoxicity, and tissue dose in zebrafish exposed to GenX and other PFAS. *Environ Health Perspect* 128:47005.
- Gallo V, Leonardi G, Genser B, Lopez-Espinosa MJ, Frisbee SJ, Karlsson L, Ducatman AM, Fletcher T. 2012. Serum perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) concentrations and liver function biomarkers in a population with elevated PFOA exposure. *Environ Health Perspect* 120:655–660.
- Gandaglia G, Ravi P, Abdollah F, Abd-El-Barr AE, Becker A, Popa I, Briganti A, Karakiewicz PI, Trinh QD, Jewett MA, Sun M. 2014. Contemporary incidence and mortality rates of kidney cancer in the United States. *Can Urol Assoc J* 8:247–252.
- Geiger SD, Xiao J, Shankar A. 2013. Positive association between perfluoroalkyl chemicals and hyperuricemia in children. *Am J Epidemiol* 177:1255–1262.
- Genser B, Teles CA, Barreto ML, Fischer JE. 2015. Within- and between-group regression for improving the robustness of causal claims in cross-sectional analysis. *Environ Health* 14:60.
- Girardi P, Merler E. 2019. A mortality study on male subjects exposed to polyfluoroalkyl acids with high internal dose of perfluorooctanoic acid. *Environ Res* 179:108743.
- Gleason JA, Post GB, Fagliano JA. 2015. Associations of perfluorinated chemical serum concentrations and biomarkers of liver function and uric acid in the US population (NHANES), 2007–2010. *Environ Res* 136:8–14.
- Gogola J, Hoffmann M, Ptak A. 2019. Persistent endocrine-disrupting chemicals found in human follicular fluid stimulate the proliferation of granulosa tumor spheroids via GPR30 and IGF1R but not via the classic estrogen receptors. *Chemosphere* 217:100–110.
- Goudarzi H, Miyashita C, Okada E, Kashino I, Chen CJ, Ito S, Araki A, Kobayashi S, Matsuura H, Kishi R. 2017. Prenatal exposure to perfluoroalkyl acids and prevalence of infectious diseases up to 4 years of age. *Environ Int* 104:132–138.
- Goulding DR, White SS, McBride SJ, Fenton SE, Harry GJ. 2017. Gestational exposure to perfluorooctanoic acid (PFOA): Alterations in motor related behaviors. *Neurotoxicology* 58:110–119.
- Graber JM, Alexander C, Laumbach RJ, Black K, Strickland PO, Georgopoulos PG, Marshall EG, Shendell DG, Alderson D, Mi Z, Mascari M, Weisel CP. 2019. Per- and polyfluoroalkyl substances (PFAS) blood levels after contamination of a community water supply and comparison with 2013–2014 NHANES. *J Expo Sci Environ Epidemiol* 29:172–182.
- Grandjean P, Andersen EW, Budtz-Jorgensen E, Nielsen F, Molbak K, Weihe P, Heilmann C. 2012. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. *JAMA* 307:391–397.
- Grandjean P, Heilmann C, Weihe P, Nielsen F, Mogensen UB, Budtz-Jorgensen E. 2017. Serum vaccine antibody concentrations in adolescents exposed to perfluorinated compounds. *Environ Health Perspect* 125:077018.
- Granum B, Haug LS, Namork E, Stolevik SB, Thomsen C, Aaberge IS, van Loveren H, Lovik M, Nygaard UC. 2013. Pre-natal exposure to perfluoroalkyl substances may be associated with altered vaccine antibody levels and immune-related health outcomes in early childhood. *J Immunotoxicol* 10:373–379.
- Guillette TC, McCord J, Guillette M, Polera ME, Rachels KT, Morgeson C, Kotlarz N, Knappe DRU, Reading BJ, Strynar M, Belcher SM. 2020. Elevated levels of per- and polyfluoroalkyl substances in Cape Fear River

- striped bass (*Morone saxatilis*) are associated with biomarkers of altered immune and liver function. *Environ Int* 136:105358.
- Guruge KS, Yeung LW, Yamanaka N, Miyazaki S, Lam PK, Giesy JP, Jones PD, Yamashita N. 2006. Gene expression profiles in rat liver treated with perfluorooctanoic acid (PFOA). *Toxicol Sci* 89:93–107.
- Gyllenhammar I, Benskin JP, Sandblom O, Berger U, Ahrens L, Lignell S, Wiberg K, Glynn A. 2018. Perfluoroalkyl acids (PFAAs) in serum from 2–4-month-old infants: Influence of maternal serum concentration, gestational age, breast-feeding, and contaminated drinking water. *Environ Sci Technol* 52:7101–7110.
- Hall JM, Greco CW. 2019. Perturbation of nuclear hormone receptors by endocrine disrupting chemicals: Mechanisms and pathological consequences of exposure. *Cells* 9:13.
- Halldorsson TI, Rytter D, Haug LS, Bech BH, Danielsen I, Becher G, Henriksen TB, Olsen SF. 2012. Prenatal exposure to perfluorooctanoate and risk of overweight at 20 yr of age: A prospective cohort study. *Environ Health Perspect* 120:668–673.
- Han X, Nabb DL, Russell MH, Kennedy GL, Rickard RW. 2012. Renal elimination of perfluorocarboxylates (PFCAs). *Chem Res Toxicol* 25:35–46.
- He X, Liu Y, Xu B, Gu L, Tang W. 2018. PFOA is associated with diabetes and metabolic alteration in US men: National Health and Nutrition Examination Survey 2003–2012. *Sci Total Environ* 625:566–574.
- Hines EP, White SS, Stanko JP, Gibbs-Flourmoy EA, Lau C, Fenton SE. 2009. Phenotypic dichotomy following developmental exposure to perfluorooctanoic acid (PFOA) in female CD-1 mice: Low doses induce elevated serum leptin and insulin, and overweight in mid-life. *Mol Cell Endocrinol* 304:97–105.
- Hoover G, Kar S, Guffey S, Leszczynski J, Sepulveda MS. 2019. In vitro and in silico modeling of perfluoroalkyl substances mixture toxicity in an amphibian fibroblast cell line. *Chemosphere* 233:25–33.
- Hu Y, Liu G, Rood J, Liang L, Bray GA, de Jonge L, Coull B, Furtado JD, Qi L, Grandjean P, Sun Q. 2019. Perfluoroalkyl substances and changes in bone mineral density: A prospective analysis in the POUNDS-LOST study. *Environ Res* 179:108775.
- Huang Q, Zhang J, Martin FL, Peng S, Tian M, Mu X, Shen H. 2013. Perfluorooctanoic acid induces apoptosis through the p53-dependent mitochondrial pathway in human hepatic cells: A proteomic study. *Toxicol Lett* 223:211–220.
- Huang R, Chen Q, Zhang L, Luo K, Chen L, Zhao S, Feng L, Zhang J. 2019. Prenatal exposure to perfluoroalkyl and polyfluoroalkyl substances and the risk of hypertensive disorders of pregnancy. *Environ Health* 18:5.
- Hui Z, Li R, Chen L. 2017. The impact of exposure to environmental contaminant on hepatocellular lipid metabolism. *Gene* 622:67–71.
- Huo X, Huang R, Gan Y, Luo K, Aimuzi R, Nian M, Ao J, Feng L, Tian Y, Wang W, Ye W, Zhang J, Shanghai Birth Cohort. 2020. Perfluoroalkyl substances in early pregnancy and risk of hypertensive disorders of pregnancy: A prospective cohort study. *Environ Int* 138:105656.
- IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. 2017. Perfluorooctanoic acid. In *Some Chemicals Used as Solvents and in Polymer Manufacture*. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 110. International Agency for Research on Cancer, Lyon, France, pp 37–110.
- Impinen A, Longnecker MP, Nygaard UC, London SJ, Ferguson KK, Haug LS, Granum B. 2019. Maternal levels of perfluoroalkyl substances (PFASs) during pregnancy and childhood allergy and asthma related outcomes and infections in the Norwegian Mother and Child (MoBa) cohort. *Environ Int* 124:462–472.
- Impinen A, Nygaard UC, Lodrup Carlsen KC, Mowinckel P, Carlsen KH, Haug LS, Granum B. 2018. Prenatal exposure to perfluoroalkyl substances (PFASs) associated with respiratory tract infections but not allergy- and asthma-related health outcomes in childhood. *Environ Res* 160: 518–523.
- Inoue K, Ritz B, Andersen SL, Ramlau-Hansen CH, Hoyer BB, Bech BH, Henriksen TB, Bonfeld-Jorgensen EC, Olsen J, Liew Z. 2019. Perfluoroalkyl substances and maternal thyroid hormones in early pregnancy; findings in the Danish National Birth Cohort. *Environ Health Perspect* 127:117002.
- Interstate Technology and Regulatory Council. 2020. Chemistry, terminology and acronyms. [cited 2020 May 19]. Available from: <https://pfas-1.itrcweb.org/2-2-chemistry-terminology-and-acronyms/>
- Jain RB. 2020. Variabilities in concentrations of selected perfluoroalkyl acids among normotensives and hypertensives across various stages of glomerular function. *Arch Environ Occup Health* 2020:1–11.
- Jain RB, Ducatman A. 2019a. Dynamics of associations between perfluoroalkyl substances and uric acid across the various stages of glomerular function. *Environ Sci Pollut Res Int* 26:12425–12434.
- Jain RB, Ducatman A. 2019b. Perfluoroalkyl acids serum concentrations and their relationship to biomarkers of renal failure: Serum and urine albumin, creatinine, and albumin creatinine ratios across the spectrum of glomerular function among US adults. *Environ Res* 174:143–151.
- Jain RB, Ducatman A. 2019c. Perfluoroalkyl substances follow inverted U-shaped distributions across various stages of glomerular function: Implications for future research. *Environ Res* 169:476–482.
- Jain RB, Ducatman A. 2019d. Roles of gender and obesity in defining correlations between perfluoroalkyl substances and lipid/lipoproteins. *Sci Total Environ* 653:74–81.
- Jain RB, Ducatman A. 2019e. Selective associations of recent low concentrations of perfluoroalkyl substances with liver function biomarkers: NHANES 2011 to 2014 data on US adults aged  $\geq 20$  years. *J Occup Environ Med* 61:293–302.
- Jensen T, Niwa K, Hisatome I, Kanbay M, Andres-Hernando A, Roncal-Jimenez CA, Sato Y, Garcia G, Ohno M, Lanasa MA, Johnson RJ, Kuwabara M. 2018. Increased serum uric acid over five years is a risk factor for developing fatty liver. *Sci Rep* 8:11735.
- Jian JM, Chen D, Han FJ, Guo Y, Zeng L, Lu X, Wang F. 2018. A short review on human exposure to and tissue distribution of per- and polyfluoroalkyl substances (PFASs). *Sci Total Environ* 636:1058–1069.
- Jin R, McConnell R, Catherine C, Xu S, Walker DI, Stratakis N, Jones DP, Miller GW, Peng C, Conti DV, Vos MB, Chatzi L. 2020. Perfluoroalkyl substances and severity of nonalcoholic fatty liver in children: An untargeted metabolomics approach. *Environ Int* 134:105220.
- Joensen UN, Bossi R, Leffers H, Jensen AA, Skakkebaek NE, Jorgensen N. 2009. Do perfluoroalkyl compounds impair human semen quality? *Environ Health Perspect* 117:923–927.
- Johnson MS, Buck RC, Cousins IT, Weis CP, Fenton SE. 2020. Estimating environmental hazard and risks from exposure to per- and polyfluoroalkyl substances (PFAS): Outcome of a SETAC focused topic meeting. *Environ Toxicol Chem* 40:543–549.
- Johnson PI, Sutton P, Atchley DS, Koustas E, Lam J, Sen S, Robinson KA, Axelrad DA, Woodruff TJ. 2014. The Navigation Guide—Evidence-based medicine meets environmental health: Systematic review of human evidence for PFOA effects on fetal growth. *Environ Health Perspect* 122:1028–1039.
- Jones PD, Hu W, De Coen W, Newsted JL, Giesy JP. 2003. Binding of perfluorinated fatty acids to serum proteins. *Environ Toxicol Chem* 22:2639–2649.
- Kang Q, Gao F, Zhang X, Wang L, Liu J, Fu M, Zhang S, Wan Y, Shen H, Hu J. 2020. Nontargeted identification of per- and polyfluoroalkyl substances in human follicular fluid and their blood-follicle transfer. *Environ Int* 139:105686.
- Karnes C, Winquist A, Steenland K. 2014. Incidence of type II diabetes in a cohort with substantial exposure to perfluorooctanoic acid. *Environ Res* 128:78–83.
- Katakura M, Kudo N, Tsuda T, Hibino Y, Mitsumoto A, Kawashima Y. 2007. Rat organic anion transporter 3 and organic anion transporting polypeptide 1 mediate perfluorooctanoic acid transport. *J Health Sci* 53:77–83.
- Kataria A, Trachtman H, Malaga-Dieguez L, Trasande L. 2015. Association between perfluoroalkyl acids and kidney function in a cross-sectional study of adolescents. *Environ Health* 14:89.
- Kato K, Wong LY, Jia LT, Kuklenyik Z, Calafat AM. 2011. Trends in exposure to polyfluoroalkyl chemicals in the U.S. population: 1999–2008. *Environ Sci Technol* 45:8037–8045.
- Khalil N, Chen A, Lee M, Czerwinski SA, Ebert JR, DeWitt JC, Kannan K. 2016. Association of perfluoroalkyl substances, bone mineral density, and osteoporosis in the U.S. population in NHANES 2009–2010. *Environ Health Perspect* 124:81–87.
- Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. 2010. Improving bioscience research reporting: The ARRIVE guidelines for reporting animal research. *PLoS Biol* 8:e1000412.
- Kim DH, Kim UJ, Kim HY, Choi SD, Oh JE. 2016. Perfluoroalkyl substances in serum from South Korean infants with congenital hypothyroidism and healthy infants—Its relationship with thyroid hormones. *Environ Res* 147:399–404.
- Kingsley SL, Walker DI, Calafat AM, Chen A, Papandonatos GD, Xu Y, Jones DP, Lanphear BP, Pennell KD, Braun JM. 2019. Metabolomics of

- childhood exposure to perfluoroalkyl substances: A cross-sectional study. *Metabolomics* 15:95.
- Kjeldsen LS, Bonefeld-Jørgensen EC. 2013. Perfluorinated compounds affect the function of sex hormone receptors. *Environ Sci Pollut Res* 20:8031–8044.
- Klaunig JE, Hocevar BA, Kamendulis LM. 2012. Mode of action analysis of perfluorooctanoic acid (PFOA) tumorigenicity and human relevance. *Reprod Toxicol* 33:410–418.
- Koponen J, Winkens K, Airaksinen R, Berger U, Vestergren R, Cousins IT, Karvonen AM, Pekkanen J, Kiviranta H. 2018. Longitudinal trends of per- and polyfluoroalkyl substances in children's serum. *Environ Int* 121:591–599.
- Koshy TT, Attina TM, Ghassabian A, Gilbert J, Burdine LK, Marmor M, Honda M, Chu DB, Han X, Shao Y, Kannan K, Urbina EM, Trasande L. 2017. Serum perfluoroalkyl substances and cardiometabolic consequences in adolescents exposed to the World Trade Center disaster and a matched comparison group. *Environ Int* 109:128–135.
- Koustas E, Lam J, Sutton P, Johnson PI, Atchley DS, Sen S, Robinson KA, Axelrad DA, Woodruff TJ. 2014. The Navigation Guide—Evidence-based medicine meets environmental health: Systematic review of nonhuman evidence for PFOA effects on fetal growth. *Environ Health Perspect* 122:1015–1027.
- Kvaalem HE, Nygaard UC, Lodrup Carlsen KC, Carlsen KH, Haug LS, Granum B. 2020. Perfluoroalkyl substances, airways infections, allergy and asthma related health outcomes—Implications of gender, exposure period and study design. *Environ Int* 134:105259.
- LaLone CA, Ankley GT, Belanger SE, Embry MR, Hodges G, Knapen D, Munn S, Perkins EJ, Rudd MA, Villeneuve DL, Whelan M, Willett C, Zhang X, Hecker M. 2017. Advancing the adverse outcome pathway framework—An international horizon scanning approach. *Environ Toxicol Chem* 36:1411–1421.
- Lam J, Koustas E, Sutton P, Johnson PI, Atchley DS, Sen S, Robinson KA, Axelrad DA, Woodruff TJ. 2014. The Navigation Guide—Evidence-based medicine meets environmental health: Integration of animal and human evidence for PFOA effects on fetal growth. *Environ Health Perspect* 122:1040–1051.
- Lau C, Anitole K, Hodes C, Lai D, Pfahles-Hutchens A, Seed J. 2007. Perfluoroalkyl acids: A review of monitoring and toxicological findings. *Toxicol Sci* 99:366–394.
- Lau C, Thibodeaux JR, Hanson RG, Narotsky MG, Rogers JM, Lindstrom AB, Strynar MJ. 2006. Effects of perfluorooctanoic acid exposure during pregnancy in the mouse. *Toxicol Sci* 90:510–518.
- Lee JE, Choi K. 2017. Perfluoroalkyl substances exposure and thyroid hormones in humans: Epidemiological observations and implications. *Ann Pediatr Endocrinol Metab* 22:6–14.
- Li C-H, Ren X-M, Cao L-Y, Qin W-P, Guo L-H. 2019. Investigation of binding and activity of perfluoroalkyl substances to the human peroxisome proliferator-activated receptor  $\beta/\delta$ . *Environ Sci Process Impacts* 21:1908–1914.
- Li K, Sun J, Yang J, Roberts SM, Zhang X, Cui X, Wei S, Ma LQ. 2017a. Molecular mechanisms of perfluorooctanoate-induced hepatocyte apoptosis in mice using proteomic techniques. *Environ Sci Technol* 51:11380–11389.
- Li Y, Barregard L, Xu Y, Scott K, Pineda D, Lindh CH, Jakobsson K, Fletcher T. 2020. Associations between perfluoroalkyl substances and serum lipids in a Swedish adult population with contaminated drinking water. *Environ Health* 19:33.
- Li Y, Cheng Y, Xie Z, Zeng F. 2017b. Perfluorinated alkyl substances in serum of the southern Chinese general population and potential impact on thyroid hormones. *Sci Rep* 7:43380.
- Li Y, Fletcher T, Mucs D, Scott K, Lindh CH, Tallving P, Jakobsson K. 2018. Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. *Occup Environ Med* 75:46–51.
- Liberatore HK, Jackson SR, Strynar MJ, McCord JP. 2020. Solvent suitability for HFPO-DA ("GenX" parent acid) in toxicological studies. *Environ Sci Technol Lett* 7:477–481.
- Liew Z, Goudarzi H, Oulhote Y. 2018. Developmental exposures to perfluoroalkyl substances (PFASs): An update of associated health outcomes. *Curr Environ Health Rep* 5:1–19.
- Lin CY, Lin LY, Chiang CK, Wang WJ, Su YN, Hung KY, Chen PC. 2010. Investigation of the associations between low-dose serum perfluorinated chemicals and liver enzymes in US adults. *Am J Gastroenterol* 105:1354–1363.
- Lin LY, Wen LL, Su TC, Chen PC, Lin CY. 2014. Negative association between serum perfluorooctane sulfate concentration and bone mineral density in US premenopausal women: NHANES, 2005–2008. *J Clin Endocrinol Metab* 99:2173–2180.
- Lin PD, Cardenas A, Hauser R, Gold DR, Kleinman KP, Hivert MF, Fleisch AF, Calafat AM, Webster TF, Horton ES, Oken E. 2019. Per- and polyfluoroalkyl substances and blood lipid levels in pre-diabetic adults: longitudinal analysis of the diabetes prevention program outcomes study. *Environ Int* 129:343–353.
- Liu G, Zhang B, Hu Y, Rood J, Liang L, Qi L, Bray GA, DeJonge L, Coull B, Grandjean P, Furtado JD, Sun Q. 2020. Associations of perfluoroalkyl substances with blood lipids and apolipoproteins in lipoprotein sub-species: The POUNDS-lost study. *Environ Health* 19:5.
- Liu S, Yang R, Yin N, Faiola F. 2020. The short-chain perfluorinated compounds PFBS, PFHxS, PFBA and PFHxA, disrupt human mesenchymal stem cell self-renewal and adipogenic differentiation. *J Environ Sci* 88:187–199.
- Looker C, Luster MI, Calafat AM, Johnson VJ, Bureson GR, Bureson FG, Fletcher T. 2014. Influenza vaccine response in adults exposed to perfluorooctanoate and perfluorooctanesulfonate. *Toxicol Sci* 138:76–88.
- Lopez-Espinosa MJ, Mondal D, Armstrong B, Bloom MS, Fletcher T. 2012. Thyroid function and perfluoroalkyl acids in children living near a chemical plant. *Environ Health Perspect* 120:1036–1041.
- Louis GM, Chen Z, Schisterman EF, Kim S, Sweeney AM, Sundaram R, Lynch CD, Gore-Langton RE, Barr DB. 2015. Perfluorochemicals and human semen quality: The LIFE study. *Environ Health Perspect* 123:57–63.
- Louis GM, Peterson CM, Chen Z, Hediger ML, Croughan MS, Sundaram R, Stanford JB, Fujimoto VY, Varner MW, Giudice LC, Kennedy A, Sun L, Wu Q, Kannan K. 2012. Perfluorochemicals and endometriosis: The ENDO study. *Epidemiology* 23:799–805.
- Luebker DJ, Hansen KJ, Bass NM, Butenhoff JL, Seacat AM. 2002. Interactions of fluorochemicals with rat liver fatty acid-binding protein. *Toxicology* 176:175–185.
- Lum KJ, Sundaram R, Barr DB, Louis TA, Buck, Louis GM. 2017. Perfluoroalkyl chemicals, menstrual cycle length, and fecundity: Findings from a prospective pregnancy study. *Epidemiology* 28:90–98.
- Lundin JI, Alexander BH, Olsen GW, Church TR. 2009. Ammonium perfluorooctanoate production and occupational mortality. *Epidemiology* 20:921–928.
- Macon MB, Villanueva LR, Tatum-Gibbs K, Zehr RD, Strynar MJ, Stanko JP, White SS, Helfant L, Fenton SE. 2011. Prenatal perfluorooctanoic acid exposure in CD-1 mice: Low-dose developmental effects and internal dosimetry. *Toxicol Sci* 122:134–145.
- Maestri L, Negri S, Ferrari M, Ghittoni S, Fabris F, Danesino P, Imbriani M. 2006. Determination of perfluorooctanoic acid and perfluorooctanesulfonate in human tissues by liquid chromatography/single quadrupole mass spectrometry. *Rapid Commun Mass Spectrom* 20:2728–2734.
- Martin MT, Brennan RJ, Hu W, Ayanoglu E, Lau C, Ren H, Wood CR, Corton JC, Kavlock RJ, Dix DJ. 2007. Toxicogenomic study of triazole fungicides and perfluoroalkyl acids in rat livers predicts toxicity and categorizes chemicals based on mechanisms of toxicity. *Toxicol Sci* 97:595–613.
- Martinsson M, Nielsen C, Bjork J, Rylander L, Malmqvist E, Lindh C, Rignell-Hydbom A. 2020. Intrauterine exposure to perfluorinated compounds and overweight at age 4: A case-control study. *PLoS One* 15:e0230137.
- Massoud O, Charlton M. 2018. Nonalcoholic fatty liver disease/nonalcoholic steatohepatitis and hepatocellular carcinoma. *Clin Liver Dis* 22:201–211.
- Mastrantonio M, Bai E, Uccelli R, Cordiano V, Screpanti A, Crosignani P. 2018. Drinking water contamination from perfluoroalkyl substances (PFAS): An ecological mortality study in the Veneto region, Italy. *Eur J Public Health* 28:180–185.
- McCord J, Strynar M. 2019. Identification of per- and polyfluoroalkyl substances in the Cape Fear River by high resolution mass spectrometry and nontargeted screening. *Environ Sci Technol* 53:4717–4727.
- Meek ME, Boobis A, Cote I, Dellarco V, Fotakis G, Munn S, Seed J, Vickers C. 2014. New developments in the evolution and application of the WHO/IPCS framework on mode of action/species concordance analysis. *J Appl Toxicol* 34:1–18.
- Melzer D, Rice N, Depledge MH, Henley WE, Galloway TS. 2010. Association between serum perfluorooctanoic acid (PFOA) and thyroid disease in the U.S. National Health and Nutrition Examination Survey. *Environ Health Perspect* 118:686–692.

- Michigan PFAS Science Advisory Panel. 2018. Scientific evidence and recommendations for managing PFAS contamination in Michigan. Lansing, MI, USA. [cited 2020 July 13]. Available from: [https://www.michigan.gov/documents/pfasresponse/Science\\_Advisory\\_Board\\_Report\\_641294\\_7.pdf](https://www.michigan.gov/documents/pfasresponse/Science_Advisory_Board_Report_641294_7.pdf)
- Nakagawa H, Hirata T, Terada T, Jutabha P, Miura D, Harada KH, Inoue K, Anzai N, Endou H, Inui K, Kanai Y, Koizumi A. 2008. Roles of organic anion transporters in the renal excretion of perfluorooctanoic acid. *Basic Clin Pharmacol Toxicol* 103:1–8.
- National Toxicology Program. 2016. Immunotoxicity associated with exposure to perfluorooctanoic acid (PFOA) or perfluorooctane sulfonate (PFOS). US Department of Health and Human Services, Research Triangle Park, NC. [cited 2020 July 13]. Available from: [https://ntp.niehs.nih.gov/ntp/ohat/pfoa\\_pfos/pfoa\\_pfosmonograph\\_508.pdf](https://ntp.niehs.nih.gov/ntp/ohat/pfoa_pfos/pfoa_pfosmonograph_508.pdf)
- National Toxicology Program. 2020a. NTP technical report on the toxicology and carcinogenesis studies of perfluorooctanoic acid (CAS no. 335-67-1) administered in feed to Sprague Dawley (Hsd:Sprague Dawley® SD®) rats. Technical Report 598. US Department of Health and Human Services, Research Triangle Park, NC. [cited 2020 September 15]. Available from: [https://ntp.niehs.nih.gov/ntp/about\\_ntp/trpanel/2019/december/tr598draft.pdf](https://ntp.niehs.nih.gov/ntp/about_ntp/trpanel/2019/december/tr598draft.pdf)
- National Toxicology Program. 2020b. P08: Statistical analysis of primary tumors—Perfluorooctanoic acid. US Department of Health and Human Services, Research Triangle Park, NC. [cited 2020 September 15]. Available from: <https://www.documentcloud.org/documents/6155302-Statistical-Analysis-Tumors.html>
- National Toxicology Program. 2020c. Testing status of perfluorooctanoic acid (PFOA) M910070. US Department of Health and Human Services, Research Triangle Park, NC. [cited 2020 May 19]. Available from: <https://ntp.niehs.nih.gov/go/ts-m910070>
- Nelson JW, Hatch EE, Webster TF. 2010. Exposure to polyfluoroalkyl chemicals and cholesterol, body weight, and insulin resistance in the general U.S. population. *Environ Health Perspect* 118:197–202.
- New Jersey Drinking Water Quality Institute Health Effects Subcommittee. 2017. Health-based maximum contaminant level support document: Perfluorooctanoic acid (PFOA). Trenton, NJ, USA. [cited 2020 July 13]. Available from: <https://www.state.nj.us/dep/watersupply/pdf/pfoa-appendix.pdf>
- Ng CA, Hungerbühler K. 2014. Bioaccumulation of perfluorinated alkyl acids: Observations and models. *Environ Sci Technol* 48:4637–4648.
- Ng CA, Hungerbuehler K. 2015. Exploring the use of molecular docking to identify bioaccumulative perfluorinated alkyl acids (PFAAs). *Environ Sci Technol* 49:12306–12314.
- Ngo HT, Hetland RB, Sabareedzovic A, Haug LS, Steffensen IL. 2014. In utero exposure to perfluorooctanoate (PFOA) or perfluorooctane sulfonate (PFOS) did not increase body weight or intestinal tumorigenesis in multiple intestinal neoplasia (Min/+) mice. *Environ Res* 132:251–263.
- Nian M, Li QQ, Bloom M, Qian ZM, Syberg KM, Vaughn MG, Wang SQ, Wei Q, Zeeshan M, Gurram N, Chu C, Wang J, Tian Y-P, Hu L-W, Liu K-K, Yang B-Y, Liu R-Q, Feng D, Zeng X-W, Dong G-H. 2019. Liver function biomarkers disorder is associated with exposure to perfluoroalkyl acids in adults: Isomers of C8 Health Project in China. *Environ Res* 172:81–88.
- Obermayr RP, Temml C, Gutjahr G, Knechtelsdorfer M, Oberbauer R, Klausner-Braun R. 2008. Elevated uric acid increases the risk for kidney disease. *J Am Soc Nephrol* 19:2407–2413.
- Olsen GW, Burris JM, Ehresman DJ, Froehlich JW, Seacat AM, Butenhoff JL, Zobel LR. 2007. Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorocarbon production workers. *Environ Health Perspect* 115:1298–1305.
- Olsen GW, Chang SC, Noker PE, Gorman GS, Ehresman DJ, Lieder PH, Butenhoff JL. 2009. A comparison of the pharmacokinetics of perfluorobutanesulfonate (PFBS) in rats, monkeys, and humans. *Toxicology* 256:65–74.
- Olsen GW, Mair DC, Lange CC, Harrington LM, Church TR, Goldberg CL, Herron RM, Hanna H, Nobiletti JB, Rios JA, Reagan WK, Ley CA. 2017. Per- and polyfluoroalkyl substances (PFAS) in American Red Cross adult blood donors, 2000–2015. *Environ Res* 157:87–95.
- Organisation for Economic Co-operation Development. 2017. Revised guidance document on developing and assessing adverse outcome pathways. Series on Testing and Assessment, No. 184. ENV/JM/MONO (2013)6. Paris, France. [cited 2020 July 13]. Available from: [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2013\)6&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2013)6&doclanguage=en)
- Organisation for Economic Co-operation Development. 2018. Toward a new comprehensive global database of per- and polyfluoroalkyl substances (PFAS): Summary report on updating the OECD 2007 list of per- and polyfluoroalkyl substances (PFASs). ENV/JM/MONO(2018)7. Series on Risk Management, No. 39. Paris, France. [cited 2020 July 13]. Available from: [https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV-JM-MONO\(2018\)7&doclanguage=en](https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV-JM-MONO(2018)7&doclanguage=en)
- Organisation for Economic Co-operation Development. 2020. AOPs. [cited 2020 May 19]. Available from: <https://aopwiki.org/aops>
- Pachkowski B, Post GB, Stern AH. 2019. The derivation of a reference dose (RfD) for perfluorooctane sulfonate (PFOS) based on immune suppression. *Environ Res* 171:452–469.
- Pan Y, Cui Q, Wang J, Sheng N, Jing J, Yao B, Dai J. 2019. Profiles of emerging and legacy per-/polyfluoroalkyl substances in matched serum and semen samples: New implications for human semen quality. *Environ Health Perspect* 127:127005.
- Papadopoulou E, Sabareedzovic A, Namork E, Nygaard UC, Granum B, Haug LS. 2016. Exposure of Norwegian toddlers to perfluoroalkyl substances (PFAS): The association with breastfeeding and maternal PFAS concentrations. *Environ Int* 94:687–694.
- Park JS, Kim J, Elghiaty A, Ham WS. 2018. Recent global trends in testicular cancer incidence and mortality. *Medicine* 97:e12390.
- Patlewicz G, Richard AM, Williams AJ, Grulke CM, Sams R, Lambert J, Noyes PD, DeVito MJ, Hines RN, Strynar M, Guiseppe-Elie A, Thomas RS. 2019. A chemical category-based prioritization approach for selecting 75 per- and polyfluoroalkyl substances (PFAS) for tiered toxicity and toxicokinetic testing. *Environ Health Perspect* 127:014501.
- Perez F, Nadal M, Navarro-Ortega A, Fabrega F, Domingo JL, Barcelo D, Farre M. 2013. Accumulation of perfluoroalkyl substances in human tissues. *Environ Int* 59:354–362.
- Perla FM, Prelati M, Lavorato M, Visicchio D, Anania C. 2017. The role of lipid and lipoprotein metabolism in non-alcoholic fatty liver disease. *Children (Basel)* 4:46.
- Post GB. 2020. Recent US state and federal drinking water guidelines for per- and polyfluoroalkyl substances (PFAS). *Environ Toxicol Chem* 40:550–563.
- Post GB, Gleason JA, Cooper KR. 2017. Key scientific issues in developing drinking water guidelines for perfluoroalkyl acids: Contaminants of emerging concern. *PLoS Biol* 15:e2002855.
- Pouwer MG, Pieterman EJ, Chang SC, Olsen GW, Caspers MPM, Verschuren L, Jukema JW, Princen HMG. 2019. Dose effects of ammonium perfluorooctanoate on lipoprotein metabolism in APOE\*3-Leiden.CETP mice. *Toxicol Sci* 168:519–534.
- Qin WP, Cao LY, Li CH, Guo LH, Colbourne J, Ren XM. 2020. Perfluoroalkyl substances stimulate insulin secretion by islet beta cells via G protein-coupled receptor 40. *Environ Sci Technol* 54:3428–3436.
- Qin XD, Qian Z, Vaughn MG, Huang J, Ward P, Zeng XW, Zhou Y, Zhu Y, Yuan P, Li M, Bai Z, Paul G, Hao Y-T, Chen W, Chen P-C, Dong G-H, Lee YL. 2016. Positive associations of serum perfluoroalkyl substances with uric acid and hyperuricemia in children from Taiwan. *Environ Pollut* 212:519–524.
- Qin XD, Qian ZM, Dharmage SC, Perret J, Geiger SD, Rigdon SE, Howard S, Zeng XW, Hu LW, Yang BY, Zhou Y, Li M, Xu S-L, Bao W-W, Zhang Y-Z, Yuan P, Wang J, Zhang C, Tian Y-P, Nian M, Xiao X, Chen W, Lee YL, Dong G-H. 2017. Association of perfluoroalkyl substances exposure with impaired lung function in children. *Environ Res* 155:15–21.
- Qiu Z, Qu K, Luan F, Liu Y, Zhu Y, Yuan Y, Li H, Zhang H, Hai Y, Zhao C. 2020. Binding specificities of estrogen receptor with perfluorinated compounds: A cross species comparison. *Environ Int* 134:105284.
- Quist EM, Filgo AJ, Cummings CA, Kissling GE, Hoenerhoff MJ, Fenton SE. 2015. Hepatic mitochondrial alteration in CD-1 mice associated with prenatal exposures to low doses of perfluorooctanoic acid (PFOA). *Toxicol Pathol* 43:546–557.
- Rabinowitz JR, Goldsmith M-R, Little SB, Pasquinelli MA. 2008. Computational molecular modeling for evaluating the toxicity of environmental chemicals: Prioritizing bioassay requirements. *Environ Health Perspect* 116:573–577.
- Rantakokko P, Mannisto V, Airaksinen R, Koponen J, Viluksela M, Kiviranta H, Pihlajamäki J. 2015. Persistent organic pollutants and non-alcoholic fatty liver disease in morbidly obese patients: A cohort study. *Environ Health* 14:79.
- Rappazzo KM, Coffman E, Hines EP. 2017. Exposure to perfluorinated alkyl substances and health outcomes in children: A systematic review of the epidemiologic literature. *Int J Environ Res Public Health* 14:691.

- Rashid F, Ramakrishnan A, Fields C, Irudayaraj J. 2020. Acute PFOA exposure promotes epigenomic alterations in mouse kidney tissues. *Toxicol Rep* 7:125–132.
- Rebholz SL, Jones T, Herrick RL, Xie C, Calafat AM, Pinney SM, Woollett LA. 2016. Hypercholesterolemia with consumption of PFOA-laced Western diets is dependent on strain and sex of mice. *Toxicol Rep* 3:46–54.
- Ren XM, Qin WP, Cao LY, Zhang J, Yang Y, Wan B, Guo LH. 2016. Binding interactions of perfluoroalkyl substances with thyroid hormone transport proteins and potential toxicological implications. *Toxicology* 366–367: 32–42.
- Romano ME, Xu Y, Calafat AM, Yoltan K, Chen A, Webster GM, Eliot MN, Howard CR, Lanphear BP, Braun JM. 2016. Maternal serum perfluoroalkyl substances during pregnancy and duration of breastfeeding. *Environ Res* 149:239–246.
- Rosen EM, Brantsaeter AL, Carroll R, Haug L, Singer AB, Zhao S, Ferguson KK. 2018. Maternal plasma concentrations of per- and polyfluoroalkyl substances and breastfeeding duration in the Norwegian Mother and Child Cohort. *Environ Epidemiol* 2:e027.
- Rosen MB, Das KP, Rooney J, Abbott B, Lau C, Corton JC. 2017. PPAR $\alpha$ -independent transcriptional targets of perfluoroalkyl acids revealed by transcript profiling. *Toxicology* 387:95–107.
- Russell MH, Nilsson H, Buck RC. 2013. Elimination kinetics of perfluorohexanoic acid in humans and comparison with mouse, rat and monkey. *Chemosphere* 93:2419–2425.
- Sabovic I, Cosci I, De Toni L, Ferramosca A, Stornaiuolo M, Di Nisio A, Dall'Acqua S, Garolla A, Foresta C. 2020. Perfluoro-octanoic acid impairs sperm motility through the alteration of plasma membrane. *J Endocrinol Invest* 43:641–652.
- Sakr CJ, Kreckmann KH, Green JW, Gillies PJ, Reynolds JL, Leonard RC. 2007a. Cross-sectional study of lipids and liver enzymes related to a serum biomarker of exposure (ammonium perfluorooctanoate or APFO) as part of a general health survey in a cohort of occupationally exposed workers. *J Occup Environ Med* 49:1086–1096.
- Sakr CJ, Leonard RC, Kreckmann KH, Slade MD, Cullen MR. 2007b. Longitudinal study of serum lipids and liver enzymes in workers with occupational exposure to ammonium perfluorooctanoate. *J Occup Environ Med* 49:872–879.
- Sakuma A, Wasada Ochi H, Yoshioka M, Yamanaka N, Ikezawa M, Guruge KS. 2019. Changes in hepato-renal gene expression in microminipigs following a single exposure to a mixture of perfluoroalkyl acids. *PLoS One* 14:e0210110.
- Salihovic S, Dickens AM, Schoultz I, Fart F, Sinisalu L, Lindeman T, Halfvarson J, Oresic M, Hyotylainen T. 2020. Simultaneous determination of perfluoroalkyl substances and bile acids in human serum using ultra-high-performance liquid chromatography-tandem mass spectrometry. *Anal Bioanal Chem* 412:2251–2259.
- Salihovic S, Fall T, Ganna A, Broeckling CD, Prenni JE, Hyotylainen T, Karrman A, Lind PM, Ingelsson E, Lind L. 2019. Identification of metabolic profiles associated with human exposure to perfluoroalkyl substances. *J Expo Sci Environ Epidemiol* 29:196–205.
- Salvagaglio M, Muscionico I, Cavallotti C. 2010. Determination of energies and sites of binding of PFOA and PFOS to human serum albumin. *J Phys Chem B* 114:14860–14874.
- Sattar N, Forrest E, Preiss D. 2014. Non-alcoholic fatty liver disease. *BMJ* 349:g4596.
- Savitz DA, Stein CR, Bartell SM, Elston B, Gong J, Shin HM, Wellenius GA. 2012. Perfluorooctanoic acid exposure and pregnancy outcome in a highly exposed community. *Epidemiology* 23:386–392.
- Schleizinger J, Puckett H, Oliver J, Nielsen G, Heiger-Bernays W, Webster T. 2020. Perfluorooctanoic acid activates multiple nuclear receptor pathways and skews expression of genes regulating cholesterol homeostasis in liver of humanized PPAR $\alpha$  mice fed an American diet. *Toxicol Appl Pharmacol* 405:115204.
- Seo SH, Son MH, Choi SD, Lee DH, Chang YS. 2018. Influence of exposure to perfluoroalkyl substances (PFASs) on the Korean general population: 10-year trend and health effects. *Environ Int* 113:149–161.
- Sha B, Schymanski EL, Ruttkies C, Cousins IT, Wang Z. 2019. Exploring open cheminformatics approaches for categorizing per- and polyfluoroalkyl substances (PFASs). *Environ Sci Process Impacts* 21:1835–1851.
- Shabalina IG, Kalinovich AV, Cannon B, Nedergaard J. 2016. Metabolically inert perfluorinated fatty acids directly activate uncoupling protein 1 in brown-fat mitochondria. *Arch Toxicol* 90:1117–1128.
- Shankar A, Xiao J, Ducatman A. 2011. Perfluoroalkyl chemicals and chronic kidney disease in US adults. *Am J Epidemiol* 174:893–900.
- Sheng N, Cui R, Wang J, Guo Y, Wang J, Dai J. 2018. Cytotoxicity of novel fluorinated alternatives to long-chain perfluoroalkyl substances to human liver cell line and their binding capacity to human liver fatty acid binding protein. *Arch Toxicol* 92:359–369.
- Skuladottir M, Ramel A, Rytter D, Haug LS, Sabaredzovic A, Bech BH, Henriksen TB, Olsen SF, Halldorsson TI. 2015. Examining confounding by diet in the association between perfluoroalkyl acids and serum cholesterol in pregnancy. *Environ Res* 143:33–38.
- Slotkin TA, MacKillop EA, Melnick RL, Thayer KA, Seidler FJ. 2008. Developmental neurotoxicity of perfluorinated chemicals modeled in vitro. *Environ Health Perspect* 116:716–722.
- Solo-Gabriele HM, Jones AS, Lindstrom AB, Lang JR. 2020. Waste type, incineration, and aeration are associated with per- and polyfluoroalkyl levels in landfill leachates. *Waste Manag* 107:191–200.
- Song M, Kim YJ, Park YK, Ryu JC. 2012. Changes in thyroid peroxidase activity in response to various chemicals. *J Environ Monit* 14:2121–2126.
- Song X, Tang S, Zhu H, Chen Z, Zang Z, Zhang Y, Niu X, Wang X, Yin H, Zeng F, He C. 2018. Biomonitoring PFASs in blood and semen samples: Investigation of a potential link between PFASs exposure and semen mobility in China. *Environ Int* 113:50–54.
- Spector AA, Yorek MA. 1985. Membrane lipid composition and cellular function. *J Lipid Res* 26:1015–1035.
- Stanifer JW, Stapleton HM, Souma T, Wittmer A, Zhao X, Boulware LE. 2018. Perfluorinated chemicals as emerging environmental threats to kidney health: A scoping review. *Clin J Am Soc Nephrol* 13:1479–1492.
- Starling AP, Engel SM, Whitworth KW, Richardson DB, Stuebe AM, Daniels JL, Haug LS, Eggesbo M, Becher G, Sabaredzovic A, Eggesbo M, Hoppin JA, Travlos GS, Wilson RE, Trostad LI, Magnus P, Longnecker MP. 2014. Perfluoroalkyl substances and lipid concentrations in plasma during pregnancy among women in the Norwegian Mother and Child Cohort Study. *Environ Int* 62:104–112.
- Steenland K, Barry V, Savitz D. 2018a. Serum perfluorooctanoic acid and birthweight: An updated meta-analysis with bias analysis. *Epidemiology* 29:765–776.
- Steenland K, Kugathasan S, Barr DB. 2018b. PFOA and ulcerative colitis. *Environ Res* 165:317–321.
- Steenland K, Tinker S, Frisbee S, Ducatman A, Vaccarino V. 2009. Association of perfluorooctanoic acid and perfluorooctane sulfonate with serum lipids among adults living near a chemical plant. *Am J Epidemiol* 170:1268–1278.
- Steenland K, Tinker S, Shankar A, Ducatman A. 2010. Association of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) with uric acid among adults with elevated community exposure to PFOA. *Environ Health Perspect* 118:229–233.
- Steenland K, Woskie S. 2012. Cohort mortality study of workers exposed to perfluorooctanoic acid. *Am J Epidemiol* 176:909–917.
- Steenland K, Zhao L, Winquist A. 2015. A cohort incidence study of workers exposed to perfluorooctanoic acid (PFOA). *Occup Environ Med* 72:373–380.
- Steenland K, Zhao L, Winquist A, Parks C. 2013. Ulcerative colitis and perfluorooctanoic acid (PFOA) in a highly exposed population of community residents and workers in the mid-Ohio Valley. *Environ Health Perspect* 121:900–905.
- Stein CR, McGovern KJ, Pajak AM, Maglione PJ, Wolff MS. 2016. Perfluoroalkyl and polyfluoroalkyl substances and indicators of immune function in children aged 12–19 y: National Health and Nutrition Examination Survey. *Pediatr Res* 79:348–357.
- Stein CR, Savitz DA, Dougan M. 2009. Serum levels of perfluorooctanoic acid and perfluorooctane sulfonate and pregnancy outcome. *Am J Epidemiol* 170:837–846.
- Stubleski J, Salihovic S, Lind L, Lind PM, van Bavel B, Karrman A. 2016. Changes in serum levels of perfluoroalkyl substances during a 10-year follow-up period in a large population-based cohort. *Environ Int* 95:86–92.
- Sun Q, Zong G, Valvi D, Nielsen F, Coull B, Grandjean P. 2018. Plasma concentrations of perfluoroalkyl substances and risk of type 2 diabetes: A prospective investigation among U.S. women. *Environ Health Perspect* 126:037001.
- Sunderland EM, Hu XC, Dassuncao C, Tokranov AK, Wagner CC, Allen JG. 2019. A review of the pathways of human exposure to poly- and

- perfluoroalkyl substances (PFASs) and present understanding of health effects. *J Expo Sci Environ Epidemiol* 29:131–147.
- Susmann HP, Schaidt LA, Rodgers KM, Rudel RA. 2019. Dietary habits related to food packaging and population exposure to PFASs. *Environ Health Perspect* 127:107003.
- Szilagyi JT, Freedman AN, Kepper SL, Keshava AM, Bangma JT, Fry RC. 2020. Per- and polyfluoroalkyl substances (PFAS) differentially inhibit placental trophoblast migration and invasion in vitro. *Toxicol Sci* 175:210–219.
- Tadic M, Cuspidi C, Vasic D, Kerkhof PLM. 2018. Cardiovascular implications of diabetes, metabolic syndrome, thyroid disease, and cardio-oncology in women. In Kerkhof PLM, Miller VM, eds, *Sex-Specific Analysis of Cardiovascular Function*. Springer International, Cham, Switzerland, pp 471–488.
- Tan X, Xie G, Sun X, Li Q, Zhong W, Qiao P, Sun X, Jia W, Zhou Z. 2013. High fat diet feeding exaggerates perfluorooctanoic acid-induced liver injury in mice via modulating multiple metabolic pathways. *PLoS One* 8:e61409.
- Temkin AM, Hocevar BA, Andrews DQ, Naidenko OV, Kamendulis LM. 2020. Application of the key characteristics of carcinogens to per and polyfluoroalkyl substances. *Int J Environ Res Public Health* 17:1668.
- Thibodeaux JR, Hanson RG, Rogers JM, Grey BE, Barbee BD, Richards JH, Butenhoff JL, Stevenson LA, Lau C. 2003. Exposure to perfluorooctane sulfonate during pregnancy in rat and mouse. I: Maternal and prenatal evaluations. *Toxicol Sci* 74:369–381.
- Tilton SC, Orner GA, Benninghoff AD, Carpenter HM, Hendricks JD, Pereira CB, Williams DE. 2008. Genomic profiling reveals an alternate mechanism for hepatic tumor promotion by perfluorooctanoic acid in rainbow trout. *Environ Health Perspect* 116:1047–1055.
- Timmermann CA, Budtz-Jorgensen E, Jensen TK, Osuna CE, Petersen MS, Steuerwald U, Nielsen F, Poulsen LK, Weihe P, Grandjean P. 2017a. Association between perfluoroalkyl substance exposure and asthma and allergic disease in children as modified by MMR vaccination. *J Immunotoxicol* 14:39–49.
- Timmermann CA, Rossing LI, Grontved A, Ried-Larsen M, Dalgard C, Andersen LB, Grandjean P, Nielsen F, Svendsen KD, Scheike T, Jensen TK. 2014. Adiposity and glycemic control in children exposed to perfluorinated compounds. *J Clin Endocrinol Metab* 99:E608–E614.
- Timmermann CAG, Budtz-Jorgensen E, Petersen MS, Weihe P, Steuerwald U, Nielsen F, Jensen TK, Grandjean P. 2017b. Shorter duration of breastfeeding at elevated exposures to perfluoroalkyl substances. *Reprod Toxicol* 68:164–170.
- Tucker DK, Macon MB, Strynar MJ, Dagnino S, Andersen E, Fenton SE. 2015. The mammary gland is a sensitive pubertal target in CD-1 and C57BL/6 mice following perinatal perfluorooctanoic acid (PFOA) exposure. *Reprod Toxicol* 54:26–36.
- US Environmental Protection Agency. 2018. PFAS structures in DSSTox. Washington, DC. [cited 2020 May 19]. Available from: [https://comptox.epa.gov/dashboard/chemical\\_lists/PFASSTRUCT](https://comptox.epa.gov/dashboard/chemical_lists/PFASSTRUCT)
- US Environmental Protection Agency. 2019. EPA's per- and polyfluoroalkyl substances (PFAS) action plan. EPA 823R18004. Washington, DC. [cited 2020 July 13]. Available from: [www.epa.gov/pfas](http://www.epa.gov/pfas)
- US Environmental Protection Agency. 2020. Announcement of preliminary regulatory determinations for contaminants on the fourth drinking water contaminant candidate list. 85 FR 14098. Washington, DC. [cited 2020 September 15]. Available from: <https://www.federalregister.gov/documents/2020/03/10/2020-04145/announcement-of-preliminary-regulatory-determinations-for-contaminants-on-the-fourth-drinking-water>
- van Esterik JCJ, Sales LB, Dollé MET, Håkansson H, Herlin M, Legler J, van der Ven LTM. 2016. Programming of metabolic effects in C57BL/6JxFVB mice by in utero and lactational exposure to perfluorooctanoic acid. *Arch Toxicol* 90:701–715.
- VanNoy BN, Lam J, Zota AR. 2018. Breastfeeding as a predictor of serum concentrations of per- and polyfluorinated alkyl substances in reproductive-aged women and young children: A rapid systematic review. *Curr Environ Health Rep* 5:213–224.
- Velez MP, Arbuckle TE, Fraser WD. 2015. Maternal exposure to perfluorinated chemicals and reduced fecundity: The MIREC study. *Hum Reprod* 30:701–709.
- Vested A, Ramlau-Hansen CH, Olsen SF, Bonde JP, Kristensen SL, Hall-dorsson TI, Becher G, Haug LS, Ernst EH, Toft G. 2013. Associations of in utero exposure to perfluorinated alkyl acids with human semen quality and reproductive hormones in adult men. *Environ Health Perspect* 121:453–458.
- Viberg H, Lee I, Eriksson P. 2013. Adult dose-dependent behavioral and cognitive disturbances after a single neonatal PFHxS dose. *Toxicology* 304:185–191.
- Vieira VM, Hoffman K, Shin HM, Weinberg JM, Webster TF, Fletcher T. 2013. Perfluorooctanoic acid exposure and cancer outcomes in a contaminated community: A geographic analysis. *Environ Health Perspect* 121:318–323.
- Wahlang B, Jin J, Beier JL, Hardesty JE, Daly EF, Schneggelberger RD, Falkner KC, Prough RA, Kirpich IA, Cave MC. 2019. Mechanisms of environmental contributions to fatty liver disease. *Curr Environ Health Rep* 6:80–94.
- Wan HT, Zhao YG, Wei X, Hui KY, Giesy JP, Wong CK. 2012. PFOS-induced hepatic steatosis, the mechanistic actions on beta-oxidation and lipid transport. *Biochim Biophys Acta* 1820:1092–1101.
- Wang B, Zhang R, Jin F, Lou H, Mao Y, Zhu W, Zhou W, Zhang P, Zhang J. 2017. Perfluoroalkyl substances and endometriosis-related infertility in Chinese women. *Environ Int* 102:207–212.
- Wang L, Wang Y, Liang Y, Li J, Liu Y, Zhang J, Zhang A, Fu J, Jiang G. 2013. Specific accumulation of lipid droplets in hepatocyte nuclei of PFOA-exposed BALB/c mice. *Sci Rep* 3:2174.
- Wang L, Wang Y, Liang Y, Li J, Liu Y, Zhang J, Zhang A, Fu J, Jiang G. 2014. PFOS induced lipid metabolism disturbances in BALB/c mice through inhibition of low density lipoproteins excretion. *Sci Rep* 4:4582.
- Wang X, Bai Y, Tang C, Cao X, Chang F, Chen L. 2018. Impact of perfluorooctane sulfonate on reproductive ability of female mice through suppression of estrogen receptor alpha-activated kisspeptin neurons. *Toxicol Sci* 165:475–486.
- Wang Z, DeWitt JC, Higgins CP, Cousins IT. 2017. A never-ending story of per- and polyfluoroalkyl substances (PFASs)? *Environ Sci Technol* 51:2508–2518.
- Waterfield G, Rogers M, Grandjean P, Auffhammer M, Sunding D. 2020. Reducing exposure to high levels of perfluorinated compounds in drinking water improves reproductive outcomes: Evidence from an intervention in Minnesota. *Environ Health* 19:42.
- Watkins DJ, Josson J, Elston B, Bartell SM, Shin HM, Vieira VM, Savitz DA, Fletcher T, Wellenius GA. 2013. Exposure to perfluoroalkyl acids and markers of kidney function among children and adolescents living near a chemical plant. *Environ Health Perspect* 121:625–630.
- Weaver YM, Ehresman DJ, Butenhoff JL, Hagenbuch B. 2009. Roles of renal organic anion transporters in transporting perfluorinated carboxylates with different chain lengths. *Toxicol Sci* 113:305–314.
- Webster GM, Rauch SA, Marie NS, Mattman A, Lanphear BP, Venners SA. 2016. Cross-sectional associations of serum perfluoroalkyl acids and thyroid hormones in U.S. adults: Variation according to TPOAb and iodine status (NHANES 2007–2008). *Environ Health Perspect* 124:935–942.
- Webster GM, Venners SA, Mattman A, Martin JW. 2014. Associations between perfluoroalkyl acids (PFASs) and maternal thyroid hormones in early pregnancy: A population-based cohort study. *Environ Res* 133:338–347.
- Wei Y, Dai J, Liu M, Wang J, Xu M, Zha J, Wang Z. 2009. Estrogen-like properties of perfluorooctanoic acid as revealed by expressing hepatic estrogen-responsive genes in rare minnows (*Gobiocypris rarus*). *Environ Toxicol Chem* 26:2440–2447.
- Wen LL, Lin CY, Chou HC, Chang CC, Lo HY, Juan SH. 2016. Perfluorooctanesulfonate mediates renal tubular cell apoptosis through PPARgamma inactivation. *PLoS One* 11:e0155190.
- White SS, Calafat AM, Kuklenyik Z, Villanueva L, Zehr RD, Helfant L, Strynar MJ, Lindstrom AB, Thibodeaux JR, Wood C, Fenton SE. 2007. Gestational PFOA exposure of mice is associated with altered mammary gland development in dams and female offspring. *Toxicol Sci* 96:133–144.
- White SS, Fenton SE, Hines EP. 2011a. Endocrine disrupting properties of perfluorooctanoic acid. *J Steroid Biochem Mol Biol* 127:16–26.
- White SS, Stanko JP, Kato K, Calafat AM, Hines EP, Fenton SE. 2011b. Gestational and chronic low-dose PFOA exposures and mammary gland growth and differentiation in three generations of CD-1 mice. *Environ Health Perspect* 119:1070–1076.
- Whitworth KW, Haug LS, Baird DD, Becher G, Hoppin JA, Skjaerven R, Thomsen C, Eggesbo M, Travlos G, Wilson R, Longnecker MP. 2012. Perfluorinated compounds and subfecundity in pregnant women. *Epidemiology* 23:257–263.
- Wikstrom S, Lin PI, Lindh CH, Shu H, Bornehag CG. 2020. Maternal serum levels of perfluoroalkyl substances in early pregnancy and offspring birth weight. *Pediatr Res* 87:1093–1099.

