Per- And Polyfluoroalkyl Substances (PFAS) and Public Health Impact: Current Evidence, Emerging Challenges, And Future Perspectives

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ABSTRACT

Per- and polyfluoroalkyl substances (PFAS) are a large and chemically diverse class of synthetic organofluorine compounds recognized as persistent environmental contaminants because of their exceptional chemical stability, widespread industrial applications, and resistance to biological and environmental degradation. Their extensive use in firefighting foams, food-contact materials, textiles, cosmetics, electronics, and numerous consumer products has resulted in global contamination of water, soil, air, wildlife, and human populations. Biomonitoring studies consistently detect PFAS in human serum worldwide, highlighting widespread exposure and increasing concerns regarding their long-term environmental and public health consequences. This review critically synthesizes current evidence on PFAS chemistry, environmental occurrence, exposure pathways, toxicokinetics, molecular mechanisms of toxicity, public health impacts, regulatory developments, and remediation technologies. A PRISMA-informed narrative review supported by thematic evidence synthesis was undertaken using peer-reviewed literature and authoritative regulatory reports published primarily between 2021 and 2025, while retaining landmark studies that underpin PFAS research. Evidence indicates that contaminated drinking water, dietary intake, occupational activities, indoor dust, and consumer products constitute the principal human exposure pathways. Current epidemiological and toxicological findings associate PFAS exposure with endocrine disruption, hepatotoxicity, immunotoxicity, thyroid dysfunction, metabolic disorders, reproductive and developmental toxicity, cardiovascular disease, neurodevelopmental impairment, reduced vaccine responses, and increased risks of kidney and testicular cancers. However, important uncertainties remain regarding the toxicity of replacement PFAS, mixture effects, chronic low-dose exposure, and limited biomonitoring data from low- and middle-income countries. Although international regulatory initiatives have strengthened PFAS management, disparities in environmental monitoring, policy implementation, quantitative risk assessment, and remediation capacity persist. Future priorities should emphasize harmonized global regulations, expanded biomonitoring, sustainable fluorine-free alternatives, innovative remediation technologies, and integrated public health interventions to reduce PFAS exposure and protect environmental and human health.

Keywords: Per- and polyfluoroalkyl substances (PFAS); environmental contamination; human exposure; toxicokinetics; public health; remediation.

INTRODUCTION

Persistent organic pollutants (POPs) remain a major environmental and public health concern because of their persistence, toxicity, bioaccumulation, and long-range environmental transport. Among these contaminants, per- and polyfluoroalkyl substances (PFAS) have received considerable scientific and regulatory attention due to their extensive industrial applications, exceptional chemical stability, and growing association with adverse health outcomes (Buck et al., 2011; Sunderland et al., 2019; Fenton et al., 2021). Their highly stable carbon–fluorine bond renders them resistant to chemical, biological, thermal, and photolytic degradation, earning them the

designation "forever chemicals." PFAS comprise over 15,000 synthetic fluorinated compounds characterized by fully or partially fluorinated carbon chains attached to functional groups such as carboxylates, sulfonates, and fluorotelomers (OECD, 2021). Since their commercial introduction in the late 1940s, they have been widely incorporated into firefighting foams, food-contact materials, textiles, non-stick cookware, cosmetics, electronics, medical devices, semiconductor manufacturing, and numerous industrial processes because of their resistance to water, oil, grease, and heat (Buck et al., 2011; Glüge et al., 2020). However, their widespread production and disposal have resulted in global environmental contamination.

PFAS have now been detected in surface and groundwater, drinking water, soils, sediments, atmospheric aerosols, wildlife, agricultural products, and remote ecosystems, including polar regions. Unlike many persistent organic pollutants that accumulate in fatty tissues, PFAS preferentially bind to proteins, resulting in accumulation within blood, liver, kidneys, placenta, and breast milk (Fenton et al., 2021). Biomonitoring programmes indicate that detectable PFAS concentrations occur in the serum of most individuals worldwide, confirming near-universal human exposure (CDC, 2024; ATSDR, 2025). Human exposure occurs primarily through contaminated drinking water and food, although inhalation of indoor dust, occupational exposure, consumer products, and maternal transfer during pregnancy and breastfeeding also contribute substantially (Sunderland et al., 2019). Populations residing near fluorochemical manufacturing facilities, airports, military bases, and waste disposal sites generally experience the highest exposure levels, while firefighters and fluorochemical workers represent particularly vulnerable occupational groups.

Growing epidemiological and toxicological evidence links PFAS exposure to dyslipidaemia, thyroid dysfunction, immune suppression, liver injury, reproductive impairment, developmental abnormalities, metabolic disorders, hypertension, and increased risks of kidney and testicular cancers (Fenton et al., 2021; ATSDR, 2025). Although regulatory restrictions have reduced production of several legacy PFAS, increasing use of replacement compounds such as GenX has raised concerns regarding regrettable substitution, as many alternatives exhibit comparable persistence and biological activity. Consequently, PFAS have become an international environmental governance priority. Regulatory actions under the Stockholm Convention, the U.S. Environmental Protection Agency (USEPA), the European Chemicals Agency (ECHA), and the Organisation for Economic Co-operation and Development (OECD) increasingly support class-based management strategies. Nevertheless, important challenges remain regarding mixture toxicity, emerging PFAS, monitoring capacity, and environmental remediation. This review therefore synthesizes current evidence on PFAS chemistry, occurrence, exposure pathways, toxicological mechanisms, public health impacts, regulation, and remediation while highlighting key knowledge gaps and future research priorities.

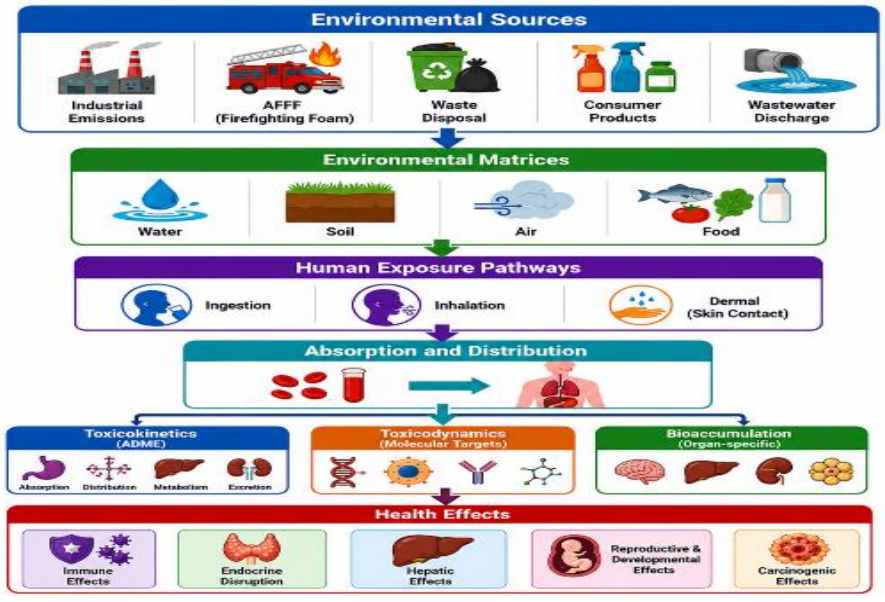

Figure 1: Environmental Transport Pathways of PFAS from Industrial Sources to Humans

