REVIEW ARTICLE OPEN Check for updates Revisiting the "forever chemicals", PFOA and PFOS exposure in drinking water

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Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), known as the most detected per- and polyfluoroalkyl substances (PFAS) in various environmental compartments, have been associated with plastic pollution and endocrine dysfunction. Over the past 180 years (1839–2019), numerous emerging contaminants have been identified, with PFOA and PFOS receiving considerable attention based on scientific evidence and publications. Between 2018 and 2019, PFOA and PFOS experienced a relatively high increase rate of 18.8% and 13.6%, respectively. While developed countries have made progress in establishing stringent guidelines, developing and underdeveloped countries often lack regulations and mechanisms to address emerging PFAS. Furthermore, advancements in PFAS removal technologies are needed to improve their efficacy and feasibility. The establishment of regulatory compliances, along with exposure assessment and risk characterization, is essential for providing precautionary advice on water source protection, water supply security, health risks, treatment efficiency, and contamination forecasting. However, a more comprehensive approach and database for evaluating exposure and risks are still imperative to effectively combat PFAS contamination. The analysis of Needs, Approaches, Benefits, and Challenges (NABC) is grounded in the current trends of PFAS in the environment and human exposure through drinking water.

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INTRODUCTION

Per- and polyfluoroalkyl substances (PFAS) are a class of highly fluorinated chemicals that have been widely synthesized and utilized since the 1940s in various industrial practices and consumer products, acting as surfactants, flame retardants, additives, lubricants, and pesticides; generated as by-products, residues, and intermediates in various processes¹⁻³. Due to their multiple carbon-fluorine (C-F) bonds, PFAS exhibit enhanced chemical and thermal stability, rendering them persistent and resistant to degradation⁴. They are also hydrophobic and lipophobic, capable of bioaccumulation and sorption, and can be transported through various modes of action in the environment, thereby posing toxicity to organisms⁵. The environmental fate of PFAS is influenced by their structural properties, including functional groups, carbon chain length, hydrophobicity, and lipophobicity^{5,6}. With over 4000 compounds belonging to this class and being utilized in various industries and products as polymers and additives, PFAS, commonly referred to as "forever chemicals", are suspected environmental contaminants and endocrine disruptors, although only a small number is currently monitored and regulated^{7,8}.

In the early 1960s, the revelation of human exposure to environmental contaminants stemming from PFAS manufacturing and application marked the emergence of a global contamination crisis⁹. PFAS are extensively utilized for their "non-stick" properties and their ability to reduce surface tension, rendering them valuable in repelling water and oil, preventing stains, and modifying surface chemistry⁸. Due to their widespread use as key components in aqueous film-forming foams (AFFF), PFAS contamination sites continue to be discovered worldwide, particularly in the vicinity of airports and military bases where AFFF is frequently used for firefighting and training activities^{3,8}. PFAS exhibits a wide range of toxic effects, including developmental toxicity, genotoxicity, carcinogenicity, hepatotoxicity, reproductive toxicity, immunotoxicity, cytotoxicity, neurotoxicity, and hormonal toxicity¹⁰. Primarily, they have been associated with elevated risks of cancer, immune responses, metabolic syndromes, developmental issues, and reproductive effects⁸. These adverse effects stem from their ability to disrupt the endocrine system through interactions with nuclear receptors, classifying PFAS as potential endocrine disruptors^{10,11}.

Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) are two of the most used PFAS compounds in various applications. Although they have been phased out globally, they persist in the environment and are listed under the Stockholm Convention on Persistent Organic Chemicals¹². The continuous concern regarding PFOA and PFOS has prompted research on their replacement, such as perfluorohexanoic acid (PFHxA), perfluorohexane sulfonic acid (PFHxS), hexafluoropropylene oxide dimer acid (HFPO-DA or GenX), and 6:2 chlorinated polyfluoroalkyl ether sulfonic acid (6:2 CI-PFAES or commercially known as F-53B), which have garnered great interest¹³⁻¹⁶. Moreover, the International Agency for Research on Cancer (IARC) has classified PFOA as "possibly carcinogenic to humans"¹⁷. Epidemiological studies have reported a strong association between both PFOA and PFOS and testicular and kidney cancer; however, conclusive results require long-term follow-up studies with large cohorts that have significant exposure contrasts¹⁸. Additionally, it is important to consider that different isomers of each PFAS may exhibit variations in toxicity¹⁹. Risk estimation based solely on traditional endpoints such as growth, reproduction, and mortality may not adequately capture PFAS toxicity. Advanced molecular biological

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