- Wikstrom S, Lindh CH, Shu H, Bornehag CG. 2019. Early pregnancy serum levels of perfluoroalkyl substances and risk of preeclampsia in Swedish women. *Sci Rep* 9:9179.
- Williams AJ, Grulke CM, Edwards J, McEachran AD, Mansouri K, Baker NC, Patlewicz G, Shah I, Wambaugh JF, Judson RS, Richard AM. 2017. The CompTox Chemistry Dashboard: A community data resource for environmental chemistry. *J Cheminform* 9:61.
- Winquist A, Steenland K. 2014a. Modeled PFOA exposure and coronary artery disease, hypertension, and high cholesterol in community and worker cohorts. *Environ Health Perspect* 122:1299–1305.
- Winquist A, Steenland K. 2014b. Perfluorooctanoic acid exposure and thyroid disease in community and worker cohorts. *Epidemiology* 25:255–264.
- Wolf CJ, Rider CV, Lau C, Abbott BD. 2014. Evaluating the additivity of perfluoroalkyl acids in binary combinations on peroxisome proliferator-activated receptor- $\alpha$  activation. *Toxicology* 316:43–54.
- Wolf CJ, Schmid JE, Lau C, Abbott BD. 2012. Activation of mouse and human peroxisome proliferator-activated receptor- $\alpha$  (PPAR $\alpha$ ) by perfluoroalkyl acids (PFAAs): Further investigation of C4-C12 compounds. *Reprod Toxicol* 33:546–551.
- Wolf CJ, Takacs ML, Schmid JE, Lau C, Abbott BD. 2008. Activation of mouse and human peroxisome proliferator-activated receptor  $\alpha$  by perfluoroalkyl acids of different functional groups and chain lengths. *Toxicol Sci* 106:162–171.
- World Health Organization. 2020. Mode of action framework (for cancer and non-cancer risk assessment). Geneva, Switzerland. [cited 2020 May 19]. Available from: <https://www.who.int/ipcs/methods/harmonization/areas/cancer/en/>
- Xiao C, Grandjean P, Valvi D, Nielsen F, Jensen TK, Weihe P, Oulhote Y. 2020. Associations of exposure to perfluoroalkyl substances with thyroid hormone concentrations and birth size. *J Clin Endocrinol Metab* 105:735–745.
- Xu HE, Lambert MH, Montana VG, Parks DJ, Blanchard SG, Brown PJ, Sternbach DD, Lehmann JM, Wisely GB, Willson TM, Klierer SA, Milburn MV. 1999. Molecular recognition of fatty acids by peroxisome proliferator-activated receptors. *Mol Cell* 3:397–403.
- Xu J, Shimpi P, Armstrong L, Salter D, Slitt AL. 2016. PFOS induces adipogenesis and glucose uptake in association with activation of Nrf2 signaling pathway. *Toxicol Appl Pharmacol* 290:21–30.
- Xu M, Liu G, Li M, Huo M, Zong W, Liu R. 2020a. Probing the cell apoptosis pathway induced by perfluorooctanoic acid and perfluorooctane sulfonate at the subcellular and molecular levels. *J Agric Food Chem* 68: 633–641.
- Xu Y, Li Y, Scott K, Lindh CH, Jakobsson K, Fletcher T, Ohlsson B, Andersson EM. 2020b. Inflammatory bowel disease and biomarkers of gut inflammation and permeability in a community with high exposure to perfluoroalkyl substances through drinking water. *Environ Res* 181:108923.
- Yamaguchi M, Arisawa K, Uemura H, Katsuura-Kamano S, Takami H, Sawachika F, Nakamoto M, Jutta T, Toda E, Mori K, Hasegawa M, Tanto M, Shima M, Sumiyoshi Y, Morinaga K, Kodama K, Suzuki T, Nagai M, Satoh H. 2013. Consumption of seafood, serum liver enzymes, and blood levels of PFOS and PFOA in the Japanese population. *J Occup Health* 55:184–194.
- Yang CH, Glover KP, Han X. 2009. Organic anion transporting polypeptide (Oatp) 1a1-mediated perfluorooctanoate transport and evidence for a renal reabsorption mechanism of Oatp1a1 in renal elimination of perfluorocarboxylates in rats. *Toxicol Lett* 190:163–171.
- Yao X, Sha S, Wang Y, Sun X, Cao J, Kang J, Jiang L, Chen M, Ma Y. 2016. Perfluorooctane sulfonate induces autophagy-dependent apoptosis through spinster 1-mediated lysosomal-mitochondrial axis and impaired mitophagy. *Toxicol Sci* 153:198–211.
- Yuan Y, Ding X, Cheng Y, Kang H, Luo T, Zhang X, Kuang H, Chen Y, Zeng X, Zhang D. 2020. PFOA evokes extracellular  $\text{Ca}^{2+}$  influx and compromises progesterone-induced response in human sperm. *Chemosphere* 241: 125074.
- Zeilmaker M, Fragki S, Verbruggen E, Bokkers B, Lijzen J. 2018. Mixture exposure to PFAS: A relative potency factor approach. RIVM-2018-0070. Rijksinstituut voor Volksgezondheid en Milieu, Bilthoven, Netherlands. [cited 2020 July 13]. Available from: <https://doi.org/10.21945/rivm-2018-0070>
- Zeng XW, Lodge CJ, Dharmage SC, Bloom MS, Yu Y, Yang M, Chu C, Li QQ, Hu LW, Liu KK, Yang B-Y, Dong G-H. 2019. Isomers of per- and polyfluoroalkyl substances and uric acid in adults: Isomers of C8 Health Project in China. *Environ Int* 133:105160.
- Zeng XW, Qian Z, Emo B, Vaughn M, Bao J, Qin XD, Zhu Y, Li J, Lee YL, Dong GH. 2015. Association of polyfluoroalkyl chemical exposure with serum lipids in children. *Sci Total Environ* 512–513:364–370.
- Zhang H, He J, Li N, Gao N, Du Q, Chen B, Chen F, Shan X, Ding Y, Zhu W, Wu Y, Tang J, Jia X. 2019. Lipid accumulation responses in the liver of *Rana nigromaculata* induced by perfluorooctanoic acid (PFOA). *Ecotoxicol Environ Saf* 167:29–35.
- Zhang J, Begum A, Brannstrom K, Grundstrom C, Iakovleva I, Olofsson A, Sauer-Eriksson AE, Andersson PL. 2016. Structure-based virtual screening protocol for in silico identification of potential thyroid disrupting chemicals targeting transthyretin. *Environ Sci Technol* 50:11984–11993.
- Zhang L, Duan X, Sun W, Sun H. 2020. Perfluorooctane sulfonate acute exposure stimulates insulin secretion via GPR40 pathway. *Sci Total Environ* 726:138498.
- Zhang L, Krishnan P, Ehresman DJ, Smith PB, Dutta M, Bagley BD, Chang SC, Butenhoff JL, Patterson AD, Peters JM. 2016. Editor's highlight: Perfluorooctane sulfonate-choline ion pair formation: A potential mechanism modulating hepatic steatosis and oxidative stress in mice. *Toxicol Sci* 153:186–197.
- Zhang Y, Beesoon S, Zhu L, Martin JW. 2013. Biomonitoring of perfluoroalkyl acids in human urine and estimates of biological half-life. *Environ Sci Technol* 47:10619–10627.
- Zhang Y, Cao X, Chen L, Qin Y, Xu Y, Tian Y, Chen L. 2020. Exposure of female mice to perfluorooctanoic acid suppresses hypothalamic kisspeptin-reproductive endocrine system through enhanced hepatic fibroblast growth factor 21 synthesis, leading to ovulation failure and prolonged dioestrus. *J Neuroendocrinol* 32:e12848.
- Zhao J, Hinton P, Chen J, Jiang J. 2020. Causal inference for the effect of environmental chemicals on chronic kidney disease. *Comput Struct Biotechnol J* 18:93–99.
- Zhou R, Cheng W, Feng Y, Wei H, Liang F, Wang Y. 2017. Interactions between three typical endocrine-disrupting chemicals (EDCs) in binary mixtures exposure on myocardial differentiation of mouse embryonic stem cell. *Chemosphere* 178:378–383.

# Landfill Gas: A Major Pathway for Neutral Per- and Polyfluoroalkyl Substance (PFAS) Release

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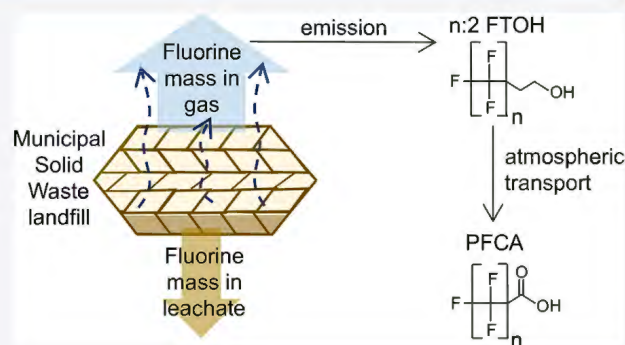
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Supporting Information

**ABSTRACT:** The undisclosed and ubiquitous use of perfluoroalkyl and polyfluoroalkyl substances (PFAS) in consumer products has led to a growing issue of environmental pollution, particularly within the solid waste community, where the fate of volatile (neutral) PFAS in landfilled refuse is not well understood. Here, three municipal solid waste landfills in Florida were assessed for neutral PFAS in landfill gas and ionic PFAS in landfill leachate to compare the relative mobility between the two pathways. Landfill gas was directly sampled using a high volume, XAD-2 resin based sampling approach developed for adsorption and analysis of 27 neutral PFAS. Across sites, 13 neutral PFAS were identified from fluorotelomer alcohol (FTOH), fluorotelomer olefin (FTO), secondary FTOH, fluorotelomer acetate (FTOAc), and fluorotelomer methyl acrylate (FTMAc) classes; however, FTOHs dominated concentrations (87–97% total neutral PFAS), with most detections surpassing utilized calibration levels. Even under conservative assumptions, the mass of fluorine leaving in landfill gas (32–76%) was comparable to or greater than the mass leaving in landfill leachate (24–68%). These findings suggest that landfill gas, a less scrutinized byproduct, serves as a major pathway for the mobility of PFAS from landfills.

**KEYWORDS:** volatile, emissions, GC, fluorotelomer alcohol



## 1. INTRODUCTION

Widespread per- and polyfluoroalkyl substance (PFAS) contamination has been a mounting environmental concern due to their chemical persistence and toxicity to human and biotic health.<sup>1–4</sup> While numerous industries are being confronted with PFAS-related management challenges, the burden of remediation and PFAS removal has often fallen on downstream industries—namely, the solid waste sector.<sup>5–9</sup> Discarded, PFAS-laden consumer products including textiles, wood products, and packaging and commonly landfilled industrial byproducts like MSW incineration ash and wastewater biosolids are known contributors to PFAS loading in landfills.<sup>10–16</sup> Existing research suggests most discarded PFAS mass is retained within landfills<sup>9,17</sup> with liquid-phase byproducts of waste decomposition, leachate and gas condensate, currently considered prevalent pathways for PFAS mobilization.<sup>2,7,9</sup> However, the extent of PFAS release to another major byproduct, landfill gas (LFG), has remained largely unscrutinized.

The bulk of PFAS characterization studies focus on nonvolatile/semivolatile (ionic) perfluoroalkyl acids (PFAAs) measured in liquid and solid matrices, in part because of a high presence and awareness of these species within the PFAS community but largely because analytical capabilities for ionic

PFAS measurement are better established.<sup>18–21</sup> Volatile (neutral) PFAS are also utilized in consumer products<sup>13,22–27,27</sup> and have been determined in a few studies on ambient air surrounding landfills and near wastewater treatment plants,<sup>28–32</sup> but a lack of volatile analytical standards and latency in methodological development has hindered the progression of gas phase research in environmental matrices. Whereas PFAS characterization in leachate is established, concentrations ranging from thousands to tens of thousands of nanograms per liter are commonly encountered;<sup>33–38</sup> only two studies characterize volatile PFAS directly in LFG.<sup>39,40</sup> Titaley et al. identified fluorotelomer alcohol (FTOH), fluorotelomer acrylate (FTAc) and fluorotelomer olefin (FTO) homologues in LFG with combined concentrations ranging from 4,600 to 14,000 ng m<sup>−3</sup> across three landfills. Goukeh et al., only assessing FTOHs, identified higher combined concentrations than Titaley et al., finding ~18,000 ng m<sup>−3</sup> (sum of 6:2 and 8:2

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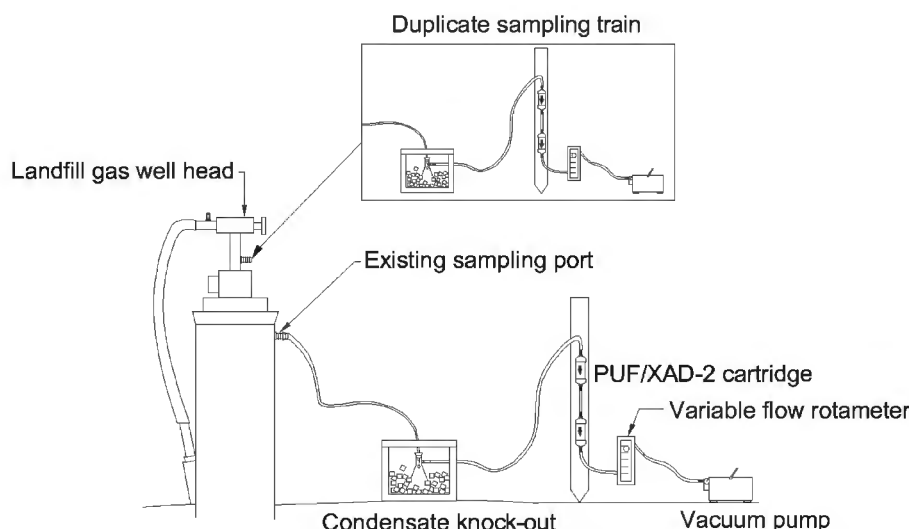


**Figure 1.** Developed system for sampling neutral PFAS directly from landfill gas well heads.

FTOH) in the one LFG sample examined. These studies suggest PFAS variability in LFG, which motivates further investigation, deploying higher sampling volumes<sup>39</sup> and larger analyte lists<sup>40</sup> to understand the potential presence of other neutral PFAS and distribution among landfills of different regions, compositions, and sizes.

With the ongoing development of PFAS regulation,<sup>19</sup> understanding the partitioning behavior of PFAS in major repositories like MSW landfills grows increasingly critical to minimize environmental and human risk. Unlike leachate, LFG is not always captured by collection systems, and management varies broadly across landfills, ranging from no treatment (i.e., passive venting) to some treatment (i.e., flaring, LFG to energy projects), but current treatment, if any, is not intended for PFAS.<sup>41,42</sup> Emerging research suggests the toxicity of volatile species (specifically 6:2 FTOH) to be significantly higher than their ionic counterparts via the inhalation pathway (a main route of exposure for volatile compounds).<sup>43–47</sup> Further, degradation of neutral species to ionic PFAAs once emitted to the atmosphere is well established.<sup>48–58</sup> The potential for long-range atmospheric transport of PFAS from landfills underscores the importance of considering neutral species and their fate during management to prevent further environmental contamination of highly scrutinized PFAAs such as perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS). As the only studies on LFG primarily identified FTOHs in LFG, the magnitude and significance of other neutral species remains unclear.

Here, LFG was sampled directly from gas well heads at three MSW landfill locations in Florida using a higher volume sampling protocol. XAD-2 resin sandwiched between polyurethane foam (PUF) was utilized for PFAS capture, then samples were analyzed for 27 volatile/semivolatile (neutral) PFAS via targeted gas chromatography high resolution mass spectrometry (GC-HRMS). To contextualize release in the gas phase, leachate was also collected at each landfill and analyzed for ionic PFAS ( $n = 93$ ) using ultrahigh pressure liquid chromatography tandem mass spectrometry (UHPLC-MS/MS). The observed LFG and leachate concentrations were normalized on a mass of fluorine basis to compare the potential mobility in gas versus leachate matrices. This study provides foundational data critical for understanding the role of

landfills in anthropogenic PFAS release and for informing LFG management.

## 2. METHODS AND MATERIALS

For brevity, materials and methods associated with ionic PFAS analysis in landfill leachate are provided in section 1 of the [Supporting Information](#) (Tables S-1 through S-4).

**2.1. Standards and Reagents.** Targeted neutral PFAS ( $\geq 97\%$  purity,  $n = 27$ ) were purchased from Wellington Laboratories Inc. (Guelph, ON, Canada), SynQuest Laboratories (Alachua, FL), and Chiron (Stiklestadveien, Trondheim, Norway). Nine classes of neutral PFAS (perfluoroalkane sulfonamides (FASAs), perfluoroalkane sulfonamidoethanols (FASEs), fluorotelomer acetates (FTOAcS), fluorotelomer methyl acrylates (FTMAcS), fluorotelomer iodides (FTIS), fluorotelomer secondary alcohols (sFTOHs), FTOHs, FTAcS, and FTOs) were measured using eight isotopically labeled internal standards (IS) from FASA, FASE, FTOH, and FTMAc classes for quantitation ([Table S-5](#)).

**2.2. Sample Preparation and Collection.** Polyvinyl chloride (PVC) cartridges filled with 4–5 g of Amberlite XAD-2 resin retained between two polyurethane foam (PUF) discs were utilized for PFAS capture.<sup>29,59,60</sup> Before use, XAD-2 sorbent was made PFAS-free through sequential Soxhlet extractions.<sup>61</sup> All cartridge components, sampling vessels, and tubing were sonicated in a mixture of Liquinox and PFAS-free water, rinsed, and then sonicated in methanol and methanol rinsed before use. Once dried and assembled, cartridges were stored in individually sealed polyethylene bags at 4 °C until sampling.

As neutral compounds were the focus of this investigation, aerosolized/particulate-bound PFAS were not specifically targeted for capture; however, a condensate collection system was included to prevent moisture interference. The developed sampling system ([Figure 1](#)) consisted of a condensate knockout (borosilicate, barbed Erlenmeyer flask contained in a cold box), two PUF/XAD-2 cartridges (installed in-series), a rotameter for flow control, a portable vacuum pump, and PFAS-free Tygon tubing. Before each sampling event, gas well head connection to the larger landfill gas collection system was disabled to create a neutral to positive pressure, workable for flow through the sampling system, then gas composition/

**Table 1. Average Concentrations ( $n = 2$ ) of 13 Neutral PFAS ( $\text{ng m}^{-3}$ ) from Three Municipal Solid Waste Landfills in Florida (Site Characteristics Are Provided in Table S-9)<sup>a</sup>**

| analyte    | concentration ( $\text{ng m}^{-3}$ ) |         |            |         |            |         |
|------------|--------------------------------------|---------|------------|---------|------------|---------|
|            | landfill 1                           | E       | landfill 2 | E       | landfill 3 | E       |
| 4:2 FTOH   | 220                                  |         | ND         |         | 57         |         |
| 6:2 FTOH   | >9,900                               | 170,000 | >6,000     | 22,000  | >6,500     | 62,000  |
| 8:2 FTOH   | >6,800                               | 200,000 | >6,000     | 140,000 | >6,500     | 740,000 |
| 10:2 FTOH  | >5,100                               | 14,000  | >3,000     | 23,000  | >5,000     | 120,000 |
| 12:2 FTOH  | 860                                  |         | 1,400      |         | 5,000      |         |
| 5:2 sFTOH  | >2,900                               | 8,800   | >1,700     | 9,000   | >1,900     | 5,900   |
| 7:2 sFTOH  | 320                                  |         | >1,300     | 13,000  | >1,400     | 11,000  |
| 8:2 FTO    | 2,500                                |         | 1,300      |         | 550        |         |
| 10:2 FTO   | 650                                  |         | 840        |         | 540        |         |
| 12:2 FTO   | 97                                   |         | 580        |         | 160        |         |
| 8:2 FTOAc  | 610                                  |         | 90         |         | 490        |         |
| 10:2 FTOAc | 99                                   |         | 19         |         | 140        |         |
| 6:2 FTMAc  | 3,800                                |         | 56         |         | 150        |         |

<sup>a</sup>Concentrations of 6:2, 8:2, and 12:2 FTOH and 5:2 and 7:2 sFTOH consistently exceeded the upper limit of developed calibration ranges; therefore, both a minimum concentration (assuming the highest calibration concentration) and a maximum extrapolated concentration are provided. Italicized values denote a minimum concentration. Column “E” presents average maximum concentrations. “ND” denotes non-detect measurements. FTAcS, FASAs, FASEs, FTIs, and 8:2 FTMAc were not detected in any samples. Analyte acronyms and details are provided in Table S-5.

temperature was recorded using an Optimax Biogas analyzer (MRU Instruments, Humble, TX). Duplicate sampling trains were connected to existing gas well sampling ports. Approximately 1,200 L was sampled through each train at a flow rate of  $5 \text{ L min}^{-1}$ . After sampling, PUF/XAD-2 cartridges were sealed and individually stored at  $\leq 4^\circ \text{C}$  for transport/storage. Quality control (QC) procedures are provided in the SI, section 2.

**2.3. Extraction and Analysis.** Spent XAD-2 from each cartridge was weighed and transferred to a 50 mL polypropylene centrifuge tube and vortexed, and approximately 2 g aliquoted for extraction. Samples were spiked with a mixture of mass labeled IS (Table S-5), rotated end-over-end for 18 h in 4 mL of 75/25% (v/v) ethyl acetate and methanol, and centrifuged for 10 min at 4,000 rpm. Supernatants were transferred to 15 mL centrifuge tubes, and the extraction process was repeated, combining supernatants from the two-fold extraction. Extracts were concentrated to 3 mL via gentle nitrogen evaporation, aliquoted, and stored no more than 30 days at  $-20^\circ \text{C}$  until analysis. QC details are provided in the SI, section 2 (Table S-6 and Figure S-1).

Targeted analysis of 27 neutral PFAS by positive chemical ionization (PCI) with selected ion monitoring (SIM) was conducted using a Thermo Scientific TRACE 1310 gas chromatograph coupled to a Thermo Scientific Orbitrap Exploris GC 240 mass spectrometer (GC-HRMS; see SI, section 2 for details regarding GC separations and instrumentation). A 12-point external calibration curve (from 1 to  $2,000 \text{ pg } \mu\text{L}^{-1}$ ) was developed for quantitation, prepared through serial gravimetrically derived dilutions of primary stock solutions. A mixture of mass labeled IS at concentrations of  $150 \text{ pg } \mu\text{L}^{-1}$  was added to each calibration level. When a labeled standard was not available for a compound, a labeled standard with a similar retention time or structure was utilized for quantitation (Table S-5).

### 3. RESULTS AND DISCUSSION

Unexpectedly, several neutral PFAS concentrations in LFG exceeded the implemented calibration levels. Because of

considerable exceedance for some compounds, dilution would reduce IS below instrument detection; therefore, in instances where sample concentrations exceeded calibration limits, two concentrations are presented (Equation S-1): a minimum value which assumes the highest calibration concentration and a maximum extrapolated concentration. Fluorine mass release calculations utilize minimum values, preventing overextrapolation while providing a conservative estimate for leachate comparison. Even under these assumptions, substantial concentrations of neutral PFAS, higher than those previously observed, were identified. Future assessments should deploy shorter sampling durations to refine findings.

**3.1. Neutral PFAS in Landfill Gas.** Except for 4:2 FTOH in one landfill, 13 PFAS were detected in duplicate samples across the three sites (site characteristics are provided in Table S-9). Observed concentrations are displayed in Table 1. At minimum, combined concentrations of neutral PFAS in LFG ranged from 22,000 to  $33,000 \text{ ng m}^{-3}$ . Considering extrapolated values, total concentrations ranged from 210,000 to  $940,000 \text{ ng m}^{-3}$ , an order of magnitude higher than those previously reported in LFG.<sup>39</sup>

**3.1.1. FTOHs and sFTOHs in Landfill Gas.** Like previous studies on LFG and air surrounding landfills, FTOHs dominated neutral PFAS concentrations;<sup>28,31,32,39,40</sup> however, extrapolated concentrations in this study surpassed previous reports in LFG, in some cases by 2 orders of magnitude, and were more comparable (although much lower) to concentrations recently identified in soil vapor near a PFAS manufacturing facility.<sup>55</sup> While there are uncertainties given the degree of extrapolation, the magnitude of FTOHs found in this study compared to existing research suggests fundamental differences potentially related to sampling methodology (e.g., much larger sampling volumes) and/or sampled landfill characteristics (e.g., waste type, age, air intrusion), although these data were not available for comparison. Across the three sites, 6:2, 8:2, and 10:2 FTOH, combined, made up 87 to 97% of total concentrations, but 8:2 FTOH alone constituted 50 to 79%. The shortest and longest analyzed homologues, 4:2 and

12:2 FTOH, were significantly lower in concentration (Table S-10). This is supported by previous FTOH distributions determined from source fluoro-telomer polymers<sup>62</sup> and observations in LFG, urban air, and air surrounding wastewater treatment/landfill sites.<sup>28–31,39,40,63</sup> Concentrations of 12:2 FTOH were of similar magnitude to those in Titaley et al., but 4:2 FTOH has not been detected in LFG, suggesting MSW landfills to be a previously unidentified potential source of atmospheric 4:2 FTOH.<sup>39</sup>

Secondary FTOHs have not been targeted in gas-phase landfill research but have been identified in condensate associated with LFG collection systems.<sup>37</sup> As intermediary byproducts of 6:2 and 8:2 FTOH biodegradation to PFAAs, 5:2 and 7:2 sFTOH, were unsurprisingly elevated, they were at least an order of magnitude lower than respective parent FTOH homologues.<sup>64–66</sup> All detections of 5:2 sFTOH and two out of three detections of 7:2 sFTOH were above calibration, combined sums attributed to 2 to 10% of total concentrations.

**3.1.2. Other Neutral PFAS in Landfill Gas.** Other neutral PFAS fell within acceptable calibration ranges and together accounted for 0.22 to 1.9% of total concentrations. FTO homologues have been encountered in other LFG and ambient air studies, but in past assessments 8:2 and 10:2 FTO were below limits of quantitation and 12:2 FTO concentrations were consistently an order of magnitude higher than those reported here.<sup>39,59</sup> To the authors' knowledge, 8:2 and 10:2 FTOAc and 6:2 FTMAC have not been determined in LFG. FTOAc are not commonly assessed analytes but are associated with fluoropolymer textile treatments and have been identified in one indoor air study from Japan.<sup>67,68</sup> Similarly, 6:2 FTMAC has only been analyzed in a few studies on cosmetics and wastewaters but at lower concentrations.<sup>69–71</sup>

**3.2. Comparative Fluorine Mass Release between Landfill Byproducts.** Normalizing PFAS concentrations on a fluorine basis allows comparisons to be drawn between different matrices and PFAS types (e.g., gas–liquid, neutral–ionic, precursor–terminal). This methodology is widely used to assess the “mass balance” of PFAS within systems, given that the long-term environmental fate of measurable PFAS is transient, whereas the mass of fluorine is conserved.<sup>17,72,73</sup>

Here, the same approach is utilized to compare the PFAS mobility in leachate versus LFG pathways. Neutral (Table 1, minimum values) and ionic (Table S-4) PFAS concentrations in LFG and leachate from this study were individually normalized to a mass of fluorine (Equation S-2) using compound specific fluorine mass fractions (Table S-8). Summed fluorine masses in leachate and LFG were then scaled according to site-specific annual generation volumes reported for each landfill (Table S-9).<sup>41</sup> A caveat of this comparison is the absence of measurements for neutral species in leachate and ionic species in LFG; however, the literature suggests FTOHs (the dominant neutral class identified) predominantly exist in the gaseous phase, while PFAAs exist in liquid or particulate phases.<sup>28,74</sup> Subsequent research should assess neutral and ionic compounds in both matrices to validate findings and further elucidate the PFAS behavior in landfills.

Even utilizing minimum concentrations observed in LFG, equal magnitudes of fluorine release are observed between LFG and leachate at each site (Figure 2)—contrasting from existing estimates of PFAS mass flow from landfills.<sup>9</sup> Existing

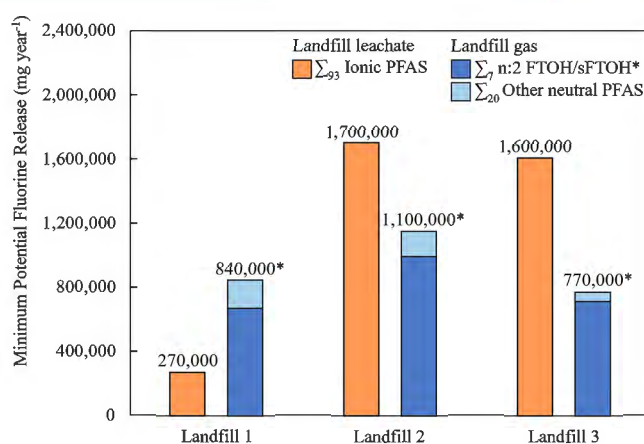


**Figure 2.** Annual fluorine mass release in landfill leachate versus landfill gas (LFG) from three municipal solid waste landfills in Florida. Fluorine masses in leachate are derived from ionic PFAS (Σ<sub>93</sub> PFAS) concentrations measured in leachate from each site (Table S-4) multiplied by the annual leachate generation volume and scaled using each detected compound's fluorine mass fraction (Tables S-8, S-9). The same methodology was applied for neutral PFAS (Σ<sub>27</sub> PFAS) in LFG by using the average of minimum concentrations (Table 1). Asterisked (\*) values denote input FTOH/sFTOH concentrations which were above calibration levels developed for this study and therefore assumed to be at the highest calibration concentration. Consequently, these findings should be viewed as minimum values which conservatively estimate the magnitude of PFAS mobility in leachate versus LFG.

estimates, based on limited data, suggest that most PFAS mass mobilized from landfills releases through leachate (~62%).<sup>9</sup> However, our data from Landfill 1, showing over 76% fluorine release in LFG, along with substantial masses released by LFG in Landfills 2 and 3 (at minimum 40% and 32%, respectively), indicate that LFG may serve as an equal, likely greater, conduit of PFAS mobility from landfills than leachate, concurring with previous reactor studies on FTOH volatilization and neutral/ionic PFAS assessments of select waste materials.<sup>17,75,76</sup>

At least 79 to 92% of the fluorine mass in LFGs were derived from FTOH/sFTOH classes, with minimal contribution from FTOs, FTOAc, and FTMACs. In this conservative assessment, fluorine from LFG surpassed leachate in only Landfill 1. Although actual fluorine emission from LFG is higher than reported here, the elevated ratio of gas-to-leachate generation at Landfill 1 likely caused this difference (Table S-9). Landfill 2, the largest site, demonstrated the highest combined fluorine release from leachate and LFG, followed by Landfill 3, and then Landfill 1, corresponding to descending waste mass in place at each location.

#### 4. IMPLICATIONS

This study provides fundamental data about neutral PFAS in LFG from MSW landfills. Unexpectedly, FTOH/sFTOH detections in LFG from this study exceeded implemented calibration levels; subsequent research should deploy shorter sampling durations. Regardless, even under more conservative assumptions these findings suggest that LFG, largely unscrutinized for PFAS, contains similar or greater magnitudes of PFAS compared to leachate, mostly attributed to midlength FTOH homologues. As landfills can be viewed as unabating PFAS repositories, the significance of LFG management in mitigating the long-term, long-range atmospheric transport of

neutral PFAS, and subsequently derived PFAAs, cannot be understated. Unlike landfill leachate, LFG collection systems (when in place) are not fully efficient, collecting an estimated ~50–70% of generated biogases.<sup>77</sup> Though this is a considerable collection efficiency of biogas and presumably neutral PFAS, management of captured LFG fractions varies globally, from no treatment to degrees of carbon filtration and thermal treatment (i.e., flaring, advanced renewable natural gas technologies). Because the feasibility of PFAS destruction through thermal treatment remains unclear, research is needed to determine the treatment/removal efficiency of existing LFG management technologies. Considering the range of LFG capture efficiency, the retention and emission of neutral PFAS via fugitive emissions (i.e., migration through the waste layer) should also be examined, along with the role of landfill waste type, age, and temperature in neutral PFAS variability.

## ■ ASSOCIATED CONTENT

### SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.estlett.4c00364>.

Acronyms, structures, and instrumental parameters for neutral PFAS via GC-HRMS and ionic PFAS via LC-MS/MS; detailed QC information and results; and fluorine mass balance/extrapolation details and assumptions (PDF)

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### Notes

The authors declare no competing financial interest.

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## ■ REFERENCES

- (1) Buck, R. C.; Franklin, J.; Berger, U.; Conder, J. M.; Cousins, I. T.; de Voogt, P.; Jensen, A. A.; Kannan, K.; Mabury, S. A.; van Leeuwen, S. P. Perfluoroalkyl and Polyfluoroalkyl Substances in the Environment: Terminology, Classification, and Origins. *Integr. Environ. Assess. Manag.* **2011**, *7* (4), 513–541.
- (2) Evich, M. G.; Davis, M. J. B.; McCord, J. P.; Acrey, B.; Awkerman, J. A.; Knappe, D. R. U.; Lindstrom, A. B.; Speth, T. F.; Tebes-Stevens, C.; Strynar, M. J.; Wang, Z.; Weber, E. J.; Henderson, W. M.; Washington, J. W. Per- and Polyfluoroalkyl Substances in the Environment. *Science* **2022**, DOI: 10.1126/science.abg9065.
- (3) Fenton, S. E.; Ducatman, A.; Boobis, A.; DeWitt, J. C.; Lau, C.; Ng, C.; Smith, J. S.; Roberts, S. M. Per- and Polyfluoroalkyl Substance Toxicity and Human Health Review: Current State of Knowledge and Strategies for Informing Future Research. *Environ. Toxicol. Chem.* **2021**, *40* (3), 606–630.
- (4) Lau, C.; Anitole, K.; Hodes, C.; Lai, D.; Pfahles-Hutchens, A.; Seed, J. Perfluoroalkyl Acids: A Review of Monitoring and Toxicological Findings. *Toxicol. Sci.* **2007**, *99* (2), 366–394.
- (5) Coffin, E. S.; Reeves, D. M.; Cassidy, D. P. PFAS in Municipal Solid Waste Landfills: Sources, Leachate Composition, Chemical Transformations, and Future Challenges. *Curr. Opin. Environ. Sci. Health* **2023**, *31*, No. 100418.
- (6) Hamid, H.; Li, L. Y.; Grace, J. R. Review of the Fate and Transformation of Per- and Polyfluoroalkyl Substances (PFASs) in Landfills. *Environ. Pollut.* **2018**, *235*, 74–84.
- (7) Lang, J. R.; Allred, B. M.; Field, J. A.; Levis, J. W.; Barlaz, M. A. National Estimate of Per- and Polyfluoroalkyl Substance (PFAS) Release to U.S. Municipal Landfill Leachate. *Environ. Sci. Technol.* **2017**, *51* (4), 2197–2205.
- (8) Stoiber, T.; Evans, S.; Naidenko, O. V. Disposal of Products and Materials Containing Per- and Polyfluoroalkyl Substances (PFAS): A Cyclical Problem. *Chemosphere* **2020**, *260*, No. 127659.
- (9) Tolaymat, T.; Robey, N.; Krause, M.; Larson, J.; Weitz, K.; Parvathikar, S.; Phelps, L.; Linak, W.; Burden, S.; Speth, T.; Krug, J. A Critical Review of Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS) Landfill Disposal in the United States. *Sci. Total Environ.* **2023**, *905*, No. 167185.
- (10) Allred, B. M.; Lang, J. R.; Barlaz, M. A.; Field, J. A. Physical and Biological Release of Poly- and Perfluoroalkyl Substances (PFASs) from Municipal Solid Waste in Anaerobic Model Landfill Reactors. *Environ. Sci. Technol.* **2015**, *49* (13), 7648–7656.
- (11) Curtzwiler, G. W.; Silva, P.; Hall, A.; Ivey, A.; Vorst, K. Significance of Perfluoroalkyl Substances (PFAS) in Food Packaging. *Integr. Environ. Assess. Manag.* **2021**, *17* (1), 7–12.
- (12) Lang, J. R.; Allred, B. M.; Peaslee, G. F.; Field, J. A.; Barlaz, M. A. Release of Per- and Polyfluoroalkyl Substances (PFASs) from Carpet and Clothing in Model Anaerobic Landfill Reactors. *Environ. Sci. Technol.* **2016**, *50* (10), S024–S032.
- (13) Li, D.; Zhu, L.; Pan, J.; Zhong, H.; Zhang, Z.; Lin, Q.; Zheng, J.; Liu, H. The Determination of Trace Per- and Polyfluoroalkyl Substances and Their Precursors Migrated into Food Simulants from Food Contact Materials by LC–MS/MS and GC–MS/MS. *LCGC N. Am.* **2019**, *37* (7), 464–475.
- (14) Li, Y.; Thompson, J.; Wang, Z.; Bräunig, J.; Zheng, Q.; Thai, P. K.; Mueller, J. F.; Yuan, Z. Transformation and Fate of Pharmaceuticals, Personal Care Products, and per- and Polyfluor-

oalkyl Substances during Aerobic Digestion of Anaerobically Digested Sludge. *Water Res.* **2022**, 219, No. 118568.

(15) Liu, Y.; Mendoza-Perilla, P.; Clavier, K. A.; Tolaymat, T. M.; Bowden, J. A.; Solo-Gabriele, H. M.; Townsend, T. G. Municipal Solid Waste Incineration (MSWI) Ash Co-Disposal: Influence on per- and Polyfluoroalkyl Substances (PFAS) Concentration in Landfill Leachate. *Waste Management* **2022**, 144, 49–56.

(16) Thompson, J. T.; Robey, N. M.; Tolaymat, T. M.; Bowden, J. A.; Solo-Gabriele, H. M.; Townsend, T. G. Underestimation of Per- and Polyfluoroalkyl Substances in Biosolids: Precursor Transformation During Conventional Treatment. *Environ. Sci. Technol.* **2023**, 57 (9), 3825–3832.

(17) Robel, A. E.; Marshall, K.; Dickinson, M.; Lunderberg, D.; Butt, C.; Peaslee, G.; Stapleton, H. M.; Field, J. A. Closing the Mass Balance on Fluorine on Papers and Textiles. *Environ. Sci. Technol.* **2017**, 51 (16), 9022–9032.

(18) *Draft Method 1633 Analysis of Per- and Polyfluoroalkyl Substances (PFAS) in Aqueous, Solid, Biosolids, and Tissue Samples by LC-MS/MS*; U.S. EPA, 2021. [https://www.epa.gov/system/files/documents/2021-09/method\\_1633\\_draft\\_aug-2021.pdf](https://www.epa.gov/system/files/documents/2021-09/method_1633_draft_aug-2021.pdf) (accessed April 4, 2022).

(19) PFAS Strategic Roadmap: EPA's Commitments to Action 2021–2024; U.S. EPA, 2021. <https://www.epa.gov/pfas/pfas-strategic-roadmap-epas-commitments-action-2021-2024> (accessed March 17, 2022).

(20) van Leeuwen, S. P. J.; de Boer, J. Extraction and Clean-up Strategies for the Analysis of Poly- and Perfluoroalkyl Substances in Environmental and Human Matrices. *J. Chromatogr. A* **2007**, 1153 (1), 172–185.

(21) Jia, S.; Marques Dos Santos, M.; Li, C.; Snyder, S. A. Recent Advances in Mass Spectrometry Analytical Techniques for Per- and Polyfluoroalkyl Substances (PFAS). *Anal. Bioanal. Chem.* **2022**, 414 (9), 2795–2807.

(22) Cahuas, L.; Muensterman, D. J.; Kim-Fu, M. L.; Reardon, P. N.; Titaley, I. A.; Field, J. A. Paints: A Source of Volatile PFAS in Air—Potential Implications for Inhalation Exposure. *Environ. Sci. Technol.* **2022**, 56 (23), 17070–17079.

(23) Morales-McDevitt, M. E.; Becanova, J.; Blum, A.; Bruton, T. A.; Vojta, S.; Woodward, M.; Lohmann, R. The Air That We Breathe: Neutral and Volatile PFAS in Indoor Air. *Environ. Sci. Technol. Lett.* **2021**, 8 (10), 897–902.

(24) Rewerts, J. N.; Morré, J. T.; Massey Simonich, S. L.; Field, J. A. In-Vial Extraction Large Volume Gas Chromatography Mass Spectrometry for Analysis of Volatile PFASs on Papers and Textiles. *Environ. Sci. Technol.* **2018**, 52 (18), 10609–10616.

(25) Roth, J.; Abusallout, I.; Hill, T.; Holton, C.; Thapa, U.; Hanigan, D. Release of Volatile Per- and Polyfluoroalkyl Substances from Aqueous Film-Forming Foam. *Environ. Sci. Technol. Lett.* **2020**, 7 (3), 164–170.

(26) Savvaides, T.; Koelmel, J. P.; Zhou, Y.; Lin, E. Z.; Stelben, P.; Aristizabal-Henao, J. J.; Bowden, J. A.; Godri Pollitt, K. J. Prevalence and Implications of Per- and Polyfluoroalkyl Substances (PFAS) in Settled Dust. *Curr. Environ. Health Rep.* **2021**, 8 (4), 323–335.

(27) Timshina, A. S.; Sobczak, W. J.; Griffin, E. K.; Lin, A. M.; Townsend, T. G.; Bowden, J. A. Up in the Air: Polyfluoroalkyl Phosphate Esters (PAPs) in Airborne Dust Captured by Air Conditioning (AC) Filters. *Chemosphere* **2023**, 325, No. 138307.

(28) Ahrens, L.; Shoenib, M.; Harner, T.; Lee, S. C.; Guo, R.; Reiner, E. J. Wastewater Treatment Plant and Landfills as Sources of Polyfluoroalkyl Compounds to the Atmosphere. *Environ. Sci. Technol.* **2011**, 45 (19), 8098–8105.

(29) Jahnke, A.; Ahrens, L.; Ebinghaus, R.; Temme, C. Urban versus Remote Air Concentrations of Fluorotelomer Alcohols and Other Polyfluorinated Alkyl Substances in Germany. *Environ. Sci. Technol.* **2007**, 41 (3), 745–752.

(30) Lin, H.; Lao, J.-Y.; Wang, Q.; Ruan, Y.; He, Y.; Lee, P. K. H.; Leung, K. M. Y.; Lam, P. K. S. Per- and Polyfluoroalkyl Substances in the Atmosphere of Waste Management Infrastructures: Uncovering

Secondary Fluorotelomer Alcohols, Particle Size Distribution, and Human Inhalation Exposure. *Environ. Int.* **2022**, 167, No. 107434.

(31) Tian, Y.; Yao, Y.; Chang, S.; Zhao, Z.; Zhao, Y.; Yuan, X.; Wu, F.; Sun, H. Occurrence and Phase Distribution of Neutral and Ionizable Per- and Polyfluoroalkyl Substances (PFASs) in the Atmosphere and Plant Leaves around Landfills: A Case Study in Tianjin, China. *Environ. Sci. Technol.* **2018**, 52 (3), 1301–1310.

(32) Weinberg, I.; Dreyer, A.; Ebinghaus, R. Landfills as Sources of Polyfluorinated Compounds, Polybrominated Diphenyl Ethers and Musk Fragrances to Ambient Air. *Atmos. Environ.* **2011**, 45 (4), 935–941.

(33) Chen, Y.; Zhang, H.; Liu, Y.; Bowden, J. A.; Tolaymat, T. M.; Townsend, T. G.; Solo-Gabriele, H. M. Evaluation of Per- and Polyfluoroalkyl Substances (PFAS) in Leachate, Gas Condensate, Stormwater and Groundwater at Landfills. *Chemosphere* **2023**, 318, No. 137903.

(34) Liu, Y.; Robey, N. M.; Bowden, J. A.; Tolaymat, T. M.; da Silva, B. F.; Solo-Gabriele, H. M.; Townsend, T. G. From Waste Collection Vehicles to Landfills: Indication of Per- and Polyfluoroalkyl Substance (PFAS) Transformation. *Environ. Sci. Technol. Lett.* **2021**, 8 (1), 66–72.

(35) Oliaei, F.; Kriens, D.; Kessler, K. Investigation of Perfluorochemical (PFC) Contamination in Minnesota Phase One; Minnesota Department of Health, 2006. <https://www.leg.mn.gov/archive/leg/minutes/database/84-s-1261-0-20060227-a.pdf> (accessed June 16, 2023).