Source: Adapted from Sunderland et al., 2019; Zhang et al., 2026

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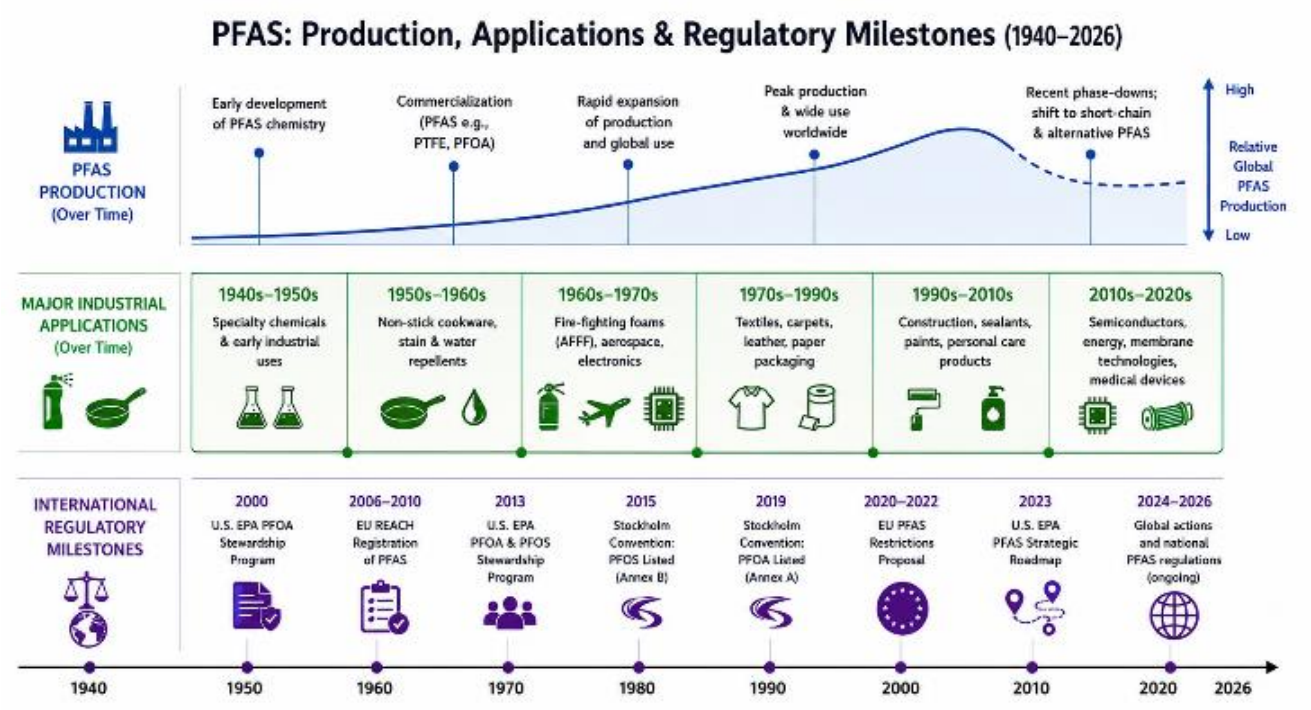


Figure 2. Historical evolution of PFAS production, major industrial applications, and international regulatory milestones (1940–2026).

REVIEW METHODOLOGY

This review employed a narrative review design supported by a thematic evidence-synthesis approach to critically evaluate current knowledge on PFAS chemistry, environmental occurrence, human exposure pathways, toxicokinetics, molecular mechanisms of toxicity, public health impacts, regulatory developments, and remediation strategies. A thematic synthesis approach was selected because it enables integration of evidence from environmental science, toxicology, epidemiology, exposure assessment, and public health while facilitating critical comparison of areas of consensus, conflicting findings, and emerging research priorities.

A comprehensive literature search was conducted between January and March 2026 using Scopus, Web of Science, PubMed, ScienceDirect, SpringerLink, Wiley Online Library, Taylor & Francis Online, and Google Scholar. To capture current regulatory and policy developments, grey literature was retrieved from the United States Environmental Protection Agency (USEPA), Agency for Toxic Substances and Disease Registry (ATSDR), Organisation for Economic Co-operation and Development (OECD), European Chemicals Agency (ECHA), World Health Organization (WHO), and the Stockholm Convention Secretariat. Search terms included combinations of "per- and polyfluoroalkyl substances (PFAS)," "PFOA," "PFOS," "environmental contamination," "drinking water," "human exposure," "toxicokinetics," "health effects," "epidemiology," "risk assessment," "regulation," and "remediation," linked using Boolean operators (AND/OR) to maximise search sensitivity and specificity.

Study selection followed a PRISMA-informed screening process to enhance transparency and reproducibility. The search yielded 1,360 records, comprising 1,286 records identified through electronic databases and 74 records obtained from grey literature sources. After removal of 286 duplicate records, 1,074 unique records remained for title and abstract screening. Of these, 930 records were excluded because they were unrelated to the review objectives or failed to satisfy the predefined eligibility criteria. The remaining 144 full-text articles were assessed for eligibility. Following critical appraisal, 99 studies were excluded because they lacked methodological quality, reported duplicate datasets, focused solely on analytical methods without environmental or public health relevance, or provided insufficient data for thematic synthesis. Consequently, 45 studies were retained for the final qualitative synthesis together with key international regulatory documents (Figure 2).

The review prioritised peer-reviewed publications published between 2021 and 2025, while retaining landmark studies that established the conceptual and scientific foundations of PFAS research, including Buck et al. (2011), Sunderland et al. (2019), Glüge et al. (2020), and Fenton et al. (2021). Eligible literature comprised systematic reviews, meta-analyses, cohort and case-control studies, biomonitoring investigations, experimental toxicology studies, environmental monitoring reports, quantitative risk assessment studies, and international regulatory documents. Editorials, conference abstracts lacking adequate methodological detail, duplicate publications, and studies unrelated to PFAS exposure or health outcomes were excluded.

To strengthen methodological rigour, included studies were critically appraised based on study design, sample size, exposure assessment methods, analytical quality, geographical coverage, risk of bias, and consistency of findings. Greater weight was assigned to systematic reviews, longitudinal cohort studies, meta-analyses, and authoritative regulatory reports because of their higher level of evidence. Evidence was synthesised thematically with emphasis on evaluating conflicting findings, causal inference, methodological limitations, and the strength of available evidence rather than providing descriptive summaries alone.

Recognising the geographical imbalance in PFAS research, particular attention was given to identifying evidence from low- and middle-income countries, where environmental monitoring and biomonitoring remain limited. The review further highlights knowledge gaps relating to replacement PFAS, mixture toxicity, chronic low-dose exposure, quantitative human health risk assessment, and public health interventions. A PRISMA-style flow diagram (Figure 3) summarises the literature identification, screening, eligibility assessment, and final study inclusion process, thereby enhancing the transparency and reproducibility of the review methodology.

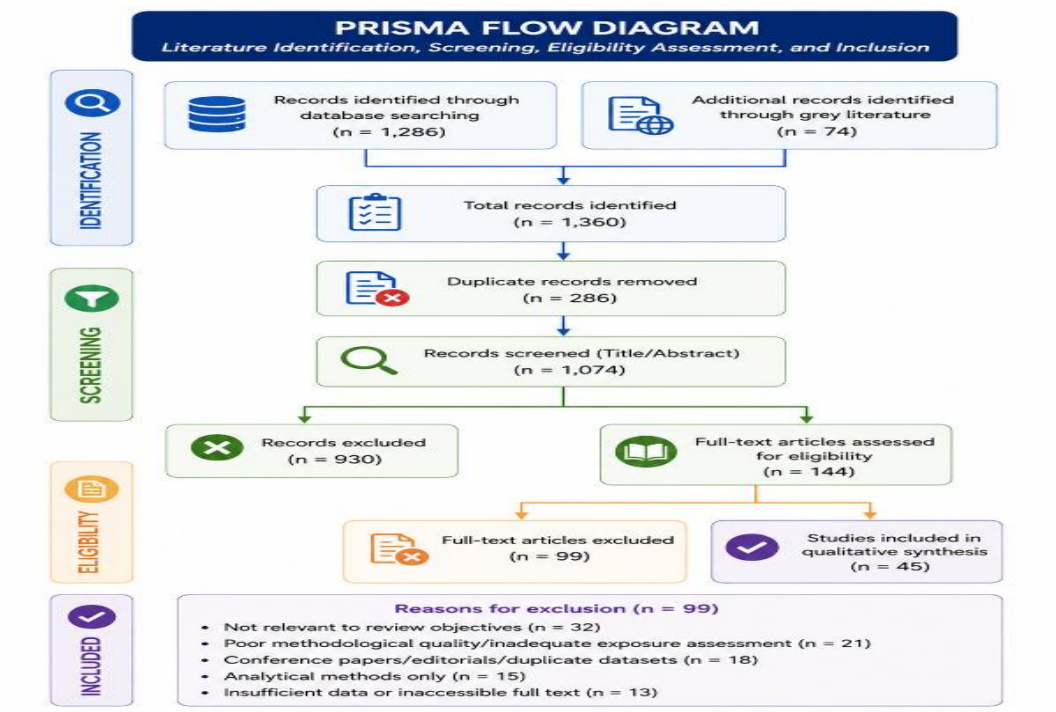


Figure 3: PRISMA Diagram

Chemistry And Classification Of Per- And Polyfluoroalkyl Substances

Chemical Characteristics of PFAS

PFAS constitute one of the largest classes of synthetic fluorinated chemicals and are defined by the presence of one or more fully fluorinated carbon atoms (OECD, 2021). Their unique physicochemical properties arise from the exceptionally strong carbon–fluorine bond, which confers remarkable resistance to chemical degradation, thermal decomposition, hydrolysis, and microbial activity (Buck et al., 2011; Glüge et al., 2020). Unlike traditional persistent organic pollutants that accumulate in fatty tissues, PFAS bind strongly to plasma proteins such as serum albumin, resulting in accumulation within blood, liver, kidneys, and other highly perfused organs

(Fenton et al., 2021). This protein-binding behaviour largely explains their prolonged biological half-lives and widespread systemic distribution.

Classification

PFAS are commonly classified according to molecular structure, carbon-chain length, and functional groups. Structurally, they are divided into perfluoroalkyl substances, in which all hydrogen atoms are replaced by fluorine, and polyfluoroalkyl substances, in which fluorination is only partial (Buck et al., 2011). Based on carbon-chain length, PFAS are categorized into long-chain compounds (e.g., PFOA, PFOS, PFNA and PFDA) and short-chain compounds (e.g., PFBS and PFHxA). Long-chain PFAS generally exhibit greater bioaccumulation, longer biological half-lives, and stronger evidence of toxicity, whereas short-chain alternatives display greater environmental mobility despite lower bioaccumulation. Restrictions on legacy PFAS have accelerated development of replacement chemicals such as GenX, ADONA, and F-53B. Although initially considered safer alternatives, increasing evidence indicates that many replacement PFAS remain environmentally persistent and biologically active, raising concerns regarding regrettable substitution (Conley et al., 2021).

Physicochemical Properties and Environmental Behaviour

The environmental behaviour of PFAS depends largely on molecular structure, carbon-chain length, and functional groups. Long-chain PFAS tend to adsorb strongly to soils, sediments, and biological tissues, whereas short-chain compounds remain highly mobile in aquatic environments, facilitating contamination of drinking-water resources (Sunderland et al., 2019). Their amphiphilic nature enables partitioning among air, water, soil, sediments, and biological systems, explaining their global distribution across both industrialized and remote environments. Consequently, many researchers now advocate class-based regulation rather than compound-specific management because the continual introduction of structurally similar replacement PFAS makes regulation of individual chemicals increasingly impractical.

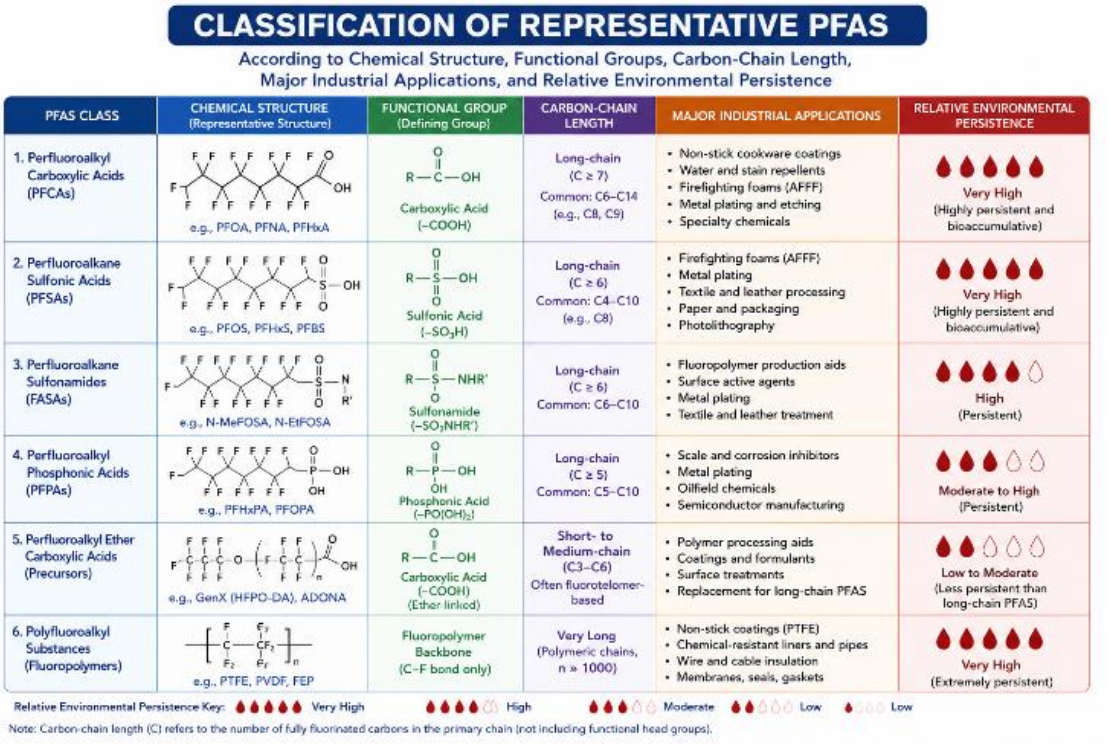


Figure 3**:** Classification of representative PFAS

Sources, Environmental Occurrence And Transport Of Per- And Polyfluoroalkyl Substances (Pfas)