(36) Robey, N. M.; da Silva, B. F.; Annable, M. D.; Townsend, T. G.; Bowden, J. A. Concentrating Per- and Polyfluoroalkyl Substances (PFAS) in Municipal Solid Waste Landfill Leachate Using Foam Separation. *Environ. Sci. Technol.* **2020**, 54 (19), 12550–12559.

(37) Smallwood, T.; Robey, N. M.; Liu, Y.; Bowden, J. A.; Tolaymat, T. M.; Solo-Gabriele, H. M.; Townsend, T. G. Per- and Polyfluoroalkyl Substances (PFAS) Distribution in Landfill Gas Collection Systems: Leachate and Gas Condensate Partitioning. *J. Hazard. Mater.* **2023**, 448, No. 130926.

(38) Solo-Gabriele, H. M.; Jones, A. S.; Lindstrom, A. B.; Lang, J. R. Waste Type, Incineration, and Aeration Are Associated with per- and Polyfluoroalkyl Levels in Landfill Leachates. *Waste Manag.* **2020**, 107, 191–200.

(39) Titaley, I. A.; De la Cruz, F. B.; Barlaz, M. A.; Field, J. A. Neutral Per- and Polyfluoroalkyl Substances in In Situ Landfill Gas by Thermal Desorption–Gas Chromatography–Mass Spectrometry. *Environ. Sci. Technol. Lett.* **2023**, 10 (3), 214–221.

(40) Goukeh, M. N.; Abichou, T.; Tang, Y. Measurement of Fluorotelomer Alcohols Based on Solid Phase Microextraction Followed by Gas Chromatography–Mass Spectrometry and Its Application in Solid Waste Study. *Chemosphere* **2023**, 345, No. 140460.

(41) LMOP Landfill and Project Database; U.S. EPA, 2016. <https://www.epa.gov/lmop/lmop-landfill-and-project-database> (accessed January 9, 2024).

(42) Townsend, T. G.; Powell, J.; Jain, P.; Xu, Q.; Tolaymat, T.; Reinhart, D. *Sustainable Practices for Landfill Design and Operation*; Springer: New York, 2015. DOI: 10.1007/978-1-4939-2662-6.

(43) McDonough, C. A.; Li, W.; Bischel, H. N.; De Silva, A. O.; DeWitt, J. C. Widening the Lens on PFASs: Direct Human Exposure to Perfluoroalkyl Acid Precursors (Pre-PFAAs). *Environ. Sci. Technol.* **2022**, 56 (10), 6004–6013.

(44) Rice, P. A.; Aungst, J.; Cooper, J.; Bandele, O.; Kabadi, S. V. Comparative Analysis of the Toxicological Databases for 6:2 Fluorotelomer Alcohol (6:2 FTOH) and Perfluorohexanoic Acid (PFHxA). *Food Chem. Toxicol.* **2020**, 138, No. 111210.

(45) Yang, Y.; Meng, K.; Chen, M.; Xie, S.; Chen, D. Fluorotelomer Alcohols' Toxicology Correlates with Oxidative Stress and Metabolism. *Rev. Environ. Contam. Toxicol.* **2020**, 256, 71–101.

(46) Xia, Y.; Hao, L.; Li, Y.; Li, Y.; Chen, J.; Li, L.; Han, X.; Liu, Y.; Wang, X.; Li, D. Embryonic 6:2 FTOH Exposure Causes Reproductive Toxicity by Disrupting the Formation of the Blood-

Testis Barrier in Offspring Mice. *Ecotoxicol. Environ. Saf.* **2023**, 250, No. 114497.

(47) Rice, P. A.; Kabadi, S. V.; Doerge, D. R.; Vanlandingham, M. M.; Churchwell, M. I.; Tryndyak, V. P.; Fisher, J. W.; Aungst, J.; Beland, F. A. Evaluating the Toxicokinetics of Some Metabolites of a C6 Polyfluorinated Compound, 6:2 Fluorotelomer Alcohol in Pregnant and Nonpregnant Rats after Oral Exposure to the Parent Compound. *Food Chem. Toxicol.* **2024**, 183, No. 114333.

(48) D'eon, J. C.; Hurley, M. D.; Wallington, T. J.; Mabury, S. A. Atmospheric Chemistry of *N*-Methyl Perfluorobutane Sulfonamidoethanol, C<sub>4</sub>F<sub>9</sub>SO<sub>2</sub>N(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>OH: Kinetics and Mechanism of Reaction with OH. *Environ. Sci. Technol.* **2006**, 40 (6), 1862–1868.

(49) Dinglasan-Panlilio, M. J. A.; Mabury, S. A. Significant Residual Fluorinated Alcohols Present in Various Fluorinated Materials. *Environ. Sci. Technol.* **2006**, 40 (5), 1447–1453.

(50) Ellis, D. A.; Martin, J. W.; Mabury, S. A.; Hurley, M. D.; Sulbaek Andersen, M. P.; Wallington, T. J. Atmospheric Lifetime of Fluorotelomer Alcohols. *Environ. Sci. Technol.* **2003**, 37 (17), 3816–3820.

(51) Ellis, D. A.; Martin, J. W.; De Silva, A. O.; Mabury, S. A.; Hurley, M. D.; Sulbaek Andersen, M. P.; Wallington, T. J. Degradation of Fluorotelomer Alcohols: A Likely Atmospheric Source of Perfluorinated Carboxylic Acids. *Environ. Sci. Technol.* **2004**, 38 (12), 3316–3321.

(52) Hammer, J.; Endo, S. Volatility and Nonspecific van Der Waals Interaction Properties of Per- and Polyfluoroalkyl Substances (PFAS): Evaluation Using Hexadecane/Air Partition Coefficients. *Environ. Sci. Technol.* **2022**, 56 (22), 15737–15745.

(53) Kim, S.-K.; Kannan, K. Perfluorinated Acids in Air, Rain, Snow, Surface Runoff, and Lakes: Relative Importance of Pathways to Contamination of Urban Lakes. *Environ. Sci. Technol.* **2007**, 41 (24), 8328–8334.

(54) Prevedouros, K.; Cousins, I. T.; Buck, R. C.; Korzeniowski, S. H. Sources, Fate and Transport of Perfluorocarboxylates. *Environ. Sci. Technol.* **2006**, 40 (1), 32–44.

(55) Schumacher, B. A.; Zimmerman, J. H.; Williams, A. C.; Lutes, C. C.; Holton, C. W.; Escobar, E.; Hayes, H.; Warrior, R. Distribution of Select Per- and Polyfluoroalkyl Substances at a Chemical Manufacturing Plant. *J. Hazard. Mater.* **2024**, 464, No. 133025.

(56) Stock, N. L.; Lau, F. K.; Ellis, D. A.; Martin, J. W.; Muir, D. C. G.; Mabury, S. A. Polyfluorinated Telomer Alcohols and Sulfonamides in the North American Troposphere. *Environ. Sci. Technol.* **2004**, 38 (4), 991–996.

(57) Dinglasan, M. J. A.; Ye, Y.; Edwards, E. A.; Mabury, S. A. Fluorotelomer Alcohol Biodegradation Yields Poly- and Perfluorinated Acids. *Environ. Sci. Technol.* **2004**, 38 (10), 2857–2864.

(58) Sulbaek Andersen, M. P.; Nielsen, O. J.; Hurley, M. D.; Ball, J. C.; Wallington, T. J.; Ellis, D. A.; Martin, J. W.; Mabury, S. A. Atmospheric Chemistry of 4:2 Fluorotelomer Alcohol (n-C<sub>4</sub>F<sub>9</sub>CH<sub>2</sub>CH<sub>2</sub>OH): Products and Mechanism of Cl Atom Initiated Oxidation in the Presence of NO<sub>x</sub>. *J. Phys. Chem. A* **2005**, 109 (9), 1849–1856.

(59) Barber, J. L.; Berger, U.; Chaemfa, C.; Huber, S.; Jahnke, A.; Temme, C.; Jones, K. C. Analysis of Per- and Polyfluorinated Alkyl Substances in Air Samples from Northwest Europe. *J. Environ. Monit.* **2007**, 9 (6), 530–541.

(60) Jahnke, A.; Ahrens, L.; Ebinghaus, R.; Berger, U.; Barber, J. L.; Temme, C. An Improved Method for the Analysis of Volatile Polyfluorinated Alkyl Substances in Environmental Air Samples. *Anal. Bioanal. Chem.* **2007**, 387 (3), 965–975.

(61) Other Test Method 45 (OTM-45) Measurement of Selected Per- and Polyfluorinated Alkyl Substances from Stationary Sources; U.S. EPA, 2021. [https://www.epa.gov/sites/production/files/2021-01/documents/otm\\_45\\_semivolatile\\_pfas\\_1-13-21.pdf](https://www.epa.gov/sites/production/files/2021-01/documents/otm_45_semivolatile_pfas_1-13-21.pdf) (accessed May 13, 2021).

(62) Washington, J. W.; Jenkins, T. M. Abiotic Hydrolysis of Fluorotelomer-Based Polymers as a Source of Perfluorocarboxylates at the Global Scale. *Environ. Sci. Technol.* **2015**, 49 (24), 14129–14135.

(63) Chen, C.; Wang, J.; Li, L.; Xu, W.; Liu, J. Comparison of Fluorotelomer Alcohol Emissions from Wastewater Treatment Plants into Atmospheric and Aquatic Environments. *Environ. Int.* **2020**, 139, No. 105718.

(64) Wang, N.; Szostek, B.; Buck, R. C.; Folsom, P. W.; Sulecki, L. M.; Gannon, J. T. 8–2 Fluorotelomer Alcohol Aerobic Soil Biodegradation: Pathways, Metabolites, and Metabolite Yields. *Chemosphere* **2009**, 75 (8), 1089–1096.

(65) Yan, P.-F.; Dong, S.; Manz, K. E.; Liu, C.; Woodcock, M. J.; Mezzari, M. P.; Abriola, L. M.; Pennell, K. D.; Cápiro, N. L. Biotransformation of 8:2 Fluorotelomer Alcohol in Soil from Aqueous Film-Forming Foams (AFFFs)-Impacted Sites under Nitrate-, Sulfate-, and Iron-Reducing Conditions. *Environ. Sci. Technol.* **2022**, 56 (19), 13728–13739.

(66) Liu, J.; Wang, N.; Szostek, B.; Buck, R. C.; Panciroli, P. K.; Folsom, P. W.; Sulecki, L. M.; Bellin, C. A. 6–2 Fluorotelomer Alcohol Aerobic Biodegradation in Soil and Mixed Bacterial Culture. *Chemosphere* **2010**, 78 (4), 437–444.

(67) Maizel, A.; Thompson, A.; Tighe, M.; Escobar Veras, S.; Rodowa, A.; Falkenstein-Smith, R.; Benner, B. A., Jr.; Hoffman, K.; Donnelly, M. K.; Hernandez, O.; Wetzler, N.; Ngu, T.; Reiner, J.; Place, B.; Kucklick, J.; Rimmer, K.; Davis, R. D. *Per- and Polyfluoroalkyl Substances in New Firefighter Turnout Gear Textiles*; NIST TN 2248; National Institute of Standards and Technology (U.S.): Gaithersburg, MD, 2023; p NIST TN 2248. DOI: 10.6028/NIST.TN.2248.

(68) Liu, W.; Takahashi, S.; Sakuramachi, Y.; Harada, K. H.; Koizumi, A. Polyfluorinated Telomers in Indoor Air of Japanese Houses. *Chemosphere* **2013**, 90 (5), 1672–1677.

(69) Whitehead, H. D.; Venier, M.; Wu, Y.; Eastman, E.; Urbanik, S.; Diamond, M. L.; Shalin, A.; Schwartz-Narbonne, H.; Bruton, T. A.; Blum, A.; Wang, Z.; Green, M.; Tighe, M.; Wilkinson, J. T.; McGuinness, S.; Peaslee, G. F. Fluorinated Compounds in North American Cosmetics. *Environ. Sci. Technol. Lett.* **2021**, 8 (7), 538–544.

(70) Dauchy, X.; Boiteux, V.; Bach, C.; Colin, A.; Hemard, J.; Rosin, C.; Munoz, J.-F. Mass Flows and Fate of Per- and Polyfluoroalkyl Substances (PFASs) in the Wastewater Treatment Plant of a Fluorochemical Manufacturing Facility. *Sci. Total Environ.* **2017**, 576, 549–558.

(71) Mok, S.; Lee, S.; Choi, Y.; Jeon, J.; Kim, Y. H.; Moon, H.-B. Target and Non-Target Analyses of Neutral per- and Polyfluoroalkyl Substances from Fluorochemical Industries Using GC-MS/MS and GC-TOF: Insights on Their Environmental Fate. *Environ. Int.* **2023**, 182, No. 108311.

(72) Li, L.; Liu, J.; Hu, J.; Wania, F. Degradation of Fluorotelomer-Based Polymers Contributes to the Global Occurrence of Fluorotelomer Alcohol and Perfluoroalkyl Carboxylates: A Combined Dynamic Substance Flow and Environmental Fate Modeling Analysis. *Environ. Sci. Technol.* **2017**, 51 (8), 4461–4470.

(73) Spaan, K. M.; van Noordenburg, C.; Plassmann, M. M.; Schultes, L.; Shaw, S.; Berger, M.; Heide-Jørgensen, M. P.; Rosing-Asvid, A.; Granquist, S. M.; Dietz, R.; Sonne, C.; Rigét, F.; Roos, A.; Benskin, J. P. Fluorine Mass Balance and Suspect Screening in Marine Mammals from the Northern Hemisphere. *Environ. Sci. Technol.* **2020**, 54 (7), 4046–4058.

(74) Dixon-Anderson, E.; Lohmann, R. Field-Testing Polyethylene Passive Samplers for the Detection of Neutral Polyfluorinated Alkyl Substances in Air and Water. *Environ. Toxicol. Chem.* **2018**, 37 (12), 3002–3010.

(75) Washington, J. W.; Jenkins, T. M.; Rankin, K.; Naile, J. E. Decades-Scale Degradation of Commercial, Side-Chain, Fluorotelomer-Based Polymers in Soils and Water. *Environ. Sci. Technol.* **2015**, 49 (2), 915–923.

(76) Washington, J. W.; Jenkins, T. M.; Weber, E. J. Identification of Unsaturated and 2H Polyfluorocarboxylate Homologous Series and Their Detection in Environmental Samples and as Polymer Degradation Products. *Environ. Sci. Technol.* **2015**, 49 (22), 13256–13263.

(77) *US Greenhouse Gas Inventory 2023*; U.S. EPA, 2023. <https://www.epa.gov/system/files/documents/2023-04/US-GHG-Inventory-2023-Main-Text.pdf> (accessed March 6, 2024).



## Review

# A critical review of perfluoroalkyl and polyfluoroalkyl substances (PFAS) landfill disposal in the United States

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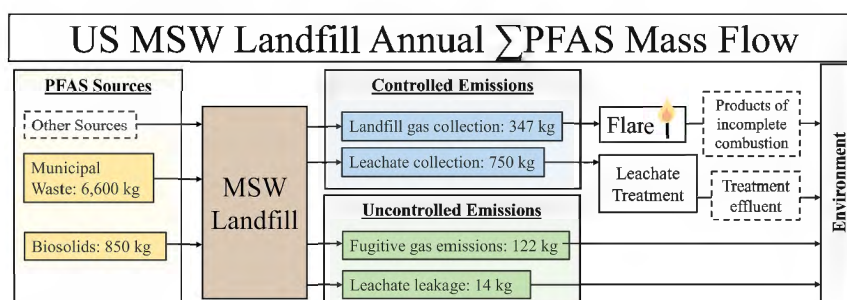
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## HIGHLIGHTS

- Solid waste management strategies impact PFAS emissions.
- PFOA has the highest ratio to its respective RSL in C&D and MSW landfill leachates.
- Unlined C&D landfills present a significant source of PFAS to the environment.
- An estimated 7.5 metric tons of PFAS enter MSW landfills annually.
- Annually, 460 kg of PFAS emitted via landfill gas, 750 kg via landfill leachate.

## GRAPHICAL ABSTRACT



## ARTICLE INFO

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## ABSTRACT

Landfills manage materials containing per- and polyfluoroalkyl substances (PFAS) from municipal solid waste (MSW) and other waste streams. This manuscript summarizes state and federal initiatives and critically reviews peer-reviewed literature to define best practices for managing these wastes and identify data gaps to guide future

**Abbreviations:** µg, Microgram; AFFF, Aqueous film-forming foams; C&D, Construction and demolition; diPAP, Polyfluoroalkyl phosphoric acid diesters; FASA, Perfluoroalkane sulfonamide; FASE, Perfluoroalkane sulfonamido ethanol; FTAc, Fluorotelomer acrylate; FTCA, Fluorotelomer carboxylic acid; FTO, Fluorotelomer olefin; FTOH, Fluorotelomer alcohol; H<sub>2</sub>S, Hydrogen sulfide gas; HAL, Health Advisory Limit; kg, Kilogram; L, Liter; LFG, Landfill gas; MCL, Maximum Contaminant Level; MeFBSAA, Methyl-n-perfluorobutanesulfonamidoacetic acid; MeFOSAA, Methyl-n-perfluorooctanesulfonamidoacetic acid; mg, Milligram; Mg, Megagram (metric ton); MPCA, Minnesota Pollution Control Agency; MSW, Municipal solid waste; MSWI, Municipal solid waste incineration; NEBRA, North East Biosolids & Residuals Association; NWRA, National Waste & Recycling Association; PFAA, Perfluoroalkyl acids; PFAS, Per- and polyfluoroalkyl substance(s); PFBS, Perfluorobutane sulfonate; PFCA, Perfluoroalkyl carboxylic acids; PFHxA, Perfluorohexanoic acid; PFHxS, perfluorohexane sulfonate; PFOA, Perfluorooctanoic acid; PFOS, Perfluorooctane sulfonic acid; PFPeA, Perfluoropentanoic acid; PFSA, Perfluoroalkyl sulfonic acids; PIC, Product of incomplete combustion; RCRA, Resource Conservation and Recovery Act; RNG, Renewable natural gas; RO, Reverse osmosis; RSL, Regional Screening Limit; SI, Supplementary information; US EPA, United States Environmental Protection Agency; WWTP, Wastewater treatment plant.

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research. The objective is to inform stakeholders about waste-derived PFAS disposed of in landfills, PFAS emissions, and the potential for related environmental impacts. Furthermore, this document highlights data gaps and uncertainties concerning the fate of PFAS during landfill disposal. Most studies on this topic measured PFAS in liquid landfill effluent (leachate); comparatively fewer have attempted to estimate PFAS loading in landfills or other effluent streams such as landfill gas (LFG). In all media, the reported total PFAS heavily depends on waste types and the number of PFAS included in the analytical method. Early studies which only measured a small number of PFAS, predominantly perfluoroalkyl acids (PFAAs), likely report a significant underestimation of total PFAS. Major findings include relationships between PFAS effluent and landfill conditions – biodegradable waste increases PFAS transformation and leaching. Based on the results of multiple studies, it is estimated that 84% of PFAS loading to MSW landfills (7.2 T total) remains in the waste mass, while 5% leaves via LFG and 11% via leachate on an annual basis. The environmental impact of landfill-derived PFAS has been well-documented. Additional research is needed on PFAS in landfilled construction and demolition debris, hazardous, and industrial waste in the US.

## 1. Introduction

Per- and polyfluoroalkyl substances (PFAS) include thousands of unique manufactured chemical compounds with a hydrophobic carbon-fluorine chain and a functional group that may be hydrophilic or hydrophobic. PFAS provides beneficial properties for many consumer products and industrial applications, mostly stick- and stain-resistance and surfactant qualities. PFAS's usefulness has led to a nearly ubiquitous presence in our lives, and PFAS's stability, due to the strength of carbon-fluorine bonds, result in long half-lives and the nickname "forever chemicals."

Human exposure to PFAS has been linked to detrimental health effects which impact all systems, including reproductive effects such as decreased fertility or increased high blood pressure in pregnant women, developmental effects or delays in children, including low birth weight, accelerated puberty, bone variations, behavioral changes, increased risk of some cancers, including prostate, kidney, and testicular cancers, reduced ability of the body's immune system to fight infections, including reduced vaccine response; interference with the body's natural hormones and increased cholesterol levels and risk of obesity (reviewed by Fenton et al., 2021). In response to the growing body of evidence identifying PFAS as a significant threat to human health and the environment, the United States Environmental Protection Agency (US EPA) is undertaking research to determine the impact of PFAS via a risk paradigm approach: (1) determine toxicity, (2) understand exposure, (3) assess risk, and (4) find and innovate effective treatment and remediation techniques and strategies. Because PFAS-containing products are disposed of at the end of their useful lives, significant PFAS quantities are managed with solid waste in the US and elsewhere. Properly managing solid waste via containment, treatment, and destruction is essential to protecting our environment and reducing the risk of harmful exposures.

Recognizing the impact of PFAS on human health and the

environment, the US EPA released its first provisional Health Advisory Levels (HALs) for PFAS in drinking water in 2009. As analytical capabilities and scientific understanding of PFAS health impacts have improved, the Agency has promulgated additional guidance and risk-based thresholds. For the first time, in 2023, the US EPA proposed enforceable drinking water regulatory limits to reduce human exposure to PFAS (US EPA, 2022d). In April of 2021, the US EPA released the PFAS Strategic Roadmap, which outlines the EPA's commitments to action for 2021 through 2024. Information about US EPA PFAS initiatives is summarized in **Table S1** of the Supplementary information (SI), and applicable limits are included in **Table 1**. The US EPA has also proposed designating PFOA and PFOS as hazardous substances under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) and is considering adding certain PFAS to the Resource Conservation and Recovery Act (RCRA) list of hazardous constituents (US EPA, 2022b).

At the State level, all the US states except Arkansas, Louisiana, Mississippi, Nebraska, Texas, and Wyoming have dedicated websites providing PFAS-specific information. Some states have banned PFAS-containing products, as summarized in **Table S2** (SI). In contrast, others have initiated their own regulatory limits and advisory guidelines, as presented in **Table S3** (SI). Eight states have undertaken specific actions and introduced or passed bills targeting PFAS in solid waste (see **Table S4**, SI). Notably, PFAS regulations are rapidly evolving, and any documentation of state-level PFAS initiatives will likely be outdated quickly.

Confronted with significant quantities of PFAS managed in landfills, the solid waste community struggles to understand the best means to manage PFAS-containing waste streams. Many studies have evaluated PFAS in landfills. However, there is a need for a critical review of the literature that would define the best methodologies for managing these wastes and identify data gaps to guide future research. This manuscript aims to inform the public and stakeholders from the solid waste industry

**Table 1**

Average concentrations (ng L<sup>-1</sup>) of select PFAS in landfill leachate and US EPA risk-based thresholds.

| Leachate matrix                 | PFOA       |     | PFOS      |     | PFNA     |     | PFBS      |      | PFHxS       |     | PFHxA       |    | 5:3 FTCA  |
|---------------------------------|------------|-----|-----------|-----|----------|-----|-----------|------|-------------|-----|-------------|----|-----------|
|                                 | Mean (n)   | DF  | Mean (n)  | DF  | Mean (n) | DF  | Mean (n)  | DF   | Mean (n)    | DF  | Mean (n)    | DF | Mean (n)  |
| MSW                             | 1400 (284) | 23  | 260 (284) | 6.6 | 69 (234) | 1.2 | 910 (234) | 0.1  | 540 (234)   | 1.4 | 2800 (225)  |    | 3500 (86) |
| CDD                             | 1100 (17)  | 19  | 660 (17)  | 17  | 50 (17)  | 0.8 | 530 (17)  | 0.1  | 2200 (17)   | 5.7 | 1600 (17)   |    | 1400 (17) |
| MSWI Ash                        | 800 (40)   | 13  | 400 (40)  | 10  | 59 (40)  | 1.1 | 1400 (40) | 0.2  | 510 (40)    | 1.3 | 1300 (40)   |    | 700 (40)  |
| HW (Primary)                    | 4900 (24)  | 81  | 4100 (24) | 102 | 530 (24) | 8.7 | 6500 (24) | 1.1  | 12,000 (24) | 32  | 12,000 (24) |    | NM        |
| HW (Secondary)                  | 100 (5)    | 1.7 | 14 (5)    | 0.4 | 40 (5)   | 0.7 | 57 (5)    | 0.01 | 86 (5)      | 0.2 | 440 (5)     |    | NM        |
| Tapwater RSL (HQ = 1.0)         | 60         |     | 40        |     | 59       |     | 6000      |      | 390         |     | n/a         |    | n/a       |
| EPA limit (ng L <sup>-1</sup> ) |            |     |           |     |          |     |           |      |             |     |             |    |           |
| Lifetime HAL                    | 0.004      |     | 0.020     |     | n/a      |     | 2000      |      | n/a         |     | n/a         |    | n/a       |
| Proposed MCL                    | 4          |     | 4         |     | n/a      |     | n/a       |      | n/a         |     | n/a         |    | n/a       |

(HAL = health advisory level; MCL = maximum contaminant level; RSL = regional screening level; HQ = hazard quotient; DF = average dilution factor required to meet RSL; NM = not measured).

Italicized values represent the controlling dilution factor.

about PFAS entering the waste stream and being disposed of in landfills, potential landfill PFAS emissions, and the related environmental impacts. Furthermore, this document highlights data gaps and uncertainties concerning the fate of PFAS during landfill disposal. Data were compiled and summarized, as described in the Methods section of the SI (Section S2 and Table S5), to provide a concise critical review of this evolving research topic.

## 2. Solid waste management in the United States

A detailed discussion of solid waste management in the US is included in the SI (Section S3). Residents, businesses, and industries in the United States (US) generate significant amounts of solid waste; overall municipal solid waste (MSW) generation in 2018 was 265 million metric tons (US EPA, 2020b). In addition to MSW, significant amounts of construction and demolition (C&D) waste (545 million metric tons), wastewater treatment plant (WWTP) biosolids (2.5 million metric tons), and varied amounts of industrial waste and disaster debris enter the US solid waste management system every year (US EPA, 2020b). Over time, MSW generation in the US has increased. While the fraction of MSW which is landfilled has decreased from over 90% in 1960 to 50% in recent years, the mass of MSW disposed of in landfills reached its highest recorded level at 133 million metric tons in 2018 (see Fig. S1 in the SI). The US's landfill design, monitoring, and classification are identified and regulated according to the RCRA described in the SI's RCRA section. RCRA and its regulations provide requirements for landfill engineering controls based on the type of waste the landfill receives (MSW (Subtitle D), Hazardous (Subtitle C), industrial, construction, and demolition (C&D) debris) as outlined in the SI.

### 2.1. Sources of PFAS in solid waste

While extensive research has been undertaken to measure PFAS in effluent from waste management activities (particularly landfill leachate), fewer studies have attempted to estimate the PFAS load entering the waste management sector. Coffin et al. (2022) estimated an extractable  $\Sigma$ PFAS concentration in MSW of  $50 \mu\text{g kg}^{-1}$  based on concentrations in MSW screenings reported by Liu et al. (2022a). Estimating PFAS loading to landfills is not only complicated by analytical challenges and the diversity of measurable PFAS, but also by the heterogeneity of MSW and other waste streams (e.g., household products, building materials, industrial waste, and "other wastes"). The following subsections focus on waste representing suspected high PFAS load or a significant fraction of the waste stream. Fig. 1 presents PFAS concentrations measured in various products and the environment compared to those measured in landfill leachate, compost, and biosolids from WWTPs.

#### 2.1.1. Municipal solid waste

In the US, household waste is among the most significant fractions of MSW. Few studies measured the PFAS concentration of suspected PFAS-containing consumer products in the context of direct exposure during product use (Buck et al., 2011; Favreau et al., 2017; Glüge et al., 2020; Guo et al., 2009; Herzke et al., 2012; ITRC, 2022; Kotthoff et al., 2015; OECD, 2022; US FDA, 2022; Ye et al., 2015). These findings indicate a significant load of PFAS remaining in products at the end of their useful life. Household waste consists of two main categories: the biodegradable fraction and the non-biodegradable fraction. Both types of waste streams contain PFAS, but the fate of their PFAS may differ.

##### 2.1.1.1. Biodegradable fraction. Paper and paperboard are the most

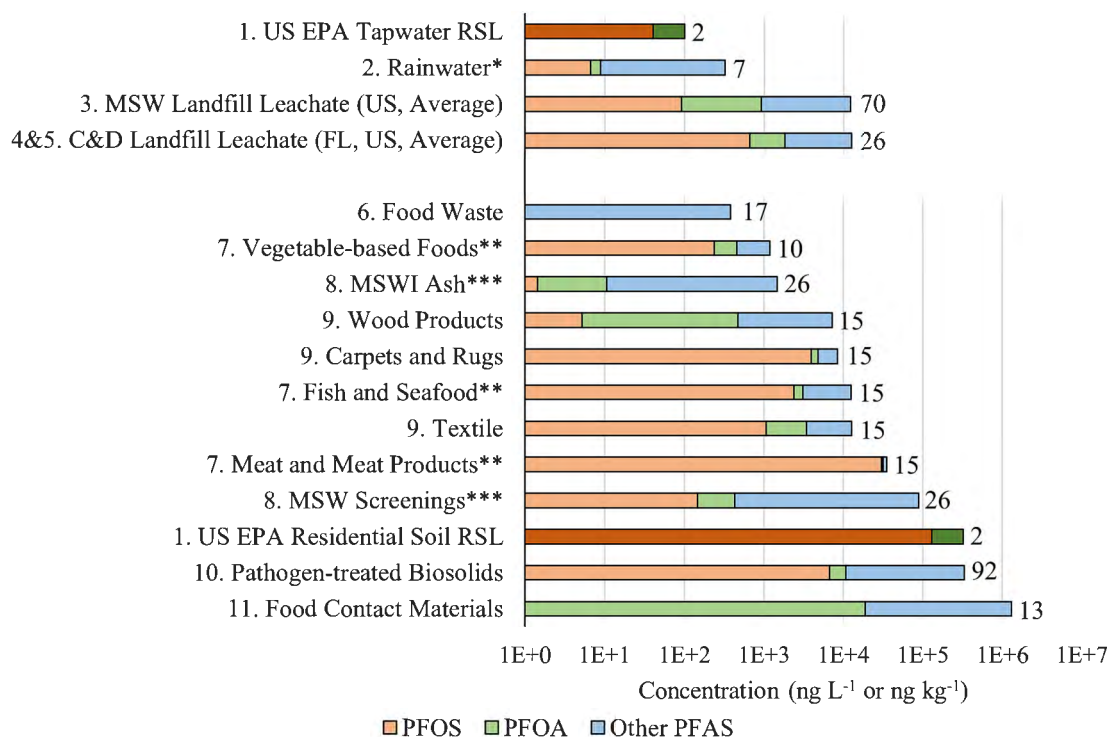


**Fig. 1.** PFAS concentrations and compositions measured in various products, wastes, and the environment compared to MSW landfill leachate.

\* includes ultra-short chain PFAS, TFA.

\*\* upper bound of the mean.

\*\*\* minimum total PFAS based on leachable fraction.

Note: numbers prior to matrix type refer to sources. Numbers to the right of the bars are the number of PFAS analytes. RSLs refer to risk-based screening levels, not enforceable regulatory limits. Sources: 1. US EPA (2022d) 2. Pike et al. (2021) 3. Lang et al. (2017) 4. Solo-Gabriele et al. (2020) 5. Chen et al. (2023) 6. Thakali et al. (2022) 7. European Food Safety Authority (2012) 8. Liu et al. (2022b) 9. Bečanová et al. (2016) 10. Thompson et al. (2023a, 2023b) 11. Siao et al. (2022).

abundant components of MSW, representing 23% of the US MSW generation in 2018 (US EPA, 2021a). PFAS are often added to paper products to improve stick and stain resistance, which results in paper products (including food packaging) consistently reported as a significant source of PFAS for human exposure and in the waste stream (Curtzwiler et al., 2021; D'eon et al., 2009; Ramírez Carnero et al., 2021; Robel et al., 2017; Seltenrich, 2020; Yuan et al., 2016; Zabaleta et al., 2016). In a review of studies that measured PFAS in food-contact materials, Siao et al. (2022) reported concentrations of  $\Sigma_{13}$ PFAS in food packaging as high as  $8500 \mu\text{g kg}^{-1}$ ; at these concentrations, paper and paper products likely contribute significantly to the overall PFAS loading in MSW, as well as contamination of food and food waste. Sapozhnikova et al. (2023) used targeted and total oxidizable precursor (TOP) assays to measure PFAS migration from food packaging into food products among 88 packaged food samples. TOP analysis identified a significant portion of total PFAS in packaging came from unknown precursor PFAS; average  $\Sigma_8$ PFAA was  $28 \mu\text{g kg}^{-1}$  before oxidation and  $380 \mu\text{g kg}^{-1}$  after oxidation. Migration from the packaging into food was found to increase over the course of the ten-day study. Unfortunately, many new products marketed as environmentally-friendly alternatives to plastic products have been found to contain PFAS (Timshina et al., 2021), and advocacy groups in the US and beyond have moved to revise compostable labeling to preclude PFAS-containing products (BioCycle, 2020). Disubstituted polyfluoroalkyl phosphates (diPAPs) have been found to represent a significant fraction of the PFAS used in paper products. However, most studies do not include diPAP as an analyte (D'eon et al., 2009; Thompson et al., 2023a). These findings suggest the concentration of  $\Sigma$ PFAS in paper products may be significantly higher than current estimates.

Another large fraction of biodegradable household waste is food waste, accounting for 22% of the MSW generated in the US in 2018 (US EPA, 2021a, 2021b, 2021c). Unlike paper products, PFAS are not intentionally added to food; contact with PFAS-containing equipment, packaging, water, feed, or soil amendments may result in residual PFAS. Several studies have been published describing the potential migration of PFAS from PFAS-impregnated food packaging (Ramírez Carnero et al., 2021). Up to 33% of extractable PFAS on the surface of food contact materials have been reported to migrate to simulated foods – the migration efficiency depends on the food type and PFAS class (Yuan et al., 2016). Additionally, some PFAS are known to bioaccumulate in the food chain. A European Food Safety Authority (2012) report lists seafood and meat as the food categories most frequently reported containing measurable concentrations of PFAS, with PFOS and PFOA quantified most commonly in 29% and 9% of samples, respectively. The same study estimated mean overall dietary exposure for PFOS and PFOA ranging from  $0.07$  to  $32 \text{ ng kg}^{-1}$  body weight per day, with lower exposure rates for 14 additional PFAS. Exposure was highest among toddlers and children due to higher food consumption for body size. Among 25 samples of food waste analyzed for PFAS by Thakali et al. (2022), 17 contained PFAS (mean  $\Sigma_{17}$ PFAS =  $0.38 \mu\text{g kg}^{-1}$ ); PFOS and PFOA were not detected in any of the samples.

Wood and yard trimmings represent approximately 18% of the US MSW generation (US EPA, 2020b). While natural wood and plant matter are unlikely to contain significant concentrations of PFAS (Thompson et al., 2023b), engineered wood building materials may be coated with PFAS to enhance performance. In a study of PFAS content in consumer and building materials, 100% of oriented strand board and wood products analyzed contained measurable PFAS concentrations, with median and maximum  $\Sigma_{15}$ PFAA of 5 and  $18 \mu\text{g kg}^{-1}$ , respectively (Bečanová et al., 2016).

**2.1.1.2. Non-biodegradable fraction.** In the non-biodegradable category of household waste, carpets, and textiles have been consistently found to contain intentionally added PFAS that provide stick and stain resistance and waterproof properties (Kallee and Santen, 2012; Kim et al., 2015;

Lang et al., 2016; Peaslee et al., 2020; van der Veen et al., 2022). A review of  $\Sigma_{15}$ PFAA in various household and consumer products found textiles, floor covering, and car interior materials represented the three highest maximum concentrations ( $78$ ,  $38$ , and  $36 \mu\text{g kg}^{-1}$ , respectively); the highest non-biodegradable median PFAS concentration was from insulation ( $3.6 \mu\text{g kg}^{-1}$ ) (Bečanová et al., 2016). PFAS and fluoropolymers are also used in non-stick cookware (Sajid and Ilyas, 2017) and electronics to provide smudge resistance, insulation, and other properties. An estimated 114 separate PFAS have been identified in electronic production (Garg et al., 2020). PFAS contamination and exposure through e-waste management have been the subject of several studies (Garg et al., 2020; Tansel, 2022; B. Zhang et al., 2020). Notably, the measurement of PFAS in e-waste itself (as opposed to through leachate, environmental contamination, or dust) is limited. A range of  $0.07$ – $0.43 \mu\text{g kg}^{-1}$  PFOS among all electronic products is provided by Garg et al. (2020).  $\Sigma_{15}$ PFAA reported by Bečanová et al. (2016) ranged as high as  $11.7 \mu\text{g kg}^{-1}$  (median:  $0.4 \mu\text{g kg}^{-1}$ ) in electronic and electrical equipment (EEE) and as high as  $2.2 \mu\text{g kg}^{-1}$  (median:  $1.4 \mu\text{g kg}^{-1}$ ) in waste EEE.

### 2.1.2. Industrial waste

Industrial processes generate waste and effluent in large volumes; processes that use PFAS, such as the leather tannery, chrome plating, and textile industries, represent a significant contribution of PFAS to the solid waste stream (ITRC, 2022) which are often disposed of in landfills. Other types of industrial processes which generate PFAS-containing waste involve the management of PFAS-contaminated materials, including the separation of wastewater biosolids as part of municipal wastewater treatment, the management of MSW incineration residuals (MSWI ash), and the disposal of PFAS-contaminated soils and other residuals generated as part of environmental cleanup processes.

**2.1.2.1. Biosolids.** WWTPs manage residential, commercial, and industrial wastewater, including landfill leachate, and have been the subject of many PFAS studies (Lenka et al., 2022). Biosolids account for a significant fraction of WWTP effluent (Fredriksson et al., 2022) and impact PFAS loading to the environment and landfills (Johnson, 2022; Thompson et al., 2023b). Reported PFAS concentrations in biosolids vary with the number of PFAS included in the analytical method. Gallen et al. (2018) reported mean  $\Sigma_9$ PFAS of  $45 \mu\text{g kg}^{-1}$  of biosolids; Thompson et al. (2023a, 2023b) reported mean  $\Sigma_{92}$ PFAS of  $500 \mu\text{g kg}^{-1}$  (dry) in untreated biosludge and  $330 \mu\text{g kg}^{-1}$  (dry) in biosolids (biosludge treated for pathogen removal), indicating that early studies of PFAS in biosolids which measured fewer PFAS, and predominantly PFAAs, did not capture a significant portion of the total PFAS. Over 5.8 million dry metric tons of biosolids were managed in the US in 2018, of which 30% was managed in landfills, 15% was incinerated, and over 50% was used as a soil amendment (NEBRA, 2022).

**2.1.2.2. MSW incineration ash.** The incineration of MSW for energy recovery (MSWI) produces two solid waste streams – bottom ash, the material that does not burn, and fly ash, fine particulate matter collected in the air pollution control system. Approximately 13% of MSW in the US is managed through incineration (US EPA, 2021a, 2021b, 2021c), resulting in an estimated 7.5 million tons of MSWI ash (Liu et al., 2019). Few studies have measured PFAS in MSWI ash. Liu et al. (2021b) reported  $\Sigma_{21}$ PFAS in fly and bottom ash from three facilities in China, with concentrations ranging from  $1.5$  to  $88 \mu\text{g kg}^{-1}$  in fly ash and from  $3.1$  to  $77 \mu\text{g kg}^{-1}$  in bottom ash. Based on the concentrations of PFAS in a laboratory leaching study, the average minimum  $\Sigma_{26}$ PFAS in MSWI ash from a US facility was  $1.5 \mu\text{g kg}^{-1}$  (Liu et al., 2022b); this represents a conservative estimate of total PFAS. These concentrations are in the same range as MSW. Incineration temperatures may not be sufficiently high to mineralize or destroy PFAS, and operational strategies likely play a significant role in the fate of PFAS during incineration. The impact

of temperatures on PFAS leaching from MSWI is discussed in greater detail in the context of MSWI ash monofill leachates.

**2.1.2.3. Manufacturing wastes.** There is extensive use of PFAS in some industries, as PFAS is added intentionally to products (i.e., to produce stain-resistant properties in textiles and paper products) and as part of the manufacturing process (i.e., to facilitate demolding). This results in unintentionally contaminated materials through contact. The Interstate Technology Review Committee (ITRC) thoroughly lists PFAS uses in the industrial and manufacturing sectors (ITRC, 2022). PFAS-laden manufacturing waste is often sent to landfills for disposal across industries.

Among specific industries and industrial wastes which have been the subject of PFAS analysis, high-concentration effluents from electronic industries have been described in the literature; photolithographic effluent in Taiwan contained 130,000 ng L<sup>-1</sup> each of PFHxS and PFOS (Lin et al., 2009); liquid effluent from television and circuit board manufacturing contained 1600 ng L<sup>-1</sup> of  $\Sigma_{11}$ PFAS (Kim et al., 2016); sludge effluent collected from an electronics industry location in South Korea contained 91  $\mu\text{g kg}^{-1}$  of  $\Sigma_{11}$ PFAAs (Kim et al., 2016). PFAS are used commonly in paper processing and treatment; a case study in Norway identified PFAS impacts downstream of a landfill used for paper factory waste disposal (Langberg et al., 2021). Chrome plating industry waste sludges are designated hazardous wastes (F006), which contain high concentrations of PFAS (ITRC, 2022) and are therefore managed in Subtitle C hazardous waste landfills. A study of chrome sludge in China identified PFOS as the most predominant PFAS at concentrations as high as 2435  $\mu\text{g kg}^{-1}$  (Qu et al., 2020). The chrome plating industry consumes an estimated 6500 kg of PFOS annually (Garg et al., 2020).

**2.1.2.4. PFAS remediation residuals.** Sites with high levels of PFAS contamination from the historical use of PFAS-containing aqueous film-forming foams (AFFF) or other releases are frequently remediated, and the contaminated media is commonly disposed of in landfills (either with the waste or used as daily cover). Remediation approaches include mobilization of PFAS and collection of the leachate, sorption of PFAS using activated carbon or other sorbents, or soil excavation for landfill disposal (Bolan et al., 2021; Ross et al., 2018). Brusseau et al. (2020) reviewed PFAS concentrations measured in soils from contaminated sites, reporting median PFOA and PFOS concentrations of 83 and 8700  $\mu\text{g kg}^{-1}$ , respectively, with concentrations as high as 50,000  $\mu\text{g kg}^{-1}$  for PFOA and 460,000  $\mu\text{g kg}^{-1}$  for PFOS.

### 3. Fate of PFAS in landfills

The fate of solid waste-derived PFAS within landfills is dominated by transformation and partitioning. Many PFAS species are persistent in the environment and PFAS that are degradable can transform into more recalcitrant, typically more environmentally mobile PFAS (Bolan et al., 2021). The partitioning behavior of PFAS are related to the chemical structure of individual species, both according to PFAS class, functional groups, and chain length among homologous species. In turn, the ongoing transformation will impact partitioning behavior (Robey et al., 2020; Zhang et al., 2020a, 2020b; Smallwood et al., 2023). In landfills, PFAS may partition to the liquid phase (leachate) and gaseous phase (landfill gas; LFG), remain sorbed to the waste, and/or interact with the engineering controls of the landfills (e.g., leachate collection systems, gas collection, and control systems). PFAS that are resistant to degradation and minimally soluble or volatile, such as certain polymeric PFAS, have historically been presumed to remain immobile and sequestered in landfills, although more recent studies have called this assumption into question (Lohmann et al., 2020).

### 3.1. PFAS transformation

Many studies observed the transformation of PFAS precursors into terminal species under abiotic and microbially active aerobic and anaerobic conditions. While this section briefly reviews these processes to provide context to PFAS in landfills, the aim is not to conduct an exhaustive review of the topic, which is available in other reviews (Lu et al., 2023).

#### 3.1.1. Abiotic transformation

PFAS transformation pathways under abiotic conditions include oxidation, photolysis, and thermal degradation (ITRC, 2020; Washington and Jenkins, 2015). While the bulk of PFAS transformations in organic-rich landfills are likely a result of biodegradation, these abiotic processes play an essential role in solid waste management systems. PFAS such as fluorotelomer alcohols (FTOHs) can volatilize under temperatures typical in landfills (35–55 °C). Once in the atmosphere, FTOH can transform via photolysis or other chemical reactions into perfluorocarboxylic acids (PFCAs) which are then deposited on land and waterbodies (Esfahani et al., 2022; Martin et al., 2006). Other abiotic processes include thermal degradation. An increase in the temperature of waste may facilitate PFAS transformation. Wastes within landfills may be exposed to temperatures insufficient to mineralize or defluorinate PFAS but which may cause precursor transformations. Thompson et al. (2023a, 2023b) measured higher concentrations of diPAPs in biosolids that had undergone any form of heat treatment, including heat drying as well as higher temperature vector reduction treatment, indicating the presence and transformation of unidentified precursors.

#### 3.1.2. Aerobic transformation

Aerobic environments exist at the early stages of landfill decomposition. The waste still contains atmospheric oxygen in its void space and likely contributes to the transformation of PFAS in waste. Thompson et al. (2023a, 2023b) observed a proportional increase in PFCAs after aerobic biosolids composting, especially short-chain (perfluoropentanoic acid, PFPeA, and perfluorohexanoic acid, PFHxA). Similarly, Li et al. (2022) found significant increases among short-chain PFAAs (including PFBS and PFOS) in aerobically treated anaerobic digester sludge. These findings are significant because short-chain PFAS are more mobile in the environment, more likely to be uptaken by plants (Ghisi et al., 2019), and more challenging to treat (Ross et al., 2018). Multiple studies have shown that aerobic decomposition facilitates the transformation of precursor PFAS to shorter-chain terminal PFAS, such as PFOA and PFOS (Hamid et al., 2020; Lee et al., 2010a; Liu et al., 2010; Lott et al., 2023; Rhoads et al., 2008; Schultz et al., 2006; Wang et al., 2009, 2011; Zhao et al., 2013).

#### 3.1.3. Anaerobic transformations

Comparatively, fewer studies have documented PFAS transformation under anaerobic or methanogenic conditions similar to landfills. Liu et al. (2021a) compared 52 PFAS in leachate from waste collection vehicles to anaerobic MSW landfill leachate and concluded the vehicle leachate contained proportionally more precursor PFAS and short-chain PFAAs compared to the landfill leachate as a result of the transformation in the anaerobic landfill environments. Studies of anaerobic precursor transformation identified FTCAs as the predominant by-product of FTOH degradation. Allred et al. (2015) reported increased MeFBSAA and FTCA leaching over abiotic reactors in biologically active landfill microcosm reactors, indicating that methanogenic biological transformation was responsible for the increase. Zhang et al. (2013) observed the accumulation of FTCAs in landfills over time, concluding that FTCAs are indicators of FTOH transformation, while Lang et al. (2016) and Weber et al. (2022) reported PFOA accumulation in leachate as a result of precursor transformation under anaerobic experimental conditions. Lang et al. (2016) attributed this to the longer experimental duration, with PFOA appearing as a significant degradation by-product only 200+

days into the 550-day experiment.

### 3.2. PFAS partitioning in landfills

#### 3.2.1. PFAS partitioning to the liquid phase

PFAS concentrations in landfill leachate are a function of multiple factors, including the PFAS profile of the incoming waste stream and conditions within the landfill, which, in turn, correspond with waste composition, stage of decomposition, and environmental factors, especially rainfall precipitation. These factors also affect the physical-chemical aspects of the leachate quality, and any discussion of PFAS in leachate should also include matrix contextualization. The number of PFAS that can be detected and quantified in landfill leachate has grown. Early methods were able to quantify 24 PFAS compounds in three classes (Huset et al., 2011), but improvements have been made; more recent studies attempted to measure 92 PFAS and detected 53, as presented in Table 2.

##### 3.2.1.1. PFAS in landfill leachate by type

**3.2.1.1.1. MSW landfills.** The vast majority of PFAS landfill leachate data are measured from MSW landfills (Allred et al., 2014; California Water Boards, 2023; Chen et al., 2022, 2023; Huset et al., 2011; Lang et al., 2017; Liu et al., 2022a; Masoner et al., 2020; NWRA, 2020; Solo-Gabriele et al., 2020). The  $\sum$ PFAS content of MSW landfill leachate in published US studies ranges from BDL - 125,000 ng L<sup>-1</sup> with an average of 10,500 ng L<sup>-1</sup> and a weighted average of 12,600 ng L<sup>-1</sup>. The weighted

average is notably similar to the estimated average  $\sum$ PFAS concentration reported by Lang et al. (2017) using Monte Carlo simulation. Often, the  $\sum$ PFAS content heavily depends on the number of unique PFAS measured in the study, which ranged from two to 70 for MSW landfill leachate (see SI Fig. S2). For comparison among studies, we will focus on PFAS with corresponding US EPA tapwater Regional Screening Levels (RSL) (i.e., PFOA, PFNA, PFBS, PFHxS, PFOS, and Gen-X), as presented in Table 1. Except for Gen-X, which has only been quantified in a single sample of landfill leachate from a North Carolina MSW landfill with a history of accepting PFAS manufacturing wastes (NWRA, 2020), the remaining five PFAS are reliably quantified in all published landfill leachate studies. Other PFAS which reliably contribute significantly to  $\sum$ PFAS in landfill leachates, PFHxA and 5:3 FTCA, are also included in Table 1.

PFAS concentrations have also been reported for leachates from MSW landfills in other countries, including Australia (Gallen et al., 2016, 2017), Europe (Ahrens et al., 2011; Busch et al., 2010; Eggen et al., 2010; Fuertes et al., 2017; Kallenborn et al., 2004; Knutsen et al., 2019; Perkola and Sainio, 2013; Woldegiorgis et al., 2005), and Asia (Huang et al., 2022; Liu et al., 2022b; Yan et al., 2015; Yin et al., 2017; Zhang et al., 2014). International differences in waste composition, sample collection, and analytical processes can impact reported PFAS concentrations, making a direct comparison of the overall PFAS content challenging. Concentrations of PFOS and PFOA, which have been reliably measured in most or all studies, are included for eight countries in Table S6 and described by Travar et al. (2020).