The extensive manufacture and application of per- and polyfluoroalkyl substances (PFAS) over the past seven decades have resulted in widespread environmental contamination. Their exceptional persistence is attributed to the highly stable carbon–fluorine bond, which resists biological, chemical, and photolytic degradation. Consequently, PFAS have been detected in surface water, groundwater, soils, sediments, atmospheric aerosols, wildlife, food products, and remote regions, demonstrating their capacity for long-range environmental transport and global dispersion (Buck et al., 2011; Sunderland et al., 2019; Glüge et al., 2020; Li et al., 2024).

Sources of PFAS Contamination

PFAS enter the environment through both **point** and **diffuse** sources. Major point sources include fluorochemical manufacturing plants, airports, military bases, wastewater treatment plants, landfills, and industrial facilities using aqueous film-forming foams (AFFFs), which have produced persistent contamination of surrounding soils and groundwater (Glüge et al., 2020; OECD, 2021; ATSDR, 2025; USEPA, 2024). Diffuse emissions originate from the production, use, and disposal of PFAS-containing consumer products, including textiles, food packaging, cosmetics, non-stick cookware, and cleaning products. Although emissions from individual products are relatively low, their cumulative contribution is environmentally significant. Furthermore, replacement PFAS such as GenX and ADONA are increasingly detected in environmental matrices, raising concerns because they remain persistent and mobile despite being introduced as safer alternatives (Conley et al., 2021; Zhang et al., 2025).

Environmental Occurrence

Aquatic systems are the principal environmental reservoirs of PFAS because these compounds are highly soluble and poorly removed by conventional wastewater treatment processes. Consequently, rivers, lakes, groundwater, and drinking-water supplies frequently receive continuous PFAS inputs through treated effluents and landfill leachates (Kurwadkar et al., 2022; Panieri et al., 2022). PFAS also accumulate in soils through atmospheric deposition and biosolid application, from where they may be absorbed by crops and transferred into the food chain. Atmospheric transport of volatile PFAS precursors further contributes to contamination of geographically remote regions (Sunderland et al., 2019; Glüge et al., 2020).

Environmental Transport

Environmental transport depends largely on molecular structure. Long-chain PFAS exhibit greater adsorption to soils and biological tissues, whereas short-chain compounds are more mobile in aquatic environments, increasing their potential to contaminate drinking-water sources (Buck et al., 2011; Sunderland et al., 2019). Unlike lipophilic pollutants, PFAS bind predominantly to proteins, facilitating bioaccumulation in wildlife and humans and biomagnification through food webs (Fenton et al., 2021; Yang et al., 2023; Xing et al., 2023). Overall, legacy contamination, continued emissions from replacement PFAS, and inadequate removal by conventional treatment technologies ensure that PFAS remain a persistent global environmental and public health challenge, necessitating integrated monitoring, class-based regulation, and the development of sustainable remediation strategies (Cousins et al., 2022; Zhang et al., 2025).

Table 1. Major Sources, Environmental Compartments, Transport Mechanisms, and Public Health Implications of PFAS

Source	Principal PFAS	Environmental compartment	Transport pathway	Public health implication
Fluorochemical industries	PFOA, PFOS, GenX	Air, water, soil	Industrial discharge	Drinking-water contamination
Firefighting foams (AFFFs)	PFOS, fluorotelomers	Soil, groundwater	Infiltration and leaching	Community exposure

Wastewater treatment plants	Mixed PFAS	Rivers, lakes	Effluent discharge	Aquatic contamination
Landfills	Mixed PFAS	Groundwater	Leachate migration	Long-term contamination
Biosolids	Short- and long-chain PFAS	Agricultural soils	Soil amendment	Crop uptake
Consumer products	Multiple PFAS	Indoor dust, wastewater	Product degradation	Chronic low-level exposure

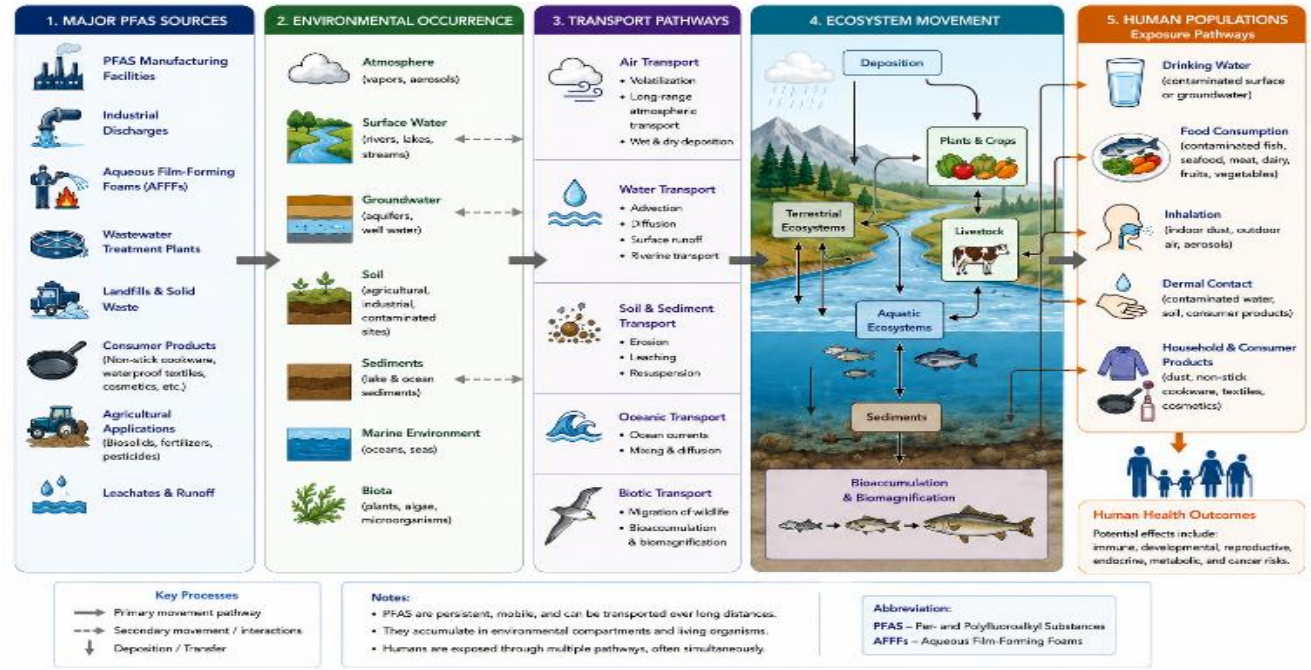


Figure 4: Major PFAS sources

Human Exposure Pathways To Per- And Polyfluoroalkyl Substances

Human exposure to per- and polyfluoroalkyl substances (PFAS) has become widespread because of their persistence and ubiquitous distribution across environmental media. Biomonitoring studies consistently detect PFAS in the serum of most individuals worldwide, indicating near-universal exposure. Although ingestion remains the predominant route, inhalation, dermal contact, occupational exposure, and maternal transfer also contribute significantly depending on population characteristics and environmental conditions (Sunderland et al., 2019; Fenton et al., 2021; ATSDR, 2025).

Drinking Water

Contaminated drinking water is the principal exposure pathway for communities located near fluorochemical manufacturing facilities, airports, military installations, landfill sites, and locations where aqueous film-forming foams (AFFFs) have been extensively used. Because many PFAS are highly soluble, chemically stable, and resistant to conventional water treatment processes, they migrate readily through groundwater and surface-water systems into municipal water supplies. Long-term consumption of contaminated drinking water has consistently been associated with elevated serum PFAS concentrations, highlighting the importance of routine environmental monitoring, improved drinking-water treatment technologies, and effective source control measures (Kurwadkar et al., 2022; USEPA, 2024).

Dietary Exposure

Dietary intake represents another major exposure pathway. Fish, seafood, meat, eggs, dairy products, and crops cultivated in contaminated environments may accumulate PFAS, facilitating their transfer through the food chain. Protein-rich animal products generally contain higher concentrations because PFAS preferentially bind to proteins rather than lipids. Food-contact materials, including grease-resistant papers, microwave popcorn bags, and takeaway packaging, have historically contributed to dietary exposure through chemical migration into food. Although regulatory restrictions have reduced the use of several legacy PFAS, concerns persist regarding replacement compounds increasingly used in food-packaging materials (Fenton et al., 2021; Xing et al., 2023; Conley et al., 2021).

Indoor Environment and Consumer Products

Indoor environments and consumer products constitute important sources of chronic low-level exposure. PFAS are gradually released from stain-resistant carpets, upholstered furniture, waterproof textiles, electronics, cosmetics, cleaning agents, and household dust through normal use and material degradation. Young children are particularly susceptible because of frequent hand-to-mouth behaviour and higher dust ingestion relative to body weight. Repeated use of PFAS-containing cosmetics and personal-care products may further increase cumulative exposure, although dermal absorption generally contributes less than oral intake (Abraham et al., 2022; Glüge et al., 2020).

Occupational Exposure

Occupational exposure is substantially higher among firefighters, fluorochemical manufacturing workers, metal-plating personnel, semiconductor workers, and waste-management employees. Firefighters are particularly vulnerable because repeated use of PFAS-containing firefighting foams and contaminated protective equipment results in combined inhalation, dermal, and incidental oral exposure. Despite increasing awareness of occupational risks, exposure monitoring programmes and workplace safety standards remain inconsistent across countries (ATSDR, 2025; Fenton et al., 2021).

Maternal and Early-Life Exposure

PFAS readily cross the placenta and are transferred through breast milk, exposing fetuses and infants during critical stages of growth and development. Infants and young children are especially vulnerable because of immature detoxification systems, greater food and water intake relative to body weight, and increased dust ingestion. Although breastfeeding remains strongly recommended because its overall health benefits far outweigh potential PFAS-related risks, reducing maternal exposure through effective environmental control remains an important public health priority (Fenton et al., 2021; ATSDR, 2025).

Overall, PFAS exposure reflects the combined influence of drinking water, diet, consumer products, occupational activities, and maternal transfer rather than any single pathway. Future exposure assessment should adopt an **exposome-based approach** capable of evaluating cumulative lifetime exposure from multiple environmental sources, thereby supporting more comprehensive risk assessment and evidence-based public health interventions (Conley et al., 2021; Zhang et al., 2025).

Table 2. Major Human Exposure Pathways to PFAS and Populations at Risk

Exposure pathway	Major source	Population most affected	Relative contribution	Key health concern
Drinking water	Contaminated groundwater and municipal supplies	General population	Very High	Chronic systemic exposure
Food consumption	Fish, seafood, meat, dairy, crops	General population	High	Bioaccumulation

Indoor dust and air	Household products	Children	Moderate	Chronic low-dose exposure
Consumer products	Cosmetics, cookware, textiles	General population	Moderate	Repeated daily exposure
Occupational exposure	Firefighting, fluorochemical manufacture	Industrial workers	Very High	Elevated body burden
Maternal transfer	Placenta and breast milk	Fetuses and infants	High	Developmental vulnerability

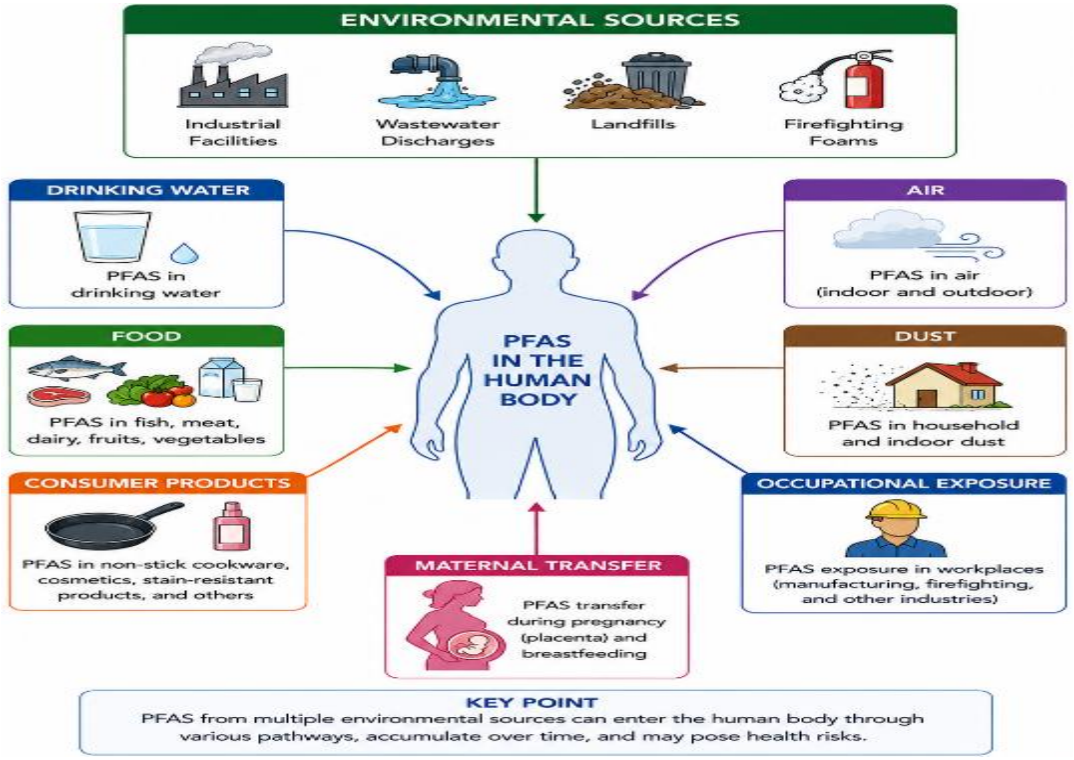


Figure 5: Major human exposure pathways showing movement of PFAS from environmental sources

Toxicokinetics And Molecular Mechanisms Of Toxicity

The toxicokinetic behaviour of per- and polyfluoroalkyl substances (PFAS) largely explains their persistence in the human body and their association with numerous chronic diseases. Unlike many environmental contaminants that undergo rapid metabolism and elimination, several PFAS possess biological half-lives of 2–8 years, permitting gradual accumulation following repeated exposure. Their resistance to degradation and strong affinity for serum proteins distinguish them from many other persistent pollutants and contribute to widespread systemic distribution (Olsen et al., 2007; Sunderland et al., 2019; Yang et al., 2023).