**Table 2**

Number of PFAS measured and  $\sum$ PFAS among published landfill leachate studies.

| Matrix            | Number of samples | Number of PFAS detected (in Method) | Average $\sum$ PFAS (ng L <sup>-1</sup> ) | $\sum$ PFAS range (ng L <sup>-1</sup> ) | Country   | Reference                      |
|-------------------|-------------------|-------------------------------------|-------------------------------------------|-----------------------------------------|-----------|--------------------------------|
| MSW LL            | 1                 | 38 (51)                             | 9700                                      | 9700                                    | USA       | Liu et al. (2021a)             |
|                   | 1                 | 32 (51)                             | 9400                                      | 9400                                    | USA       | Robey et al. (2020)            |
|                   | 78                | 25 (26)                             | 12,700                                    | 300–58,000                              | USA       | Chen et al. (2023)             |
|                   | 4                 | 10 (11)                             | 17,200                                    | 15,000–18,000                           | USA       | Solo-Gabriele et al. (2020)    |
|                   | 6                 | 24 (24)                             | 4700                                      | 2700–7400                               | USA       | Huset et al. (2011)            |
|                   | 40                | 30 (70)                             | 12,200                                    | 2000–29,000                             | USA       | Lang et al. (2017)             |
|                   | 11                | 2 (2)                               | 840                                       | 330–2600                                | USA       | Clarke et al. (2015)           |
|                   | 19                | 28 (28)                             | 5400                                      | 230–29,000                              | USA       | Helmer et al. (2022)           |
|                   | 39                | 2 (2)                               | 1500                                      | 47–3400                                 | USA       | EGLE (2019)                    |
|                   | 9                 | 22 (25)                             | 24,300                                    | 1400–125,000                            | USA       | NWRA (2020)                    |
|                   | 131               | 31 (40)                             | 17,500                                    | BDL – 104,000                           | USA       | California Water Boards (2023) |
|                   | 17                | 14 (14)                             | 3000                                      | 33–15,000                               | Australia | Gallen et al. (2016)           |
|                   | 94                | 9 (9)                               | 6100                                      | 210–46,000                              | Australia | Gallen et al. (2017)           |
|                   | 22                | 15 (15)                             | 7000                                      | Not reported                            | Australia | Simmons (2019)                 |
|                   | 6                 | 25 (43)                             | 6100                                      | 31–13,000                               | Germany   | Busch et al. (2010)            |
|                   | 11                | 24 (24)                             | 9800                                      | 2500–36,000                             | Canada    | Benskin et al. (2012)          |
|                   | 31                | 16 (18)                             | 2700                                      | 700–6400                                | Canada    | Li (2009)                      |
|                   | 10                | 2 (2)                               | *                                         | 50–2300                                 | Canada    | Gewurtz et al. (2013)          |
|                   | 2                 | 16 (27)                             | 4200                                      | 2200–6100                               | Norway    | Eggen et al. (2010)            |
|                   | 5                 | 7 (8)                               | 770                                       | 200–1500                                | Norway    | Kallenborn et al. (2004)       |
|                   | 2                 | 4 (4)                               | 400                                       | 210–610                                 | Finland   | Perkola and Sainio (2013)      |
|                   | 48                | 7 (10)                              | 2400                                      | 14–17,500                               | Ireland   | Harrad et al. (2019)           |
|                   | 4                 | 8 (16)                              | 1100                                      | 640–1400                                | Spain     | Fuertes et al. (2017)          |
|                   | 12                | 28 (30)                             | 1700                                      | 320–11,000                              | Norway    | Knutsen et al. (2019)          |
|                   | 10                | 17 (26)                             | 490                                       | 0.3–1300                                | Sweden    | Gobelius et al. (2018)         |
|                   | 5                 | 11 (14)                             | 82,100                                    | 7300–290,000                            | China     | Yan et al. (2015)              |
|                   | 9                 | 33 (57)                             | 42,900                                    | 3040–109,000                            | China     | Liu et al. (2022b)             |
|                   | 6                 | 17 (17)                             | 14,200                                    | 1800–43,300                             | China     | Huang et al. (2022)            |
|                   | 12                | 18 (18)                             | 4060                                      | 1270–7660                               | Singapore | Yin et al. (2017)              |
|                   | 5                 | 8 (9)                               | 6000                                      | 4200–11,000                             | Australia | Gallen et al. (2017)           |
| CDD LL            | 13                | 24 (26)                             | 9500                                      | 270–30,500                              | USA       | Chen et al. (2023)             |
| MSWIA LL          | 2                 | 11 (11)                             | 15,500                                    | 14,000–16,000                           | USA       | Solo-Gabriele et al. (2020)    |
|                   | 2                 | 9 (11)                              | 3100                                      | 2800–3400                               | USA       | Solo-Gabriele et al. (2020)    |
| MSW GC            | 31                | 26 (26)                             | 7300                                      | 39–54,500                               | USA       | Chen et al. (2023)             |
|                   | 21                | 26 (26)                             | 12,200                                    | 199–80,900                              | USA       | Chen et al. (2023)             |
| HW LL (Primary)   | 12                | 53 (92)                             | 19,000                                    | 3000–50,000                             | USA       | Smallwood et al. (2023)        |
|                   | 24                | 17 (28)                             | 68,000                                    | 570–377,000                             | USA       | California Water Boards (2023) |
| HW LL (Secondary) | 5                 | 13 (24)                             | 1800                                      | 25–3700                                 | USA       | California Water Boards (2023) |

(LL = landfill leachate; MSW = municipal solid waste; CDD = construction and demolition debris; MSWIA = MSW incineration ash; GC = gas condensate).

\* Gewurtz et al. (2013) do not provide detailed data to calculate average  $\sum$ PFAS.

**3.2.1.1.2. C&D landfills.** PFAS were detected in all C&D landfill leachate samples analyzed across three studies with  $\sum$ PFAS ranging from 270 to 30,500 ng L<sup>-1</sup> (weighted average 10,300 ng L<sup>-1</sup>). Solo-Gabriele et al. (2020) and Chen et al. (2023) found no significant difference in the total measured PFAS between leachate from MSW and C&D landfills. The analytical method used by Chen et al. (2023) included 18 terminal PFAS (PFAAs) and eight precursors (FASAs, FTCAs, and FTSs). The study, however, reported a significant difference in the fraction of  $\sum$ Terminal and  $\sum$ Precursor species between MSW and C&D landfill leachates. C&D leachate contained, on average, 86% terminal PFAS, while MSW leachate contained 64% terminal PFAS (Chen et al., 2023). This could be attributed to the different types of PFAS present in each waste stream and the type of biological activity prevalent in each landfill type. Because C&D landfills contain proportionally less food waste and more concrete and gypsum drywall, the prevailing landfill conditions result in higher pH leachate and proportionally more sulfate chemical species in the leachate as opposed to ammonia, which is typically at higher concentrations in MSW landfill leachate (Townsend et al., 1999). Further, due to those differences in leachate conditions, microbial differences result from presence of different carbon sources as well as electron donors and acceptors. Generally, sulfur-reducing bacteria are found in higher concentrations at C&D landfills due to higher amounts of sulfate, while methanogens are more prevalent at conventional landfills (Meyer-Dombard et al., 2020).

Fig. 2 includes the range of concentrations for PFAS with RSLs for MSW and C&D landfill leachate; average PFHxS concentrations were higher in C&D landfill leachate than in MSW landfill leachate, and PFBS concentrations were lower in C&D landfill leachate. Waste composition is highly variable between landfills as well as over time at an individual landfill, so, while limited studies may suggest potential sources of select PFAS in C&D debris (e.g., higher concentrations of PFHxS may be attributed to their use in carpeting and other building materials (Beeson et al., 2012; Jin et al., 2011)), generalizations about specific sources may not be appropriate. Gallen et al. (2017) measured nine terminal PFAS in Australian C&D landfill leachates (n = 5), reporting average  $\sum_9$ PFAS concentrations of 6000 ng L<sup>-1</sup> (compared to 6100 ng L<sup>-1</sup> in 94 MSW leachates from the same study).

Unlike MSW landfills, at the US federal level, C&D landfills do not require a bottom liner and leachate collection systems. This contributes to the lower number of studies describing PFAS in C&D relative to MSW landfill leachate and an increase in the probability of groundwater contamination from C&D compared to MSW landfills. Average

concentrations of PFOA, PFOS, PFNA, PFBS, and PFHxS, along with corresponding US EPA risk-based thresholds (HALs, MCLs, and RSLs), are included in Table 1. PFOA poses the most significant challenge as its concentration in C&D landfill leachate would have to be diluted by 19 to meet the tapwater RSL or by 287 to meet the US EPA proposed MCL.

**3.2.1.1.3. MSWI Ash monofills.** Solo-Gabriele et al. (2020) and Chen et al. (2023) found leachate from MSWI ash monofills to have lower  $\sum$ PFAS concentrations than leachate from MSW landfills. Solo-Gabriele et al. (2020) reported  $\sum_{11}$ PFAS in MSWI ash monofill leachates ranging from 2800 to 3400 ng L<sup>-1</sup> and inversely correlated with incineration temperature.  $\sum_{11}$ PFAS in leachate from MSWI ash that underwent incineration at 800 °C was almost three times higher than after incineration at 950 °C. The decrease indicates loss of measurable PFAS via mineralization (i.e., destruction), volatilization (i.e., air emission), or transformation to PFAS species which are not measured in standard analytical methods (e.g., products of incomplete combustion or PICs). Leachates from MSWI ash which had undergone incineration at 950 °C, still contained >2000 ng L<sup>-1</sup> of PFAS, indicating PFAS are not fully mineralized at these operating conditions. Liu et al. (2021b) reported substantially higher  $\sum_{21}$ PFAS in MSWI ash leachate from three facilities in China, with concentrations ranging from 127,000–450,000 ng L<sup>-1</sup>. The study did not report incineration temperatures or other operating conditions.

However, when MSWI ash was co-disposed with other wastes, such as MSW or biosolids,  $\sum$ PFAS concentration in the leachate was on par with that in MSW landfill leachate (Solo-Gabriele et al., 2020; Liu et al., 2022a). Liu et al. (2022a) found the co-disposal of a small fraction (e.g., 4%) of MSW, including biosolids, with MSWI ash resulted in leachate concentrations that were comparable to MSW landfill leachate, suggesting liquids are preferentially flowing through and leaching PFAS from the non-incinerated waste as opposed to the ash. While MSWI ash-derived leachates have lower concentrations of PFAS, these studies suggest care should be taken to dispose of MSW and MSWI ash separately, and more research is needed to understand the fate of PFAS during MSW incineration.

**3.2.1.1.4. Industrial landfills.** Unlined industrial landfills that received residuals from manufacturing PFAS and PFAS-containing products have been linked to contamination of local groundwater sources. Notable examples include the House Street landfill in Belmont, Michigan which received tannery waste (US EPA, 2022e); Crown Vantage landfills in Parchment, Michigan (MPART, 2020), that were used to dispose of paper mill waste from the production of laminated paper

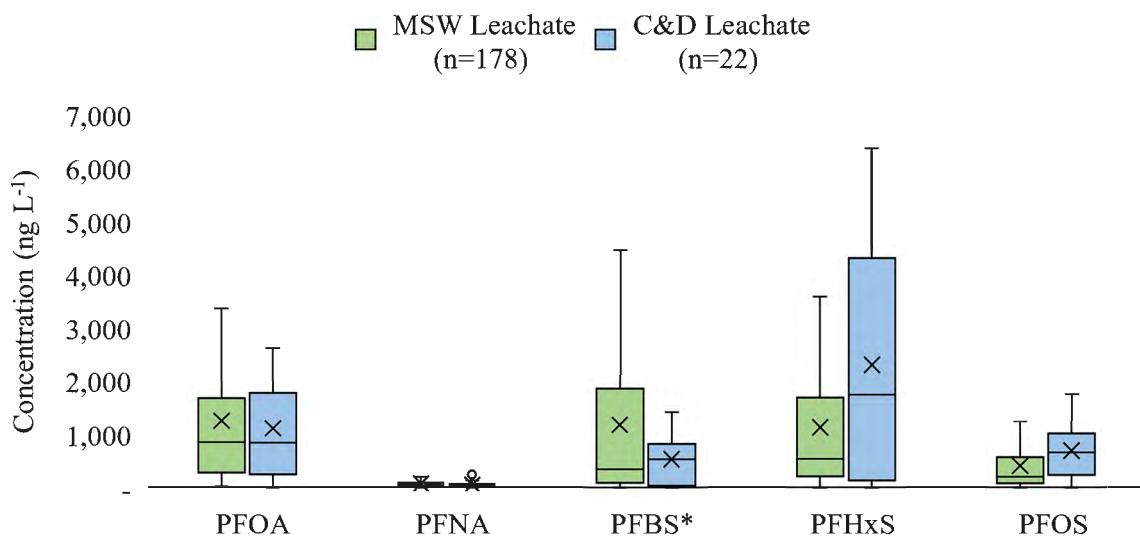


Fig. 2. Average concentrations of five PFAS with US EPA tapwater RSLs. Data from Gallen et al. (2017), Solo-Gabriele et al. (2020), and Chen et al. (2023).

\* Gallen et al. (2017) did not include PFBS analysis.

products; and the 3M Woodbury disposal site in Washington County, Minnesota, that was used to dispose of PFAS production waste. As part of this literature search, no leachate PFAS concentration data from industrial landfills in the US were located. However, Kameoka et al. (2022) measured PFAS in leachate from three industrial landfills in Japan;  $\sum_{17}\text{PFAS}$  concentrations averaged  $45,000 \text{ ng L}^{-1}$ .

**3.2.1.1.5. Hazardous waste landfills.** Although PFAS are not federally regulated as listed hazardous wastes, some solid wastes managed in Subtitle C hazardous waste landfills contain PFAS (as discussed in Section 2.1.2, e.g., chrome-plating sludge), while other PFAS-containing wastes may meet hazardous waste characteristic criteria (e.g., flammable, corrosive, etc.). Some hazardous waste landfills have also reported receipt of AFFF waste at their sites. No peer-reviewed studies have evaluated PFAS concentrations in leachate collected from hazardous waste landfills; however, California Water Boards have released PFAS concentrations for landfill leachate, including two hazardous waste landfills in California (California Water Boards, 2023). The data for these sites are included in the SI Table S7. Among 29 samples from the two sites,  $\sum_{24}\text{PFAS}$  and  $\sum_{28}\text{PFAS}$  concentration was as high as  $377,000 \text{ ng L}^{-1}$  (average  $68,000 \text{ ng L}^{-1}$ ), substantially higher than MSW, C&D debris, or MSWI ash landfill leachates (see Table 2). In the US, hazardous waste landfill disposal requires waste pre-treatment to minimize contaminant mobility – land disposal restrictions for hazardous waste are described in the Code of Federal Regulations (CFR; 40 CFR § 268). Leaching studies have shown minimal PFAS immobilization using traditional solidification techniques (Barth et al., 2021), which may explain elevated PFAS concentrations in the leachate.

US hazardous waste landfills must also use secondary leachate collection systems; California's database includes five samples of secondary hazardous waste landfill leachate from one site, with  $\sum_{24}\text{PFAS}$  averaging  $1800 \text{ ng L}^{-1}$  (see Table 2). Without exception, for all sampling locations with both primary and secondary leachate PFAS data, concentrations for individual and  $\sum_{24}\text{PFAS}$  were higher in the primary compared to the secondary leachate. While the absence of biological decomposition in hazardous waste landfills may minimize the microbially-mediated precursor transformation to PFAAs, waste treatment methods (e.g., lime treatment) may also impact transformation and partitioning, possibly oxidizing precursor PFAS. Hazardous waste pretreatment standards are designed to minimize traditional hazardous waste constituent leaching (e.g., lime treatment stabilizes metals and neutralizes acidic waste) and have not been optimized for PFAS stabilization; PFAS fate, transport, and transformations under hazardous waste pretreatment processes are not well understood. Because of the strict Subtitle C landfill operation requirements and the pre-treatment of wastes, leachate generation in these landfills is typically minimal, and any leachate which is produced is often managed as hazardous waste (i.e., not discharged to WWTP, as other landfill leachates often are).

### 3.2.1.2. Other factors impacting PFAS concentrations in leachate

**3.2.1.2.1. Waste age.** As waste degrades under the anaerobic conditions of biologically active landfills, the overall PFAS concentrations in the leachate and the ratio of the terminal to precursor species have been found to increase. Lang et al. (2017) reported leachate from waste older than ten years had significantly lower concentrations of PFNA, 8:2 FTCA, 5:3 FTCA, PFBS, MeFBSAA, and MeFOSAA than leachate from younger waste. These differences could be attributed to changes in the PFAS formulations in commercial products and/or the conversion of PFAA precursors. Liu et al. (2021a) measured PFAS in leachate from waste collection vehicles alongside leachate from the receiving MSW landfill. The study found significantly higher  $\sum_{51}\text{PFAS}$  concentrations in landfill leachate which had undergone further biological decomposition. Furthermore, Liu et al. (2021a) also reported a difference in PFAS profiles likely caused by the transformation of precursor PFAS in landfill environments.

**3.2.1.2.2. Leachate quality.** Although most PFAS behavior and

solution chemistry studies focus on remediation technologies, generalizations regarding PFAS phase partitioning also apply to landfill leaching (Z. Du et al., 2014). Comparatively, fewer studies have explored PFAS partitioning in the context of leachate chemistry. In a landfill simulator study, Allred et al. (2015) observed increases in longer-chain PFCA and perfluoroalkyl sulfonic acids (PFSA) concentrations when biodegradation reached the methanogenic stage. At this stage, increased methanogenic and secondary fermentation and decreased volatile fatty acid concentrations from the acidogenic stage result in increased pH, more neutral pH, which is theorized to deprotonate waste surfaces, resulting in less sorption of PFAS to the degrading organic matter. This theory is supported by the results described by Solo-Gabriele et al. (2020), where a significant positive correlation was reported between PFAS concentrations and increasing leachate pH. This effect has also been observed in several previous landfill leachate sampling studies (Benskin et al., 2012; Gallen et al., 2017; Hamid et al., 2018; Yan et al., 2015).

In addition to partitioning behavior, the PFAS profile of landfill leachate is a function of PFAA precursor transformation resulting from biodegradation. Biological activity is catalyzed by landfill moisture, resulting in higher landfilled waste temperatures and more PFAS transformation. In a study of WWTP biosolids pathogen removal, precursor transformation and apparent increases in  $\sum_{92}\text{PFAS}$ , driven by increased PFAA content, resulted after aerobic composting and increased diPAP concentrations from heat treatment (Thompson et al., 2023b). Based on a nationwide study of 95 leachate samples collected from 18 landfills, leachate from MSW landfills in US regions with high annual precipitation showed significantly greater  $\sum_{19}\text{PFAS}$  than comparable landfills in arid locations (Lang et al., 2017); see Table 2 for all US-based studies included in this review. Further, leachate generation volume is significantly higher in regions that experience more precipitation. As a result, landfills in arid regions are estimated to contribute <1% of the nationwide landfill leachate PFAS mass load (Lang et al., 2017). When studies have evaluated the short-term impacts of precipitation on PFAS in landfill leachate, however, leachate PFAS concentration decreased within a day of a precipitation event due to dilution (Benskin et al., 2012; Gallen et al., 2017). Normalization of PFAS concentrations to bulk parameters such as chloride or total dissolved solids may be able to account for such dilution.

### 3.2.2. PFAS partitioning to the gas phase

MSW contains a proportionally more biodegradable organic matter which undergoes anaerobic decomposition in landfill environments compared to other waste streams (e.g., C&D). The decomposition of organic matter produces MSW LFG, which is, on average, about 50% methane ( $\text{CH}_4$ ), and 50% carbon dioxide ( $\text{CO}_2$ ), with a small fraction consisting of other gaseous and volatile constituents (Wang et al., 2021). LFG at MSW landfills is collected and managed according to the requirements of the US EPA New Source Performance Standards (US Clean Air Act, 40 CFR § 60). According to the US EPA's Landfill Methane Outreach Program (LMOP) August 2022 database, 1230 of the 2635 MSW landfills in the US have gas collection systems in place, and 1157 have flares in place (US EPA, 2022a). C&D LFG is rarely collected in the US, as C&D landfills contain less biodegradable organic matter and produce less LFG than MSW landfills. Additionally, C&D LFG contains proportionally more  $\text{H}_2\text{S}_{(\text{g})}$  produced by sulfur-reducing bacteria and the decomposition of gypsum disposed of as drywall.

Gas generation and composition at other landfill types has yet to be the subject of significant research. MSWI ash monofills are not expected to generate LFG because there is minimal biodegradable matter in the ash; however, the co-disposal of WWTP biosolids, MSW, or any degradable organic matter with MSWI ash will produce biogas as a result of decomposition. Gas generation at industrial landfill sites is primarily a function of the type of waste deposited. Organic waste like pulp and paper mill sludges will likely generate gas requiring management. In general, Subtitle C hazardous waste landfills in the US do not contain

putrescible organic waste and do not generate biogas.

**3.2.2.1.1. PFAS in MSW landfill gas.** PFAS volatilization and release from MSW landfills within the gaseous phase is receiving an increased focus driven by advances in volatile PFAS measurement (Riedel et al., 2019) and an improved understanding of PFAS chemistry. The partitioning coefficients (e.g., Henry's constant) for ionizable PFAS are significantly lower than neutral PFAS (Abusallout et al., 2022), making ionizable PFAS less likely to volatilize under typical MSW landfill conditions. Experimental measurement of PFAS vapor pressures similarly suggests FTOHs (i.e., neutral PFAS) are more readily volatilized than PFCAs (i.e., ionizable PFAS) and that vapor pressure decreases logarithmically with carbon chain length in homologous species (M. Zhang et al., 2020). Measurement and data of PFAS in actual MSW LFG are still minimal.

In a 2007 analysis of landfills that accepted PFAS-containing industrial wastes, the MPCA detected several PFAS (12 PFAAs and perfluorooctane sulfonamide, PFOSA) in MSW LFG with  $\sum_{13}$ PFAS ranging from 4.1 to 18.7 ng m<sup>-3</sup> (MPCA, 2010). Titaley et al. (2023) measured neutral PFAS in LFG of three active MSW landfills (n = 12 samples) and reported concentrations of four n:2 FTOHs (n = 6, 8, 10, and 12), one fluorotelomer acrylate (6:2 FTA), and one fluorotelomer olefins (12:2 FTO). Concentrations for individual PFAS range from 270 to 4900 ng m<sup>-3</sup>, and the total measured neutral PFAS for each landfill was, on average, between 4600 and 14,000 ng m<sup>-3</sup> (weighted average across all samples: 10,200 ng m<sup>-3</sup>). Smallwood et al. (2023) reported FTOH in LFG condensate, which, when normalized to gas volume, was three orders of magnitude lower than the gaseous phase concentrations reported by Titaley et al. (see SI Table S8 for calculations), indicating FTOHs preferentially partition to the gas phase; FTOHs may transform in the atmosphere into PFCAs, such as PFOA, which have known and suspected toxic effects.

**3.2.2.1.2. PFAS in C&D landfill gas.** While no data exist on the concentration of PFAS in C&D LFG, it can be conservatively assumed, based on data from MSW LFG measurements, that PFAS also leave C&D landfills via gas effluent. As previously described, PFAS-containing wastes are disposed of at C&D landfills, and it is highly likely C&D debris contains volatile PFAS, such as FTOHs, which readily transform into FTCAs and PFCAs as a result of biodegradation and environmental oxidation, respectively. Lower rates of biological activity in C&D landfills may result in slower biodegradation of PFAS like FTOH (and other volatile precursors) may persist longer in C&D compared to MSW landfills and therefore have more opportunity to volatilize and leave the landfill via LFG. This is likely offset by the lower volume of LFG generated overall at C&D landfills compared to MSW. Nonetheless, this read-across should be validated by experimental data.

### 3.3. Fate of PFAS in traditional landfill leachate and gas management systems

Most landfills compliant with New Source Performance Standards (Clean Air Act) and RCRA must capture gas effluent and leachate to minimize environmental impacts. Leachate is often intercepted using a low-permeability bottom liner made of high-density polyethylene, collected, and may be transported off-site to a WWTP, disposed of using deep well injection, or otherwise managed and treated on-site.

PFAS interactions with low-permeability landfill liners have been the subject of limited studies. Most landfill liners are constructed from polyethylene geomembranes. Laboratory studies of PFAS diffusion through linear low-density polyethylene report below detection diffusion rates (Di Battista et al., 2020). Diffusion through high-density polyethylene has yet to be reported but maybe even lower due to differences in material structure. Landfill liner integrity – the absence of flaws or holes – is the most critical factor in preventing PFAS

transmission through geomembrane and composite liners (Di Battista et al., 2020). An analysis of landfill liner performance reported median leakage rates of 44 and 33 L ha<sup>-1</sup> day<sup>-1</sup> for geomembrane and composite liners, respectively, with an overall liner collection efficiency of 98% (Jain et al., 2023). Compacted clay liners, which are more common in older landfills and C&D landfills, do not adsorb PFAS, which are reported to pass through bentonite clay at the same rate as other mobile leachate constituents like chloride (Li et al., 2015). PFAS profile, leachate quality, and soil characteristics all play a role in soil interaction, and decisions should be made on a site-specific basis (Li et al., 2019; Gates et al., 2020; Mukhopadhyay et al., 2021).

Management of leachate in the US is dependent on climate – in dry regions, leachate generation is minimal, and many facilities use atmospheric evaporation. In contrast, in wet regions, leachate management presents a significant challenge (US EPA, 2021c). A nationwide survey found approximately 60% of US Subtitle D landfills conveyed their leachate to WWTPs for off-site treatment, 28% recirculated leachate or use other techniques resulting in no necessary leachate treatment, and 12% used on-site treatment (US EPA, 2021c). A breakdown of on-site leachate treatment strategies is included in SI Fig. S3. Traditional leachate treatment typically targets non-PFAS leachate constituents of concern, such as ammonia and chemical oxygen demand (COD). The fate of PFAS in existing leachate treatment systems and wastewater treatment systems that manage leachate have been the subject of several studies and have been reviewed previously (Appleman et al., 2014; Lu et al., 2023; Meegoda et al., 2020; Travar et al., 2020; Zhang et al., 2022). To generalize, the treatment of ammonia and COD relies on chemical or biological oxidation, which do not effectively treat PFAS but often have the unintended effect of transforming precursor PFAS to terminal PFAS (US EPA, 2021b). Furthermore, during treatment, PFAS may partition into solids (e.g., biosolids) to a limited extent, which results in additional management challenges (Thompson et al., 2023b). Studies have recommended PFAS removal prior to such treatment (Lott et al., 2023). The targeted treatment of PFAS via removal or destruction in landfill leachate has been the subject of multiple reviews (Bandala et al., 2021; Berg et al., 2022; Lu et al., 2023; Ross et al., 2018; Travar et al., 2020) which have thoroughly discussed the effectiveness of different technologies and which are, here, summarized in Table 3.

PFAS separation technologies typically rely on adsorption over materials, such as activated carbons and ion exchange resins (US EPA, 2022c; Chow et al., 2022; Crone et al., 2019; Appleman et al., 2013), the use of high-pressure membrane separation (US EPA, 2022c; Lipp et al., 2010; Steinle-Darling and Reinhard, 2008), and newer technologies such as ozo- and foam-fractionation with the aim of concentrating the PFAS into a smaller volume of either a solid phase or concentrated liquid residual to either be disposed or destroyed via a subsequent high-energy destructive treatment method (Du et al., 2021; Labiadh et al., 2016). Several novel technologies are being investigated for the destructive treatment of landfill leachate – most require large amounts of energy in the form of chemical reactions or localized high temperatures to break the C–F bond. MSWI for energy recovery is not currently optimized to target PFAS destruction. Additional research is ongoing to define the conditions needed for PFAS destruction in MSWI and other incineration approaches, such as sewage sludge incineration.

Flaring and combustion are common LFG management techniques. Flaring is typically carried out in an open (candle) or enclosed flare. Combustion processes can generate energy on-site (e.g., a combustion engine) or off-site in a gas-fired power generation system. MSW LFG regulations target the destruction of nonmethane organic compounds (NMOCs), not PFAS. Flares generally operate at ~650 °C to 850 °C and temperatures in combustion engines or boiler systems could be lower (Wade, 2022). PFAS separation treatment has not been applied to LFG, however, laboratory-scale thermal PFAS destruction experiments indicate that temperatures higher than 1000 °C are necessary to achieve the mineralization of PFAS (Winchell et al., 2021). MSW LFG flare temperatures and the time that gaseous PFAS are in the presence of high

**Table 3**

Summary of treatment methods for PFAS in landfill leachate (Bandala et al., 2021; Berg et al., 2022; Lu et al., 2023; Ross et al., 2018; Travar et al., 2020; Wei et al., 2019).

|                          | Technology                    | Pros                                                                                                                                                                                                                                                                                                                                      | Cons                                                                                                                                                                                                                                                                                                    | Matrix       | References                                                                                                                                                               |
|--------------------------|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Separation technologies  | Activated carbon (GAC, PAC)   | <ul style="list-style-type: none"> <li>High maturity level</li> <li>Highly effective for long-chain PFAS</li> </ul>                                                                                                                                                                                                                       | <ul style="list-style-type: none"> <li>Generates large quantities of spent sorbent that need additional treatment and disposal</li> </ul>                                                                                                                                                               | GW           | Busch et al. (2010); McCleaf et al. (2017), Pan et al. (2016), Ross et al. (2018); Bao et al. (2014), Pan et al. (2016); Malovanyy et al. (2023)                         |
|                          | Ion exchange resins           | <ul style="list-style-type: none"> <li>High maturity level</li> <li>Can remove compounds such as GenX</li> </ul>                                                                                                                                                                                                                          | <ul style="list-style-type: none"> <li>Needs secondary treatment and disposal</li> </ul>                                                                                                                                                                                                                | GW, LL       | Gao et al. (2015); Dixit et al. (2021); McCleaf et al. (2017); Ross et al. (2018); Boyer et al. (2021); Park et al. (2020); Ellis et al. (2022); Malovanyy et al. (2023) |
|                          | Membranes (RO, UF, NF)        | <ul style="list-style-type: none"> <li>High maturity level and commonly practiced</li> <li>2-stage RO most effective on raw leachate</li> </ul>                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>Membrane fouling</li> <li>Secondary stream with high PFAS concentrations and volume requires treatment</li> <li>UF might not be effective</li> </ul>                                                                                                             | GW, LL       | Das and Ronen (2022); Enzminger et al. (1987); Wei et al. (2019); Ross et al. (2018); Boo et al. (2018); Malovanyy et al. (2023)                                         |
|                          | Foam/ozofractionation         | <ul style="list-style-type: none"> <li>High maturity level and commercially available pilot-scale technology</li> <li>Potentially low cost</li> <li>Highly effective method</li> <li>Can be used for regeneration of spent materials</li> </ul>                                                                                           | <ul style="list-style-type: none"> <li>Pretreatment of leachate might be required</li> <li>Secondary treatment of concentrated PFAS required</li> <li>As a standalone method, not practical for large volumes of leachate</li> <li>Uses additional chemicals for treatment</li> </ul>                   | GW, AFFF, LL | Smith et al. (2022); Robey et al. (2020); Malovanyy et al. (2023)                                                                                                        |
|                          | Incineration                  |                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                         |              |                                                                                                                                                                          |
|                          | Chemical Oxidation            | <ul style="list-style-type: none"> <li>Controllable by varying pH and temperatures</li> </ul>                                                                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>Low effectiveness of removal</li> <li>Needs to be paired with other methods such as UV for higher effectiveness</li> </ul>                                                                                                                                       | LL           | Abu Amr et al. (2013); Lin et al. (2012)                                                                                                                                 |
| Destruction technologies | Electrochemical               | <ul style="list-style-type: none"> <li>98–99.7% effectiveness demonstrated</li> <li>Operates at ambient temperatures</li> <li>No chemicals required</li> <li>Lower energy consumption compared to incineration</li> </ul>                                                                                                                 | <ul style="list-style-type: none"> <li>Expensive electrode materials</li> <li>Perchlorates could be formed</li> </ul>                                                                                                                                                                                   | LL           | Labiadh et al. (2016); Du et al. (2021); Gomez-Ruiz et al. (2017); Witt et al. (2020); Krause et al. (2021)                                                              |
|                          | Photocatalysis                | <ul style="list-style-type: none"> <li>94–99% degradation reported</li> <li>Can also potentially mineralize PFAS</li> </ul>                                                                                                                                                                                                               | <ul style="list-style-type: none"> <li>Slow kinetics</li> <li>Lab-scale testing only</li> <li>Difficult to scale for larger volumes</li> </ul>                                                                                                                                                          |              | Esfahani et al. (2022)                                                                                                                                                   |
|                          | Sonolysis                     | <ul style="list-style-type: none"> <li>Can destroy short-chain and long-chain molecules</li> <li>Effective for high concentration samples</li> <li>Can be combined with chemical oxidation to lower costs</li> <li>Can be used to regenerate GACs</li> <li>Catalytic microwave treatment could result in ~65–67% effectiveness</li> </ul> | <ul style="list-style-type: none"> <li>High capital costs</li> </ul>                                                                                                                                                                                                                                    |              | Moriwaki et al. (2005); Vecitis et al. (2008); Babu et al. (2016)                                                                                                        |
|                          | Microwaves                    |                                                                                                                                                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>Expensive for large-scale use</li> </ul>                                                                                                                                                                                                                         |              | Gagliano et al. (2021); Lee et al. (2010b); Liu et al. (2020)                                                                                                            |
|                          | Subcritical water oxidation   | <ul style="list-style-type: none"> <li>Effective for short-chain PFAS</li> </ul>                                                                                                                                                                                                                                                          | <ul style="list-style-type: none"> <li>Additional chemicals (e.g., zero-valent iron) needed for higher effectiveness</li> <li>Slower kinetics</li> <li>Full fluorine balance needed</li> </ul>                                                                                                          |              | Hori et al. (2006)                                                                                                                                                       |
|                          | Supercritical water oxidation | <ul style="list-style-type: none"> <li>High maturity and close to commercialization</li> <li>Low residence times required</li> </ul>                                                                                                                                                                                                      | <ul style="list-style-type: none"> <li>High-pressure and temperature processes can be energy intensive</li> </ul>                                                                                                                                                                                       | GW, AFFF, LL | Pinkard et al. (2021); Hori et al. (2006); Krause et al. (2022)                                                                                                          |
|                          | Wet Air Oxidation             | <ul style="list-style-type: none"> <li>No demonstrated benefits for PFAS treatment</li> </ul>                                                                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>Converts FTOH precursors to PFCAs</li> <li>Laboratory demonstrations only and thus low technology readiness level</li> </ul>                                                                                                                                     | LL           | Travar et al. (2020)                                                                                                                                                     |
|                          | Biological processes          | <ul style="list-style-type: none"> <li>Limited aerobic and anaerobic degradation of PFOS by bacteria and fungi reported</li> </ul>                                                                                                                                                                                                        | <ul style="list-style-type: none"> <li>Slow kinetics</li> <li>Longer-chain PFAS converted to shorter-chain; no mineralization</li> <li>Unlikely to be effective</li> <li>Does not result in a concentrated PFAS stream that can be adequately managed</li> <li>Environmental release of PFAS</li> </ul> |              | Berhanu et al. (2023); Huang and Jaffé (2019)                                                                                                                            |
|                          | Constructed wetlands          | <ul style="list-style-type: none"> <li>No demonstrated benefits for PFAS treatment</li> </ul>                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                         | LL           | Yin et al. (2017, 2019); Awad et al. (2022); Lott et al. (2023)                                                                                                          |
|                          |                               |                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                         |              |                                                                                                                                                                          |

(GAC = granular activated carbon; PAC = powder activated carbon; RO = reverse osmosis; UF = ultrafiltrations; NF = nanofiltration; GW = groundwater; LL = landfill leachate; AFFF = aqueous film-forming foam).

temperatures are too low to completely mineralize PFAS, but may result in the transformation of volatile PFAS into products of incomplete combustion (PICs). Notably, several PICs have been identified as significant greenhouse gases (Ahmed et al., 2020; Hong et al., 2013; Longendyke et al., 2022).

#### 4. Environmental impact of PFAS emissions from landfills

Waste-derived PFAS may be emitted from landfills through multiple pathways, primarily in leachate or LFG effluent. While most RCRA-compliant landfills are operated to minimize environmental impacts, controls have yet to be designed to manage PFAS, and there is a subclass of small landfills in the US that are not required to install bottom liners as they are exempt from RCRA requirements (40 CFR § 258.1(f)(1)).

PFAS may be released into the atmosphere via fugitive gas emissions or gas flares. No data were found on PFAS concentrations in the ambient air surrounding C&D landfills, hazardous waste landfills, or industrial landfills; however, PFAS concentrations in the ambient air close to MSW landfills have been the subject of studies in the US, Germany, and China. Ahrens et al. (2011) reported average total FTOH concentrations of 2.6 and 26 ng m<sup>-3</sup> at two US MSW landfills, representing 93% and 98% of total gas phase PFAS, with the remaining fraction consisting of perfluoroalkane sulfonamide (FASAs), perfluoroalkane sulfonamido ethanols (FASEs), and PFAAs. Weinberg et al. (2011) reported average total FTOH concentrations at two German landfill sites of 0.086 and 0.271 ng m<sup>-3</sup>, representing 80% and 92% of total gas phase PFAS. Tian et al. (2018) measured PFAS in air sampled on-site at two landfills as well as downwind. The PFAS profile of the on-site air samples was more evenly split among classes. Total FTOHs were 0.61 and 2.1 ng m<sup>-3</sup> at the two sites, representing 42% and 76% of  $\sum_6$ PFAS, with PFAAs representing the bulk of the remaining fraction. PFAS concentrations downwind of the two landfill sites were lower than on-site but elevated relative to control sites, indicating atmospheric transport of PFAS. Lower concentrations downwind may indicate dilution or deposition of volatile PFAS. Neutral PFAS readily transform in the environment – studies have shown the degradation of FTOHs into PFCAs via photooxidation (Esfahani et al., 2022; Martin et al., 2006). Tian et al. (2018) reported elevated neutral and ionizable PFAS in dry deposition samples on-site and downwind of landfills, driven primarily by PFBA and PFOA. Ahmadireskety et al. (2020) reported PFAS concentrations in landfill cover soils of approximately 8 µg kg<sup>-1</sup>, similarly driven by PFCAs.

Deposition of PFAS from landfill-impacted air may also contribute to PFAS measured in surface water on landfill sites. Chen et al. (2023) reported  $\sum_{26}$ PFAS concentrations in stormwater at MSW landfill sites averaging 470 ng L<sup>-1</sup>, significantly lower than leachate concentrations from the same study but significantly higher than groundwater samples, which averaged 140 ng L<sup>-1</sup> of  $\sum_{26}$ PFAS. PFAS may be present in both surface and groundwater due to leachate contamination. At the same time, particulate transport from the working face or atmospheric transport and deposition of PFAS are more likely to impact surface water. The MPCA (2010) reported PFAS contamination in groundwater impacted by landfills accepting PFAS-laden industrial waste. Hepburn et al. (2019) measured PFAS and other landfill leachate indicators in groundwater impacted by legacy landfills in Australia, where PFOA represented >10% of total PFAAs, likely associated with legacy landfills.

Using the landfill liner collection efficiency reported by Jain et al. (2023) and overall leachate leakage rate of 1.9% with the leachate generation rate reported in Lang et al. (2017) (61 billion L year<sup>-1</sup>), approximately 1.2 billion L of MSW landfill leachate enter the groundwater directly as a result of liner imperfections every year (14.3 kg of total PFAS using the average  $\sum_{19}$ PFAS from Lang et al. (2017)). This represents a conservative estimate, as Lang et al. (2017) note that most but not all landfills contributing to the total estimated leachate generation are lined. Although C&D leachate generation rates are not readily available, using leachate generation rates calculated for 17 MSW landfills in six US states, Jain et al. (2023) reported an average collection rate

of 6900 L ha<sup>-1</sup> day<sup>-1</sup>. Assuming similar leachate generation rates for C&D landfills, this corresponds to approximately 2.5 million L of C&D leachate entering the groundwater per hectare of C&D landfill annually, representing a  $\sum$ PFAS mass of 26 g of PFAS per hectare of C&D landfill (see Table S9 in the SI for more calculation information). In 2012, the US EPA inventoried 1504 active C&D landfills (US EPA, 2012).

In the US, most landfill leachate generated from RCRA-permitted landfills is managed off-site (again, many C&D landfills are not required to collect leachate and thus operate without a bottom liner). This represents a significant flux of PFAS leaving the landfill. Multiple studies in the US and Australia have estimated the contribution of PFAS to municipal WWTP from landfill leachate and the environmental impact of PFAS in WWTP effluent. Masoner et al. (2020) estimated the PFAS load in landfill leachates and receiving WWTPs. They reported that landfill leachate while representing, on average, <2% of WWTP influent by volume across three sites, contributed 18% of influent PFAS. Gallen et al. (2017) reported similar contributions of PFAS to WWTPs from landfill leachates. PFAS are not effectively treated with traditional WWTP processes and are released to the environment via WWTP liquid effluent, land-applied biosolids, landfills, and possibly incineration of biosludge (Barisci and Suri, 2021; Coggan et al., 2019; Gallen et al., 2018; Helmer et al., 2022; Tavasoli et al., 2021).

#### 5. Estimate of US MSW landfill PFAS mass balance

Estabrooks and Zemba (2019) evaluated landfill PFAS mass balance at an MSW landfill in Vermont, identifying the PFAS load from targeted waste types suspected to contain PFAS, not including residential MSW, and found that approximately 7% of the PFAS load entering landfills is emitted via leachate annually, and hypothesize the majority of PFAS remain in the waste mass within the landfill. Coffin et al. (2022) propose an estimated extractable  $\sum$ PFAS load in MSW entering landfills of 50 ng g<sup>-1</sup> based on the findings in Liu et al. (2022a). This, combined with US EPA estimation of landfilled MSW in 2018 (the most recent year for which MSW generation data is available for the US), corresponds to 6600 kg of extractable PFAS entering MSW landfills in 2018 with MSW (US EPA, 2020b). Biosludge and biosolids also contribute a significant fraction of PFAS loading in MSW landfills. Using  $\sum_{92}$ PFAS in treated biosolids reported by Thompson et al. (2023b) and biosolids management statistics reported by NEBRA (2022), the 1.74 million dry metric tons of biosolids landfilled each year contribute an additional estimated 850 kg of PFAS to MSW landfills. Based on our calculations, a conservative estimate of 7480 kg of extractable PFAS entered US MSW landfills in 2018. This estimate does not include PFAS polymers.

As described earlier, PFAS can be emitted from landfills via the gaseous and liquid phase. MSW landfills in the US collect approximately 93.5 million m<sup>3</sup> of gas daily according to the US EPA LMOP database. This translates to nearly 1 kg of neutral PFAS emitted via MSW LFG per day (347 kg annually) based on the concentrations reported by Titaley et al. (2023). The US EPA estimates MSW LFG collection efficiency of approximately 75% (US EPA, 2020a), indicating an additional 31.2 million m<sup>3</sup> of LFG are released via fugitive emissions from MSW landfills annually. Leachate generation in the US, estimated by Lang et al. (2017), is 61.1 billion L year<sup>-1</sup> which corresponds to 750 kg of PFAS emitted from MSW landfills via leachate annually (using the weighted average  $\sum$ PFAS concentration of 12,300 ng L<sup>-1</sup> calculated in this study). See Fig. 3 for a flowchart representing PFAS sources, controlled emissions, and uncontrolled emissions to the environment corresponding to MSW landfills, and Fig. 4 for a graphical presentation of the fraction of PFAS entering landfills from MSW and biosolids and corresponding emissions; the majority of PFAS entering landfills remain in the waste (84% annually) and significant mass of PFAS have likely accumulated since PFAS use in consumer products began. Detailed calculations for Fig. 3 are included in the SI Table S10.

One can estimate the total PFAS released via the gaseous phase per ton of MSW based on the potential methane generation capacity (L<sub>0</sub>) of

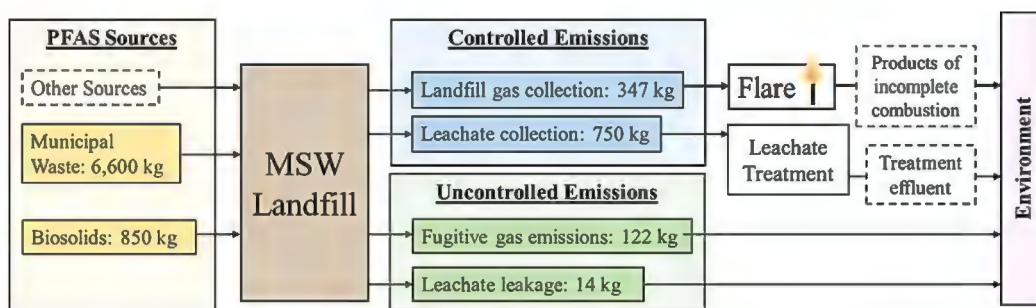


**Fig. 3.** Flowchart depiction of annual  $\Sigma$ PFAS loading and release at MSW and C&D debris landfills based on current understanding in the literature. Dashed lines represent PFAS streams which have not been quantified to any extent in the literature.

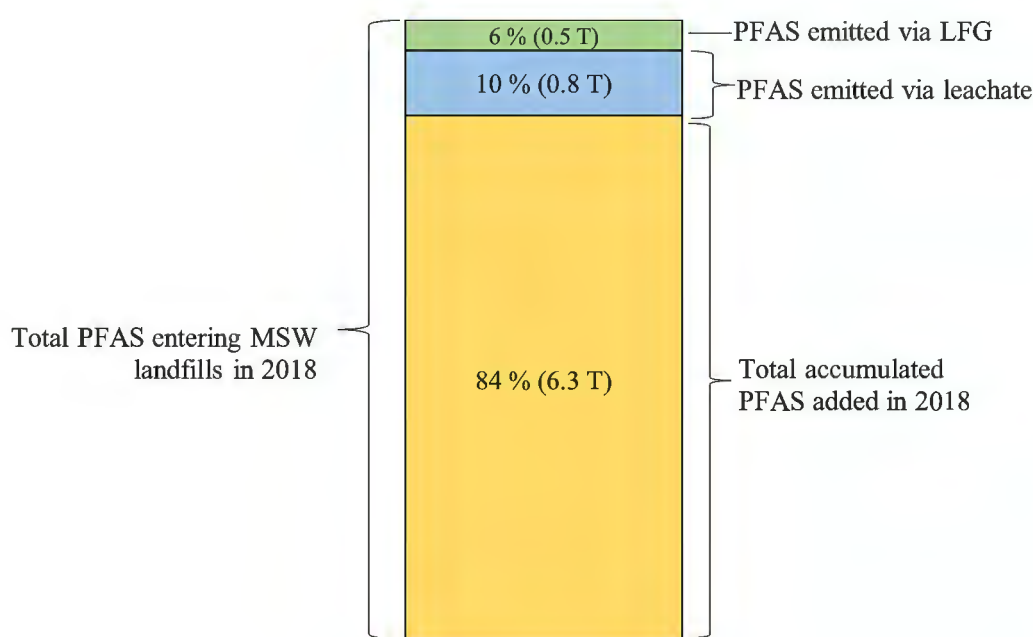


**Fig. 4.** Estimated PFAS mass balance for US MSW landfills.

MSW. Jain et al. (2021) estimated MSW methane emissions of 68 m<sup>3</sup> of methane per metric ton (Mg) of waste, or approximately 136 m<sup>3</sup> of LFG per Mg of waste; using these values and the Titaley et al. (2023) LFG PFAS concentrations suggest 1.38 mg of PFAS are released, cumulatively, via LFG for every Mg of MSW.

### 5.1. Limitations

The estimated PFAS mass loading and emissions presented here are based on multiple assumptions and, in some cases, limited data, resulting in significant uncertainty. We have not provided additional data quality assurance in this review process. A small number of studies have explored changes in landfill leachate PFAS profile over time, and no studies have looked for similar relationships in LFG; for this critical review, it was assumed that  $\Sigma$ PFAS reported in leachate and gas are representative of a range of waste ages and stages of decomposition and, overall, are expected to remain consistent over time. Even fewer studies have looked at C&D debris landfills in the US, and those studies are limited to Florida landfills. This critical review of previous analyses provides perspective, not precise values, which should be derived through additional empirical studies.

## 6. Conclusions and data gaps

The bulk of studies of PFAS in solid waste and landfills focus on MSW landfill leachate, with comparatively fewer studies estimating overall PFAS loading in other types of landfill leachate, in the solid waste itself, or gaseous effluent. Regardless of the type of landfill, in all studies across all locations, PFAS were quantified in all leachate samples. PFAS concentrations in leachates vary across studies, which may be a function of waste type, leachate qualities, climate, and the analytical method.

US MSW and C&D landfill leachates have similar  $\Sigma$ PFAS concentrations. However, C&D leachate contains proportionally more terminal PFAS. This is likely due to the PFAS present and the conditions within each landfill type. Concentrations of the five PFAS which have been the subject of proposed US EPA regulations (i.e., PFBS, PFHxS, PFOS, PFOA, and PFNA) consistently exceed US EPA tapwater RSLs in both MSW and C&D landfill leachates by a factor as high as 20 (PFOA) and in HW landfill leachates by a factor as high as 104 (PFOS); as presented in Table 1 and Fig. 2.

MSWI ash leachates have lower PFAS concentrations than other leachates, however, co-disposal of ash with other wastes results in disproportionately high PFAS concentrations in leachate. To minimize PFAS leaching from MSWI ash landfills, care should be taken to dispose of unburned waste which contains higher concentrations of PFAS separately from MSWI ash. No peer-reviewed studies have reported

PFAS concentrations in effluent from hazardous waste (Subtitle C) landfills, although hazardous waste management methods are likely to reduce PFAS leaching. Since some hazardous waste landfills likely accept PFAS-laden industrial waste at relatively high levels, it would be helpful to have more information on effluent generated from these facilities.

Traditional leachate treatment methods that use oxidation (e.g., a treatment that targets ammonia, COD) are likely to increase the transformation rate of precursor PFAS to terminal PFAS, such as regulated PFAAs. Treatment that relies on volatilization, such as evaporation, likely contributes significant quantities of PFAS to the atmosphere and surrounding environment, increasing off-site transport. Separating PFAS from leachate prior to additional treatment would avoid these issues. Though there are many aqueous treatment technologies for the targeted removal or destruction of PFAS, few have been tested for effectiveness on landfill leachate. Those tested on leachate and have shown promise include supercritical water oxidation, electrochemical oxidation, reverse osmosis, and foam separation. Assuming treatment efficacy is comparable across PFAAs, reducing PFOA concentration to its limit (e.g., MCL) will reduce all other PFAS to below their respective limits. PFAS treatment of liquid wastes often produces a secondary residual waste requiring additional management.