Absorption

PFAS enter the human body primarily through oral ingestion of contaminated drinking water and food, with gastrointestinal absorption exceeding 90% for several legacy compounds, including PFOA and PFOS. Additional exposure occurs through inhalation of contaminated air and dust, particularly in occupational settings, whereas dermal absorption contributes relatively little because most ionic PFAS penetrate the skin poorly. Maternal transfer through the placenta and breast milk exposes fetuses and infants during critical developmental stages (Fenton et al., 2021; ATSDR, 2025).

Distribution

Following absorption, PFAS bind extensively to serum albumin and other transport proteins, facilitating systemic circulation. Unlike lipophilic pollutants that accumulate in adipose tissue, PFAS concentrate in highly perfused organs, including the liver, kidneys, thyroid, blood, and placenta. Long-chain PFAS generally exhibit greater tissue retention and longer biological half-lives than short-chain analogues, although the latter are typically more environmentally mobile (Fenton et al., 2021; Yang et al., 2023).

Metabolism and Excretion

Most legacy PFAS undergo little or no metabolic transformation because mammalian enzymes cannot readily degrade the carbon–fluorine bond. However, some fluorinated precursor compounds are converted into persistent perfluoroalkyl acids, complicating exposure assessment. Elimination occurs mainly through renal excretion, but efficient tubular reabsorption markedly prolongs biological persistence. Physiological processes such as menstruation, pregnancy, and lactation contribute to lower serum PFAS concentrations in women while simultaneously transferring PFAS to developing fetuses and infants (Olsen et al., 2007; Yang et al., 2023).

Molecular Mechanisms of Toxicity

PFAS exert toxicity through multiple interconnected molecular pathways. Activation of peroxisome proliferator-activated receptors (PPARs) disrupts lipid metabolism, glucose homeostasis, and inflammatory signalling, while oxidative stress promotes mitochondrial dysfunction, lipid peroxidation, DNA damage, and chronic inflammation. PFAS also function as endocrine-disrupting chemicals by interfering with thyroid and steroid hormone signalling and suppress immune function through impaired antibody production and altered cytokine expression. Emerging evidence further implicates epigenetic modifications, including altered DNA methylation and microRNA expression, suggesting potential long-term and transgenerational effects. Although oxidative stress, endocrine disruption, immune dysregulation, and epigenetic alterations are recognised mechanisms, uncertainties remain regarding mixture toxicity and the health effects of emerging replacement PFAS (Cao et al., 2022; Manojkumar et al., 2023; Grandjean et al., 2012; Conley et al., 2021; Zhang et al., 2025).

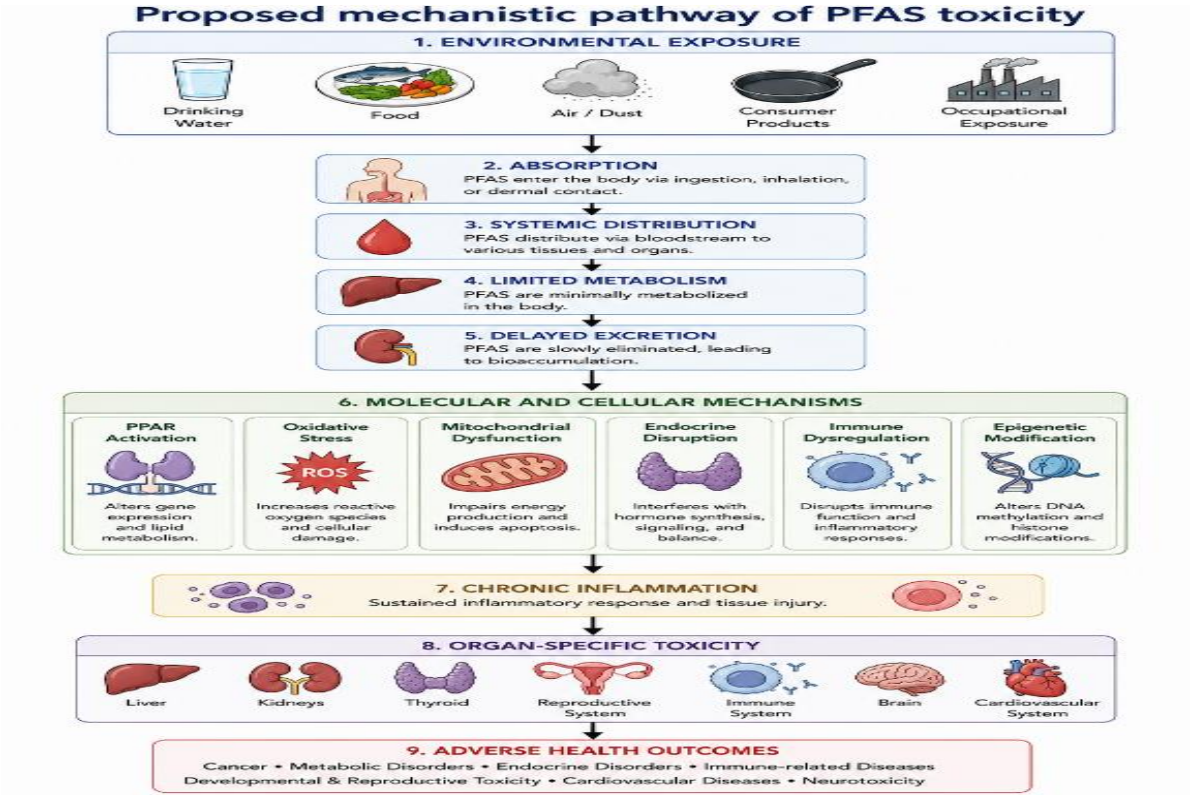


Figure 6: Proposed mechanistic pathway of PFAS toxicity

Public Health Impacts Of Per- And Polyfluoroalkyl Substances

Growing epidemiological and experimental evidence identifies per- and polyfluoroalkyl substances (PFAS) as contaminants capable of affecting multiple organ systems. Although the strongest evidence relates to legacy compounds such as PFOA and PFOS, concerns increasingly extend to replacement PFAS because of their persistence and biological activity. Current evidence consistently links PFAS exposure with metabolic disorders, liver and kidney disease, immune dysfunction, reproductive toxicity, developmental abnormalities, and selected cancers (Sunderland et al., 2019; Fenton et al., 2021; ATSDR, 2025).

Endocrine and Metabolic Effects

PFAS are recognised endocrine-disrupting chemicals that interfere with thyroid hormone regulation, lipid metabolism, and glucose homeostasis. Epidemiological studies consistently associate elevated serum PFAS concentrations with dyslipidaemia, particularly increased total cholesterol and low-density lipoprotein (LDL) cholesterol. Evidence also suggests possible associations with obesity, insulin resistance, type 2 diabetes, and gestational diabetes, although findings remain less consistent across populations (Fenton et al., 2021; ATSDR, 2025).

Hepatic and Renal Toxicity

The liver is a major target organ because of its central role in metabolism and xenobiotic processing. Experimental studies demonstrate hepatocellular hypertrophy, oxidative stress, mitochondrial dysfunction, and hepatic inflammation, while epidemiological evidence links PFAS exposure with elevated liver enzymes and non-alcoholic fatty liver disease. Renal accumulation resulting from active tubular reabsorption has also been associated with impaired kidney function and chronic kidney disease. Prolonged PFOA exposure is strongly associated with kidney cancer, supporting its classification as carcinogenic to humans by the International Agency for Research on Cancer (Cao et al., 2022; Manojkumar et al., 2023; IARC, 2023).

Immunotoxicity

PFAS-induced immunotoxicity is among the most consistently documented health effects. Cohort studies demonstrate reduced antibody responses following childhood vaccination, altered cytokine production, impaired immune-cell function, and increased susceptibility to infectious diseases. Experimental findings similarly indicate suppression of both innate and adaptive immune responses following chronic exposure (Grandjean et al., 2012; Fenton et al., 2021; ATSDR, 2025).

Reproductive and Developmental Toxicity

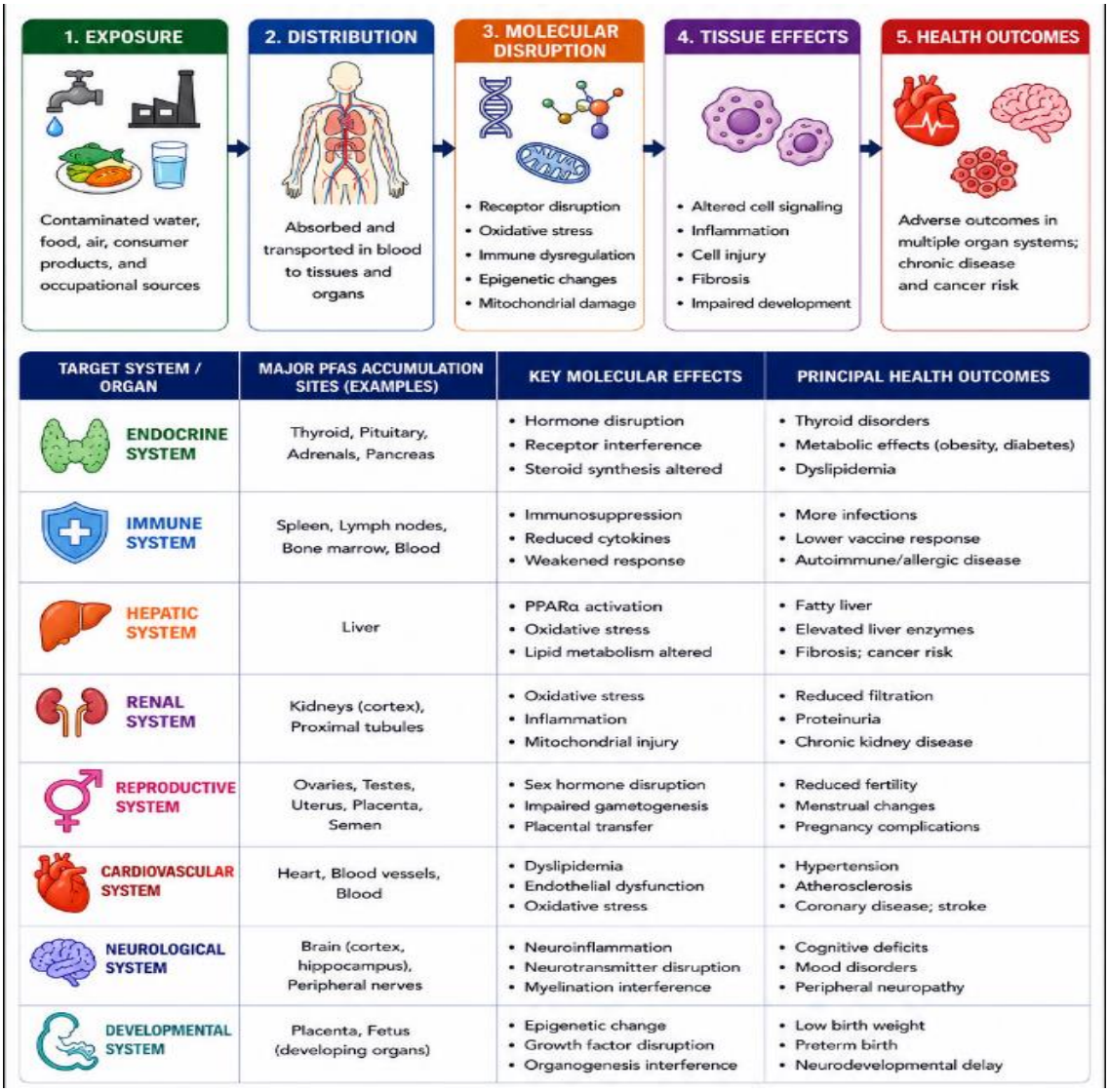
Maternal PFAS exposure has been associated with reduced fertility, pregnancy complications, preterm birth, low birth weight, and impaired fetal growth. Because PFAS readily cross the placenta and are transferred through breast milk, fetal exposure begins before birth. Prenatal exposure has also been associated with altered neurodevelopment, behavioural disorders, impaired cognitive function, immune dysfunction, and increased asthma risk, although the magnitude of these effects varies among studies (Fenton et al., 2021; ATSDR, 2025).

Cardiovascular, Neurological and Carcinogenic Effects

Emerging evidence links PFAS exposure with hypertension, endothelial dysfunction, oxidative stress, and chronic inflammation, suggesting potential contributions to cardiovascular disease. Neurological studies indicate possible effects on neurotransmission and cognitive development, although evidence remains limited. Strong epidemiological evidence supports associations between prolonged PFOA exposure and kidney and testicular cancers, whereas evidence for other cancers remains suggestive but inconclusive (Fenton et al., 2021; IARC, 2023; ATSDR, 2025).

Overall, PFAS exert multisystem toxicity through interconnected molecular mechanisms rather than isolated pathways. Although evidence is strongest for dyslipidaemia, immunotoxicity, reproductive toxicity, kidney disease, and selected cancers, uncertainties persist regarding replacement PFAS, chronic low-dose exposure, and

cumulative mixture effects, highlighting important priorities for future research (Conley et al., 2021; Zhang et al., 2025).