PFAS are expected to be present in LFG as a product of volatilization and the anaerobic decomposition of biodegradable waste but have been quantified only in MSW LFG. PFAS have not been measured in C&D LFG. However, based on PFAS profiles in C&D landfill leachate, similar PFAS concentrations are likely present in C&D LFG, although LFG generation rates from C&D debris is lower. To reduce gaseous emissions of PFAS, biodegradable waste should be disposed of separately from other PFAS-containing waste. Data do not exist on the effectiveness of PFAS destruction from LFG combustion within flares and internal combustion engines or PFAS removal from LFG to RNG conversion processes. However, the temperatures reached in LFG flares are expected to transform volatile PFAS into terminal PFAS and possible PICs, with minimal mineralization.

Based on our estimate of the PFAS entering and leaving landfills, significant quantities of PFAS are emitted in both LFG and leachate; however, the bulk of PFAS remains within the waste mass on a per-year basis (see Fig. 3). This suggests landfills will be a source of PFAS emissions for the foreseeable future. Studies have demonstrated down-gradient impacts on groundwater from landfills. C&D landfills pose the highest risk of environmental contamination since they are not required (at the federal level) to install liners to collect leachate. Even among lined landfills, the average liner collection efficiency is approximately 98%, corresponding to an annual flux of 14.3 kg PFAS entering groundwater via liner imperfections.

Elevated PFAS concentrations were measured in ambient air at landfills across several studies. The highest concentrations were found among FTOHs, which transform into PFAAs in the environment. Atmospheric PFAS may deposit and contribute to soil and surface water concentrations. Even if LFG collection systems were equipped to operate at temperatures and residence times sufficient to destroy PFAS, current MSW LFG collection efficiency is only 75%, and landfills not required to collect LFG will continue to emit PFAS into the atmosphere. The fate of PFAS in LFG that passes through landfill cover soil should be analyzed in future studies.

This review has identified several data gaps for PFAS emissions from US landfills. Data are needed from hazardous waste landfill sites and relevant industrial waste landfills. Furthermore, US C&D landfill leachate data are limited to Florida landfills, and additional efforts should be made to collect information from other states. C&D waste streams may vary due to regional construction requirements. The measurement of PFAS in LFG and other gaseous emissions is an area of emerging study. More research is needed on both controlled and uncontrolled landfill gaseous emissions. A closer evaluation of the fate of PFAS during leachate treatment and LFG management is needed to help

decision-makers guide the solid waste community. Geomembrane liners are the most effective tools for the protection from and collection of PFAS-containing liquids, such as landfill leachate. More research is needed to understand long-term interactions between PFAS and liner systems, especially in complex matrices such as landfill leachate. More research is needed to evaluate the long-term implications of PFAS in the landfill environment since the bulk of PFAS remains within the solid waste mass. This review focused on landfilling as a management option for solid waste; evaluation of PFAS fate during other solid waste management processes (e.g., anaerobic digestion, thermal treatment, composting, and recycling) is needed.

#### CRediT authorship contribution statement

**Thabet Tolaymat:** conceptualization, approach, methodology, writing-reviewing, editing, funding, **Nicole Robey:** data curation, methodology, calculations, writing-original draft, writing and editing. **Max Krause:** writing and editing, **Judd Larson, Keith Weitz, Sameer Parvathikar:** data curation, original draft preparation, editing, **Lara Phelps, William Linak, Susan Burden, Tom Speth, Jonathan Krug:** writing and editing

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Data availability

Data will be made available on request.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2023.167185>.

#### References

- Abu Amr, S.S., Aziz, H.A., Adlan, M.N., 2013. Optimization of stabilized leachate treatment using ozone/persulfate in the advanced oxidation process. *Waste Manag.* 33 (6), 1434–1441. <https://doi.org/10.1016/j.wasman.2013.01.039>.
- Abusallout, I., Holton, C., Wang, J., Hanigan, D., 2022. Henry's law constants of 15 per- and polyfluoroalkyl substances determined by static headspace analysis. *J. Hazard. Mater. Lett.* 3, 100070. <https://doi.org/10.1016/j.hazl.2022.100070>.
- Ahmadireskety, A., Da Silva, B.F., Townsend, T.G., Yost, R.A., Solo-Gabriele, H.M., Bowden, J.A., 2020. Evaluation of extraction workflows for quantitative analysis of per- and polyfluoroalkyl substances: a case study using soil adjacent to a landfill. *Sci. Total Environ.* 143944 <https://doi.org/10.1016/j.scitotenv.2020.143944>.
- Ahmed, M.B., Alam, Md.M., Zhou, J.L., Xu, B., Johir, M.A.H., Karmakar, A.K., Rahman, Md.S., Hossen, J., Hasan, A.T.M.K., Moni, M.A., 2020. Advanced treatment technologies efficacies and mechanism of per- and poly-fluoroalkyl substances removal from water. *Process. Saf. Environ. Prot.* 136, 1–14. <https://doi.org/10.1016/j.psep.2020.01.005>.
- Ahrens, L., Shoeib, M., Harner, T., Lee, S.C., Guo, R., Reiner, E.J., 2011. Wastewater treatment plant and landfills as sources of polyfluoroalkyl compounds to the atmosphere<sup>†</sup>. *Environ. Sci. Technol.* 45 (19), 8098–8105. <https://doi.org/10.1021/es1036173>.

- Allred, B.M., Lang, J.R., Barlaz, M.A., Field, J.A., 2014. Orthogonal zirconium diol/C18 liquid chromatography–tandem mass spectrometry analysis of poly and perfluoroalkyl substances in landfill leachate. *J. Chromatogr. A* 1359, 202–211. <https://doi.org/10.1016/j.chroma.2014.07.056>.
- Allred, B.M., Lang, J.R., Barlaz, M.A., Field, J., 2015. Physical and biological release of poly- and perfluoroalkyl substances (PFAS) from municipal solid waste in anaerobic model landfill reactors. *Environ. Sci. Technol.* 49 (13), 7648–7656.
- Appleman, T.D., Dickenson, E.R.V., Bellona, C., Higgins, C.P., 2013. Nanofiltration and granular activated carbon treatment of perfluoroalkyl acids. *J. Hazard. Mater.* 260, 740–746.
- Appleman, T.D., Higgins, C.P., Quiñones, O., Vanderford, B.J., Kolstad, C., Zeigler-Holady, J.C., Dickenson, E.R.V., 2014. Treatment of poly- and perfluoroalkyl substances in U.S. full-scale water treatment systems. *Water Res.* 51, 246–255. <https://doi.org/10.1016/j.watres.2013.10.067>.
- Awad, J., Brunetti, G., Juhasz, A., Williams, M., Navarro, D., Drigo, B., Bougoure, J., Vanderzalm, J., Beecham, S., 2022. Application of native plants in constructed floating wetlands as a passive remediation approach for PFAS-impacted surface water. *J. Hazard. Mater.* 429, 128326. <https://doi.org/10.1016/j.jhazmat.2022.128326>.
- Babu, S.G., Ashokkumar, M., Neppolian, B., 2016. The role of ultrasound on advanced oxidation processes. *Top. Curr. Chem.* 374 (5), 75. <https://doi.org/10.1007/s41061-016-0072-9>.
- Bandala, E.R., Liu, A., Wijesiri, B., Zeidman, A.B., Goonetilleke, A., 2021. Emerging materials and technologies for landfill leachate treatment: a critical review. *Environ. Pollut.* 291, 118133. <https://doi.org/10.1016/j.envpol.2021.118133>.
- Bao, Y., Niu, J., Xu, Z., Gao, D., Shi, J., Sun, X., Huang, Q., 2014. Removal of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) from water by coagulation: mechanisms and influencing factors. *J. Colloid Interface Sci.* 434, 59–64. <https://doi.org/10.1016/j.jcis.2014.07.041>.
- Barisci, S., Suri, R., 2021. Occurrence and removal of poly/perfluoroalkyl substances (PFAS) in municipal and industrial wastewater treatment plants. *Water Sci. Technol.* 84 (12), 3442–3468. <https://doi.org/10.2166/wst.2021.484>.
- Barth, E., McKernan, J., Bless, D., Dasu, K., 2021. Investigation of an immobilization process for PFAS contaminated soils. *J. Environ. Manag.* 296, 113069. <https://doi.org/10.1016/j.jenvman.2021.113069>.
- Bečanová, J., Melymuk, L., Vojta, S., Komprdová, K., Klánová, J., 2016. Screening for perfluoroalkyl acids in consumer products, building materials and wastes. *Chemosphere* 164, 322–329. <https://doi.org/10.1016/j.chemosphere.2016.08.112>.
- Beesoon, S., Genuis, S.J., Benskin, J.P., Martin, J.W., 2012. Exceptionally high serum concentrations of perfluorohexanesulfonate in a Canadian family are linked to home carpet treatment applications. *Environ. Sci. Technol.* 46, 12960–12967. <https://doi.org/10.1021/es3034654>.
- Benskin, J.P., Li, B., Ikonomou, M.G., Grace, J.R., Li, L.Y., 2012. Per- and polyfluoroalkyl substances in landfill leachate: patterns, time trends, and sources. *Environ. Sci. Technol.* 46 (21), 11532–11540. <https://doi.org/10.1021/es302471n>.
- Berg, C., Crone, B., Gullett, B., Higuchi, M., Krause, M.J., Lemieux, P.M., Martin, T., Shields, E.P., Lohman Struble, E., Thoma, E., Whitehill, A., 2022. Developing innovative treatment technologies for PFAS-containing wastes. *J. Air Waste Manage. Assoc.* 72 (6), 540–555. <https://doi.org/10.1080/10962247.2021.2000903>.
- Berhanu, A., Mutanda, I., Taolin, J., Qaria, M.A., Yang, B., Zhu, D., 2023. A review of microbial degradation of per- and polyfluoroalkyl substances (PFAS): biotransformation routes and enzymes. *Sci. Total Environ.* 859, 160010. <https://doi.org/10.1016/j.scitotenv.2022.160010>.
- BioCycle, 2020. PFAS at Minnesota composting sites. <https://www.biocycle.net/pfas-minnesota-composting-sites/>.
- Bolan, N., Sarkar, B., Yan, Y., Li, Q., Wijesekara, H., Kannan, K., Tsang, D.C.W., Schauer, M., Bosch, J., Noll, H., Ok, Y.S., Scheckel, K., Kumpiene, J., Gobindal, K., Kah, M., Sperry, J., Kirkham, M.B., Yang, H., Tsang, Y.F., Rinklebe, J., 2021. Remediation of poly- and perfluoroalkyl substances (PFAS) contaminated soils – to mobilize or to immobilize or to degrade? *J. Hazard. Mater.* 401, 123892. <https://doi.org/10.1016/j.jhazmat.2020.123892>.
- Boo, C., Wang, Y., Zucker, I., Choo, Y., Osuji, C.O., Elimelech, M., 2018. High performance nanofiltration membrane for effective removal of perfluoroalkyl substances at high water recovery. *Environ. Sci. Technol.* 52, 7279–7288. <https://doi.org/10.1021/acs.est.8b01040>.
- Boyer, T.H., Fang, Y., Ellis, A., Dietz, R., Choi, Y.J., Schaefer, C.E., Higgins, C.P., Strathmann, T.J., 2021. Anion exchange resin removal of per- and polyfluoroalkyl substances (PFAS) from impacted water: a critical review. *Water Res.* 200, 117244. <https://doi.org/10.1016/j.watres.2021.117244>.
- Brusseau, M.L., Anderson, R.H., Guo, B., 2020. PFAS concentrations in soils: background levels versus contaminated sites. *Sci. Total Environ.* 740, 140017. <https://doi.org/10.1016/j.scitotenv.2020.140017>.
- Buck, R., Franklin, J., Berger, U., Conder, J., Cousins, I., Voogt, P. d., Jensen, A., Kannan, K., Mabury, S., Leeuwen, S., 2011. Perfluoroalkyl and polyfluoroalkyl substances in the environment: terminology, classifications, and origins. *Integr. Environ. Assess. Manag.* 7, 513–571. <https://doi.org/10.1002/ieam.258>.
- Busch, J., Ahrens, L., Sturm, R., Ebinghaus, R., 2010. Polyfluoroalkyl compounds in landfill leachates. *Environ. Pollut.* 158 (5), 1467–1471. <https://doi.org/10.1016/j.envpol.2009.12.031>.
- California Water Boards, 2023. GeoTracker PFAS Map [Interactive Tool] (April 19). [http://s://geotracker.waterboards.ca.gov/map/pfas\\_map](http://s://geotracker.waterboards.ca.gov/map/pfas_map).
- Chen, Y., Zhang, H., Liu, Y., Bowden, J.A., Tolaymat, T.M., Townsend, T.G., Solo-Gabriele, H.M., 2022. Concentrations of perfluoroalkyl and polyfluoroalkyl substances before and after full-scale landfill leachate treatment. *Waste Manag.* 153, 110–120. <https://doi.org/10.1016/j.wasman.2022.08.024>.
- Chen, Y., Zhang, H., Liu, Y., Bowden, J.A., Tolaymat, T.M., Townsend, T.G., Solo-Gabriele, H.M., 2023. Evaluation of per- and polyfluoroalkyl substances (PFAS) in leachate, gas condensate, stormwater and groundwater at landfills. *Chemosphere* 318, 137903. <https://doi.org/10.1016/j.chemosphere.2023.137903>.
- Chow, S.J., Croll, H.C., Ojeda, N., Klammer, J., Capelle, R., Oppenheimer, J., Jacangelo, J.G., Schwab, K.J., Prasse, C., 2022. Comparative investigation of PFAS adsorption onto activated carbon and anion exchange resins during long-term operation of a pilot treatment plant. *Water Res.* 226, 119198. <https://doi.org/10.1016/j.watres.2022.119198>.
- Clarke, B.O., Anumol, T., Barlaz, M., Snyder, S.A., 2015. Investigating landfill leachate as a source of trace organic pollutants. *Chemosphere* 127, 269–275. <https://doi.org/10.1016/j.chemosphere.2015.02.030>.
- Coffin, E.S., Reeves, D.M., Cassidy, D.P., 2022. PFAS in municipal solid waste landfills: sources, leachate composition, chemical transformations, and future challenges. *Curr. Opin. Environ. Sci. Health* 100418.
- Coggan, T.L., Moodie, D., Kolobaric, A., Szabo, D., Shimeta, J., Crosbie, N.D., Lee, E., Fernandes, M., Clarke, B.O., 2019. An investigation into per- and polyfluoroalkyl substances (PFAS) in nineteen Australian wastewater treatment plants (WWTPs). *Heliyon* 5 (8), e02316. <https://doi.org/10.1016/j.heliyon.2019.e02316>.
- Crone, B.C., Speth, T.F., Wahman, D.G., Smith, S.J., Abulikemu, G., Kleiner, E.J., Pressman, J.G., 2019. Occurrence of per- and polyfluoroalkyl substances (PFAS) in source water and their treatment in drinking water. *Crit. Rev. Environ. Sci. Technol.* 1–38. <https://doi.org/10.1080/10643389.2019.1614848>.
- Curtzwiler, G.W., Silva, P., Hall, A., Ivey, A., Vorst, K., 2021. Significance of perfluoroalkyl substances (PFAS) in food packaging. *Integr. Environ. Assess. Manag.* 17 (1), 7–12. <https://doi.org/10.1002/ieam.4346>.
- Das, S., Ronen, A., 2022. A review on removal and destruction of per- and polyfluoroalkyl substances (PFAS) by novel membranes. *Membranes* (12). <https://doi.org/10.3390/membranes12070662>.
- D'eon, J.C., Crozier, P.W., Furdul, V.I., Reiner, E.J., Libelo, E.L., Mabury, S.A., 2009. Observation of a commercial fluorinated material, the polyfluoroalkyl phosphoric acid diesters, in human sera, wastewater treatment plant sludge, and paper fibers. *Environ. Sci. Technol.* 43 (12), 4589–4594. <https://doi.org/10.1021/es900100d>.
- Di Battista, V., Rowe, R.K., Patch, D., Weber, K., 2020. PFOA and PFOS diffusion through LLDPE and LLDPE coextruded with EVOH at 22 °C, 35 °C, and 50 °C. *Waste Manag.* 117, 93–103. <https://doi.org/10.1016/j.wasman.2020.07.036>.
- Dixit, F., Dutta, R., Barbeau, B., Berube, P., Mohseni, M., 2021. PFAS removal by ion exchange resins: a review. *Chemosphere* 272, 129777. <https://doi.org/10.1016/j.chemosphere.2021.129777>.
- Du, X., Li, Z., Xiao, M., Mo, Z., Wang, Z., Li, X., Yang, Y., 2021. An electro-oxidation reactor for treatment of nanofiltration concentrate towards zero liquid discharge. *Sci. Total Environ.* 783, 146990. <https://doi.org/10.1016/j.scitotenv.2021.146990>.
- Du, Z., Deng, S., Bei, Y., Huang, Q., Wang, B., Huang, J., Yu, G., 2014. Adsorption behavior and mechanism of perfluorinated compounds on various adsorbents—a review. *J. Hazard. Mater.* 274, 443–454. <https://doi.org/10.1016/j.jhazmat.2014.04.038>.
- Eggen, T., Moeder, M., Arukwe, A., 2010. Municipal landfill leachates: a significant source for new and emerging pollutants. *Sci. Total Environ.* 408 (21), 5147–5157. <https://doi.org/10.1016/j.scitotenv.2010.07.049>.
- EGLE, 2019. Statewide Study on Landfill Leachate PFOA and PFOS Impact on Water Resource Recovery Facility Influent. Michigan Waste & Recycling Association, p. 25 (<https://www.bridgemi.com/sites/default/files/mwra-technical-report.pdf>).
- Ellis, A.C., Liu, C.J., Fang, Y., Boyer, T.H., Schaefer, C.E., Higgins, C.P., Strathmann, T.J., 2022. Pilot study comparison of regenerable and emerging single-use anion exchange resins for treatment of groundwater contaminated by per- and polyfluoroalkyl substances (PFASs). *Water Res.* 223, 119019. <https://doi.org/10.1016/j.watres.2022.119019>.
- Enzminger, J.D., Robertson, D., Ahlert, R.C., Kosson, D.S., 1987. Treatment of landfill leachates. *J. Hazard. Mater.* 14 (1), 83–101. [https://doi.org/10.1016/0304-3894\(87\)87007-3](https://doi.org/10.1016/0304-3894(87)87007-3).
- Esfahani, E.B., Zeidabadi, F.A., Zhang, S., Mohseni, M., 2022. Photo-chemical/catalytic oxidative/reductive decomposition of per- and poly-fluoroalkyl substances (PFAS), decomposition mechanisms and effects of key factors: A review. *Environ. Sci.: Water Res. Technol.* 8 (4), 698–728. <https://doi.org/10.1039/D1EW00774B>.
- Estabrooks, M., Zemba, S., 2019. PFAS Waste Source Testing Report—Sanborn Head & Associates. <https://anrweb.vt.gov/PubDocs/DEC/SolidWaste/OL510/OL510%202019.10.15%20NEWSVT%20PFAS%20Source%20Testing%20Rpt%20%20Final.pdf>.
- European Food Safety Authority, 2012. Perfluoroalkylated substances in food: occurrence and dietary exposure. *EFSA J.* 10 (6), 2743. <https://doi.org/10.2903/j.efsa.2012.2743>.
- Favreau, P., Poncioni-Rothlisberger, C., Place, B.J., Bouchex-Bellomie, H., Weber, A., Tremp, J., Field, J.A., Kohler, M., 2017. Multianalyte profiling of per- and polyfluoroalkyl substances (PFASs) in liquid commercial products. *Chemosphere* 171, 491–501. <https://doi.org/10.1016/j.chemosphere.2016.11.127>.
- Fenton, S.E., Ducatman, A., Boobis, A., DeWitt, J.C., Lau, C., Ng, C., Smith, J.S., Roberts, S.M., 2021. Per- and polyfluoroalkyl substance toxicity and human health review: current state of knowledge and strategies for informing future research. *Environ. Toxicol. Chem.* 40 (3), 606–630. <https://doi.org/10.1002/etc.4890>.
- Fredriksson, F., Eriksson, U., Kärrman, A., Yeung, L.W.Y., 2022. Per- and polyfluoroalkyl substances (PFAS) in sludge from wastewater treatment plants in Sweden—first findings of novel fluorinated copolymers in Europe including temporal analysis. *Sci. Total Environ.* 846, 157406. <https://doi.org/10.1016/j.scitotenv.2022.157406>.
- Fuertes, I., Gómez-Lavín, S., Elizalde, M.P., Urtiaga, A., 2017. Perfluorinated alkyl substances (PFAS) in northern Spain municipal solid waste landfill leachates. *Chemosphere* 168, 399–407. <https://doi.org/10.1016/j.chemosphere.2016.10.072>.

- Gagliano, E., Falciglia, P.P., Zaker, Y., Karanfil, T., Roccaro, P., 2021. Microwave regeneration of granular activated carbon saturated with PFAS. *Water Res.* 198, 117121. <https://doi.org/10.1016/j.watres.2021.117121>.
- Gallen, C., Gallen, M., Drage, D., Kaserzon, S., Baduel, C., Banks, A., Broomhall, S., Mueller, J.F., 2016. Occurrence and distribution of brominated flame retardants and perfluoroalkyl substances in Australian landfill leachate and biosolids. *J. Hazard. Mater.* 312, 55–64.
- Gallen, C., Drage, D., Eaglesham, G., Grant, S., Bowman, M., Mueller, J.F., 2017. Australia-wide assessment of perfluoroalkyl substances (PFASs) in landfill leachates. *J. Hazard. Mater.* 331, 132–141. <https://doi.org/10.1016/j.jhazmat.2017.02.006>.
- Gallen, C., Eaglesham, G., Drage, D., Nguyen, T.H., Mueller, J.F., 2018. A mass estimate of perfluoroalkyl substance (PFAS) release from Australian wastewater treatment plants. *Chemosphere* 208, 975–983. <https://doi.org/10.1016/j.chemosphere.2018.06.024>.
- Gao, J., Oloibiri, V., Chys, M., Audenaert, W., Decostere, B., He, Y., Van Langenhove, H., Demestere, K., Van Hulle, S.W.H., 2015. The present status of landfill leachate treatment and its development trend from a technological point of view. *Rev. Environ. Sci. Biotechnol.* 14 (1), 93–122. <https://doi.org/10.1007/s11157-014-9349-z>.
- Garg, S., Kumar, P., Mishra, V., Guijt, R., Singh, P., Dumée, L.F., Sharma, R.S., 2020. A review on the sources, occurrence and health risks of per-/poly-fluoroalkyl substances (PFAS) arising from the manufacture and disposal of electric and electronic products. *J. Water Process Eng.* 38, 101683. <https://doi.org/10.1016/j.jwpe.2020.101683>.
- Gates, W.P., MacLeod, A.J.N., Fehervari, A., Bouazza, A., Gibbs, D., Hackney, R., Callahan, D.L., Watts, M., 2020. Interactions of per- and polyfluoroalkyl substances (PFAS) with landfill liners. *Adv. Environ. Eng. Res.* 1 (4), 4. <https://doi.org/10.21926/aer.2004007>.
- Gewurtz, S.B., Backus, S.M., De Silva, A.O., Ahrens, L., Armellin, A., Evans, M., Fraser, S., Gledhill, M., Guerra, P., Harner, T., Helm, P.A., Hung, H., Khera, N., Kim, M.G., King, M., Lee, S.C., Letcher, R.J., Martin, P., Marvin, C., Waltho, J., 2013. Perfluoroalkyl acids in the Canadian environment: multi-media assessment of current status and trends. *Environ. Int.* 59, 183–200. <https://doi.org/10.1016/j.envint.2013.05.008>.
- Ghisi, R., Vamerali, T., Manzetti, S., 2019. Accumulation of perfluorinated alkyl substances (PFAS) in agricultural plants: a review. *Environ. Res.* 169, 326–341. <https://doi.org/10.1016/j.envres.2018.10.023>.
- Glüge, J., Scheringer, M., Cousins, I.T., DeWitt, J.C., Goldenman, G., Herzke, D., Lohmann, R., Ng, C.A., Trier, X., Wang, Z., 2020. An overview of the uses of per- and polyfluoroalkyl substances (PFAS). *Environ. Sci. Process Impacts* 22 (12), 2345–2373. <https://doi.org/10.1039/D0EM00291G>.
- Gobelius, L., Hedlund, J., Dürig, W., Tröger, R., Lilja, K., Wiberg, K., Ahrens, L., 2018. Per- and polyfluoroalkyl substances in Swedish groundwater and surface water: implications for environmental quality standards and drinking water guidelines. *Environ. Sci. Technol.* 52, 4340–4349. <https://doi.org/10.1021/acs.est.7b05718>.
- Gomez-Ruiz, B., Gómez-Lavín, S., Diban, N., Boiteux, V., Colin, A., Dauchy, X., Urtiaga, A., 2017. Efficient electrochemical degradation of poly- and perfluoroalkyl substances (PFASs) from the effluents of an industrial wastewater treatment plant. *Chem. Eng. J.* 322, 196–204. <https://doi.org/10.1016/j.cej.2017.04.040>.
- Guo, Z., Liu, X., Krebs, K.A., 2009. Perfluorocarboxylic Acid Content in 116 Articles of Commerce (EPA/600/R-09/033). National Risk Management Research Laboratory, Office of Research and Development, US EPA.
- Hamid, H., Li, L.Y., Grace, J.R., 2018. Review of the fate and transformation of per- and polyfluoroalkyl substances (PFAS) in landfills. *Environ. Pollut.* 235, 74–84.
- Hamid, H., Li, L.Y., Grace, J.R., 2020. Aerobic biotransformation of fluorotelomer compounds in landfill leachate-sediment. *Sci. Total Environ.* 713, 136547. <https://doi.org/10.1016/j.scitotenv.2020.136547>.
- Harrad, S., Drage, D.S., Sharkey, M., Berresheim, H., 2019. Brominated flame retardants and perfluoroalkyl substances in landfill leachate from Ireland. *Sci. Total Environ.* 695, 133810. <https://doi.org/10.1016/j.scitotenv.2019.133810>.
- Helmer, R.W., Reeves, D.M., Cassidy, D.P., 2022. Per- and polyfluorinated alkyl substances (PFAS) cycling within Michigan: contaminated sites, landfills and wastewater treatment plants. *Water Res.* 210, 117983. <https://doi.org/10.1016/j.watres.2021.117983>.
- Hepburn, E., Madden, C., Szabo, D., Coggan, T.L., Clarke, B., Currell, M., 2019. Contamination of groundwater with per- and polyfluoroalkyl substances (PFAS) from legacy landfills in an urban re-development precinct. *Environ. Pollut.* 248, 101–113. <https://doi.org/10.1016/j.envpol.2019.02.018>.
- Herzke, D., Olsson, E., Posner, S., 2012. Perfluoroalkyl and polyfluoroalkyl substances (PFASs) in consumer products in Norway – a pilot study. *Chemosphere* 88 (8), 980–987. <https://doi.org/10.1016/j.chemosphere.2012.03.035>.
- Hong, A.C., Young, C.J., Hurley, M.D., Wallington, T.J., Mabury, S.A., 2013. Perfluorotributylamine: a novel long-lived greenhouse gas. *Geophys. Res. Lett.* 40 (22), 6010–6015. <https://doi.org/10.1002/2013GL058010>.
- Hori, H., Nagaoka, Y., Yamamoto, A., Sano, T., Yamashita, N., Taniyasu, S., Kutsuna, S., Osaka, I., Arakawa, R., 2006. Efficient decomposition of environmentally persistent perfluorooctanesulfonate and related fluorochemicals using zerovalent iron in subcritical water. *Environ. Sci. Technol.* 40 (3), 1049–1054. <https://doi.org/10.1021/es0517419>.
- Huang, S., Jaffé, P.R., 2019. Defluorination of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) by *Acidimicrobium* sp. strain A6. *Environ. Sci. Technol.* 53, 11410–11419. <https://doi.org/10.1021/acs.est.9b04047>.
- Huang, X., Wei, X., Liu, H., Li, W., Shi, D., Qian, S., Sun, W., Yue, D., Wang, X., 2022. Occurrence of per- and polyfluoroalkyl substances (PFAS) in municipal solid waste landfill leachates from western China. *Environ. Sci. Pollut. Res.* 29 (46), 69588–69598.
- Huset, C.A., Barlaz, M.A., Barofsky, D.F., Field, J.A., 2011. Quantitative determination of fluorochemicals in municipal landfill leachates. *Chemosphere* 82 (10), 1380–1386. <https://doi.org/10.1016/j.chemosphere.2010.11.072>.
- ITRC, 2020. Fate and transport of per- and polyfluoroalkyl substances (PFAS), Interstate Technology Regulatory Council. [https://pfas-1.itrcweb.org/wp-content/uploads/2020/10/f\\_and\\_t\\_508\\_2020Aug.pdf](https://pfas-1.itrcweb.org/wp-content/uploads/2020/10/f_and_t_508_2020Aug.pdf).
- ITRC, 2022. 2.5 PFAS uses (June). <https://pfas-1.itrcweb.org/2-5-pfas-uses/>.
- Jain, P., Wally, J., Townsend, T.G., Krause, M., Tolaymat, T., 2021. Greenhouse gas reporting data improves understanding of regional climate impact on landfill methane production and collection. *PLoS ONE* 16 (2), e0246334. <https://doi.org/10.1371/journal.pone.0246334>.
- Jain, P., Winslow, K.M., Townsend, T.G., Krause, M.J., Tolaymat, T.M., 2023. Assessment of municipal solid waste landfill liner performance. *ASCE J. Environ. Eng.* 149 (9). [https://doi.org/10.1061/\(ASCE\)JEEENG-7218](https://doi.org/10.1061/(ASCE)JEEENG-7218).
- Jin, C.F., Sun, Y.H., Islam, Ahmed, Qian, Y., Ducatman, A., 2011. Perfluoroalkyl acids including perfluorooctane sulfonate and perfluorohexane sulfonate in firefighters. *J. Occup. Environ. Med.* 53 (3), 324–328. <http://www.jstor.org/stable/45009711>.
- Johnson, G.R., 2022. PFAS in soil and groundwater following historical land application of biosolids. *Water Res.* 211, 118035. <https://doi.org/10.1016/j.watres.2021.118035>.
- Kaleel, U., Santen, M., 2012. Greenpeace Tests Outdoor Clothes for Per- and Polyfluorinated Chemicals. Greenpeace. <https://doi.org/10.13140/2.1.1726.4007>.
- Kallenborn, R., Berger, U., Järnberg, U., Dam, M., Hedlund, B., Lundgren, A., Bügel, B., Sigurdsson, S., 2004. Perfluorinated alkylated substances (PFAS) in the nordic environment. In: AIP 2004: 552. Nordic Council of Ministers, Copenhagen.
- Kameoka, H., Ito, K., Ono, J., Banno, A., Matsumura, C., Haga, Y., Endo, K., Mizutani, S., Yabuki, Y., 2022. Investigation of perfluoroalkyl carboxylic and sulfonic acids in leachates from industrial and municipal solid waste landfills, and their treated waters and effluents from their closest leachate treatment plants. *J. Mater. Cycles Waste Manag.* 24 (1), 287–296. <https://doi.org/10.1007/s10163-021-01319-z>.
- Kim, H.-Y., Seok, H.-W., Kwon, H.-O., Choi, S.-D., Seok, K.-S., Oh, J.E., 2016. A national discharge load of perfluoroalkyl acids derived from industrial wastewater treatment plants in Korea. *Sci. Total Environ.* 563–564, 530–537. <https://doi.org/10.1016/j.scitotenv.2016.04.077>.
- Kim, M., Li, L.Y., Grace, J.R., Benskin, J.P., Ikonomou, M.G., 2015. Compositional effects on leaching of stain-guarded (perfluoroalkyl and polyfluoroalkyl substance-treated) carpet in landfill leachate. *Environ. Sci. Technol.* 49 (11), 6564–6573. <https://doi.org/10.1021/es505333y>.
- Knutsen, H., Mæhlum, T., Haarstad, K., Slinde, G.A., H. A. H. P., 2019. Leachate emissions of short- and long-chain per- and polyfluoroalkyl substances (PFASs) from various Norwegian landfills. *Environ. Sci. Process Impacts* 21 (11), 1970–1979. <https://doi.org/10.1039/C9EM00170K>.
- Kotthoff, M., Müller, J., Jüring, H., Schlummer, M., Fiedler, D., 2015. Perfluoroalkyl and polyfluoroalkyl substances in consumer products. *Environ. Sci. Pollut. Res.* 22 (19), 14546–14559.
- Krause, M., Magnuson, M., Crone, B., 2021. Potential PFAS destruction technology: electrochemical oxidation, U.S. EPA Office of Research and Development Research Brief. [https://www.epa.gov/sites/default/files/2021-01/documents/pitt\\_research\\_brief\\_electrochemical\\_oxidation\\_final\\_jan\\_25\\_2021\\_508.pdf](https://www.epa.gov/sites/default/files/2021-01/documents/pitt_research_brief_electrochemical_oxidation_final_jan_25_2021_508.pdf).
- Krause, M.J., Thoma, E., Sahle-Damesessie, E., Crone, B., Whitehill, A., Shields, E., Gullett, B., 2022. Supercritical water oxidation as an innovative technology for PFAS destruction. *J. Environ. Eng.* 148, 05021006. [https://doi.org/10.1061/\(ASCE\)EE.1943-7870.0001957](https://doi.org/10.1061/(ASCE)EE.1943-7870.0001957).
- Labiadh, L., Fernandes, A., Ciriaco, L., Pacheco, M.J., Gadri, A., Ammar, S., Lopes, A., 2016. Electrochemical treatment of concentrate from reverse osmosis of sanitary landfill leachate. *J. Environ. Manag.* 181, 515–521. <https://doi.org/10.1016/j.jenvman.2016.06.069>.
- Lang, J.R., Allred, B.M., Peaslee, G.F., Field, J.A., Barlaz, M.A., 2016. Release of per- and polyfluoroalkyl substances (PFAS) from carpet and clothing in model anaerobic landfill reactors. *Environ. Sci. Technol.* 50 (10), 5024–5032.
- Lang, J.R., Allred, B.M., Field, J.A., Levis, J.W., Barlaz, M.A., 2017. National estimate of per- and polyfluoroalkyl substance (PFAS) release to U.S. municipal landfill leachate. *Environ. Sci. Technol.* 51 (4), 2197–2205. <https://doi.org/10.1021/acs.est.6b05005>.
- Langberg, H.A., Arp, H.P.H., Breedveld, G.D., Slinde, G.A., Høiseter, Å., Grønning, H.M., Jartun, M., Rundberget, T., Jenssen, B.M., Hale, S.E., 2021. Paper product production identified as the main source of per- and polyfluoroalkyl substances (PFAS) in a Norwegian lake: source and historic emission tracking. *Environ. Pollut.* 273, 116259. <https://doi.org/10.1016/j.envpol.2020.116259>.
- Lee, H., D'eon, J., Mabury, S.A., 2010a. Biodegradation of polyfluoroalkyl phosphates as a source of perfluorinated acids to the environment. *Environ. Sci. Technol.* 44 (9), 3305–3310. <https://doi.org/10.1021/es9028183>.
- Lee, Y.C., Lo, S.L., Chiueh, P.T., Liou, Y.H., Chen, M.L., 2010b. Microwave-hydrothermal decomposition of perfluorooctanoic acid in water by iron-activated persulfate oxidation. *Water Res.* 44 (3), 886–892. <https://doi.org/10.1016/j.watres.2009.09.055>.
- Lenka, S.P., Kah, M., Padhye, L.P., 2022. Occurrence and fate of poly- and perfluoroalkyl substances (PFAS) in urban waters of New Zealand. *J. Hazard. Mater.* 428, 128257. <https://doi.org/10.1016/j.jhazmat.2022.128257>.
- Li, B., 2009. Perfluorinated Compounds in Landfill Leachate and Their Effect on the Performance of Sodium Bentonite Landfill Liners (B.A.Sc.). The University of British Columbia.
- Li, B., Li, L.Y., Grace, J.R., 2015. Adsorption and hydraulic conductivity of landfill-leachate perfluorinated compounds in bentonite barrier mixtures. *J. Environ. Manag.* 156, 236–243. <https://doi.org/10.1016/j.jenvman.2015.04.003>.

- Li, F., Fang, X., Zhou, Z., Liao, X., Zou, J., Yuan, B., Sun, W., 2019. Adsorption of perfluorinated acids onto soils: kinetics, isotherms, and influences of soil properties. *Sci. Total Environ.* 649, 504–514. <https://doi.org/10.1016/j.scitotenv.2018.08.209>.
- Li, Y., Thompson, J., Wang, Z., Bräunig, J., Zheng, Q., Thai, P.K., Mueller, J.F., Yuan, Z., 2022. Transformation and fate of pharmaceuticals, personal care products, and per- and polyfluoroalkyl substances during aerobic digestion of anaerobically digested sludge. *Water Res.* 219, 118568. <https://doi.org/10.1016/j.watres.2022.118568>.
- Lin, A.Y., Panchangam, S.C., Chang, C.Y., Hong, P.K., Hsueh, H.F., 2012. Removal of perfluorooctanoic acid and perfluorooctane sulfonate via ozonation under alkaline condition. *J. Hazard. Mater.* 243, 272–277. <https://doi.org/10.1016/j.jhazmat.2012.10.029>.
- Lin, A.Y.-C., Panchangam, S.C., Lo, C.-C., 2009. The impact of semiconductor, electronics and optoelectronic industries on downstream perfluorinated chemical contamination in Taiwanese rivers. *Environ. Pollut.* 157 (4), 1365–1372. <https://doi.org/10.1016/j.envpol.2008.11.033>.
- Lipp, P., Sacher, F., Baldauf, G., 2010. Removal of organic micro-pollutants during drinking water treatment by nanofiltration and reverse osmosis. *Desalin. Water Treat.* 13, 226–237. <https://doi.org/10.5004/dwt.2010.1063>.
- Liu, J., Wang, N., Szostek, B., Buck, R.C., Panciroli, P.K., Folsom, P.W., Sulecki, L.M., Bellin, C.A., 2010. 6-2 Fluorotelomer alcohol aerobic biodegradation in soil and mixed bacterial culture. *Chemosphere* 78 (4), 437–444. <https://doi.org/10.1016/j.chemosphere.2009.10.044>.
- Liu, Y., Clavier, K.A., Spreadbury, C., Townsend, T.G., 2019. Limitations of the TCLP fluid determination step for hazardous waste characterization of US municipal waste incineration ash. *Waste Manag.* 87, 590–596. <https://doi.org/10.1016/j.wasman.2019.02.045>.
- Liu, F., Hua, L., Zhang, W., 2020. Influences of microwave irradiation on performances of membrane filtration and catalytic degradation of perfluorooctanoic acid (PFOA). *Environ. Int.* 143, 105969. <https://doi.org/10.1016/j.envint.2020.105969>.
- Liu, Y., Robey, N.M., Bowden, J.A., Tolaymat, T.M., da Silva, B.F., Solo-Gabriele, H.M., Townsend, T.G., 2021a. From waste collection vehicles to landfills: indication of per- and polyfluoroalkyl substance (PFAS) transformation. *Environ. Sci. Technol. Lett.* 8, 66–72. <https://doi.org/10.1021/acs.estlett.0c00819>.
- Liu, S., Zhao, S., Liang, Z., Wang, F., Sun, F., Chen, D., 2021b. Perfluoroalkyl substances (PFASs) in leachate, fly ash, and bottom ash from waste incineration plants: implications for the environmental release of PFAS. *Sci. Total Environ.* 795, 148468. <https://doi.org/10.1016/j.scitotenv.2021.148468>.
- Liu, Y., Mendoza-Perilla, P., Clavier, K.A., Tolaymat, T.M., Bowden, J.A., Solo-Gabriele, H.M., Townsend, T.G., 2022a. Municipal solid waste incineration (MSWI) ash co-disposal: influence on per- and polyfluoroalkyl substances (PFAS) concentration in landfill leachate. *Waste Manag.* 144, 49–56. <https://doi.org/10.1016/j.wasman.2022.03.009>.
- Liu, T., Hu, L.-X., Han, Y., Dong, L.-L., Wang, Y.-Q., Zhao, J.-H., Liu, Y.-S., Zhao, J.-L., Ying, G.-G., 2022b. Non-target and target screening of per- and polyfluoroalkyl substances in landfill leachate and impact on groundwater in Guangzhou, China. *Sci. Total Environ.* 844, 157021.
- Lohmann, R., Cousins, I.T., DeWitt, J.C., Glüge, J., Goldenman, G., Herzke, D., Lindstrom, A.B., Miller, M.F., Ng, C.A., Patton, S., Scheringer, M., Trier, X., Wang, Z., 2020. Are fluoropolymers really of low concern for human and environmental health and separate from other PFAS? *Environ. Sci. Technol.* 54 (20), 12820–12828. <https://doi.org/10.1021/acs.est.0c03244>.
- Longendyke, G., Katel, S., Wang, Y., 2022. PFAS fate and destruction mechanisms during thermal treatment: a comprehensive review. *Environ. Sci. Process Impacts* 24 (2), 196–208. <https://doi.org/10.1039/D1EM00465D>.
- Lott, D.J., Robey, N.M., Fonseca, R., Bowden, J.A., Townsend, T.G., 2023. Behavior of per- and polyfluoroalkyl substances (PFAS) in pilot-scale vertical flow constructed wetlands treating landfill leachate. *Waste Manag.* 161, 187–192. <https://doi.org/10.1016/j.wasman.2023.03.001>.
- Lu, J., Lu, H., Liang, D., Feng, S., Li, Y., Li, J., 2023. A review of the occurrence, monitoring, and removal technologies for the remediation of per- and polyfluoroalkyl substances (PFAS) from landfill leachate. *Chemosphere* 332, 138824. <https://doi.org/10.1016/j.chemosphere.2023.138824>.
- Malovany, A., Hedman, F., Bergh, L., Liljeros, E., Lund, T., Suokko, J., Hinrichsen, H., 2023. Comparative study of per- and polyfluoroalkyl substances (PFAS) removal from landfill leachate. *J. Hazard. Mater.* 460, 132505. <https://doi.org/10.1016/j.jhazmat.2023.132505>.
- Martin, J.W., Ellis, D.A., Mabury, S.A., Hurley, M.D., Wallington, T.J., 2006. Atmospheric chemistry of perfluoroalkanesulfonamides: kinetic and product studies of the OH radical and Cl atom initiated oxidation of N-ethyl perfluorobutanesulfonamide. *Environ. Sci. Technol.* 40 (3), 864–872. <https://doi.org/10.1021/es051362f>.
- Masoner, J.R., Kolpin, D.W., Cozzarelli, I.M., Smalling, K.L., Bolyard, S.C., Field, J.A., Furlong, E.T., Gray, J.L., Lozinski, D., Reinhard, D., Rodowa, A., M. B. P., 2020. Landfill leachate contributes per-/poly-fluoroalkyl substances (PFAS) and pharmaceuticals to municipal wastewater. *Environ. Sci. Water Res. Technol.* 6 (5), 1300–1311. <https://doi.org/10.1039/D0EW00045K>.
- McClellan, P., Englund, S., Östlund, A., Lindegren, K., Wiberg, K., Ahrens, L., 2017. Removal efficiency of multiple poly- and perfluoroalkyl substances (PFASs) in drinking water using granular activated carbon (GAC) and anion exchange (AE) column tests. *Water Res.* 120, 77–87. <https://doi.org/10.1016/j.watres.2017.04.057>.
- Meegoda, J.N., Kewalramani, J.A., Li, B., Marsh, R.W., 2020. A review of the applications, environmental release, and remediation technologies of per- and polyfluoroalkyl substances. *Int. J. Environ. Res. Public Health* 17 (21), 8117. <https://doi.org/10.3390/ijerph17218117>.
- Meyer-Dombard, D.R., Bogner, J.E., Malas, J., 2020. A review of landfill microbiology and ecology: a call for modernization with ‘Next Generation’ technology. *Front. Microbiol.* 11.
- Moriwaki, H., Takagi, Y., Tanaka, M., Tsuruho, K., Okitsu, K., Maeda, Y., 2005. Sonochemical decomposition of perfluorooctane sulfonate and perfluorooctanoic acid. *Environ. Sci. Technol.* 39 (9), 3388–3392. <https://doi.org/10.1021/es040342v>.
- MPART, 2020. Crown Vantage Property (Parchment, Kalamazoo County). Michigan PFAS Action Response Team. <https://www.michigan.gov/pfasresponse/investigations/sites-aoi/kalamazoo-county/crown-vantage-property>.
- MPCA, 2010. 2005–2008 perfluorochemical evaluation at solid waste facilities in Minnesota technical evaluation and regulatory management approach, Minnesota Pollution Control Agency. <https://www.pca.state.mn.us/sites/default/files/c-pf4-01.pdf>.
- Mukhopadhyay, R., Sarkar, B., Palansooriya, K.N., Dar, J.Y., Bolan, N.S., Parikh, S.J., Sonne, C., Ok, Y.S., 2021. Natural and engineered clays and clay minerals for the removal of poly- and perfluoroalkyl substances from water: state-of-the-art and future perspectives. *Adv. Colloid Interf. Sci.* 297, 102537. <https://doi.org/10.1016/j.cis.2021.102537>.
- NEBRA, 2022. Data on biosolids management in the United States, National Biosolids Data Project. <https://www.biosolidsdata.org/national-summary>.
- NWRA, 2020. Collective study of PFAS and 1,4-dioxane in landfill leachate and estimated influence on wastewater treatment plant facility influent (NWA-001), National Waste & Recycling Association - Carolinas Chapter. <https://www.deq.nc.gov/waste-management/dwm/nc-collective-study-rpt-03-10-2020/download>.
- OECD, 2022. Per- and polyfluoroalkyl substances and alternatives in coatings, paints and varnishes (CPVs). In Report on the commercial availability and current uses. <https://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/per-and-polyfluoroalkyl-substances-alternatives-in-coatings-paints-varnishes.pdf>.
- Pan, C.-G., Liu, Y.-S., Ying, G.-G., 2016. Perfluoroalkyl substances (PFASs) in wastewater treatment plants and drinking water treatment plants: removal efficiency and exposure risk. *Water Res.* 106, 562–570. <https://doi.org/10.1016/j.watres.2016.10.045>.
- Park, M., Daniels, K.D., Wu, S., Ziska, A.D., Snyder, S.A., 2020. Magnetic ion-exchange (MIEX) resin for perfluorinated alkyl substance (PFAS) removal in groundwater: roles of atomic charges for adsorption. *Water Res.* 181, 115897. <https://doi.org/10.1016/j.watres.2020.115897>.
- Peaslee, G.F., Wilkinson, J.T., McGuinness, S.R., Tighe, M., Caterisano, N., Lee, S., Gonzales, A., Roddy, M., Mills, S., Mitchell, K., 2020. Another pathway for firefighter exposure to per- and polyfluoroalkyl substances: firefighter textiles. *Environ. Sci. Technol. Lett.* 7 (8), 594–599. <https://doi.org/10.1021/acs.estlett.0c00410>.
- Perkola, N., Sainio, P., 2013. Survey of perfluorinated alkyl acids in Finnish effluents, storm water, landfill leachate and sludge. *Environ. Sci. Pollut. Res.* 20 (11), 7979–7987. <https://doi.org/10.1007/s11356-013-1518-z>.
- Pike, K.A., Edmiston, P.L., Morrison, J.J., Faust, J.A., 2021. Correlation analysis of perfluoroalkyl substances in regional U.S. precipitation events. *Water Res.* 190, 116685. <https://doi.org/10.1016/j.watres.2020.116685>.
- Pinkard, B.R., Shetty, S., Stritzinger, D., Bellona, C., Novosselov, I.V., 2021. Destruction of perfluorooctanesulfonate (PFOS) in a batch supercritical water oxidation reactor. *Chemosphere* 279, 130834. <https://doi.org/10.1016/j.chemosphere.2021.130834>.
- Qu, Y., Huang, J., Willand, W., Weber, R., 2020. Occurrence, removal and emission of per- and polyfluorinated alkyl substances (PFASs) from chrome plating industry: a case study in Southeast China. *Emerg. Contam.* 6, 376–384. <https://doi.org/10.1016/j.emcon.2020.10.001>.
- Ramírez Carnero, A., Lestido-Cardama, A., Vazquez Loureiro, P., Barbosa-Pereira, L., Rodríguez Bernaldo de Quirós, A., Sendón, R., 2021. Presence of perfluoroalkyl and polyfluoroalkyl substances (PFAS) in food contact materials (FCM) and its migration to food. *Foods* 10 (7), 7. <https://doi.org/10.3390/foods10071443>.
- Rhoads, K.R., Janssen, E.M.-L., Luthy, R.G., Criddle, C.S., 2008. Aerobic biotransformation and fate of N-ethyl perfluorooctane sulfonamidoethanol (N-EtFOSE) in activated sludge. *Environ. Sci. Technol.* 42 (8), 2873–2878. <https://doi.org/10.1021/es702866c>.
- Riedel, T.P., Lang, J.R., Strynar, M.J., Lindstrom, A.B., Offenberg, J.H., 2019. Gas-phase detection of fluorotelomer alcohols and other oxygenated per- and polyfluoroalkyl substances by chemical ionization mass spectrometry. *Environ. Sci. Technol. Lett.* 6 (5), 289–293. <https://doi.org/10.1021/acs.estlett.9b00196>.
- Robel, A.E., Marshall, K., Dickinson, M., Lunderberg, D., Butt, C., Peaslee, G., Stapleton, H.M., Field, J.A., 2017. Closing the mass balance on fluorine on papers and textiles. *Environ. Sci. Technol.* 51 (16), 9022–9032. <https://doi.org/10.1021/acs.est.7b02080>.
- Robey, N.M., da Silva, B.F., Annable, M.D., Townsend, T.G., Bowden, J.A., 2020. Concentrating per- and polyfluoroalkyl substances (PFAS) in municipal solid waste landfill leachate using foam separation. *Environ. Sci. Technol.* 54 (19), 12550–12559. <https://doi.org/10.1021/acs.est.0c01266>.
- Ross, I., McDonough, J., Miles, J., Storch, P., Thelakkat Kochunarayanan, P., Kalve, E., Hurst, J., Dasgupta, S., S., & Burdick, J., 2018. A review of emerging technologies for remediation of PFASs. *Remediat. J.* 28 (2), 101–126. <https://doi.org/10.1002/rem.21553>.
- Sajid, M., Ilyas, M., 2017. PTFE-coated non-stick cookware and toxicity concerns: a perspective. *Environ. Sci. Pollut. Res.* 24 (30), 23436–23440. <https://doi.org/10.1007/s11356-017-0095-y>.
- Sapozhnikova, Y., Taylor, R.B., Bedi, M., Ng, C., 2023. Assessing per- and polyfluoroalkyl substances in globally sourced food packaging. *Chemosphere* 337, 139381. <https://doi.org/10.1016/j.chemosphere.2023.139381>.

- Schultz, M.M., Higgins, C.P., Huset, C.A., Luthy, R.G., Barofsky, D.F., Field, J.A., 2006. Fluorochemical mass flows in a municipal wastewater treatment facility. *Environ. Sci. Technol.* 40 (23), 7350–7357. <https://doi.org/10.1021/es061025m>.
- Seltenrich, N., 2020. PFAS in food packaging: a hot, greasy exposure. *Environ. Health Perspect.* 128 (5), 054002 <https://doi.org/10.1289/EHP6335>.
- Siao, P., Tseng, S.-H., Chen, C.-Y., 2022. Determination of perfluoroalkyl substances in food packaging in Taiwan using ultrasonic extraction and ultra-performance liquid chromatography/tandem mass spectrometry. *J. Food Drug Anal.* 30 (1), 11–25. <https://doi.org/10.38212/2224-6614.3397>.
- Simmons, N., 2019. PFAS Concentrations of Landfill Leachates in Victoria, Australia - Implications for Discharge of Leachate to Sewer.
- Smallwood, T.J., Robey, N.M., Liu, Y., Bowden, J.A., Tolaymat, T.M., Solo-Gabriele, H.M., Townsend, T.G., 2023. Per- and polyfluoroalkyl substances (PFAS) distribution in landfill gas collection systems: leachate and gas condensate partitioning. *J. Hazard. Mater.* 448, 130926. <https://doi.org/10.1016/j.jhazmat.2023.130926>.
- Smith, S.J., Wiberg, K., McCleaf, P., Ahrens, L., 2022. Pilot-scale continuous foam fractionation for the removal of per- and polyfluoroalkyl substances (PFAS) from landfill leachate. *ACS ES&T Water* 2 (5), 841–851. <https://doi.org/10.1021/acsestwater.2c00032>.
- Solo-Gabriele, H.M., Jones, A.S., Lindstrom, A.B., Lang, J.R., 2020. Waste type, incineration, and aeration are associated with per-and polyfluoroalkyl levels in landfill leachates. *Waste Manag.* 107, 191–200.
- Steinle-Darling, E.K., Reinhard, M., 2008. ENVR 64-Removal of perfluorochemicals via nanofiltration. In: *Abstracts of Papers of the (Vol. 235)*. 1155. American Chemical Society, NW, Washington, DC, USA, p. 16TH. April.
- Tansel, B., 2022. PFAS use in electronic products and exposure risks during handling and processing of e-waste: a review. *J. Environ. Manag.* 316, 115291. <https://doi.org/10.1016/j.jenvman.2022.115291>.
- Tavasoli, E., Luek, J.L., Malley, J.P., Mouser, P.J., 2021. Distribution and fate of per- and polyfluoroalkyl substances (PFAS) in wastewater treatment facilities. *Environ Sci Process Impacts* 23 (6), 903–913. <https://doi.org/10.1039/D1EM00032B>.
- Thakali, A., MacRae, J.D., Isenhour, C., Blackmer, T., 2022. Composition and contamination of source separated food waste from different sources and regulatory environments. *J. Environ. Manag.* 314, 115043. <https://doi.org/10.1016/j.jenvman.2022.115043>.
- Thompson, J.T., Chen, B., Bowden, J.A., Townsend, T.G., 2023a. Per- and polyfluoroalkyl substances in toilet paper and the impact on wastewater systems. *Environ. Sci. Technol. Lett.* 10 (3), 234–239. <https://doi.org/10.1021/acs.estlett.3c00094>.
- Thompson, J.T., Robey, N.M., Tolaymat, T.M., Bowden, J.A., Solo-Gabriele, H.M., Townsend, T.G., 2023b. Underestimation of per- and polyfluoroalkyl substances in biosolids: precursor transformation during conventional treatment. *Environ. Sci. Technol.* <https://doi.org/10.1021/acs.est.2c06189>.
- Tian, Y., Yao, Y., Chang, S., Zhao, Z., Zhao, Y., Yuan, X., Wu, F., Sun, H., 2018. Occurrence and phase distribution of neutral and ionizable per- and polyfluoroalkyl substances (PFASs) in the atmosphere and plant leaves around landfills: a case study in Tianjin, China. *Environ. Sci. Technol.* 52 (3), 1301–1310. <https://doi.org/10.1021/acs.est.7b05385>.
- Timshina, A., Aristizabal-Henao, J.J., Da Silva, B.F., Bowden, J.A., 2021. The last straw: characterization of per- and polyfluoroalkyl substances in commercially-available plant-based drinking straws. *Chemosphere* 277, 130238. <https://doi.org/10.1016/j.chemosphere.2021.130238>.
- Titaley, I.A., De la Cruz, F.B., Barlaz, M.A., Field, J.A., 2023. Neutral per- and polyfluoroalkyl substances in situ landfill gas by thermal desorption-gas chromatography–mass spectrometry. *Environ. Sci. Technol. Lett.* 10 (3), 214–221. <https://doi.org/10.1021/acs.estlett.3c00037>.
- Townsend, T.G., Jang, Y., Thurn, L.G., 1999. Simulation of construction and demolition waste leachate. *J. Environ. Eng.* 125, 1071–1081. [https://doi.org/10.1061/\(ASCE\)0733-9372\(1999\)125:11\(1071\)](https://doi.org/10.1061/(ASCE)0733-9372(1999)125:11(1071)).
- Travar, I., Uwayezu, J., Kumpiene, J., Yeung, L., 2020. Challenges in the PFAS remediation of soil and landfill leachate: a review. *Adv. Environ. Eng. Res.* 02, 1. <https://doi.org/10.21926/aer.2102006>.
- US EPA, 2012. Data Gap Analysis and Damage Case Studies: Risk Analysis From Construction and Demolition Debris Landfills and Recycling Facilities (EPA/600/R-13/303). Office of Research and Development.
- US EPA, 2020a. AP 42, Fifth Edition, Volume I Chapter 2: Solid Waste Disposal. <http://www.epa.gov/air-emissions-factors-and-quantification/ap-42-fifth-edition-volume-i-chapter-2-solid-waste-0>.
- US EPA, 2020b. Advancing Sustainable Materials Management: 2018 Fact Sheet (EPA 530-F-20-009). Office of Land and Emergency Management, p. 25.
- US EPA, 2021a. Other Test Method 45 (OTM-45) Measurement of selected per- and polyfluorinated alkyl substances from stationary sources. [https://www.epa.gov/sites/default/files/2021-01/documents/otm\\_45\\_semivolatile\\_pfahs\\_1-13-21.pdf](https://www.epa.gov/sites/default/files/2021-01/documents/otm_45_semivolatile_pfahs_1-13-21.pdf).
- US EPA, 2021b. PFAS Strategic Roadmap: EPA's Commitments to Action 2021–2024. [https://www.epa.gov/system/files/documents/2021-10/pfas-roadmap\\_final-508.pdf](https://www.epa.gov/system/files/documents/2021-10/pfas-roadmap_final-508.pdf).
- US EPA, 2021c. State of the Practice of Onsite Leachate Treatment at Municipal Solid Waste Landfills (EPA/600/R-21/xxx). Office of Research and Development.
- US EPA, 2022a. Data File of Landfill Methane Outreach Program (LMOP). <https://www.epa.gov/lmop/landfill-technical-data>.
- US EPA, 2022b. EPA Proposes Designating Certain PFAS Chemicals as Hazardous Substances Under Superfund to Protect people's Health. US Environmental Protection Agency.
- US EPA, 2022c. PFAS Treatment in Drinking Water and Wastewater - State of the Science [WWW Document]. URL. <https://www.epa.gov/research-states/pfas-treatment-drinking-water-and-wastewater-state-science>.
- US EPA, 2022d. Regional Screening Levels (RSLs)—generic tables. <https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables>.
- US EPA, 2022e. Wolverine World Wide Tannery [WWW Document]. US Environmental Protection Agency. URL. <https://www.epa.gov/mi/wolverine-world-wide-tannery>.
- US FDA, 2022. Per and polyfluoroalkyl substances (PFAS) in cosmetics. <https://www.fda.gov/cosmetics/cosmetic-ingredients/and-polyfluoroalkyl-substances-pfas-cosmetics>.
- van der Veen, I., Schellenberger, S., Hanning, A.-C., Stare, A., de Boer, J., Weiss, J.M., Leonards, P.E.G., 2022. Fate of per- and polyfluoroalkyl substances from durable water-repellent clothing during use. *Environ. Sci. Technol.* 56 (9), 5886–5897. <https://doi.org/10.1021/acs.est.1c07876>.
- Vecitis, C.D., Park, H., Cheng, J., Mader, B.T., Hoffmann, M.R., 2008. Kinetics and mechanism of the sonolytic conversion of the aqueous perfluorinated surfactants, perfluorooctanoate (PFOA), and perfluorooctane sulfonate (PFOS) into inorganic products. *J. Phys. Chem. A* 112 (18), 4261–4270. <https://doi.org/10.1021/jp801081y>.
- Wang, N., Szostek, B., Buck, R.C., Folsom, P.W., Sulecki, L.M., Gannon, J.T., 2009. 8-2 Fluorotelomer alcohol aerobic soil biodegradation: pathways, metabolites, and metabolite yields. *Chemosphere* 75 (8), 1089–1096. <https://doi.org/10.1016/j.chemosphere.2009.01.033>.
- Wang, N., Liu, J., Buck, R.C., Korzeniowski, S.H., Wolstenholme, B.W., Folsom, P.W., Sulecki, L.M., 2011. 6:2 Fluorotelomer sulfonate aerobic biotransformation in activated sludge of waste water treatment plants. *Chemosphere* 82 (6), 853–858. <https://doi.org/10.1016/j.chemosphere.2010.11.003>.
- Wade, A., 2022. Management of PFAS in landfill leachate, liquids, and gases. Presented at the MRRA Solid Waste Summit. October 25, 2022. <https://mrra.net/wp-content/uploads/2022/05/TRC-2022-MRRA-PFAS-in-Landfills.pdf>.
- Wang, Y., Li, L., Qiu, Z., Yang, K., Han, Y., Chai, F., Li, P., Wang, Y., 2021. Trace volatile compounds in the air of domestic waste landfill site: identification, olfactory effect and cancer risk. *Chemosphere* 272, 129582. <https://doi.org/10.1016/j.chemosphere.2021.129582>.
- Washington, J.W., Jenkins, T.M., 2015. Abiotic hydrolysis of fluorotelomer-based polymers as a source of perfluorocarboxylates at the global scale. *Environ. Sci. Technol.* 49 (24), 14129–14135. <https://doi.org/10.1021/acs.est.5b03686>.
- Weber, E., Tebes-Stevens, C., Washington, J.W., Gladstone, R., 2022. Development of a PFAS reaction library: identifying plausible transformation pathways in environmental and biological systems. *Environ Sci Process Impacts* 24 (5), 689–753. <https://doi.org/10.1039/D1EM00445J>.
- Wei, Z., Xu, T., Zhao, D., 2019. Treatment of per- and polyfluoroalkyl substances in landfill leachate: status, chemistry and prospects. *Environ. Sci.: Water Res. Technol.* 5 (11), 1814–1835. <https://doi.org/10.1039/C9EW00645A>.
- Weinberg, I., Dreyer, A., Ebinghaus, R., 2011. Landfills as sources of polyfluorinated compounds, polybrominated diphenyl ethers and musk fragrances to ambient air. *Atmos. Environ.* 45 (4), 935–941.
- Winchell, L.J., Ross, J.J., Wells, M.J.M., Fonoll, X., Norton Jr., J.W., Bell, K.Y., 2021. Per- and polyfluoroalkyl substances thermal destruction at water resource recovery facilities: a state of the science review. *Water Environ. Res.* 93, 826–843. <https://doi.org/10.1002/wer.1483>.
- Witt, S., Rancis, N., Ensich, M., Maldonado, V., 2020. Electrochemical destruction of 'forever chemicals': the right solution at the right time. *Electrochem. Soc. Interface* 29, 73–76. <https://doi.org/10.1149/2.F11202IF>.
- Woldegiorgis, A., Andersson, J., Remberger, M., Kaj, L., Ekheden, Y., Blom, L., Brorström-Lundén, E., 2005. Results from the Swedish National Screening Programme 2005. Subreport 3: Perfluorinated Alkylated Substances (PFAS). Swedish Environmental Research Institute.
- Yan, H., Cousins, I.T., Zhang, C., Zhou, Q., 2015. Perfluoroalkyl acids in municipal landfill leachates from China: occurrence, fate during leachate treatment and potential impact on groundwater. *Sci. Total Environ.* 524–525, 23–31. <https://doi.org/10.1016/j.scitotenv.2015.03.111>.
- Ye, F., Zushi, Y., Masunaga, S., 2015. Survey of perfluoroalkyl acids (PFAAs) and their precursors present in Japanese consumer products. *Chemosphere* 127, 262–268.
- Yin, T., Chen, H., Reinhard, M., Yi, X., He, Y., Gin, K.Y.-H., 2017. Perfluoroalkyl and polyfluoroalkyl substances removal in a full-scale tropical constructed wetland system treating landfill leachate. *Water Res.* 125, 418–426. <https://doi.org/10.1016/j.watres.2017.08.071>.
- Yin, T., Tran, N.H., Huiting, C., He, Y., Gin, K.Y.-H., 2019. Biotransformation of polyfluoroalkyl substances by microbial consortia from constructed wetlands under aerobic and anoxic conditions. *Chemosphere* 233, 101–109. <https://doi.org/10.1016/j.chemosphere.2019.05.227>.
- Yuan, G., Peng, H., Huang, C., Hu, J., 2016. Ubiquitous occurrence of fluorotelomer alcohols in eco-friendly paper-made food-contact materials and their implication for human exposure. *Environ. Sci. Technol.* 50 (2), 942–950. <https://doi.org/10.1021/acs.est.5b03806>.
- Zabaleta, I., Bizkarguenaga, E., Bilbao, D., Etxebarria, N., Prieto, A., Zuloaga, O., 2016. Fast and simple determination of perfluorinated compounds and their potential precursors in different packaging materials. *Talanta* 152, 353–363. <https://doi.org/10.1016/j.talanta.2016.02.022>.
- Zhang, B., He, Y., Huang, Y., Hong, D., Yao, Y., Wang, L., Sun, W., Yang, B., Huang, X., Song, S., Bai, X., Guo, Y., Zhang, T., Sun, H., 2020. Novel and legacy poly- and perfluoroalkyl substances (PFASs) in indoor dust from urban, industrial, and e-waste dismantling areas: the emergence of PFAS alternatives in China. *Environ. Pollut.* 263, 114461. <https://doi.org/10.1016/j.envpol.2020.114461>.
- Zhang, H., Chen, Y., Liu, Y., Bowden, J.A., Townsend, T.G., Solo-Gabriele, H.M., 2022. Do PFAS changes in landfill leachate treatment systems correlate with changes in physical chemical parameters? *Waste Manag.* 151, 49–59. <https://doi.org/10.1016/j.wasman.2022.07.030>.

- Zhang, M., Yamada, K., Bourguet, S., Guelfo, J., Suuberg, E.M., 2020. Vapor pressure of nine perfluoroalkyl substances (PFASs) determined using the Knudsen effusion method. *J. Chem. Eng. Data* 65 (5), 2332–2342. <https://doi.org/10.1021/acs.jced.9b00922>.
- Zhang, R., Yan, W., Jing, C., 2014. Mechanistic study of PFOS adsorption on kaolinite and montmorillonite. *Colloids Surf. A Physicochem. Eng. Asp.* 462, 252–258. <https://doi.org/10.1016/j.colsurfa.2014.09.019>.
- Zhang, S., Szostek, B., McCausland, P.K., Wolstenholme, B.W., Lu, X., Wang, N., Buck, R. C., 2013. 6:2 and 8:2 fluorotelomer alcohol anaerobic biotransformation in digester sludge from a WWTP under methanogenic conditions. *Environ. Sci. Technol.* 47 (9), 4227–4235. <https://doi.org/10.1021/es4000824>.
- Zhao, L., McCausland, P.K., Folsom, P.W., Wolstenholme, B.W., Sun, H., Wang, N., Buck, R.C., 2013. 6:2 fluorotelomer alcohol aerobic biotransformation in activated sludge from two domestic wastewater treatment plants. *Chemosphere* 92 (4), 464–470. <https://doi.org/10.1016/j.chemosphere.2013.02.032>.

## Review

# Making the Connection Between PFASs and Agriculture Using the Example of Minnesota, USA: A Review

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## Abstract

Exposure to per- and polyfluoroalkyl substances (PFASs) can cause detrimental health effects. The consumption of contaminated food is viewed as a major exposure pathway for humans, but the relationship between agriculture and PFASs has not been investigated thoroughly, and it is becoming a pressing issue since health advisories are continuously being reassessed. This semi-systematic literature review connects the release, environmental fate, and agriculture uptake of PFASs to enhance comprehension and identify knowledge gaps which limit accurate risk assessment. It focuses on the heavily agricultural state of Minnesota, USA, which is representative of the large Midwestern US Corn Belt in terms of agricultural activities, because PFASs have been monitored in Minnesota since the beginning of the 21st century. PFAS contamination is a complex issue due to the over 14,000 individual PFAS compounds which have unique chemical properties that interact differently with air, water, soil, and biological systems. Moreover, the lack of field studies and monitoring of agricultural sites makes accurate risk assessments challenging. Researchers, policymakers, and farmers must work closely together to reduce the risk of PFAS exposure as the understanding of their potential health effects increases and legacy PFASs are displaced with shorter fluorinated replacements.



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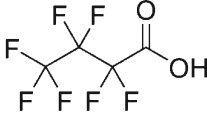
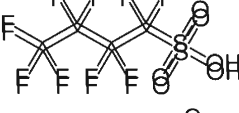
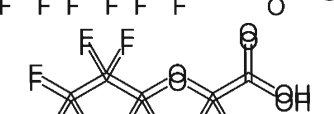
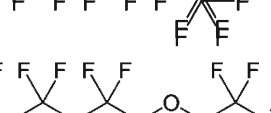
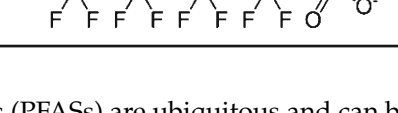
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**Keywords:** PFAS; agriculture; environmental fate; knowledge gaps; mitigation; Midwest

## 1. Introduction

PFASs are defined as aliphatic substances which contain at least one carbon atom on which all hydrogen atoms have been replaced with fluorine atoms. Perfluoroalkyl substances are substances in which all hydrogen atoms attached to the carbon chain have been substituted by fluorine, and polyfluoroalkyl substances are not fully fluorinated [1]. The Organisation for Economic Co-operation and Development proposes a broader definition by suggesting that any compound containing at least one fully fluorinated methyl or methylene group be referred to as a PFAS [2]. There are currently over 14,000 chemicals listed as PFASs in the United States Environmental Protection Agency toxicity databases [3]. Some of the most relevant representatives are presented in Table 1.

**Table 1.** A list of the most relevant PFASs. \* The ammonium salt of HFPO-DA is also known as GenX.

| Name                                            | Abbreviation | Chemical Formula   | Structural Formulas                                                                   |
|-------------------------------------------------|--------------|--------------------|---------------------------------------------------------------------------------------|
| Perfluorobutanoic acid                          | PFBA         | $C_4HF_7O_2$       |    |
| Perfluorobutanesulfonic acid                    | PFBS         | $C_4HF_9O_3S$      |    |
| Perfluorohexanoic acid                          | PFHxA        | $C_6HF_{11}O_2$    |    |
| Perfluorohexanesulfonic acid                    | PFHxS        | $C_6HF_{13}O_3S$   |    |
| Perfluorooctanoic acid                          | PFOA         | $C_8HF_{15}O_2$    |    |
| Perfluorooctanesulfonic acid                    | PFOS         | $C_8HF_{17}O_3S$   |   |
| 6:2-Fluorotelomersulfonic acid                  | 6:2 FTS      | $C_8H_5F_{13}O_3S$ |  |
| Hexafluoropropylene oxide dimer acid *          | HFPO-DA *    | $C_6HF_{11}O_3$    |  |
| 6:2 chlorinated polyfluoroalkyl ether sulfonate | F-53B        | $C_8ClF_{16}KO_4S$ |  |

Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are ubiquitous and can be detected in the environment, wildlife, human serum, and tissue [4–7]. PFASs can accumulate in the human body over time and cause different toxicological effects [8,9], such as cancer, kidney and liver disease, and adverse effects on reproductivity and development [10]. The mean half lives of some of the most common PFASs, namely perfluorooctane sulfonic acid (PFOS), perfluorohexane sulfonic acid (PFHxS), and perfluorooctanoic acid (PFOA), are 5.4 years, 8.5 years, and 3.8 years, respectively [11].

PFASs can be found in many products, such as firefighting foams, food packaging materials, household products, medical devices, pesticide formulations, and surfactants [12]. The widespread industrial and commercial utilization of these substances is based on their chemical and physicochemical properties. The carbon–fluorine bond is the strongest bond in organic chemistry, with a dissociation energy of up to 536 kJ/mol [13]. Therefore, the PFAS family of chemicals shows exceptionally high chemical and thermal stability [14–16]. Due to their polar nature, most PFASs show high solubility in water [17] and are therefore environmentally mobile [18]. Four main activities are responsible for the contamination of PFASs in the air, water, and soil. These include leakages and emissions of PFASs at

manufacturing sites, use of aqueous film-forming foam (AFFF) for firefighting activities, leaching from landfills, and the application of biosolids for wastewater treatment [19–22].

Although PFASs have multiple potential exposure paths to humans, a significant exposure route of concern is the consumption of contaminated food [23]. PFASs can accumulate from the environment in crops and produce that are consumed directly by humans [24], and the PFASs in fodder and grain used to feed livestock can lead to the contamination of the animals and their related food products [25,26]. In Maine, USA, dairy farms were shut down due to PFAS contamination in their products, with PFASs being detected on more than 50 farms [27–30]. Most environmental research has primarily focused on PFAS sources and the fate of these substances in the air, water, and soil [31]. Research on downstream biological systems, such as agricultural crops and livestock, experiencing PFAS contamination is lacking. Understanding the relationship between PFASs in the environment and agriculture is critical as humans are dependent on food production and approximately 44% of habitable land surface is used for agricultural purposes [32].

The research objective of this study is to detail the sources of PFAS contaminations in agriculture, determine the environmental fate of PFASs, and outline the connection to agriculture to fill knowledge gaps. The history, contamination levels, and actions regarding PFASs are discussed for a typical Midwestern state (Minnesota, USA) so that the findings can be put into the historical context, and other agricultural areas can assess their paths towards protecting their agricultural sector from contamination issues. This work aims to make meaningful contributions to public health by reducing the risk of PFAS exposure by suggesting sensible actions based on our findings. Furthermore, we suggest future research directions to close dangerous knowledge gaps.

## 2. Materials and Methods

A semi-systematic literature was carried out to address the link between PFAS contamination and agriculture. Different databases and search engines (i.e., SciFinder (web-based, Chemical Abstracts Services, Columbus, OH, USA), Scopus (web-based, Elsevier, Amsterdam, Netherlands), Web of Science (web-based, Clarivate, Philadelphia, PA, USA), PubMed (web-based, U.S. National Library of Medicine, Bethesda, MD, USA), Google Scholar (web-based, Google LLC, Mountain View, CA, USA), and ScienceDirect (web-based, Elsevier, Amsterdam, Netherlands)) were utilized to identify relevant peer-reviewed articles. Governmental databases (e.g., Minnesota Groundwater Atlas) and reports (e.g., Minnesota's PFAS Blueprint) were examined from multiple agencies to gather Minnesota-related and other important information. Various single and combined search terms were employed due to the complexity and diversity of the presented research objective. For example, the number of publications per year for a typical query (i.e., PFAS \* and agriculture \*) is shown in Figure 1. Excluding most sources from Section 3.1.1, the majority of relevant papers were published from 2019 onward and no publications were found prior to 2007 regarding PFAS in agriculture specifically. The exponential growth of the number of publications indicates the increasing scholarly attention regarding this issue to address pressing knowledge gaps and lacking mitigation strategies.

Multiple qualitative criteria were used for the inclusion or exclusion of the respective sources. These encompassed the (1) relevance, (2) originality (primary and field studies were preferred), (3) publication date (papers published between 2000 and 2024 were considered; this does not apply to historic documents and a few exceptions), (4) overall quality (e.g., methodology, sample size, transparency, etc.), and (5) impact (i.e., number of citations or legislative documents).

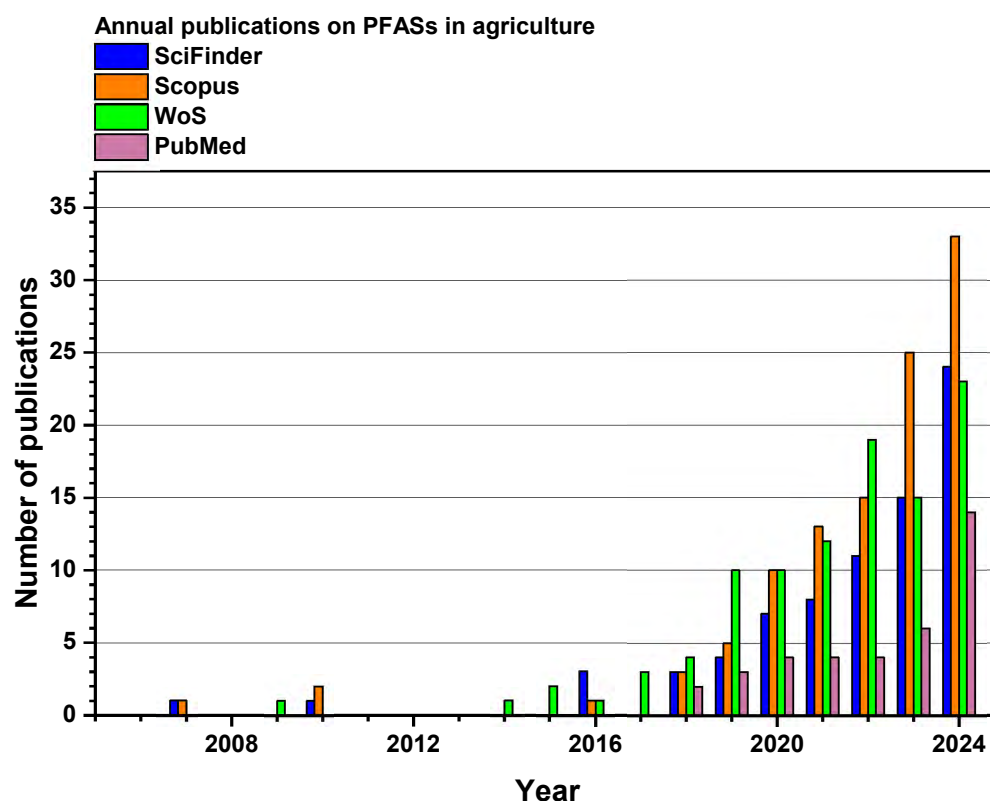


**Figure 1.** A plot of annual publications for the query “PFAS \* AND agriculture \*” between 2005 and 2024.

### 3. Results and Discussions

#### 3.1. PFASs in Minnesota

##### 3.1.1. History of PFASs in Minnesota

Minnesota’s experience with PFASs is deeply intertwined with the beginning of PFAS production in the 1940s. PFOS- and PFOA-related substances and other fluorochemicals were manufactured at Minnesota Mining and Manufacturing (officially renamed 3M in 2002) production facility in Cottage Grove, MN [33]. As early as 1955, research indicated that PFOS could impact biological systems, as protein binding properties were observed in PFOS [34]. In 1961, DuPont researchers found that these chemicals can potentially increase the liver size in rats and rabbits [35]. In 1997, 3M was selling almost 1900 metric tons of PFASs in the US. [36]. Waste products, sludges, and wastewater were generated, disposed of at landfills or discharged to the Mississippi River [37]. In 2002, 3M informed the Minnesota Pollution Control Agency (MPCA) that PFOA and PFOS had been detected in groundwater reservoirs used near production and disposal sites [38].

A number of locations linked to PFAS wastes in and around Cottage Grove, MN, were investigated to examine the extent of contamination [39]. While Cottage Grove and the surrounding areas with contamination were more rural areas when 3M began disposal of PFAS wastes, their population grew to become part of the greater Twin Cities (Minneapolis–St. Paul) metropolitan area. According to the MPCA, 3M’s manufacturing activities led to the contamination of groundwater covering more than 150 square miles, which affected the drinking water quality of more than 140,000 Minnesotans. Different PFASs were detected at varying concentrations in all samples, including groundwater, surface water, municipal wells, sediment, sludges, influent/effluent, fish, plants, leachates, and gas condensates at landfills [37,39]. Further research analyzed the PFAS contamination in the air [40], fish and bald eagles [41,42], leachate and gas condensates from landfills [43], and yard

waste sites [44]. Statistical evaluations showed that residents of affected communities (e.g., Oakdale) were 30% more likely to be diagnosed with prostate cancer, and infants were 34% more likely to be born with low birth weight compared to unaffected communities [45].

3M decided to terminate the manufacturing of PFOS- and PFOA-related compounds after the initial discovery of contamination [5,46]. In 2010, the Minnesota Attorney General sued over contaminated drinking water and natural resource findings [47]. More recently, 3M announced that it will cease all PFAS manufacturing and stop selling products containing PFASs by 2025 due to the “rapidly evolving external regulatory [...] landscape” [48]. Communities are still tremendously concerned about PFAS exposure and the associated health effects and urgently demand that appropriate actions be taken.

### 3.1.2. Contamination in Minnesota

The detection of major contamination around the Twin Cities metropolitan area led to a larger effort to examine PFAS contamination and spread than is seen in other communities and states. While Cottage Grove was the single most sampled area, rural areas throughout Minnesota were also heavily sampled. Much of the data has been reported to the MPCA, who publishes it as part of their role in investigating and regulating pollution in the state [49]. With this extensive data set, Minnesota provides a temporally and geographically complete example for assessing issues related to PFAS contamination. That said, these datasets are complex and difficult to interpret because of the many unique PFAS chemical species and behaviors, in addition to changing testing protocols as the field has advanced.

#### Drinking Water Standards as a Guide

The potential human health risks of consuming contaminated drinking water have meant that most Minnesota and nationwide PFAS investigations have concentrated on the contaminant levels in drinking water [49,50]. However, the extent of the problem has meant that Minnesota has expanded testing to surface and groundwater statewide. While the dangers represented by contaminated drinking water are different than agricultural PFAS contamination, water data provides the best guide to understanding contamination in agriculture. The vast PFAS water data from different sites and examining different types of PFASs require that a metric be established to help evaluate locations where contamination levels are potentially detrimental to health.

The Health Index (HI) was adopted by Minnesota in 2002 to evaluate the associated risk of consuming drinking water, and it is continuing to be updated as new data emerges [51]. The HI uses drinking water guidance values for perfluorobutanoic acid (PFBA) (7.000 µg/L), perfluorobutanesulfonic acid (PFBS) (2.000 µg/L), perfluorohexanoic acid (PFHxA) (0.200 µg/L), PFHxS (0.047 µg/L), PFOA (0.035 µg/L), and PFOS (0.015 µg/L) (see Equation (1)) [52].

$$\text{HI} = ([\text{PFBA}]) / (7 \text{ } \mu\text{g/L}) + ([\text{PFBS}]) / (2 \text{ } \mu\text{g/L}) + ([\text{PFHxA}]) / (0.2 \text{ } \mu\text{g/L}) + ([\text{PFHxS}]) / (0.047 \text{ } \mu\text{g/L}) + ([\text{PFOA}]) / (0.035 \text{ } \mu\text{g/L}) + ([\text{PFOS}]) / (0.015 \text{ } \mu\text{g/L}) \quad (1)$$

If the HI is greater than 1, the drinking water is considered to have potentially adverse health implications. More information on the regulation of PFAS contamination levels is provided in Section 3.5.

As of July 2024, 919 Community Water Systems out of 966 have been tested by the MPCA, with 5 exceeding the proposed HI. The contaminated Community Water Systems are in larger urban areas, except for Swanville, a small community in central Minnesota. Most Community Water Systems showing PFAS contamination are located in the Twin Cities metropolitan area, which can be linked to 3M production in Cottage Grove (see Section 3.1.1) [49].

The geospatial distribution of wells that contain at least one PFAS that exceeds health-based guidance values and their proximity to wellhead protection areas, which surround public water supply wells and where groundwater contributes to the respective wells, are shown in Figure 2. Out of 13,884 locations/timepoint sampling combinations, 17% contained at least one exceedance and 4189 total exceedances were detected [53]. These were found both in urban and rural/agricultural regions (see Figure 2).

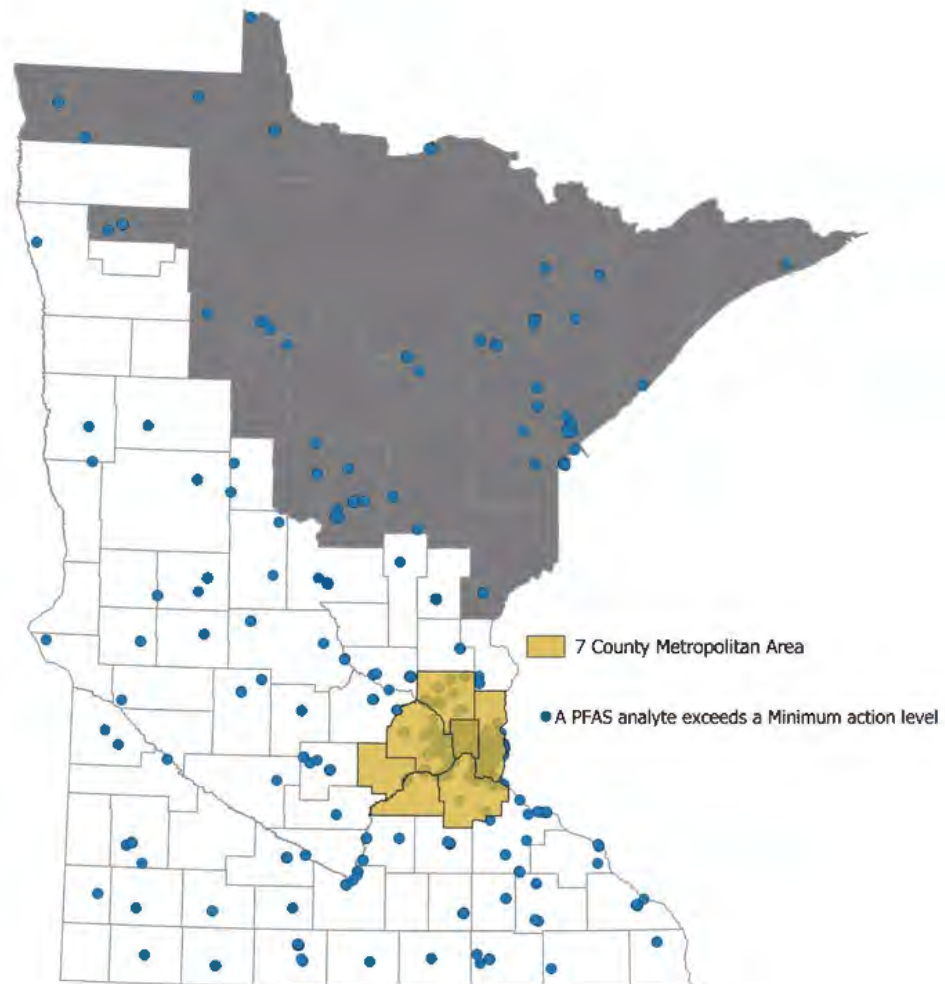


**Figure 2.** PFAS exceedance data obtained from the MPCA by request. Regions in black represent counties with less than 2.7% of county land area used for corn production. The Twin Cities metropolitan area is excluded. White regions represent counties with greater than 2.7% of county land area used for corn production.

#### Air Pollution

The first extensive study on PFAS levels in ambient air was published by the MPCA in April of 2022 [40]. Researchers sampled the ambient air at four different sites. Three sites were located near PFAS-emitting sites in urban areas (Duluth, St. Louis Park, and Eagan), while the fourth site (Grand Portage) was in a rural area and was expected to be a low-PFAS reference site. During the observation duration, 17 different PFASs were detected, varying in concentration and time of observation. The MPCA found PFBA, PFBS, PFOA, and PFOS in all air samples, with PFBA contributing approximately between 47% and 70% of the total PFAS concentration. The authors attribute the abundant occurrence of PFBS to the direct emission and degradation of precursors in the atmosphere. Precursors are used as intermediates in the manufacturing process of surfactants or fluoropolymers. They are also used as substitutes for chlorofluorocarbons, coolants, solvents, or fire suppressors [54].

Additionally, 6:2 fluorotelomer sulfonate is known to replace PFOS at chrome plating facilities (e.g., at the St. Louis Park site) and is additionally applied in AFFFs. Therefore, 6:2 fluorotelomer sulfonate was regularly detected in ambient air [40].

Though Grand Portage was chosen due to its remote location, low population (684 in 2019), and limited industry, it showed the second highest airborne PFAS contamination with a mean concentration of about 100 pg/m<sup>3</sup>. The authors hypothesize that this surprising finding is likely due to emissions from the local fire department and the solid waste transfer station. They also speculate that long-distance atmospheric transport might contribute to the relatively high concentrations. The findings that the rural community of Grand Portage could have high detectable levels of airborne PFAS indicates that rural/agricultural areas should not assume that their relative isolation is potentially sufficient to limit exposure to airborne PFASs.

### 3.2. Significant Sources of PFASs in the Environment

#### 3.2.1. Release of PFASs During Their Production, Use, and Disposal Phases

Manufacturing plants that produce PFASs or use PFASs in production of other products contribute significantly to environmental contamination by PFASs [55]. During the manufacturing process, PFASs can be emitted into the atmosphere [40,56] or discharged as contaminated wastewater that is often not sufficiently treated at wastewater treatment plants before it enters the aquatic environment [37,55]. Hazardous wastes containing PFASs can also be generated during the production process, which may not always be mitigated when incinerated or disposed of; improper storage or burial might contaminate the environment [57].

PFASs can enter the environment during the use of the PFAS-containing products [15]. For example, some carpets contain PFASs to repel stains, which might be released from carpet fibers over time [58]. Functional textiles (e.g., outdoor clothing) are also treated to have water-repelling properties. They are exposed to radiation, rain, heat, and abrasive stress that can cause the emission of repellents [59]. Many non-stick pans are coated using PFAS precursors, which can flake off during cooking or during the cleaning process. PFASs are present in more than 200 use categories [15], which have the potential to lead to unintentional PFAS release.

After their use, roughly 146 million metric tons (50%) of solid wastes were landfilled in 2018 in the US. [60]. Solid waste management facilities are viewed as important point sources of PFAS pollution, and thus, many researchers have investigated the PFAS concentration in landfill leachates [61–63]. PFASs undergo long-term leaching, and precursors degrade [64] as they are exposed to sunlight, microbial activity, varying redox conditions (available oxygen, pH-value, content of redox active species, etc.), or wastewater treatment [65]. PFAS leachate and gas condensates at solid waste landfills were evaluated across the state by the MPCA between 2005 and 2008. Down-gradient (points where water flows away from landfill) and upgradient (points where water flows to the landfill) groundwater samples were taken and found to have significant differences in concentrations of PFBA and PFOA, with PFAS concentrations being higher in the water leaving the sites. PFOS was detected in 10% of the samples. There were noteworthy differences between the median PFOA and PFBA concentrations in the groundwater at lined and unlined landfills. The median concentrations at lined landfills were 2.39 ng/L and 33.2 ng/L, respectively. The median concentrations of PFOA and PFBA at unlined landfills were 0.36 ng/L and 7.29 ng/L, respectively. The same study also showed that gas condensates were contaminated [43].

In total, the MPCA investigated the groundwater at 102 out of 111 landfills of interest. Out of those, 98% showed elevated PFAS levels, and the drinking water guidance values of the Minnesota Department of Health (MDH) were exceeded at 62 sites [66]. The landfills

included both metro and rural landfills. Rural landfills are often outside cities and adjacent to active farming operations. Most of the rural landfills analyzed in these efforts are landfills that were closed or consolidated as more stringent environmental rules increased requirements for siting and management. However, these closed landfills are likely to have been leaching PFASs for decades. They are typical of small town/county size landfills found throughout the US Midwest.

Mass balancing PFAS leachates and estimating total releases is challenging as they depend on various fluctuating factors (e.g., rainfall, number/concentration of PFASs) [67]. Lang et al. estimated that the total PFAS mass release from leachates at landfills in the US is approximately 600 kg/year [61].

### 3.2.2. Aqueous Film-Forming Foam (AFFF)

Over 240 individual PFAS compounds (e.g., perfluoroalkyl carboxylic acids (PFCAs), perfluorosulfonic acids (PFSAs), and perfluoroalkyl sulfonamido compounds) are used in aqueous film-forming foam (AFFF) formulations [68,69] to enhance wetting at the hydrocarbon–water and air–water interfaces [15,69]. In practical terms, this allows fire-fighting foams with AFFF to more easily encapsulate flammable liquid fuels and starve them of oxygen when attempting to stop a fuel fire. Firefighting and training activities (e.g., at airports, fire training areas, or military sites) have resulted in the contamination of surrounding surface waters and groundwater. However, data describing the lower-volume AFFF use at smaller airports has not been collected, so it is difficult to assess how significant this problem may be at rural airports. As many precursors present in these foams undergo transformation processes [70,71], the fate of AFFF-contaminated sites is not fully understood [68].

Many rural airports are located immediately adjacent to agricultural fields, which provide the open land needed for runway safety. The use of AFFF at these sites, either for training or to combat an actual fire, has the potential to contaminate nearby groundwater and fields.

### 3.2.3. Biosolids from Wastewater Treatment

Biosolids consist of organic matter that is recovered from sewage during wastewater treatment. They are often applied in agriculture to improve soil fertility by enriching it with nutrients and organic matter [72]. Biosolids are heterogeneous and have varying concentrations of organic matter, microorganisms, bacterial constituents, inorganic materials, and water [73]. As a result, PFASs can bind to various sites of these components with different strengths [74–76]. PFAS-contaminated biosolids are generated in the wastewater treatment process because PFASs cannot be efficiently removed from sewage being treated during biosolid separation. Some studies even showed that the concentration of stable perfluoroalkyl acids increases during treatment due to the oxidation of precursors (e.g., fluorotelomer alcohols) [77,78]. Hence, wastewater treatment plants are considered an important point source of PFAS [16]. Although sewage and treated biosolids from residential sanitation systems are known to contain somewhat higher levels of background PFASs, sewage from industrial wastewater treatment is a primary source of more highly contaminated biosolids [79].

Once the contaminated biosolids are applied on a field, the fate of the PFASs is influenced by physicochemical properties of the respective substances and soil. It was shown that the half-lives of different PFASs in soils can range from a few days to years depending on their chain length, functional groups, and their dissociation constant [80,81]. Furthermore, substances can be accumulated by various plants [82–84] or leach into the groundwater [23,85]. As a result, PFASs were detected in livestock, and thus, food pro-

duction can be an exposure pathway to consumers [86]. Lindstrom et al. investigated well water and surface water close to fields where contaminated biosolids were applied for 12 years and observed elevated PFAS concentrations (up to 11 µg/L for PFOA in surface water) [87].

The Environmental Protection Agency (EPA) estimated that 1.15 million dry metric tons of biosolids were applied to agricultural land in 2021 [88]. The yearly loading of PFASs on agricultural land in the US is estimated at 1375–2070 kg/year [89]. Thus, concerns arise about whether and to what extent biosolids pose a threat to food supply and, therefore, the economic security of farmers [90]. While a typical application of biosolids is not expected to dramatically increase PFAS concentrations in the soil, there is a concern that multiple biosolid applications or the use of heavily contaminated biosolids may increase soil contamination to the point where food or livestock feed would have high levels of PFASs.

Regulatory agencies became aware of the contamination potential of biosolids in 2016, when elevated PFAS levels were detected in milk products of a dairy farm in Maine. The Maine Department of Environmental Protection found combined PFOA and PFOS concentrations of up to 1.420 µg/L. In addition, a PFOS concentration of 32.200 µg/L was detected in dairy products on another farm in 2020 [90].

#### 3.2.4. PFASs in Pesticide Formulations

Approximately 68,000 metric tons of pesticides are applied yearly in the Midwestern US [91]. PFASs have been part of some pesticide formulations as active ingredients or identified as inert ingredients in the past [92]. However, it is not fully clear how many currently used pesticides in the US contain PFASs as active ingredients or for other reasons. Lasee et al. found that 6 out of 10 insecticide formulations contained PFAS concentrations between 3.92 mg/kg and 19.2 mg/kg [93]. However, these results could not be verified in a separate investigation, and no PFASs were detected above the detection limit of 0.2 µg/L [94].

International pesticide active ingredient and application differences also increase the difficulty of quantifying PFAS applications to land. N-ethyl perfluorooctane sulfonamide, also called sulfuramid, is an effective insecticide used to control leaf cutting ants (*Atta* and *Acromyrmex*) [95]. It can be transformed into PFOS in the environment. Even though sulfuramid was internationally phased out by 2016 [96], it is still used in South America. Estimates are that Brazilian sulfuramid use has been responsible for the release of up to 487 metric tons of PFOS/perfluorooctanesulfonamide between 2004 and 2015 [97].

Storage containers can also be a PFAS source in pesticides via leaching. Nguyen observed gradual leaching from fluorinated high-density polyethylene containers. The total PFAS concentration was 15 µg/L when methanol was used as a solvent and 3 µg/L in water [98]. However, the relatively small contribution of PFAS from a container to any applied chemical would be difficult to detect. Consider an example of a container that holds 9 L of pesticide covering 4 hectares of crops, which could leach 15 µg PFAS per liter of pesticide, and leaching would result in 34 µg/ha or 3.3 ng/m<sup>2</sup>. This is below the background levels, as noted by Qian and French [94]. Generally, pesticide use is very crop, weather, and geographically specific. Thus, the load of pesticide-related PFASs must be calculated on a case-by-case basis.

#### 3.2.5. PFASs in Rural Versus Urban Communities

It is evident that rural and urban areas are impacted by different PFAS contaminant sources as they vastly differ in their industrial activities, population density, and land use [99]. This is reflected by site-specific contamination patterns, which reveal information about PFAS discharge in the area [100].

The background levels should be lower in rural areas due to reduced human activities, but similarly to urban areas, point sources are primarily responsible for pollution in rural areas. It is important to explicitly discuss sites likely to face contamination issues in agricultural and rural areas. While a significant amount of contamination has been observed in areas near PFAS production sites and in industries utilizing PFASs, such occurrences are relatively uncommon in rural areas. Very few facilities produce PFASs nation-wide, and facilities using large volumes of PFASs in industrial application tend to be closer to urban centers that can supply labor. Therefore, most contamination in rural areas occurs from the application of high-PFAS-concentration biosolids, the use of AFFF, the application of PFAS containing pesticides, or leaching from landfills. While some species of PFASs are spread by air in rural environments, it should not be significantly different than the global background levels. Lastly, in total, there are 321 airports, seaplane bases, and heliports statewide in Minnesota that are generally linked to enhanced contamination levels [101].

### *3.3. The Behavior and Transport of PFASs in the Agricultural Environment*

The fate of PFASs in the environment and its entry into agricultural ecosystems depends on various parameters. The physicochemical properties of particular PFAS species determine their movement, partitioning, and transformation behavior, also called environmental fate [102]. The PFAS chain length [103] and functional groups [104] significantly impact their solubility, mobility, and bioavailability. Thus, each substance has a unique environmental fate, which makes it challenging to develop predictive models in agricultural soils, plants, and livestock [105].

#### *3.3.1. PFASs in the Atmosphere*

Non-ionic PFASs (typically precursors) are often sufficiently volatile such that they are transported in the atmosphere [106]. Long-range transport of PFASs, on the order of days to weeks, can occur in the atmosphere. For example, researchers attributed the contamination of the European Arctic to long-atmospheric transport processes, the resulting degradation processes and local sources (e.g., consumer products and AFFFs) [107,108]. The total historical global emissions of PFCAs due to indirect air emissions are estimated to be as high as 350 metric tons, which contributes between 4.8% and 10.9% of the total historical PFCA emissions [109].

Airborne PFASs can migrate to the soil or into surface water via dry (direct deposition) or wet deposition (ab- or adsorption by/at water) [107,110–112]. Compared with other types of movement of PFASs, airborne movement likely spreads material over a wider area at a lower concentration. This compares to PFAS movement in water, biosolids, or other solid/liquid mediums. This is likely a primary mechanism for the background PFASs found in many isolated rural communities, both agricultural and non-agricultural.

#### *3.3.2. PFASs in Surface Water, Sediment, and Groundwater*

About 40 different PFASs have been detected in the aquatic environment [106]. PFASs with low pKa values and vapor pressure (e.g., PFCAs and PFSAAs) are ionic at common environmental pH values. These ionic PFASs are mainly observed in water or bound to particles and sediment [109,113]. The PFASs that persist in the aquatic environment can be transported downstream by rivers until they end up in the marine environment, where PFASs can reenter the atmosphere via sea spray [114]. During this process, the total PFAS concentration decreases downstream until it reaches the oceans [106].