TARGET SYSTEM / ORGAN	MAJOR PFAS ACCUMULATION SITES (EXAMPLES)	KEY MOLECULAR EFFECTS	PRINCIPAL HEALTH OUTCOMES
ENDOCRINE SYSTEM	Thyroid, Pituitary, Adrenals, Pancreas	• Hormone disruption • Receptor interference • Steroid synthesis altered	• Thyroid disorders • Metabolic effects (obesity, diabetes) • Dyslipidemia
IMMUNE SYSTEM	Spleen, Lymph nodes, Bone marrow, Blood	• Immunosuppression • Reduced cytokines • Weakened response	• More infections • Lower vaccine response • Autoimmune/allergic disease
HEPATIC SYSTEM	Liver	• PPARα activation • Oxidative stress • Lipid metabolism altered	• Fatty liver • Elevated liver enzymes • Fibrosis; cancer risk
RENAL SYSTEM	Kidneys (cortex), Proximal tubules	• Oxidative stress • Inflammation • Mitochondrial injury	• Reduced filtration • Proteinuria • Chronic kidney disease
REPRODUCTIVE SYSTEM	Ovaries, Testes, Uterus, Placenta, Semen	• Sex hormone disruption • Impaired gametogenesis • Placental transfer	• Reduced fertility • Menstrual changes • Pregnancy complications
CARDIOVASCULAR SYSTEM	Heart, Blood vessels, Blood	• Dyslipidemia • Endothelial dysfunction • Oxidative stress	• Hypertension • Atherosclerosis • Coronary disease; stroke
NEUROLOGICAL SYSTEM	Brain (cortex, hippocampus), Peripheral nerves	• Neuroinflammation • Neurotransmitter disruption • Myelination interference	• Cognitive deficits • Mood disorders • Peripheral neuropathy
DEVELOPMENTAL SYSTEM	Placenta, Fetus (developing organs)	• Epigenetic change • Growth factor disruption • Organogenesis interference	• Low birth weight • Preterm birth • Neurodevelopmental delay

Figure 7: Target organs and principal adverse health outcomes associated with PFAS exposure

Regulatory Framework

The global response to PFAS contamination has evolved rapidly over the past decade, reflecting growing scientific evidence of their persistence, bioaccumulation, and adverse health effects. Initial regulatory efforts focused primarily on legacy compounds such as PFOS and PFOA; however, increasing recognition of thousands of structurally related PFAS has prompted a shift towards regulating PFAS as chemical classes rather than individual substances (OECD, 2021; Cousins et al., 2023).

Internationally, the Stockholm Convention on Persistent Organic Pollutants has listed PFOS, PFOA, and perfluorohexane sulfonic acid (PFHxS) for global restriction or elimination because of their persistence and long-range environmental transport (UNEP, 2023). Within Europe, the European Chemicals Agency (ECHA) is progressing a comprehensive proposal to restrict thousands of PFAS under the REACH Regulation, representing one of the most ambitious chemical control initiatives to date (ECHA, 2024). Similarly, the United States Environmental Protection Agency (USEPA) established legally enforceable maximum contaminant levels (MCLs) for selected PFAS in drinking water and designated PFOA and PFOS as hazardous substances under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) (USEPA, 2024).

Despite these advances, regulatory implementation remains uneven globally, particularly in many low- and middle-income countries where PFAS monitoring capacity, environmental standards, and risk management frameworks are still developing. Future regulation should therefore prioritize class-based approaches, harmonized international monitoring, and precautionary substitution with demonstrably safer alternatives.

Remediation Technologies

The exceptional persistence and mobility of PFAS present major challenges for environmental remediation because conventional water and wastewater treatment processes remove these compounds inefficiently (Ross et al., 2020; Panieri et al., 2022). Consequently, considerable research has focused on developing technologies capable of both removing and destroying PFAS.

Current treatment methods rely primarily on adsorption and separation technologies. Granular activated carbon (GAC) remains widely used for removing long-chain PFAS from drinking water, whereas ion-exchange resins generally demonstrate higher removal efficiencies across a broader range of PFAS compounds (Ross et al., 2020). Reverse osmosis and nanofiltration effectively remove most PFAS but generate concentrated waste streams requiring further treatment.

Destructive technologies are increasingly receiving attention because they permanently degrade PFAS rather than transferring them to another environmental medium. Advanced oxidation, electrochemical oxidation, plasma treatment, sonolysis, supercritical water oxidation, and photocatalytic degradation have shown encouraging laboratory and pilot-scale results (Nzeribe et al., 2024). However, high operational costs, energy demands, and limited large-scale implementation currently constrain widespread application. Continued innovation is therefore required to develop cost-effective, environmentally sustainable remediation technologies capable of treating complex PFAS mixtures.

Knowledge Gaps And Future Perspectives

1. Despite substantial advances in PFAS research, important scientific uncertainties remain. Most toxicological and epidemiological studies continue to focus on a relatively small number of legacy PFAS, whereas thousands of replacement compounds remain poorly characterized. Consequently, the environmental persistence, toxicokinetics, and health effects of many emerging PFAS remain largely unknown.

2. Another important limitation involves mixture toxicity. Human populations are exposed simultaneously to numerous PFAS and other environmental contaminants, yet most risk assessments evaluate individual compounds in isolation. Improved understanding of cumulative exposure and chemical interactions is therefore essential for more realistic health-risk assessment. Additionally, environmental monitoring remains concentrated in North America and Europe, with comparatively limited data from Africa, Latin America, and many developing regions.

3. Future research should integrate exposomics, high-resolution mass spectrometry, multi-omics technologies, artificial intelligence-assisted exposure modelling, and physiologically based pharmacokinetic (PBPK) models to improve prediction of long-term health risks. Simultaneously, governments should strengthen biomonitoring programmes, encourage development of fluorine-free alternatives, and adopt class-based regulatory approaches that prevent regrettable substitution of one persistent PFAS with another structurally similar compound.

CONCLUSIONS

Per- and polyfluoroalkyl substances (PFAS) have become one of the most significant environmental and public health concerns because of their exceptional persistence, widespread industrial use, and global environmental distribution. This review demonstrates that PFAS contaminate water, soil, air, food chains, wildlife, and human populations, resulting in continuous exposure through drinking water, food, consumer products, occupational activities, indoor environments, and maternal transfer. Current evidence indicates that PFAS exert multisystem

toxicity through interconnected mechanisms involving oxidative stress, endocrine disruption, immune dysregulation, mitochondrial dysfunction, and chronic inflammation. Epidemiological and experimental studies consistently associate PFAS exposure with metabolic, hepatic, renal, reproductive, developmental, immunological, cardiovascular, neurological, and carcinogenic effects. However, important uncertainties remain regarding replacement PFAS, mixture toxicity, chronic low-dose exposure, and the long-term health implications of emerging fluorinated compounds.

Although international regulatory efforts have expanded, significant challenges persist in environmental monitoring, quantitative risk assessment, remediation, and policy implementation, particularly in low- and middle-income countries. Addressing these challenges requires harmonized global regulations, expanded biomonitoring, improved environmental surveillance, sustainable fluorine-free alternatives, and innovative remediation technologies. Continued multidisciplinary research and stronger international collaboration will be essential to improve risk assessment, reduce PFAS exposure, manage legacy contamination, and translate scientific evidence into effective public health and environmental protection policies for present and future generations.

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