Multiple studies have investigated the sorption behavior of PFASs between water and different sediments/soils [104,113,115,116]. Sediments can store organic pollutants over a long period since sediments show hydrophobic behavior in the aquatic atmosphere [117], and trends of released PFASs (e.g., replacing PFOA with HFPO-DA) can be observed in

sediment cores [118]. Other important parameters for sorption are the pH value, organic carbon content, and the coexistence of certain metal cations (e.g.,  $\text{Ca}^{2+}$ ) [104,113,115,116].

Generally, PFCAs with a chain length shorter than seven carbon atoms were exclusively found in the liquid phase [104], and every extra  $\text{CF}_2$  moiety on the molecule increases binding affinity to the solid phase. Moreover, the sulfonate group enhances the absorption strength further in comparison to the PFCA analogs [116]. Linear PFAS isomers tend to sorb to sediments due to their lower hydrophilicity compared to their branched isomers [119].

Many worldwide studies have investigated groundwater contamination levels [120–124]. Groundwater contamination can be attenuated by the vadose zone due to sorption phenomena [85], and surface water was identified as a key source of groundwater contamination [125–127]. In contrast to the atmosphere and deposition on surface water, which retain PFASs for short periods, groundwater (and soil column) contamination reflects the long-term retention of PFASs [128].

The biotransformation of precursors is another important factor in evaluating whether aquifer contamination is a potential source of danger for the environment [121] or human health [9,129]. Biotransformations are highly dependent on the toxic conditions of the soil [70,130,131].

As groundwater enters springs, lakes, rivers, and wetlands or is used for irrigation [132], PFASs that are present can reenter the water cycle [121] and thus might be reintegrated into the biosphere. Overall, PFAS groundwater contamination processes are not well understood, and further research is needed to improve modeling [133].

### 3.3.3. Behavior and Uptake of PFASs in Soils

#### PFAS Sorption

The modeling of soil PFAS adsorption is complicated by the wide variation in soil components and the resulting soil's physical and chemical properties. Soils are a mix of mineral, organic, and biologically active materials and other compounds that can change over the distance of a few meters. These variations interact in concert with the chemical property differences in PFAS species. Some soils simultaneously have surface sites that are charged positively and negatively. The surface charge strongly depends on the pH and on the soil type [134,135]. At the same time, several PFASs occur in an ionic or zwitterionic state (equal number of positively and negatively charged functional groups present in the molecule) in the environment [136,137].

Several studies investigated the vertical distribution of PFASs in the ground after contamination due to biosolids application or AFFF use [6,21,138–140]. In most cases, the observation was that the vertical loading of PFASs in the vadose zone decreased sharply with increasing depths. In contrast, Nickerson et al. found that total PFAS concentrations increased along the vertical profile of the soil, and the maximum concentrations were observed at a depth of 3–5 m [141]. The retention and lifetime of PFASs, especially precursors, differ vastly depending on the soil [142–144].

The factors influencing the adsorption of PFASs (mainly PFOA and PFOS) onto soils have been thoroughly investigated. It is apparent that the sorption of PFASs is not dependent on one factor and that models must use multiple parameters to describe sorption accurately. Organic carbon is often attributed as the driving parameter of PFAS adsorption in the soil [116,145–149].

Another important factor is the content of dissolved inorganic salts in the soil column since they can change the properties of the aqueous phase. Investigations showed a positive correlation between the ionic strength and the sorption of anionic PFAS onto soils [116,146,147,150,151]. It was found that with increasing ion concentrations, the mo-

bility of PFASs along the soil profile decreased (especially for long-chain PFASs with  $C > 10$ ) [151].

Most sorption processes of PFASs might be explainable when considering the organic carbon, pH, and the clay content due to the importance of electrostatic interaction for the sorption processes. More data is needed to conduct multivariate data analysis techniques, which might provide a more accurate understanding [76]. This would be very helpful as values of the field- and laboratory-derived partitioning coefficients for PFOS, PFOA, PFNA, and PFDA in the literature vary by factors of 1.6, 10.9, 1.9, and 1.7, respectively. All field-derived values are larger than the laboratory-derived values [76]. More soil adsorption research is needed, which should include a precise characterization of the soil properties to facilitate future analysis of sorption processes. If the sorption mechanisms are fully understood, farms and areas that are likely to have the potential to have a high concentration of sorbed PFASs can be identified. This ensures effective employment of resources in mitigation efforts.

### PFAS Retention

The retention of PFASs in soils depends not only on the interactions between the compound and the soil but also on (1) adsorption at the air–water interfaces, (2) partitioning to soil gases, (3) adsorption at non-aqueous phase liquid (NAPL)–water interfaces, and (4) partitioning to the NAPL [152,153]. The combination of general partitioning mechanisms might not be sufficient to predict retention in some cases [154]. One field study investigated the PFAS partitioning behavior at AFFF-affected sites and observed that at 87% of the examined sites, the concentration levels in the soil exceeded those of the groundwater, indicating the significance of the retention [154].

However, a laboratory study revealed that between 80% and 90% of the ten investigated PFASs were eluted in the flow-through soil column experiments [155]. It is questionable to what extent the results of the study can be transferred to environmental conditions. A further important contributor to PFAS transport is the presence of co-contaminations [156]. Those can increase sorption by providing additional binding sites or lower PFAS sorption by competing for existing sorption sites in the soil [157].

### PFASs in Agricultural and Rural Soils

PFAS release mechanisms of concern for agriculture are all point sources of contamination that first impact specific release sites. Thus, preventing agricultural plant and animal systems from being exposed to PFASs requires an understanding of local point sources of contamination and the potential for movement into the agricultural environment.

Depending on factors such as surface and sub-surface water flows and soil types, the areas adjacent to the initial contamination sites can become polluted over time. As described above, the rate of movement is dependent on many different soil, water, and PFAS physical and chemical properties as well as concentration gradients. Based on the data from Minnesota contamination sites, it is likely that sub-surface movement of PFASs from a contamination site can take several years per kilometer of movement in typical soils. This time is reduced in soils with high groundwater flows. In contrast, contamination moves very quickly in surface waters.

The risk of PFAS translocation should be insignificant for the consumer if the products were grown on fields with no history of direct PFAS application and that underwent minimal industrial processing. However, the general lack of monitoring of agricultural sites makes it challenging to perform accurate risk assessments.

### 3.4. PFASs in Plant and Animal Systems

Agricultural plants and animals are in direct, constant interaction with the outdoor environment, and thus, they can take up PFASs from their surroundings. A better understanding of the uptake mechanism of agricultural plants and animals consuming plants is required to reduce the potential risks of human exposure to PFAS from agricultural products. This section describes the current understanding of these interactions and the potential for contamination of agricultural goods during production.

#### 3.4.1. Plant Uptake of PFASs

##### PFAS Uptake Mechanisms in Plants

The predominant pathway for plant accumulation is root uptake [158–161]. Above-ground parts of the plant can also absorb airborne PFASs to a smaller degree [162–164]. In the first step of the root uptake process, the contaminants diffuse passively into the surface tissue of the root system. The PFASs are then gradually distributed and accumulate in the root tissue. This only occurs in cell walls that have not sufficiently developed protective layers (e.g., cuticle layer) [165]. If the molecule has sufficient lipid solubility, it can pass the lipid bilayer of the membrane and enter the aqueous phase inside the cell. Charged or polar particles might be hindered from entering the cell membrane by the lipid bilayer, but proteins can function as a transport system [166] due to the high affinity between PFASs and proteins [167]. After they enter the root tissue, PFASs can be absorbed by apoplastic cell wall tissue outside root cell membranes and be transferred through the xylem up to the plant's shoot (see Figure 3). Here, the Casparian strip inhibits the translocation of long-chain PFCAs, PFASs, FOSAs, and chlorinated polyfluorinated ether sulfonates by sealing the space between the cell membranes and cells [83]. As a result, long-chain PFASs are mainly limited to the root system and accumulate in the shoot system in a smaller amount [84,159,168].

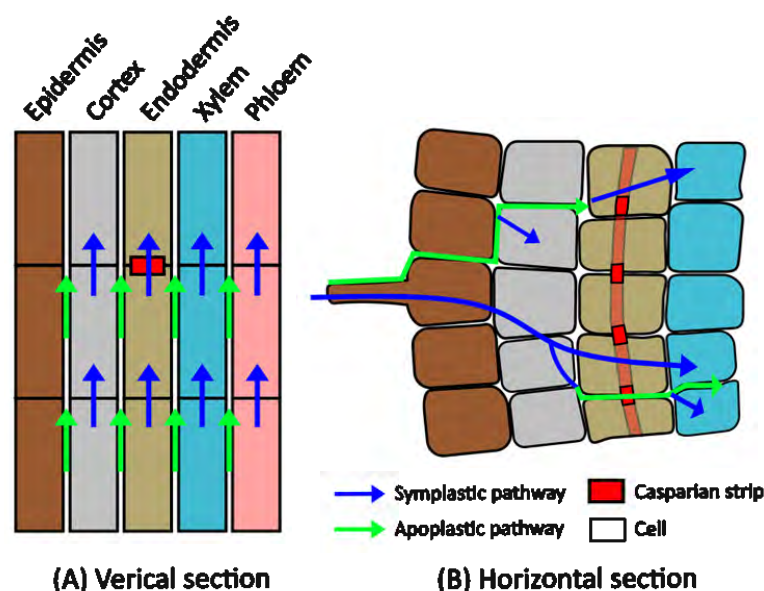


**Figure 3.** A schematic illustration of the possible pathways of PFAS translocation in plants. A vertical root section and transportation (A); PFAS movement in a root cross section (B). The movement along cell walls (apoplastic) is indicated with green arrows, and the translocation through cells (sym-plastic) is displayed with blue arrows [169].

PFAS concentrations in fruits decrease further due to additional barriers as the contaminants are translocated in the aboveground plant tissue [170]. It is important to note that uptake mechanisms are plant specific [83]. For example, Liu et al. linked differences

in PFAS uptake in different crops to the varying lipid and protein contents [56]. Another study showed that the shoot accumulation of long-chain PFASs might be related to the surface-area-to-tissue ratio and is enhanced with an increasing surface area [171].

#### Uptake Rates of Different Crops

Since most plant uptake experiments have utilized varying conditions (e.g., soil vs. hydroponic cultivation, different plants or soil types, contamination levels, etc.), uptake metrics have been developed to improve the comparability of plant uptake across different studies. The bioaccumulation factor (BAF) gives the ratio of the PFAS concentration in the plant to the concentration levels in the surrounding environment (Equation (2)) [172]. The second important factor is the translocation factor (TF), which describes the distribution of the compound of interest within the plant (e.g., TF<sub>leaf/root</sub>) and is calculated similarly to the BAF (Equation (3)) [173].

$$\text{BAF} = [\text{PFAS}_{\text{plant tissue}}]/[\text{PFAS}_{\text{soil}}] \quad (2)$$

$$\text{TF} = [\text{PFAS}_{\text{leaf}}]/[\text{PFAS}_{\text{root}}] \quad (3)$$

The literature shows a direct positive correlation between the PFAS concentration in the soil and the plant [83,84,174]. Moreover, the bioaccumulation of PFASs by plants depends on various plant and soil factors. The physicochemical properties of the respective PFASs, contamination levels, plant type, and environmental conditions all interact to determine the uptake rate. An interesting trend observed was that, while TFs varied throughout the plant, BAFs were higher for vegetative plant parts than reproductive and storage organs [84,173]. The Casparian strip plays an important role in impeding the translocation within the plant, and translocation is also decreased by a relatively low protein content in the aboveground tissue [169].

Krippner et al. investigated the influence of the chain length (C4 to C10 for PFCA; C4, C6, and C8 for PFSAs) on the uptake and distribution of PFCAs and PFSAs in corn and observed that the uptake rates (BAF) exhibited a U-shaped trend. The lowest uptake rates were observed for PFHpA and PFHxS [175]. In contrast, the TF showed a negative correlation with the chain length for the tested PFCAs and PFSAs. Longer-chain-length PFASs possess a higher affinity for the lipid bilayer of membranes, which reduces overall movement within the plant [175]. PFOS showed the highest mean uptake rates, possibly due to different uptake mechanisms [176]. However, the BAFs for PFOS in different plants are generally considerably lower than those for PFOA or PFHxS [177]. It is apparent that translocation is more hindered with increasing chain lengths, and the risk of exposure is higher for short-chain PFASs that are less studied [178]. It should be noted that Krippner et al. grew plants in nutrient solutions, which is a less realistic approach since the interactions with soil components are missing [175].

In a case study, Liu et al. [56] examined the PFAS concentration in the soil and crops from a mega fluorochemical industrial park at two distances (0.3 km and 10 km). The soil had total contamination levels between 79.9 µg/kg and 200 µg/kg, with PFOA being the most abundant substance. The PFAS levels in the crops were between 58.8 µg/kg and 8050 µg/kg, with the BAFs of edible parts reaching levels of up to 48.0 µg/kg (radish) in shoot vegetables. The ranking for BAFs in terms of highest bioaccumulation of the different plants grown at the field 0.3 km from the pollution source were shoot vegetables (24.3 µg/kg) > fruit vegetables (6.63 µg/kg) > flower vegetables (4.23 µg/kg) > grain crops (4.05 µg/kg) > root vegetables (3.58 µg/kg).

PFASs' impacts on plant health were examined by Stahl et al., who studied the uptake of PFOA and PFOS by different plants by spiking the soil with concentrations between 0

and 50 mg/kg. They found that exposure to a concentration of 50 mg/kg led to a significant reduction in corn (*Zea mays*) yield, mainly due to reduced ear mass [160]. However, these high contamination levels are only likely found at sites where PFASs are directly released (e.g., manufacturing or AFFF affected sites) [179], and studies investigating PFAS uptake at more typical environmentally relevant concentration levels are lacking [180].

### 3.4.2. PFAS Contamination in Livestock

The primary mechanism for PFAS contamination of livestock, and the resulting animal-based productions they provide, is the consumption of contaminated feed or water. PFASs can be absorbed by the gastrointestinal tract [181,182] and bind to blood serum proteins [183,184]. The distribution in animal tissue is PFAS and species dependent. For example, PFOA, PFOS, and PFBS accumulate to a higher degree in the liver in most species, whereas PFBA and PFHxS can be found to a higher degree in the blood serum [182].

Kowalczyk et al. [25] investigated the kinetics of PFBS, PFHxS, PFOS, and PFOA in dairy cows by feeding them contaminated grass silage and hay for 21 days. The plasma concentration levels of PFBS (mean =  $1.8 \pm 0.8$  µg/L) and PFOA (mean =  $8.5 \pm 5.7$  µg/L) were relatively low compared to those of PFOS ( $2462 \pm 411$  µg/L on day 44) and PFHxS ( $419 \pm 172$  µg/L on day 29). Additionally, the concentrations in the milk samples were proportional to blood serum levels, and the highest cumulative secretion was observed for PFOS ( $14 \pm 3.6\%$  µg/L). PFBS ( $0.01 \pm 0.02\%$  µg/L) and PFOA ( $0.1 \pm 0.06\%$  µg/L) were secreted into the milk in a low amount. Similarly, it was shown that PFOA is excreted significantly faster compared to PFOS in sheep. PFOA was mainly excreted with urine (51–55%) and could not be detected after day 42. In contrast, the highest PFOS excretion was detected in feces (4–5%) followed by milk. The PFOS levels in the tissue of the sheep did not decrease during the 21-day PFAS-free feeding period [26]. Since the animals were exposed to contaminated fodder for a relatively short time, serum and/or tissue concentrations might have not reached a steady state, possibly leading to a significant underestimation of these values [185].

In general, few studies have focused on PFASs in livestock, and their focus was on uptake and elimination. Potential adverse health effects were hardly investigated for different animal species, especially livestock [86]. Studies in monkeys showed a link between the exposure of PFASs and liver toxicity, altered thyroid hormone concentrations, decreased cholesterol serum concentrations, weight loss, and glycogen metabolism [186]. It is assumed that animals are capable of tolerating high PFAS concentrations [86], but more research is needed to investigate potential adverse health effects in livestock. Hlousova et al. found that PFAS concentrations from common farm livestock decrease in the following order: pig/bovine liver > egg > meat > dairy products (butter) [187]. Pasecnaja et al. summarized several studies that assessed the contamination levels in the European food market. They found that the most important sources were fish, meat, eggs, fruits, and vegetables, with fruits and vegetables exceeding the levels found in meat [188].

### 3.4.3. PFAS Transfer Through the Food Chain

Several parameters influence PFASs as they move through the food production chain (Figure 4). The descriptions of the environmental fate of PFASs described above can be transferred to food production. Bioaccumulation can occur at every step if a contamination source is present. This is critical if the source continuously emits PFASs or if large amounts are released over a brief period. Crops grown on soil with high PFAS loadings will uptake the surrounding contaminants to an often times unknown extent. If these crops are used as feed, the livestock and the produced meat will be affected as well and might show stronger contamination levels compared to the fed crop. For example, Tefera et al. estimated the

total daily mean dietary PFAS intakes for firefighters. They showed that food (i.e., eggs, fruits, and vegetables) which was produced at fire stations was responsible for 82% (i.e., 1250 ng/d) of the total PFAS intake [189].

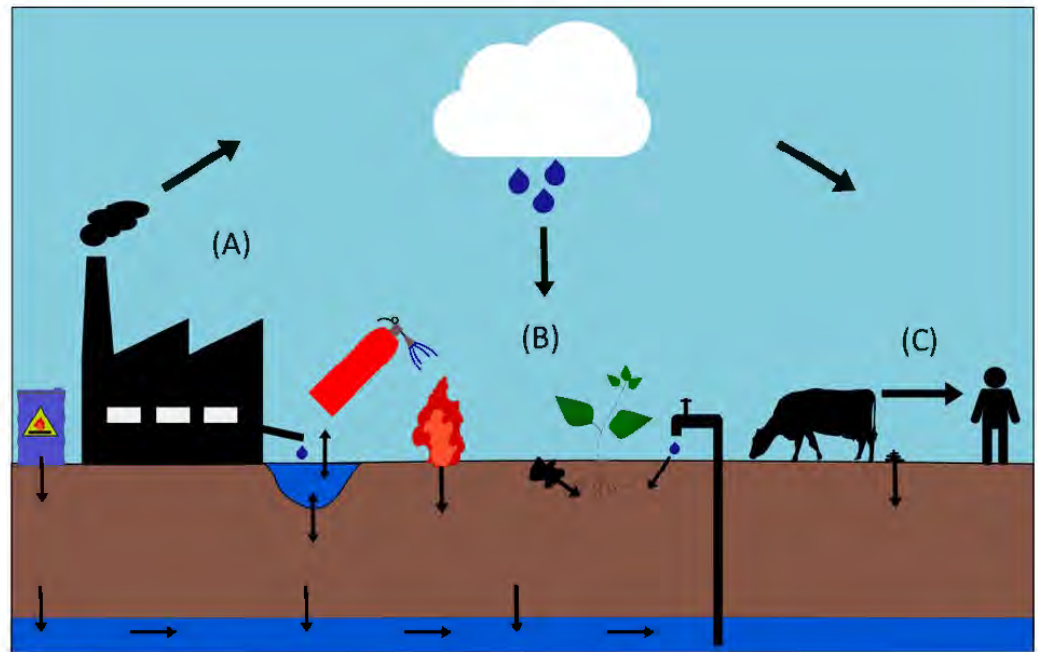


**Figure 4.** An illustration of the PFAS cycle in relation to agriculture. (A) shows the release of PFASs by point sources (manufacturing sites, landfills, AFFFs, and biosolids), which is followed by (B) uptake by crops and livestock. Lastly, (C) contaminated products are consumed. The arrows indicate the direction of PFAS translocation and accumulation along the food production process.

The large number of individual PFAS molecules and their unique fates make it challenging to conduct highly accurate PFAS risk assessments [23] for food production systems. While short-chain PFASs have not been the focus of research, they show the highest mobility in the environment and across the food web, and their emissions are expected to increase. Recent studies showed that they might cause adverse health effects similar to long-chain PFASs [178,190,191], indicating the dire need for intensive investigations on shorter-chain PFASs.

There seems to be a disconnection between the fact that diet is a major exposure pathway [23] and the limited resources being used to address PFASs in agriculture. This might be partially due to early studies suggesting that dietary exposure is neglectable [192]. However, recent studies suggest that even exposure to an extremely low concentration might cause detrimental health effects, which is underlined by the EPA's updated drinking water health guidance values [193] (see Figure 5).

The complexity of soil-to-plant, plant-to-human/livestock, and milk/meat-to-human PFAS interactions combined with the vast number of PFAS species limits our understanding of how and which PFASs are transferred through the food web. Another dimension of complexity is added when considering PFASs present in food contact materials (e.g., fast food wrappers or baking plates) [194]. This makes accurate assessments of the posed threat to consumers nearly impossible without more information.

### 3.5. Policy and Regulations

In the US, regulation and policy for pollution issues often occur at both the federal and state levels. There are currently no nationwide restrictions on PFAS contamination levels in food in the US. The State of Maine Department of Agriculture, Conservation and Forestry established PFOS action levels for beef (3.4  $\mu\text{g}/\text{kg}$ ) and milk (0.21  $\mu\text{g}/\text{L}$ ) [195].

The European Food Safety Authority set a tolerable weekly intake (TWI) for the sum of PFOA, PFNA, PFHxS, and PFOS at 4.4 (ng/kg food)/(week · kg bw) [196].

Most PFAS regulation and research funding have been directed at drinking water standards. Due to Minnesota's longer history of PFAS pollution issues, Minnesota has had much earlier PFAS drinking water standards than the federal government. In the past few years, the federal government has begun to set more stringent requirements for drinking water (Figure 5).

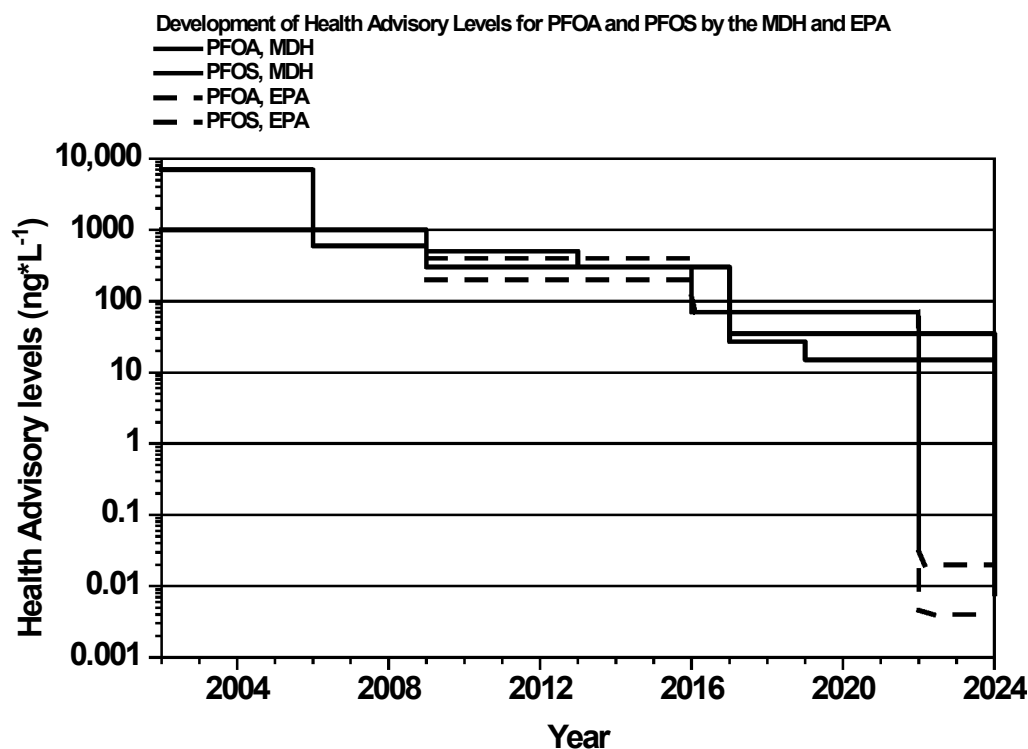


**Figure 5.** A comparison of the proposed health advisory levels for PFOA (black) and PFOS (gray) drinking water standards by the Minnesota Department of Health (MDH) (continuous) and US Environmental Protection Agency (EPA) (dotted) between 2002 and 2024 [196,197]. Note that the scale is a log scale, so proposed standards for 2024 are on the order of 100,000 times more stringent than in 2002.

Until recently, neither the state nor federal government had addressed PFAS contamination issues in agriculture. In 2023, the Minnesota Legislature passed bills (SF 1955 and HF 2310) regulating pesticide products that contain intentionally added PFASs [197]. One of the new laws requires pesticide registrants to inform the Minnesota Department of Agriculture if a pesticide product contains intentionally added PFASs. The EPA is studying this issue and determining the scope and scale of pesticide-related PFAS issues.

Both Minnesota and the federal government have set up near-term plans for further research and rulemaking on PFAS-related issues. Minnesota's PFAS staff group has observed that it is challenging to manage PFASs sufficiently through regulatory actions as several vital areas (e.g., pollution prevention and waste management or understanding risks and how they relate to exposure through food/water) are overlapping [198]. The EPA's roadmap's goals for 2021 to 2024 are to increase the understanding of the effects of PFAS exposure on human health and ecological systems, prevent the release of those substances into the environment, and facilitate remediation efforts at contaminated sites [199].

In Minnesota, the MPCA, MDH, Department of Natural Resources, and Minnesota Department of Agriculture published Minnesota's PFAS Blueprint for addressing the PFAS problem systematically and efficiently at the beginning of 2021.

Minnesota's blueprint lists the following areas of concern: (1) preventing PFAS pollution, (2) measuring PFAS effectively and consistently, (3) quantifying PFAS risks to human health, (4) limiting PFAS exposure from drinking water, (5) reducing PFAS exposure from consuming fish and game, (6) limiting PFAS exposure from food, (7) understanding risks from PFAS in the air, (8) protecting ecosystem health, and (9) remediating PFAS-contaminated sites [198].

While all agree that the potential for PFAS contamination in food production needs to be addressed [83], regulating agriculture is often made more difficult due to political and practical issues. Minnesota's Department of Employment and Economic Development estimated that the agricultural sector in Minnesota generated about USD 17 billion in sales, with USD 8.85 billion being contributed from the cultivation of crops in the year 2022 [200]. Similar economic impacts are generated by agriculture in states throughout the US Midwest. Agriculture is an important industry that supplies the planet with needed food; thus, state and federal regulators are often cautious about changing rules for agriculture. However, care needs to be taken to reduce the potential that agricultural products are a source of exposure to PFAS in people. Poorly addressing PFAS issues has the potential to negatively impact human health, threaten economic sustainability, and cause consumer backlash.

The PFAS cycle must be broken long term to prevent further contamination on agricultural sites. This requires far-reaching regulations governing the production, use, and disposal of PFASs as it is very challenging to prevent the emission of PFASs into the environment over their life cycle [201]. Therefore, restricting production and utilization is the best option to prevent further contamination. For example, the state of Minnesota banned the use of PFAS-containing firefighting foam with a few exceptions and limited intentionally adding PFASs to food packaging material in 2024 [202]. Banning the commercialization of PFAS-containing products is especially important if the PFAS-provided properties are not necessarily required for the respective application. This step must also include thorough and mandatory testing of PFAS substitutes to ensure their biocompatibility and biodegradability. Biosolids for land application should be thoroughly investigated, and PFAS contaminants exceeding a set threshold should be treated as they are primary contamination sources in rural areas. The Maine legislature went so far as to ban land application in August 2022 [203]. Existing wastes should be handled adequately so they will not enter the groundwater or atmosphere. Furthermore, law makers should address PFAS-containing food contact material and restrict their use if necessary. Consequentially, legally binding maximum PFAS levels in food should be established, which should include the most common legacy PFASs (e.g., PFBA, PFBS, PFHxA, PFxS, PFOA, PFOS, and fluorotelomer sulfonates) and upcoming alternatives (e.g., GenX, F-53B, OBS).

Lastly, agencies should facilitate mitigation strategies, which are still energy- and cost-intensive. It is self-explanatory that the required actions require enormous resources and the parties responsible for the pollution to be held accountable.

### *3.6. Future Research Recommendations and Challenges*

It is clear that the US agriculture community faces challenges in identifying the risks that PFASs present to today's agriculture-based food systems. More work across all areas is needed to understand the scope of these challenges and develop long-term strategies for mitigating related risks. It is also important to recognize that there is a difficult question of responsibility for PFAS contamination as farms are most likely contaminated without the knowledge of the farmers. However, they may suffer financial losses due to contamination or mitigation. A rapid response and sufficient resources are needed for establishing a framework to tackle the PFAS crisis.

### 3.6.1. Agricultural Challenges and Strategies for PFAS Mitigation

Arguably, most US farmers have not heard of the term PFAS. Thus, a knowledge gap in the farming community is an initial barrier to mitigating risks to agriculture and the food supply. Little guidance and studies in the literature are available that are geared towards informing agricultural practitioners about PFASs. The agriculture sector is already under heavy pressure to act on other environmental issues (e.g., greenhouse gases, nitrates, fossil fuels, and pesticides), which makes it difficult to incorporate additional information about PFASs in outreach materials to producers and their cropping advisors. Without this information, farmers are unlikely to even be aware that they should consider potential risks to their crop or livestock products from PFASs.

It is also clear that the outlined knowledge gaps need to be addressed regarding translocation in agricultural plants and livestock. Therefore, more research on PFAS translocation and presence is needed in every step of food production (soil sorption, plant uptake/translocation, transfer to livestock, and consumption). In many products, long-chain PFASs have been replaced with shorter alternatives (e.g., GenX), which are more mobile in agricultural systems. However, there are uncertainties about their toxicological potential that must be studied. Field studies that deal with plant uptake are needed to enhance the understanding of the respective uptake mechanisms. Clinical studies that expose the livestock to relatively high PFAS loads have limited applicability as well, which makes it challenging for regulators to establish suitable action plans. One helpful measure would be to develop TWI values to increase the transparency and trust of consumers.

These suggested efforts require immediate action, many resources, and the bundling of expertise across biological, chemical, and medical fields as the question of under which conditions crops and livestock can be safely grown must be answered.

Finding data on PFAS-contaminated agricultural sites that present risks to farm operations is also difficult. States with robust environmental protection policies or a known existing issue with PFASs may have a well-developed database on PFAS manufacture, use, or contamination sites. For example, Minnesota has a repository of PFAS-related test data available online in raw and searchable (map based) formats [50]. A further challenge for producers that have identified a potential PFAS contamination risk is the lack of resources on subsequent steps to verify the risks. Educational and consulting resources for farmers in the US are typically centered on state universities and their federally funded agricultural extension staff. Extension staff in some states have begun outreach efforts on agricultural PFAS issues [204], typically in states with known significant PFAS problems. However, the majority of state universities do not have staff focused on the issue. Farmers at high risk for PFAS contamination will likely need to refer to information from other states or outside the agricultural sector.

Should a producer believe that they may be at risk for PFAS issues in their operations, the next step would be testing. The availability of testing labs and methods needed for performing soil/plant/animal testing will be another challenge for farmers. Tests for PFASs are very sensitive, detecting these materials at the parts per billion or trillion level. A simple web-based search indicates that most certified labs testing drinking water samples in the US charge between USD 250 and USD 600 per sample. It is likely that testing soil or products would add additional costs. Between the costs of tests and sampling work, it is likely that farmers would find testing unaffordable. Moreover, financial support should be provided for contaminated farms so that farmers do not fear testing. It may be necessary for states to assist with the expertise and cost of conducting PFAS tests. There is also the issue of interpreting test results as there are currently no guidelines for defining soil contamination in an agricultural context.

### 3.6.2. Strategies for PFAS Risk Reduction on Farms

Understanding the sources and associated entry of PFASs into the environment is crucial to identify locations with higher associated risks and to develop mitigation strategies to ensure efficient use of resources [205]. Based on the findings in Minnesota, these include rural sites located by landfills or airports or sites that have undergone application of contaminated biosolids. In the case of landfills and airports, these are typically matters of public record. Farmers who have been applying biosolids will typically know how much and how often they have applied them to their land. This work can all be performed at the individual farm level or by mapping farms adjacent to known contamination sites.

Another approach to identifying risks of PFASs in agriculture that may play an increasing role in the future is machine learning (e.g., for farms in proximity to airports or military sites). Maine is already examining machine learning-related methods [195]. However, extensive PFAS and environmental monitoring data is required for these methods to be efficiently applied.

Once identified, sites with elevated contamination levels or at high risk for new contamination must be further evaluated to assess whether and how farming can be continued. Remediating agricultural sites is currently not economically feasible due to the energy and cost-intensive nature of the respective methods. Alternative crops that have lower BAFs or are not used for food production (e.g., bioenergy or fiber crops) may need to be produced on contaminated land. PFASs would still be present on both land and crops but would not put livestock or humans at risk.

Another contamination-related issue is irrigation and groundwater. Agricultural lands may not necessarily be heavily contaminated, but irrigation water pumped from contaminated aquifers could pose a risk. Again, the primary rural source of contamination for water is landfills; thus, it is prudent to test irrigation water being pumped from wells near landfills. This should also be performed for drinking water provided to livestock.

At present, these are concrete steps that can be taken to mitigate PFAS risks. They will likely need to be re-evaluated and updated as more information becomes available on both PFASs in general and its linkage to agriculture in particular. The rapid development of strict drinking water standards suggests that PFAS regulation will be developed for agriculture in the near future so that we can reduce the potential for PFAS contamination in food supply.

## 4. Conclusions

The experience with PFASs in Minnesota makes it evident that PFAS contamination in agriculture is an area of concern that needs to be more fully examined by the scientific community, policymakers, and farmers to mitigate risks for the environment and consumers. Minnesota, with its historical relationship to PFASs and a strong agricultural sector, provides a glimpse into the major sources of agricultural contamination (landfills, biosolids, and airports) and can be used as a model region for other rural areas. Adaptations must be made based on local geographical features, its contamination history, and individual food production chains.

Knowledge gaps are a critical issue, as consuming PFAS-contaminated foodstuffs is identified as an important exposure pathway. Our findings suggest that more field studies which investigate the PFAS partitioning behavior in all soil types, PFAS uptake by crops cultivated in different soil types, and PFAS uptake/distribution/accumulation in livestock are direly needed. Studies in a controlled environment can expand the understanding of certain factors but can only be applied to real conditions to a limited extent. Often times, environmental conditions are not investigated, but unrealistic high PFAS levels are used. Epidemiological studies are lacking in this area, as well as data and reports specifically

evaluating contamination levels at agricultural sites. The amount and type of specific PFASs detected in the environment will change in the near future due to manufacturing adaptations made by the industry. This poses a great challenge to the scientific community and must be tackled quickly so that research, regulations, and public health measures do not only address legacy PFASs.

The high complexity, knowledge gaps in critical areas, and interdisciplinary nature of the PFAS crisis do not allow reliant risk assessments at the present time. No simple approaches will adequately meet this problem, and complex approaches, such as machine learning or intergovernmental cooperation, will be of utmost importance.

Our findings suggest that the consumption of produce from areas with no direct PFAS application should pose no significant threat to the consumer. Animal products, especially offal, generally show higher contamination levels compared to plant-based foods. It is advisable to establish a monitoring system in agricultural areas and across the food chain. Farms and foods with a higher associated risk of contamination (e.g., close to manufacturing sites, airports, or landfills; those that have undergone historic biosolid application; or those in contact with contaminated surface water) should be preferred during the planning phase of such systems. Legally binding regulations dealing with PFASs in agriculture and food production are basically non-existent, which shows the need for immediate action.

The current strategies to limit agricultural PFAS contamination rely on avoiding known contamination from these sources or leachates spreading in groundwater. Remediation efforts will likely play a significant role in the future for some agricultural sites as the methods become economically competitive or are required by future regulations. However, there are currently no sensible remediation strategies in the context of agriculture. Established methods, such as the excavation or washing of contaminated soils, do not meet the requirements, and more attention needs to be paid to this aspect.

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## References

1. Buck, R.C.; Franklin, J.; Berger, U.; Conder, J.M.; Cousins, I.T.; Voogt, P.d.; Jensen, A.A.; Kannan, K.; Ma-bury, S.A.; van Leeuwen, S.P.J. Perfluoroalkyl and polyfluoroalkyl substances in the environment: Terminology, classification, and origins. *Integr. Environ. Assess. Manag.* **2011**, *7*, 513–541. [[CrossRef](#)]
2. OECD. Reconciling Terminology of the Universe of Per- and Polyfluoroalkyl Substances: Recommendations and Practical Guidance. Available online: [https://www.oecd.org/en/publications/reconciling-terminology-of-the-universe-of-per-and-polyfluoroalkyl-substances\\_e458e796-en.html](https://www.oecd.org/en/publications/reconciling-terminology-of-the-universe-of-per-and-polyfluoroalkyl-substances_e458e796-en.html) (accessed on 9 July 2024).
3. EPA. PFAS Structures in DSSTox. Available online: <https://comptox.epa.gov/dashboard/chemical-lists/PFASSTRUCT> (accessed on 10 July 2024).

4. Rankin, K.; Mabury, S.A.; Jenkins, T.M.; Washington, J.W. A North American and global survey of perfluoroalkyl substances in surface soils: Distribution patterns and mode of occurrence. *Chemosphere* **2016**, *161*, 333–341. [CrossRef]
5. Giesy, J.P.; Kannan, K. Global distribution of perfluorooctane sulfonate in wildlife. *Environ. Sci. Technol.* **2001**, *35*, 1339–1342. [CrossRef]
6. Jian, J.-M.; Chen, D.; Han, F.-J.; Guo, Y.; Zeng, L.; Lu, X.; Wang, F. A short review on human exposure to and tissue distribution of per- and polyfluoroalkyl substances (PFASs). *Sci. Total Environ.* **2018**, *636*, 1058–1069. [CrossRef]
7. Lewis, R.C.; Johns, L.E.; Meeker, J.D. Serum Biomarkers of Exposure to Perfluoroalkyl Substances in Relation to Serum Testosterone and Measures of Thyroid Function among Adults and Adolescents from NHANES 2011–2012. *Int. J. Environ. Res. Public Health* **2015**, *12*, 6098–6114. [CrossRef]
8. Pérez, F.; Nadal, M.; Navarro-Ortega, A.; Fàbrega, F.; Domingo, J.L.; Barceló, D.; Farré, M. Accumulation of perfluoroalkyl substances in human tissues. *Environ. Int.* **2013**, *59*, 354–362. [CrossRef] [PubMed]
9. Sunderland, E.M.; Hu, X.C.; Dassuncao, C.; Tokranov, A.K.; Wagner, C.C.; Allen, J.G. A Review of the Pathways of Human Exposure to Poly- and Perfluoroalkyl Substances (PFASs) and Present Understanding of Health Effects. *J. Expo. Sci. Environ. Epidemiol.* **2018**, *29*, 131–147. [CrossRef] [PubMed]
10. Fenton, S.E.; Ducatman, A.; Boobis, A.; DeWitt, J.C.; Lau, C.; Ng, C.; Smith, J.S.; Roberts, S.M. Per- and Polyfluoroalkyl Substance Toxicity and Human Health Review: Current State of Knowledge and Strategies for Informing Future Research. *Environ. Toxicol. Chem.* **2020**, *40*, 606–630. [CrossRef] [PubMed]
11. Olsen, G.W.; Burris, J.M.; Ehresman, D.J.; Froehlich, J.W.; Seacat, A.M.; Butenhoff, J.L.; Zobel, L.R. Half-life of Serum Elimination of Perfluorooctanesulfonate, Perfluorohexanesulfonate, and Perfluorooctanoate in Retired Fluorochemical Production Workers. *Environ. Health Perspect.* **2007**, *115*, 1298–1305. [CrossRef]
12. Wang, Z.; DeWitt, J.C.; Higgins, C.P.; Cousins, I.T. A Never-Ending Story of Per- and Polyfluoroalkyl Substances (PFASs)? *Environ. Sci. Technol.* **2017**, *51*, 2508–2518. [CrossRef]
13. Ross, I.; McDonough, J.; Miles, J.; Storch, P.; Kochunarayanan, P.T.; Kalve, E.; Hurst, J.; Dasgupta, S.S.; Burdick, J. A review of emerging technologies for remediation of PFASs. *Remediat. J.* **2018**, *28*, 101–126. [CrossRef]
14. Bolan, N.; Sarkar, B.; Yan, Y.; Li, Q.; Wijesekara, H.; Kannan, K.; Tsang, D.C.W.; Schauerte, M.; Bosch, J.; Noll, H.; et al. Remediation of poly- and perfluoroalkyl substances (PFAS) contaminated soils—To mobilize or to immobilize or to degrade? *J. Hazard. Mater.* **2021**, *401*, 123892. [CrossRef]
15. Glüge, J.; Scheringer, M.; Cousins, I.T.; DeWitt, J.C.; Goldenman, G.; Herzke, D.; Lohmann, R.; Ng, C.A.; Trier, X.; Wang, Z. An overview of the uses of per- and polyfluoroalkyl substances (PFAS). *Environ. Sci. Process. Impacts* **2020**, *22*, 2345–2373. [CrossRef]
16. Meegoda, J.N.; Kewalramani, J.A.; Li, B.; Marsh, R.W. A Review of the Applications, Environmental Release, and Remediation Technologies of Per- and Polyfluoroalkyl Substances. *Int. J. Environ. Res. Public Health* **2020**, *17*, 8117. [CrossRef] [PubMed]
17. EPA. Emerging Contaminants: Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA). Available online: <https://semspub.epa.gov/work/HQ/100002767.pdf> (accessed on 2 July 2024).
18. Barlow, C.A.; Boyd, C.A.; Kemp, M.J.; Hoppe Parr, K.A. PFAS Toxicology: What is Driving Variation in Drinking Water Standards? 2019. Available online: <https://portal.ct.gov/-/media/DEEP/PFASTaskForce/HHCBarlowBoydKempHoppeParr2019PFASToxicologypdf.pdf> (accessed on 17 June 2024).
19. Carey, G.R.; Hakimabadi, S.G.; Singh, M.; McGregor, R.; Woodfield, C.; van Geel, P.J.; Pham, A.L.-T. Longevity of colloidal activated carbon for in situ PFAS remediation at AFFF-contaminated airport sites. *Remediat. J.* **2022**, *33*, 3–23. [CrossRef]
20. Helmer, R.W.; Reeves, D.M.; Cassidy, D.P. Per- and Polyfluorinated Alkyl Substances (PFAS) cycling within Michigan: Contaminated sites, landfills and wastewater treatment plants. *Water Res.* **2022**, *210*, 117983. [CrossRef] [PubMed]
21. Johnson, G.R. PFAS in soil and groundwater following historical land application of biosolids. *Water Res.* **2022**, *211*, 118035. [CrossRef]
22. Salvatore, D.; Mok, K.; Garrett, K.K.; Poudrier, G.; Brown, P.; Birnbaum, L.S.; Goldenman, G.; Miller, M.F.; Patton, S.; Poehlein, M.; et al. Presumptive Contamination: A New Approach to PFAS Contamination Based on Likely Sources. *Environ. Sci. Technol. Lett.* **2022**, *9*, 983–990. [CrossRef]
23. Silva, A.O.d.; Armitage, J.M.; Bruton, T.A.; Dassuncao, C.; Heiger-Bernays, W.; Hu, X.C.; Kärrman, A.; Kelly, B.; Ng, C.; Robuck, A.; et al. PFAS Exposure Pathways for Humans and Wildlife: A Synthesis of Current Knowledge and Key Gaps in Understanding. *Environ. Toxicol. Chem.* **2020**, *40*, 631–657. [CrossRef]
24. Klenow, S.; Heinemeyer, G.; Brambilla, G.; Dellatte, E.; Herzke, D.; Voogt, P.d. Dietary exposure to selected perfluoroalkyl acids (PFAAs) in four European regions. *Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess.* **2013**, *30*, 2141–2151. [CrossRef]
25. Kowalczyk, J.; Ehlers, S.; Oberhausen, A.; Tischer, M.; Fürst, P.; Schafft, H.; Lahrssen-Wiederholt, M. Absorption, Distribution, and Milk Secretion of the Perfluoroalkyl Acids PFBS, PFHxS, PFOS, and PFOA by Dairy Cows Fed Naturally Contaminated Feed. *J. Agric. Food Chem.* **2013**, *61*, 2903–2912. [CrossRef]

26. Kowalczyk, J.; Ehlers, S.; Fürst, P.; Schafft, H.; Lahrssen-Wiederholt, M. Transfer of Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS) from Contaminated Feed into Milk and Meat of Sheep: Pilot Study. *Arch. Environ. Contam. Toxicol.* **2012**, *63*, 288–298. [CrossRef]
27. Treat, S.A. With a Second Farm Shuttered Due to Massive PFAS Contamination, Maine Legislators Weigh Easing Access to the Courts. Available online: <https://www.iatp.org/blog/202007/second-farm-shuttered-due-massive-pfas-contamination-maine-legislators-weigh-easing> (accessed on 11 July 2024).
28. Leigh, V. There Are No Tears Left Arundel Dairy Farmer Devastated by PFAS Fights for State Help, 2022. Available online: <https://www.newscentermaine.com/article/tech/science/environment/pfas/there-are-no-tears-left-arundel-dairy-farmer-devastated-by-pfas-fights-for-state-help-maine-agriculture/97-1d7f1b97-84f5-4dd3-8f51-90f36e72af6e> (accessed on 14 April 2024).
29. Miller, K. More Than 50 Maine Farms Impacted by PFAS, but State Officials See ‘Glimmer of Hope’. Available online: <https://www.mainepublic.org/environment-and-outdoors/2023-02-01/more-than-50-maine-farms-impacted-by-pfas-but-state-officials-see-glimmer-of-hope> (accessed on 10 July 2024).
30. O’Brien, K. ‘Forever Chemicals’ Upended a Maine Farm—And Point to Larger Problem. *The Washington Post*, April 11, 2022. Available online: <https://www.washingtonpost.com/nation/2022/04/11/pfas-forever-chemicals-maine-farm/> (accessed on 14 April 2023).
31. Kolpin, D.W.; Hubbard, L.E.; Cwiertny, D.M.; Meppelink, S.M.; Thompson, D.A.; Gray, J.L. A Comprehensive Statewide Spatiotemporal Stream Assessment of Per- and Polyfluoroalkyl Substances (PFAS) in an Agricultural Region of the United States. *Environ. Sci. Technol. Lett.* **2021**, *8*, 981–988. [CrossRef]
32. Ritchie, H.; Roser, M. Land Use, 2019. Available online: [https://ourworldindata.org/land-use#:~:text=Almost%20half%20\(44%25\)%20of,land%20is%20used%20for%20agriculture.&text=In%20total%20it%20is%20an,size%20of%20the%20United%20States](https://ourworldindata.org/land-use#:~:text=Almost%20half%20(44%25)%20of,land%20is%20used%20for%20agriculture.&text=In%20total%20it%20is%20an,size%20of%20the%20United%20States) (accessed on 26 March 2024).
33. 3M. Perfluorochemical Release at the 3M–Cottage Grove Facility, 2005. Available online: <https://www.health.state.mn.us/communities/environment/hazardous/docs/sites/washington/3mcg0205.pdf> (accessed on 19 July 2024).
34. Nordby, G.L.; Luck, J.M. Perfluorooctanoic acid interactions with human serum albumin. *J. Biol. Chem.* **1955**, *219*, 399–404. [CrossRef]
35. Rich, N. The Lawyer Who Became DuPont’s Worst Nightmare. Available online: <https://www.nytimes.com/2016/01/10/magazine/the-lawyer-who-became-duponts-worst-nightmare.html> (accessed on 10 July 2024).
36. 3M. Fluorochemical Use, Distribution and Release Overview, 1999. Available online: <https://www.regulations.gov/document/EPA-HQ-OPPT-2002-0051-0003> (accessed on 19 July 2023).
37. Oliaei, F.; Kriens, D.; Weber, R.; Watson, A. PFOS and PFC releases and associated pollution from a PFC production plant in Minnesota (USA). *Environ. Sci. Pollut. Res.* **2013**, *20*, 1977–1992. [CrossRef]
38. State of Minnesota. Settlement Agreement and Consent Order, 2007. Available online: <https://www.pca.state.mn.us/sites/default/files/c-pfc2-11c.pdf> (accessed on 19 July 2024).
39. Oliaei, F.; Kriens, D.; Kessler, K. Investigation of Perfluorochemical (PFC) Contamination in Minnesota: Phase One, 2006. Available online: <https://www.leg.mn.gov/archive/leg/minutes/database/84-s-1261-0-20060227-a.pdf> (accessed on 18 April 2024).
40. MPCA. PFAS Air and Deposition Monitoring Report, 2022. Available online: <https://www.pca.state.mn.us/sites/default/files/tdr-g1-23.pdf> (accessed on 26 April 2023).
41. MPCA. 2007 MPCA Metro Lakes PFC Fish Data—First 10 of 30 Lakes, 2007. Available online: <https://www.pca.state.mn.us/sites/default/files/pfc-metro-lakes-fish.pdf> (accessed on 27 April 2024).
42. MPCA. Update: Urban Lakes PFCs Study, 2008. Available online: <https://www.pca.state.mn.us/sites/default/files/pfc-fishdata.pdf> (accessed on 27 April 2024).
43. MPCA. 2005–2008 Perfluorochemical Evaluation at Solid Waste Facilities in Minnesota Technical Evaluation and Regulatory Management Approach, 2010. Available online: <https://www.pca.state.mn.us/sites/default/files/c-pfc4-01.pdf> (accessed on 27 April 2023).
44. Wood. Site Investigation Report: Investigation of Per- and Polyfluoroalkyl Substances at Select Source Separated Organic Material and Yard Waste Sites, Minnesota, 2019. Available online: <https://www.pca.state.mn.us/sites/default/files/w-sw4-37.pdf> (accessed on 26 April 2024).
45. Sunding, D.L. Damage to Minnesota’s Natural Resources Resulting from 3M’s Disposal of PFCs in Washington County, MN, 2017. Available online: <https://minnesotareformer.com/wp-content/uploads/2022/12/David-Sunding-Expert-Witness-Report-1.pdf> (accessed on 20 August 2024).
46. Olsen, G.W.; Mair, D.C.; Reagen, W.K.; Ellefson, M.E.; Ehresman, D.J.; Butenhoff, J.L.; Zobel, L.R. Preliminary evidence of a decline in perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) concentrations in American Red Cross blood donors. *Chemosphere* **2007**, *68*, 105–111. [CrossRef] [PubMed]

47. MPCA. East Metro | 3M PFAS Contamination. Available online: <https://www.pca.state.mn.us/local-sites-and-projects/east-metro-3m-pfas-contamination#:~:text=The%203M%20chemicals%20that%20contain,its%20Cottage%20Grove%20manufacturing%20facility> (accessed on 10 July 2024).
48. 3M. 3M to Exit PFAS Manufacturing by the End of 2025. Available online: <https://news.3m.com/2022-12-20-3M-to-Exit-PFAS-Manufacturing-by-the-End-of-2025> (accessed on 2 July 2024).
49. MPCA. PFAS Testing of Minnesota Community Water Systems, 2024. Available online: <https://mdh.maps.arcgis.com/apps/MapSeries/index.html?appid=63515695237f425ea7120d1aac1fd09a> (accessed on 17 July 2024).
50. EWG. PFAS Contamination in the U.S., 2022. Available online: [https://www.ewg.org/interactive-maps/pfas\\_contamination/?gad\\_source=1&gad\\_campaignid=6485693431&gbraid=0AAAAAD\\_iHo6be2j\\_2aLgTUIOTJIBA EKZ5&gclid=Cj0KCQjws4fEBhD-ARIsACC3d28k9wrjaab2hMNQ#9HOFImLVuqwiSSrI2GoX8vsxrUehvXpYhoGklsaAnq3EALw\\_wcB](https://www.ewg.org/interactive-maps/pfas_contamination/?gad_source=1&gad_campaignid=6485693431&gbraid=0AAAAAD_iHo6be2j_2aLgTUIOTJIBA EKZ5&gclid=Cj0KCQjws4fEBhD-ARIsACC3d28k9wrjaab2hMNQ#9HOFImLVuqwiSSrI2GoX8vsxrUehvXpYhoGklsaAnq3EALw_wcB) (accessed on 26 April 2024).
51. MDH. History of MDH Activities—Per- and Polyfluoroalkyl Substances (PFAS), 2024. Available online: <https://www.health.state.mn.us/communities/environment/hazardous/topics/history.html> (accessed on 17 November 2024).
52. Croll, H.; Capelle, R. Cottage Grove Pilot Study Final Report, 2022. Available online: <https://3msettlement.state.mn.us/sites/3msettlement/files/2023-02/c-pfc3-22.pdf> (accessed on 28 April 2024).
53. Minnesota Geospatial Commons. Minnesota Groundwater Contamination Atlas. Available online: <https://gisdata.mn.gov/dataset/env-mn-gw-contamination-atlas> (accessed on 8 July 2024).
54. Young, C.J.; Mabury, S.A. Atmospheric Perfluorinated Acid Precursors: Chemistry, Occurrence, and Impacts. *Rev. Environ. Contam. Toxicol.* **2010**, *208*, 1–109. [CrossRef]
55. Valsecchi, S.; Rusconi, M.; Mazzoni, M.; Viviano, G.; Pagnotta, R.; Zaghi, C.; Serrini, G.; Polesello, S. Occurrence and sources of perfluoroalkyl acids in Italian river basins. *Chemosphere* **2015**, *129*, 126–134. [CrossRef]
56. Liu, Z.; Lu, Y.; Song, X.; Jones, K.; Sweetman, A.J.; Johnson, A.C.; Zhang, M.; Lu, X.; Su, C. Multiple crop bioaccumulation and human exposure of perfluoroalkyl substances around a mega fluorochemical industrial park, China: Implication for planting optimization and food safety. *Environ. Int.* **2019**, *127*, 671–684. [CrossRef]
57. Neely, N.; Gillespie, D.; Schauf, F.; Walsh, J. Remedial Actions at Hazardous Waste Sites: Survey and Case studies, 1981. Available online: <https://nepis.epa.gov/Exe/ZyPDF.cgi/9101OX8Y.PDF?Dockey=9101OX8Y.PDF> (accessed on 21 August 2024).
58. Wu, Y.; Romanak, K.; Bruton, T.; Blum, A.; Venier, M. Per- and polyfluoroalkyl substances in paired dust and carpets from childcare centers. *Chemosphere* **2020**, *251*, 126771. [CrossRef]
59. Schellenberger, S.; Liagkouridis, I.; Awad, R.; Khan, S.; Plassmann, M.; Peters, G.; Benskin, J.P.; Cousins, I.T. An Outdoor Aging Study to Investigate the Release of Per- And Polyfluoroalkyl Substances (PFAS) from Functional Textiles. *Environ. Sci. Technol.* **2022**, *56*, 3471–3479. [CrossRef] [PubMed]
60. EPA. National Overview: Facts and Figures on Materials, Wastes and Recycling. Available online: <https://www.epa.gov/facts-and-figures-about-materials-waste-and-recycling/national-overview-facts-and-figures-materials> (accessed on 4 July 2024).
61. Lang, J.R.; Allred, B.M.; Field, J.A.; Levis, J.W.; Barlaz, M.A. National Estimate of Per- and Polyfluoroalkyl Substance (PFAS) Release to U.S. Municipal Landfill Leachate. *Environ. Sci. Technol.* **2017**, *51*, 2197–2205. [CrossRef] [PubMed]
62. Zhang, M.; Zhao, X.; Zhao, D.; Soong, T.-Y.; Tian, S. Poly- and Perfluoroalkyl Substances (PFAS) in Landfills: Occurrence, Transformation and Treatment. *Waste Manag.* **2023**, *155*, 162–178. [CrossRef] [PubMed]
63. Huset, C.A.; Barlaz, M.A.; Barofsky, D.F.; Field, J.A. Quantitative determination of fluorochemicals in municipal landfill leachates. *Chemosphere* **2011**, *82*, 1380–1386. [CrossRef]
64. Yan, H.; Cousins, I.T.; Zhang, C.; Zhou, Q. Perfluoroalkyl acids in municipal landfill leachates from China: Occurrence, fate during leachate treatment and potential impact on groundwater. *Sci. Total Environ.* **2015**, *524–525*, 23–31. [CrossRef]
65. Capozzi, S.L.; Leang, A.L.; Rodenburg, L.A.; Chandramouli, B.; Delistraty, D.A.; Carter, C.H. PFAS in municipal landfill leachate: Occurrence, transformation, and sources. *Chemosphere* **2023**, *334*, 138924. [CrossRef]
66. MPCA. PFAS and Closed Landfills. Available online: <https://www.pca.state.mn.us/air-water-land-climate/pfas-and-closed-landfills> (accessed on 22 July 2024).
67. Hamid, H.; Li, L.Y.; Grace, J.R. Review of the fate and transformation of per- and polyfluoroalkyl substances (PFASs) in landfills. *Environ. Pollut.* **2018**, *235*, 74–84. [CrossRef]
68. Barzen-Hanson, K.A.; Roberts, S.C.; Choyke, S.; Oetjen, K.; McAlees, A.; Riddell, N.; McCrindle, R.; Ferguson, P.L.; Higgins, C.P.; Field, J.A. Discovery of 40 Classes of Per- and Polyfluoroalkyl Substances in Historical Aqueous Film-Forming Foams (AFFFs) and AFFF-Impacted Groundwater. *Environ. Sci. Technol.* **2017**, *51*, 2047–2057. [CrossRef]
69. Moody, C.A.; Field, J.A. Perfluorinated Surfactants and the Environmental Implications of Their Use in Fire-Fighting Foams. *Environ. Sci. Technol.* **2000**, *34*, 3864–3870. [CrossRef]
70. Harding-Marjanovic, K.C.; Houtz, E.F.; Yi, S.; Field, J.A.; Sedlak, D.L.; Alvarez-Cohen, L. Aerobic Biotransformation of Fluorotelomer Thioether Amido Sulfonate (Lodyne) in AFFF-Amended Microcosms. *Environ. Sci. Technol.* **2015**, *49*, 7666–7674. [CrossRef]

71. Yi, S.; Harding-Marjanovic, K.C.; Houtz, E.F.; Gao, Y.; Lawrence, J.E.; Nichiporuk, R.V.; Iavarone, A.T.; Zhuang, W.-Q.; Hansen, M.; Field, J.A.; et al. Biotransformation of AFFF Component 6:2 Fluorotelomer Thioether Amido Sulfonate Generates 6:2 Fluorotelomer Thioether Carboxylate under Sulfate-Reducing Conditions. *Environ. Sci. Technol. Lett.* **2018**, *5*, 283–288. [\[CrossRef\]](#)
72. Collivignarelli, M.C.; Canato, M.; Abbà, A.; Miino, M.C. Biosolids: What are the different types of reuse? *J. Clean. Prod.* **2019**, *238*, 117844. [\[CrossRef\]](#)
73. Uggetti, E.; Ferrer, I.; Nielsen, S.; Arias, C.; Brix, H.; García, J. Characteristics of biosolids from sludge treatment wetlands for agricultural reuse. *Ecol. Eng.* **2012**, *40*, 210–216. [\[CrossRef\]](#)
74. Hellsing, M.S.; Josefsson, S.; Hughes, A.V.; Ahrens, L. Sorption of perfluoroalkyl substances to two types of minerals. *Chemosphere* **2016**, *159*, 385–391. [\[CrossRef\]](#) [\[PubMed\]](#)
75. Johnson, R.L.; Anschutz, A.J.; Smolen, J.M.; Simcik, M.F.; Penn, R.L. The Adsorption of Perfluorooctane Sulfonate onto Sand, Clay, and Iron Oxide Surfaces. *J. Chem. Eng. Data* **2007**, *52*, 1165–1170. [\[CrossRef\]](#)
76. Li, Y.; Oliver, D.P.; Kookana, R.S. A critical analysis of published data to discern the role of soil and sediment properties in determining sorption of per and polyfluoroalkyl substances (PFASs). *Sci. Total Environ.* **2018**, *628–629*, 110–120. [\[CrossRef\]](#)
77. Arvaniti, O.S.; Stasinakis, A.S. Review on the occurrence, fate and removal of perfluorinated compounds during wastewater treatment. *Sci. Total Environ.* **2015**, *524–525*, 81–92. [\[CrossRef\]](#)
78. Lenka, S.P.; Kah, M.; Padhye, L.P. A review of the occurrence, transformation, and removal of poly- and perfluoroalkyl substances (PFAS) in wastewater treatment plants. *Water Res.* **2021**, *199*, 117187. [\[CrossRef\]](#)
79. Fredriksson, F.; Eriksson, U.; Kärrman, A.; Yeung, L.W.Y. Per- and polyfluoroalkyl substances (PFAS) in sludge from wastewater treatment plants in Sweden—First findings of novel fluorinated copolymers in Europe including temporal analysis. *Sci. Total Environ.* **2022**, *846*, 157406. [\[CrossRef\]](#)
80. Sharifan, H.; Bagheri, M.; Wang, D.; Burken, J.G.; Higgins, C.P.; Liang, Y.; Liu, J.; Schaefer, C.E.; Blotvogel, J. Fate and transport of per- and polyfluoroalkyl substances (PFASs) in the vadose zone. *Sci. Total Environ.* **2021**, *771*, 145427. [\[CrossRef\]](#)
81. Guo, B.; Zeng, J.; Brusseau, M.L. A Mathematical Model for the Release, Transport, and Retention of Per- and Polyfluoroalkyl Substances (PFAS) in the Vadose Zone. *Water Resour. Res.* **2020**, *56*, e2019WR026667. [\[CrossRef\]](#) [\[PubMed\]](#)
82. Sivaram, A.K.; Lee, E.; Curnow, A.; Surapaneni, A.; Kannan, K.; Megharaj, M. Uptake, accumulation, and toxicity of per- and polyfluoroalkyl substances in *Allium cepa* grown in soils amended with biosolids. *Environ. Chall.* **2023**, *10*, 100670. [\[CrossRef\]](#)
83. Costello, M.C.S.; Lee, L.S. Sources, Fate, and Plant Uptake in Agricultural Systems of Per- and Polyfluoroalkyl Substances. *Curr. Pollut. Rep.* **2020**, *10*, 799–819. [\[CrossRef\]](#)
84. Ghisi, R.; Vamerali, T.; Manzetti, S. Accumulation of perfluorinated alkyl substances (PFAS) in agricultural plants: A review. *Environ. Res.* **2019**, *169*, 326–341. [\[CrossRef\]](#)
85. Xiao, F.; Simcik, M.F.; Halbach, T.R.; Gulliver, J.S. Perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in soils and groundwater of a U.S. metropolitan area: Migration and implications for human exposure. *Water Res.* **2015**, *72*, 64–74. [\[CrossRef\]](#)
86. Death, C.; Bell, C.; Champness, D.; Milne, C.; Reichman, S.; Hagen, T. Per- and polyfluoroalkyl substances (PFAS) in livestock and game species: A review. *Sci. Total Environ.* **2021**, *774*, 144795. [\[CrossRef\]](#)
87. Lindstrom, A.B.; Strynar, M.J.; Delinsky, A.D.; Nakayama, S.F.; McMillan, L.; Libelo, E.L.; Neill, M.; Thomas, L. Application of WWTP biosolids and resulting perfluorinated compound contamination of surface and well water in Decatur, Alabama, USA. *Environ. Sci. Technol.* **2011**, *45*, 8015–8021. [\[CrossRef\]](#)
88. EPA. Basic Information About Biosolids. Available online: <https://www.epa.gov/biosolids/basic-information-about-biosolids> (accessed on 16 July 2024).
89. Venkatesan, A.K.; Halden, R.U. National inventory of perfluoroalkyl substances in archived U.S. biosolids from the 2001 EPA National Sewage Sludge Survey. *J. Hazard. Mater.* **2013**, *252–253*, 413–418. [\[CrossRef\]](#)
90. Moavenzadeh Ghaznavi, S.; Zimmerman, C.; Shea, M.E.; MacRae, J.D.; Peckenham, J.M.; Noblet, C.L.; Apul, O.G.; Kopec, A.D. Management of per- and polyfluoroalkyl substances (PFAS)-laden wastewater sludge in Maine: Perspectives on a wicked problem. *Biointerphases* **2023**, *18*, 041004. [\[CrossRef\]](#)
91. United States Geological Survey. One Hundred Small Streams in the Midwest Were Tested for Pesticides During the 2013 Growing Season and Found to Contain, on Average, 52 Pesticides per Stream. Available online: <https://www.usgs.gov/news/national-news-release/pesticides-prevalent-midwestern-streams#:~:text=%E2%80%9CAbout%20150%20million%20pounds%20of,lead%20scientist%20for%20the%20study> (accessed on 16 July 2024).
92. Gaines, L.G.T. Historical and current usage of per- and polyfluoroalkyl substances (PFAS): A literature review. *Am. J. Ind. Med.* **2023**, *66*, 353–378. [\[CrossRef\]](#)
93. Lasee, S.; McDermett, K.; Kumar, N.; Guelfo, J.; Payton, P.; Yang, Z.; Anderson, T.A. Targeted analysis and Total Oxidizable Precursor assay of several insecticides for PFAS. *J. Hazard. Mater. Lett.* **2022**, *3*, 100067. [\[CrossRef\]](#)
94. Qian, Y.; French, D. Verification Analysis for PFAS in Pesticide Products, 2023. Available online: <https://www.epa.gov/system/files/documents/2023-05/BEAD%20PFAS%20Study%20Results%202023.pdf> (accessed on 23 July 2024).

95. Guida, Y.; Torres, F.B.M.; Barizon, R.R.M.; Assalin, M.R.; Rosa, M.A. Confirming sulfluramid (EtFOSA) application as a precursor of perfluorooctanesulfonic acid (PFOS) in Brazilian agricultural soils. *Chemosphere* **2023**, *325*, 138370. [CrossRef]
96. UNEP. SC-4/17: Listing of Perfluorooctane Sulfonic Acid, Its Salts and Perfluorooctane Sulfonyl Fluoride, 2009. Available online: <http://www.pops.int/Portals/0/download.aspx?d=UNEP-POPS-COP.4-SC-4-17.English.pdf> (accessed on 23 July 2024).
97. Löfstedt Gilljam, J.; Leonel, J.; Cousins, I.T.; Benskin, J.P. Is Ongoing Sulfluramid Use in South America a Significant Source of Perfluorooctanesulfonate (PFOS)? Production Inventories, Environmental Fate, and Local Occurrence. *Environ. Sci. Technol.* **2016**, *50*, 653–659. [CrossRef] [PubMed]
98. Nguyen, T. Results of EPA's Analytical Chemistry Branch Laboratory Study of PFAS Leaching from Fluorinated HDPE Containers, 2022. Available online: [https://www.epa.gov/system/files/documents/2022-09/EPA%20PFAS%20Container%20Leaching%20Study%2008122022\\_0.pdf](https://www.epa.gov/system/files/documents/2022-09/EPA%20PFAS%20Container%20Leaching%20Study%2008122022_0.pdf) (accessed on 26 July 2024).
99. Ratcliffe, M.; Burd, C.; Holder, K.; Fields, A. Defining Rural at the U.S. Census Bureau, 2016. Available online: [https://www.researchgate.net/profile/Michael-Ratcliffe-2/publication/311533270\\_Defining\\_Rural\\_at\\_the\\_US\\_Census\\_Bureau/links/584aad3708aeb19dcb758910/Defining-Rural-at-the-US-Census-Bureau.pdf](https://www.researchgate.net/profile/Michael-Ratcliffe-2/publication/311533270_Defining_Rural_at_the_US_Census_Bureau/links/584aad3708aeb19dcb758910/Defining-Rural-at-the-US-Census-Bureau.pdf) (accessed on 22 August 2024).
100. Simcik, M.F.; Dorweiler, K.J. Ratio of Perfluorochemical Concentrations as a Tracer of Atmospheric Deposition to Surface Waters. *Environ. Sci. Technol.* **2005**, *39*, 8678–8683. [CrossRef] [PubMed]
101. MnDOT. Minnesota Airports. Available online: <https://www.dot.state.mn.us/aero/operations/minnesotaairports.html> (accessed on 30 July 2024).
102. Ahrens, L.; Bundschuh, M. Fate and effects of poly- and perfluoroalkyl substances in the aquatic environment: A review. *Environ. Toxicol. Chem.* **2014**, *33*, 1921–1929. [CrossRef]
103. Martin, J.W.; Mabury, S.A.; Solomon, K.R.; Muir, D.C.G. Bioconcentration and tissue distribution of perfluorinated acids in rainbow trout (*Oncorhynchus mykiss*). *Environ. Toxicol. Chem.* **2002**, *22*, 196–204. [CrossRef]
104. Ahrens, L.; Taniyasu, S.; Yeung, L.W.Y.; Yamashita, N.; Lam, P.K.S.; Ebinghaus, R. Distribution of polyfluoroalkyl compounds in water, suspended particulate matter and sediment from Tokyo Bay, Japan. *Chemosphere* **2010**, *79*, 266–272. [CrossRef]
105. Naidu, R.; Nadebaum, P.; Fang, C.; Cousins, I.; Pennell, K.; Conder, J.; Newell, C.J.; Longpré, D.; Warner, S.; Crosbie, N.D.; et al. Per- and poly-fluoroalkyl substances (PFAS): Current status and research needs. *Environ. Technol. Innov.* **2020**, *19*, 100915. [CrossRef]
106. Ahrens, L. Polyfluoroalkyl compounds in the aquatic environment: A review of their occurrence and fate. *J. Environ. Monit.* **2011**, *13*, 20–31. [CrossRef]
107. Kallenborn, R.; Berger, U.; Järnberg, U. *Perfluorinated Alkylated Substances (PFAS) in the Nordic Environment*; Nordic Council of Ministers' Publishing House: Copenhagen, Denmark, 2004; ISBN 9789289310512.
108. Kwok, K.Y.; Yamazaki, E.; Yamashita, N.; Taniyasu, S.; Murphy, M.B.; Horii, Y.; Petrick, G.; Kallerborn, R.; Kannan, K.; Murano, K.; et al. Transport of perfluoroalkyl substances (PFAS) from an arctic glacier to downstream locations: Implications for sources. *Sci. Total Environ.* **2013**, *447*, 46–55. [CrossRef]
109. Prevedouros, K.; Cousins, I.T.; Buck, R.C.; Korzeniowski, S.H. Sources, Fate and Transport of Perfluorocarboxylates. *Environ. Sci. Technol.* **2006**, *40*, 32–44. [CrossRef]
110. Kwok, K.Y.; Taniyasu, S.; Yeung, L.W.Y.; Murphy, M.B.; Lam, P.K.S.; Horii, Y.; Kannan, K.; Petrick, G.; Sinha, R.K.; Yamashita, N. Flux of Perfluorinated Chemicals through Wet Deposition in Japan, the United States, And Several Other Countries. *Environ. Sci. Technol.* **2010**, *44*, 7043–7049. [CrossRef]
111. Liu, W.; Jin, Y.; Quan, X.; Sasaki, K.; Saito, N.; Nakayama, S.F.; Sato, I.; Tsuda, S. Perfluorosulfonates and perfluorocarboxylates in snow and rain in Dalian, China. *Environ. Int.* **2009**, *35*, 737–742. [CrossRef]
112. Chen, H.; Zhang, L.; Li, M.; Yao, Y.; Zhao, Z.; Munoz, G.; Sun, H. Per- and polyfluoroalkyl substances (PFASs) in precipitation from mainland China: Contributions of unknown precursors and short-chain (C2–C3) perfluoroalkyl carboxylic acids. *Water Res.* **2019**, *153*, 169–177. [CrossRef] [PubMed]
113. Ahrens, L.; Yamashita, N.; Yeung, L.W.Y.; Taniyasu, S.; Horii, Y.; Lam, P.K.S.; Ebinghaus, R. Partitioning behavior of per- and polyfluoroalkyl compounds between pore water and sediment in two sediment cores from Tokyo Bay, Japan. *Environ. Sci. Technol.* **2009**, *43*, 6969–6975. [CrossRef] [PubMed]
114. Li, L.; Zheng, H.; Wang, T.; Cai, M.; Wang, P. Perfluoroalkyl acids in surface seawater from the North Pacific to the Arctic Ocean: Contamination, distribution and transportation. *Environ. Pollut.* **2018**, *238*, 168–176. [CrossRef] [PubMed]
115. Liu, J.; Lee, L.S. Solubility and Sorption by Soils of 8:2 Fluorotelomer Alcohol in Water and Cosolvent Systems. *Environ. Sci. Technol.* **2005**, *39*, 7535–7540. [CrossRef]
116. Higgins, C.P.; Luthy, R.G. Sorption of Perfluorinated Surfactants on Sediments. *Environ. Sci. Technol.* **2006**, *40*, 7251–7256. [CrossRef]
117. Bigus, P.; Tobiszewski, M.; Namieśnik, J. Historical records of organic pollutants in sediment cores. *Mar. Pollut. Bull.* **2014**, *78*, 26–42. [CrossRef]

118. Zhong, H.; Zheng, M.; Liang, Y.; Wang, Y.; Gao, W.; Wang, Y.; Jiang, G. Legacy and emerging per- and polyfluoroalkyl substances (PFAS) in sediments from the East China Sea and the Yellow Sea: Occurrence, source apportionment and environmental risk assessment. *Chemosphere* **2021**, *282*, 131042. [[CrossRef](#)]
119. Schulz, K.; Silva, M.R.; Klaper, R. Distribution and effects of branched versus linear isomers of PFOA, PFOS, and PFHxS: A review of recent literature. *Sci. Total Environ.* **2020**, *733*, 139186. [[CrossRef](#)] [[PubMed](#)]
120. Sammut, G.; Sinagra, E.; Sapiano, M.; Helmus, R.; Voogt, P.d. Perfluoroalkyl substances in the Maltese environment—(II) sediments, soils and groundwater. *Sci. Total Environ.* **2019**, *682*, 180–189. [[CrossRef](#)] [[PubMed](#)]
121. Pétré, M.-A.; Genereux, D.P.; Koropecjy-Cox, L.; Knappe, D.R.U.; Duboscq, S.; Gilmore, T.E.; Hopkins, Z.R. Per- and Polyfluoroalkyl Substance (PFAS) Transport from Groundwater to Streams near a PFAS Manufacturing Facility in North Carolina, USA. *Environ. Sci. Technol.* **2021**, *55*, 5848–5856. [[CrossRef](#)] [[PubMed](#)]
122. Ng, K.; Alygizakis, N.; Androulakakis, A.; Galani, A.; Aalizadeh, R.; Thomaidis, N.S.; Slobodnik, J. Target and suspect screening of 4777 per- and polyfluoroalkyl substances (PFAS) in river water, wastewater, groundwater and biota samples in the Danube River Basin. *J. Hazard. Mater.* **2022**, *436*, 129276. [[CrossRef](#)]
123. Hepburn, E.; Madden, C.; Szabo, D.; Coggan, T.L.; Clarke, B.; Currell, M. Contamination of groundwater with per- and polyfluoroalkyl substances (PFAS) from legacy landfills in an urban re-development precinct. *Environ. Pollut.* **2019**, *248*, 101–113. [[CrossRef](#)]
124. Chen, S.; Jiao, X.-C.; Gai, N.; Li, X.-J.; Wang, X.-C.; Lu, G.-H.; Piao, H.-T.; Rao, Z.; Yang, Y.-L. Perfluorinated compounds in soil, surface water, and groundwater from rural areas in eastern China. *Environ. Pollut.* **2016**, *211*, 124–131. [[CrossRef](#)]
125. Davis, K.L.; Aucoin, M.D.; Larsen, B.S.; Kaiser, M.A.; Hartten, A.S. Transport of ammonium perfluorooctanoate in environmental media near a fluoropolymer manufacturing facility. *Chemosphere* **2007**, *67*, 2011–2019. [[CrossRef](#)]
126. Liu, Z.; Lu, Y.; Wang, T.; Wang, P.; Li, Q.; Johnson, A.C.; Sarvajayakesavalu, S.; Sweetman, A.J. Risk assessment and source identification of perfluoroalkyl acids in surface and ground water: Spatial distribution around a mega-fluorochemical industrial park, China. *Environ. Int.* **2016**, *91*, 69–77. [[CrossRef](#)]
127. Xu, B.; Liu, S.; Zhou, J.L.; Zheng, C.; Weifeng, J.; Chen, B.; Zhang, T.; Qiu, W. PFAS and their substitutes in groundwater: Occurrence, transformation and remediation. *J. Hazard. Mater.* **2021**, *412*, 125159. [[CrossRef](#)]
128. Shin, H.-M.; Vieira, V.M.; Ryan, P.B.; Detwiler, R.; Sanders, B.; Steenland, K.; Bartell, S.M. Environmental Fate and Transport Modeling for Perfluorooctanoic Acid Emitted from the Washington Works Facility in West Virginia. *Environ. Sci. Technol.* **2011**, *45*, 1435–1442. [[CrossRef](#)]
129. Sharma, B.M.; Bharat, G.K.; Tayal, S.; Larssen, T.; Bečanová, J.; Karásková, P.; Whitehead, P.G.; Futter, M.N.; Butterfield, D.; Nizzetto, L. Perfluoroalkyl substances (PFAS) in river and ground/drinking water of the Ganges River basin: Emissions and implications for human exposure. *Environ. Pollut.* **2016**, *208*, 704–713. [[CrossRef](#)] [[PubMed](#)]
130. Zhang, S.; Szostek, B.; McCausland, P.K.; Wolstenholme, B.W.; Lu, X.; Wang, N.; Buck, R.C. 6:2 and 8:2 Fluorotelomer Alcohol Anaerobic Biotransformation in Digester Sludge from a WWTP under Methanogenic Conditions. *Environ. Sci. Technol.* **2013**, *47*, 4227–4235. [[CrossRef](#)] [[PubMed](#)]
131. Zhang, S.; Lu, X.; Wang, N.; Buck, R.C. Biotransformation potential of 6:2 fluorotelomer sulfonate (6:2 FTSA) in aerobic and anaerobic sediment. *Chemosphere* **2016**, *154*, 224–230. [[CrossRef](#)]
132. Siebert, S.; Burke, J.; Faures, J.M.; Frenken, K.; Hoogeveen, J.; Döll, P.; Portmann, F.T. Groundwater use for irrigation—A global inventory. *Hydrol. Earth Syst. Sci.* **2010**, *14*, 1863–1880. [[CrossRef](#)]
133. Tokranov, A.K.; LeBlanc, D.R.; Pickard, H.M.; Ruyle, B.J.; Barber, L.B.; Hull, R.B.; Sunderland, E.M.; Vecitis, C.D. Surface-water/groundwater boundaries affect seasonal PFAS concentrations and PFAA precursor transformations. *Environ. Sci. Process. Impacts* **2021**, *23*, 1893–1905. [[CrossRef](#)]
134. Tombácz, E.; Szekeres, M. Surface charge heterogeneity of kaolinite in aqueous suspension in comparison with montmorillonite. *Appl. Clay Sci.* **2006**, *34*, 105–124. [[CrossRef](#)]
135. Qafoku, N.P.; van Ranst, E.; Noble, A.; Baert, G. Variable Charge Soils: Their Mineralogy, Chemistry and Management. *Adv. Agron.* **2004**, *84*, 159–215.
136. Gao, X.; Chorover, J. Adsorption of perfluorooctanoic acid and perfluorooctanesulfonic acid to iron oxide surfaces as studied by flow-through ATR-FTIR spectroscopy. *Environ. Chem.* **2012**, *9*, 148–157. [[CrossRef](#)]
137. Du, Z.; Deng, S.; Bei, Y.; Huang, Q.; Wang, B.; Huang, J.; Yu, G. Adsorption behavior and mechanism of perfluorinated compounds on various adsorbents: A review. *J. Hazard. Mater.* **2014**, *274*, 443–454. [[CrossRef](#)]
138. Liu, M.; Munoz, G.; Vo Duy, S.; Sauv  , S.; Liu, J. Per- and Polyfluoroalkyl Substances in Contaminated Soil and Groundwater at Airports: A Canadian Case Study. *Environ. Sci. Technol.* **2022**, *56*, 885–895. [[CrossRef](#)]
139. Washington, J.W.; Yoo, H.; Ellington, J.J.; Jenkins, T.M.; Libelo, E.L. Concentrations, Distribution, and Persistence of Perfluoroalkylates in Sludge-Applied Soils near Decatur, Alabama, USA. *Environ. Sci. Technol.* **2010**, *44*, 8390–8396. [[CrossRef](#)]

140. Baduel, C.; Mueller, J.F.; Rotander, A.; Corfield, J.; Gomez-Ramos, M.-J. Discovery of novel per- and polyfluoroalkyl substances (PFASs) at a fire fighting training ground and preliminary investigation of their fate and mobility. *Chemosphere* **2017**, *185*, 1030–1038. [[CrossRef](#)] [[PubMed](#)]
141. Nickerson, A.; Rodowa, A.E.; Adamson, D.T.; Field, J.A.; Kulkarni, P.R.; Kornuc, J.J.; Higgins, C.P. Spatial Trends of Anionic, Zwitterionic, and Cationic PFASs at an AFFF-Impacted Site. *Environ. Sci. Technol.* **2021**, *55*, 313–323. [[CrossRef](#)] [[PubMed](#)]
142. Yoo, H.; Washington, J.W.; Ellington, J.J.; Jenkins, T.M.; Neill, M.P. Concentrations, Distribution, and Persistence of Fluorotelomer Alcohols in Sludge-Applied Soils near Decatur, Alabama, USA. *Environ. Sci. Technol.* **2010**, *44*, 8397–8402. [[CrossRef](#)] [[PubMed](#)]
143. Wang, N.; Szostek, B.; Buck, R.C.; Folsom, P.W.; Sulecki, L.M.; Gannon, J.T. 8-2 fluorotelomer alcohol aerobic soil biodegradation: Pathways, metabolites, and metabolite yields. *Chemosphere* **2009**, *75*, 1089–1096. [[CrossRef](#)]
144. Mejia-Avendaño, S.; Vo Duy, S.; Sauv  , S.; Liu, J. Generation of Perfluoroalkyl Acids from Aerobic Biotransformation of Quaternary Ammonium Polyfluoroalkyl Surfactants. *Environ. Sci. Technol.* **2016**, *50*, 9923–9932. [[CrossRef](#)]
145. Ahrens, L.; Yeung, L.W.Y.; Taniyasu, S.; Lam, P.K.S.; Yamashita, N. Partitioning of perfluorooctanoate (PFOA), perfluorooctane sulfonate (PFOS) and perfluorooctane sulfonamide (PFOSA) between water and sediment. *Chemosphere* **2011**, *85*, 731–737. [[CrossRef](#)]
146. Chen, Y.-C.; Lo, S.-L.; Li, N.-H.; Lee, Y.-C.; Kuo, J. Sorption of perfluoroalkyl substances (PFASs) onto wetland soils. *Desalination Water Treat.* **2013**, *51*, 7469–7475. [[CrossRef](#)]
147. Chen, H.; Zhang, C.; Yu, Y.; Han, J. Sorption of perfluorooctane sulfonate (PFOS) on marine sediments. *Mar. Pollut. Bull.* **2012**, *64*, 902–906. [[CrossRef](#)]
148. Li, F.; Fang, X.; Zhou, Z.; Liao, X.; Zou, J.; Yuan, B.; Sun, W. Adsorption of perfluorinated acids onto soils: Kinetics, isotherms, and influences of soil properties. *Sci. Total Environ.* **2019**, *649*, 504–514. [[CrossRef](#)]
149. Milinovic, J.; Lacorte, S.; Vidal, M.; Rigol, A. Sorption behaviour of perfluoroalkyl substances in soils. *Sci. Total Environ.* **2015**, *511*, 63–71. [[CrossRef](#)]
150. You, C.; Jia, C.; Pan, G. Effect of salinity and sediment characteristics on the sorption and desorption of perfluorooctane sulfonate at sediment-water interface. *Environ. Pollut.* **2010**, *158*, 1343–1347. [[CrossRef](#)] [[PubMed](#)]
151. Cai, W.; Navarro, D.A.; Du, J.; Ying, G.; Yang, B.; McLaughlin, M.J.; Kookana, R.S. Increasing ionic strength and valency of cations enhance sorption through hydrophobic interactions of PFAS with soil surfaces. *Sci. Total Environ.* **2022**, *817*, 152975. [[CrossRef](#)] [[PubMed](#)]
152. Lyu, Y.; Brusseau, M.L.; Chen, W.; Yan, N.; Fu, X.; Lin, X. Adsorption of PFOA at the Air–Water Interface during Transport in Unsaturated Porous Media. *Environ. Sci. Technol.* **2018**, *52*, 7745–7753. [[CrossRef](#)] [[PubMed](#)]
153. Brusseau, M.L. Assessing the potential contributions of additional retention processes to PFAS retardation in the subsurface. *Sci. Total Environ.* **2018**, *613–614*, 176–185. [[CrossRef](#)]
154. Hunter Anderson, R.; Adamson, D.T.; Stroo, H.F. Partitioning of poly- and perfluoroalkyl substances from soil to groundwater within aqueous film-forming foam source zones. *J. Contam. Hydrol.* **2019**, *220*, 59–65. [[CrossRef](#)]
155. Gellrich, V.; Stahl, T.; Knepper, T.P. Behavior of perfluorinated compounds in soils during leaching experiments. *Chemosphere* **2012**, *87*, 1052–1056. [[CrossRef](#)]
156. Guelfo, J.L.; Higgins, C.P. Subsurface Transport Potential of Perfluoroalkyl Acids at Aqueous Film-Forming Foam (AFFF)-Impacted Sites. *Environ. Sci. Technol.* **2013**, *47*, 4164–4171. [[CrossRef](#)]
157. Hatton, J.; Holton, C.; DiGuseppi, B. Occurrence and behavior of per- and polyfluoroalkyl substances from aqueous film-forming foam in groundwater systems. *Remediat. J.* **2018**, *28*, 89–99. [[CrossRef](#)]
158. Lechner, M.; Knapp, H. Carryover of Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS) from Soil to Plant and Distribution to the Different Plant Compartments Studied in Cultures of Carrots (*Daucus carota* ssp. *Sativus*), Potatoes (*Solanum tuberosum*), and Cucumbers (*Cucumis sativus*). *J. Agric. Food Chem.* **2011**, *59*, 11011–11018. [[CrossRef](#)]
159. Wen, B.; Li, L.; Zhang, H.; Ma, Y.; Shan, X.-Q.; Zhang, S. Field study on the uptake and translocation of perfluoroalkyl acids (PFAAs) by wheat (*Triticum aestivum* L.) grown in biosolids-amended soils. *Environ. Pollut.* **2014**, *184*, 547–554. [[CrossRef](#)]
160. Stahl, T.; Heyn, J.; Thiele, H.; H  ther, J.; Failing, K.; Georgii, S.; Brunn, H. Carryover of Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS) from Soil to Plants. *Arch. Environ. Contam. Toxicol.* **2009**, *57*, 289–298. [[CrossRef](#)] [[PubMed](#)]
161. Lee, H.; Tevlin, A.G.; Mabury, S.A.; Mabury, S.A. Fate of Polyfluoroalkyl Phosphate Diesters and Their Metabolites in Biosolids-Applied Soil: Biodegradation and Plant Uptake in Greenhouse and Field Experiments. *Environ. Sci. Technol.* **2014**, *48*, 340–349. [[CrossRef](#)] [[PubMed](#)]
162. Chen, H.; Yao, Y.; Zhao, Z.; Wang, Y.; Wang, Q.; Ren, C.; Wang, B.; Sun, H.; Alder, A.C.; Kannan, K. Multimedia Distribution and Transfer of Per- and Polyfluoroalkyl Substances (PFASs) Surrounding Two Fluorochemical Manufacturing Facilities in Fuxin, China. *Environ. Sci. Technol.* **2018**, *52*, 8263–8271. [[CrossRef](#)] [[PubMed](#)]
163. Collins, C.; Fryer, M.; Grosso, A. Plant Uptake of Non-Ionic Organic Chemicals. *Environ. Sci. Technol.* **2006**, *40*, 45–52. [[CrossRef](#)]
164. Shan, G.; Wei, M.; Zhu, L.; Liu, Z.; Zhang, Y. Concentration profiles and spatial distribution of perfluoroalkyl substances in an industrial center with condensed fluorochemical facilities. *Sci. Total Environ.* **2014**, *490*, 351–359. [[CrossRef](#)]

165. Kvesitadze, E.; Sadunishvili, T.; Kvesitadze, G. Mechanisms of Organic Contaminants Uptake and Degradation in Plants. *Int. J. Biol. Biomol. Agric. Food Biotechnol. Eng.* **2009**, *2009*, 361–371.
166. Briskin, D.P. Membranes and Transport Systems in Plants: An Overview. *Weed Sci.* **1994**, *42*, 255–262. [\[CrossRef\]](#)
167. Wen, B.; Wu, Y.; Zhang, H.; Liu, Y.; Hu, X.; Huang, H.; Zhang, S. The roles of protein and lipid in the accumulation and distribution of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in plants grown in biosolids-amended soils. *Environ. Pollut.* **2016**, *216*, 682–688. [\[CrossRef\]](#)
168. Zhang, L.; Sun, H.; Wang, Q.; Chen, H.; Yao, Y.; Zhao, Z.; Alder, A.C. Uptake mechanisms of perfluoroalkyl acids with different carbon chain lengths (C2–C8) by wheat (*Triticum aestivum* L.). *Sci. Total Environ.* **2019**, *654*, 19–27. [\[CrossRef\]](#)
169. Mei, W.; Sun, H.; Song, M.; Jiang, L.; Li, Y.; Lu, W.; Ying, G.-G.; Luo, C.; Zhang, G. Per- and polyfluoroalkyl substances (PFASs) in the soil-plant system: Sorption, root uptake, and translocation. *Environ. Int.* **2021**, *156*, 106642. [\[CrossRef\]](#)
170. Blaine, A.C.; Rich, C.D.; Sedlacko, E.M.; Hundal, L.S.; Kumar, K.; Lau, C.; Mills, M.A.; Harris, K.M.; Higgins, C.P. Perfluoroalkyl Acid Distribution in Various Plant Compartments of Edible Crops Grown in Biosolids-Amended Soils. *Environ. Sci. Technol.* **2014**, *48*, 7858–7865. [\[CrossRef\]](#)
171. Müller, C.E.; LeFevre, G.H.; Timofte, A.E.; Hussain, F.A.; Sattely, E.S.; Luthy, R.G. Competing mechanisms for perfluoroalkyl acid accumulation in plants revealed using an Arabidopsis model system. *Environ. Toxicol. Chem.* **2015**, *35*, 1138–1147. [\[CrossRef\]](#)
172. Zhang, D.Q.; Wang, M.; He, Q.; Niu, X.; Liang, Y. Distribution of perfluoroalkyl substances (PFASs) in aquatic plant-based systems: From soil adsorption and plant uptake to effects on microbial community. *Environ. Pollut.* **2020**, *257*, 113575. [\[CrossRef\]](#) [\[PubMed\]](#)
173. Lesmeister, L.; Lange, F.T.; Breuer, J.; Biegel-Engler, A.; Giese, E.; Scheurer, M. Extending the knowledge about PFAS bioaccumulation factors for agricultural plants: A review. *Sci. Total Environ.* **2021**, *766*, 142640. [\[CrossRef\]](#) [\[PubMed\]](#)
174. Krippner, J.; Falk, S.; Brunn, H.; Georgii, S.; Schubert, S.; Stahl, T. Accumulation Potentials of Perfluoroalkyl Carboxylic Acids (PFCAs) and Perfluoroalkyl Sulfonic Acids (PFASs) in Maize (*Zea mays*). *J. Agric. Food Chem.* **2015**, *63*, 3646–3653. [\[CrossRef\]](#) [\[PubMed\]](#)
175. Krippner, J.; Brunn, H.; Falk, S.; Georgii, S.; Schubert, S.; Stahl, T. Effects of chain length and pH on the uptake and distribution of perfluoroalkyl substances in maize (*Zea mays*). *Chemosphere* **2014**, *94*, 85–90. [\[CrossRef\]](#)
176. Wen, B.; Li, L.; Liu, Y.; Zhang, H.; Hu, X.; Shan, X.-Q.; Zhang, S. Mechanistic studies of perfluorooctane sulfonate, perfluorooctanoic acid uptake by maize (*Zea mays* L. cv. TY2). *Plant Soil* **2013**, *370*, 345–354. [\[CrossRef\]](#)
177. Knight, E.R.; Bräunig, J.; Janik, L.J.; Navarro, D.A.; Kookana, R.S.; Mueller, J.F.; McLaughlin, M.J. An investigation into the long-term binding and uptake of PFOS, PFOA and PFHxS in soil—Plant systems. *J. Hazard. Mater.* **2021**, *404*, 124065. [\[CrossRef\]](#)
178. Ateia, M.; Maroli, A.; Tharayil, N.; Karanfil, T. The overlooked short- and ultrashort-chain poly- and perfluorinated substances: A review. *Chemosphere* **2019**, *220*, 866–882. [\[CrossRef\]](#)
179. Brusseau, M.L.; Anderson, R.H.; Guo, B. PFAS concentrations in soils: Background levels versus contaminated sites. *Sci. Total Environ.* **2020**, *740*, 140017. [\[CrossRef\]](#)
180. Li, J.; Sun, J.; Li, P. Exposure routes, bioaccumulation and toxic effects of per- and polyfluoroalkyl substances (PFASs) on plants: A critical review. *Environ. Int.* **2022**, *158*, 106891. [\[CrossRef\]](#)
181. DeWitt, J.C. *Toxicological Effects of Perfluoroalkyl and Polyfluoroalkyl Substances*; Springer International Publishing: Cham, Switzerland, 2015; ISBN 978-3-319-15518-0.
182. Pizzurro, D.M.; Seeley, M.; Kerper, L.E.; Beck, B.D. Interspecies differences in perfluoroalkyl substances (PFAS) toxicokinetics and application to health-based criteria. *Regul. Toxicol. Pharmacol.* **2019**, *106*, 239–250. [\[CrossRef\]](#) [\[PubMed\]](#)
183. Ylinen, M.; Auriola, S. Tissue Distribution and Elimination of Perfluorodecanoic Acid in the Rat after Single Intraperitoneal Administration. *Pharmacol. Toxicol.* **1990**, *66*, 45–48. [\[CrossRef\]](#) [\[PubMed\]](#)
184. Jones, P.D.; Hu, W.; Coen, W.d.; Newsted, J.L.; Giesy, J.P. Binding of perfluorinated fatty acids to serum proteins. *Environ. Toxicol. Chem.* **2003**, *22*, 2639–2649. [\[CrossRef\]](#) [\[PubMed\]](#)
185. Drew, R.; Hagen, T.G.; Champness, D. Accumulation of PFAS by livestock—Determination of transfer factors from water to serum for cattle and sheep in Australia. *Food Addit. Contam. Part A* **2021**, *38*, 1897–1913. [\[CrossRef\]](#)
186. Seacat, A.M.; Thomford, P.J.; Hansen, K.J.; Olsen, G.W.; Case, M.T.; Butenhoff, J.L. Subchronic toxicity studies on perfluorooctane-sulfonate potassium salt in cynomolgus monkeys. *Toxicol. Sci.* **2002**, *68*, 249–264. [\[CrossRef\]](#)
187. Hlouskova, V.; Hradkova, P.; Poustka, J.; Brambilla, G.; Filipps, S.P.d.; D'Hollander, W.; Bervoets, L.; Herzke, D.; Huber, S.; Voegt, P.d.; et al. Occurrence of perfluoroalkyl substances (PFASs) in various food items of animal origin collected in four European countries. *Food Addit. Contam. Part A* **2013**, *30*, 1918–1932. [\[CrossRef\]](#)
188. Pasecnaja, E.; Bartkevics, V.; Zacs, D. Occurrence of selected per- and polyfluorinated alkyl substances (PFASs) in food available on the European market—A review on levels and human exposure assessment. *Chemosphere* **2022**, *287*, 132378. [\[CrossRef\]](#)
189. Mesfin Tefera, Y.; Gaskin, S.; Mitchell, K.; Springer, D.; Mills, S.; Pisaniello, D. Food grown on fire stations as a potential pathway for firefighters' exposure to per- and poly-fluoroalkyl substances (PFAS). *Environ. Int.* **2022**, *168*, 107455. [\[CrossRef\]](#)

190. Pan, Y.; Zhang, H.; Cui, Q.; Sheng, N.; Yeung, L.W.Y.; Guo, Y.; Sun, Y.; Dai, J. First Report on the Occurrence and Bioaccumulation of Hexafluoropropylene Oxide Trimer Acid: An Emerging Concern. *Environ. Sci. Technol.* **2017**, *51*, 9553–9560. [CrossRef] [PubMed]
191. Brendel, S.; Fetter, É.; Staude, C.; Vierke, L.; Biegel-Engler, A. Short-chain perfluoroalkyl acids: Environmental concerns and a regulatory strategy under REACH. *Environ. Sci. Eur.* **2018**, *30*, 9. [CrossRef]
192. EFSA. Perfluoroalkylated substances in food: Occurrence and dietary exposure. *EFSA J.* **2012**, *10*, 2743. [CrossRef]
193. EPA. Per- and Polyfluoroalkyl Substances National Primary Drinking Water Regulation. Available online: <https://www.regulations.gov/document/EPA-HQ-OW-2022-0114-0027> (accessed on 16 July 2024).
194. Ramírez Carnero, A.; Lestido-Cardama, A.; Vazquez Loureiro, P.; Barbosa-Pereira, L.; Rodríguez Ber-naldo de Quirós, A.; Sendón, R. Presence of Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS) in Food Contact Materials (FCM) and Its Migration to Food. *Foods* **2021**, *10*, 1443. [CrossRef]
195. DACF. PFAS Response, 2021. Available online: <https://www.maine.gov/dacf/ag/pfas/pfas-response.shtml> (accessed on 3 April 2024).
196. Schrenk, D.; Bignami, M.; Bodin, L.; Chipman, J.K.; Del Mazo, J.; Grasl-Kraupp, B.; Hogstrand, C.; Hoo-genboom, L.R.; Leblanc, J.-C.; Nebbia, C.S.; et al. Risk to human health related to the presence of perfluoroalkyl substances in food. *EFSA J.* **2020**, *18*, e06223. [CrossRef]
197. MDA. Products with Added PFAS, 2023. Available online: <https://www.mda.state.mn.us/environment-sustainability/products-added-pfas> (accessed on 3 April 2024).
198. MPCA. Minnesota’s PFAS Blueprint, 2021. Available online: <https://www.pca.state.mn.us/sites/default/files/p-gen1-22.pdf> (accessed on 8 August 2024).
199. EPA. PFAS Strategic Roadmap: EPA’s Commitments to Action 2021–2024. 2021. Available online: [https://www.epa.gov/system/files/documents/2021-10/pfas-roadmap\\_final-508.pdf](https://www.epa.gov/system/files/documents/2021-10/pfas-roadmap_final-508.pdf) (accessed on 3 May 2024).
200. DEED. Food & Agriculture: We Hope You’re Hungry. There’s a Lot to Take in. Available online: <https://mn.gov/deed/joinusmn/key-industries/food-agriculture/> (accessed on 17 July 2024).
201. Evich, M.G.; Davis, M.J.B.; McCord, J.P.; Acrey, B.; Awkerman, J.A.; Knappe, D.R.U.; Lindstrom, A.B.; Speth, T.F.; Tebes-Stevens, C.; Strynar, M.J.; et al. Per- and polyfluoroalkyl substances in the environment. *Science* **2022**, *375*, eabg9065. [CrossRef]
202. MPCA. PFAS Use Prohibitions, 2023. Available online: <https://www.pca.state.mn.us/air-water-land-climate/pfas-use-prohibitions> (accessed on 8 April 2024).
203. DACF. Per- and Polyfluoroalkyl Substances (PFAS), 2023. Available online: <https://www.maine.gov/dep/spills/topics/pfas/> (accessed on 8 April 2024).
204. University of Maine. Cooperative Extension: Agriculture: Guide to Investigating PFAS Risk on Your Farm, 2022. Available online: <https://extension.umaine.edu/agriculture/guide-to-investigating-pfas-risk-on-your-farm/> (accessed on 3 April 2024).
205. Hu, X.C.; Andrews, D.Q.; Lindstrom, A.B.; Bruton, T.A.; Schaidler, L.A.; Grandjean, P.; Lohmann, R.; Carignan, C.C.; Blum, A.; Balan, S.A.; et al. Detection of Poly- and Perfluoroalkyl Substances (PFASs) in U.S. Drinking Water Linked to Industrial Sites, Military Fire Training Areas, and Wastewater Treatment Plants. *Environ. Sci. Technol. Lett.* **2016**, *3*, 344–350. [CrossRef]

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