

Molecular and Integrative Toxicology

Jamie C. DeWitt *Editor*

Toxicological Effects of Perfluoroalkyl and Polyfluoroalkyl Substances

 Humana Press

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Toxicological Effects of Perfluoroalkyl and Polyfluoroalkyl Substances

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Preface

This book will be of interest to toxicologists, environmental chemists, risk assessors, and others with an interest in the class of compounds known as perfluoroalkyl and polyfluoroalkyl substances (PFASs). Most of the chapters are written for those with a background in toxicology or chemistry, but background information and references to review articles are included to provide a starting point for those seeking additional information.

PFASs are commonly used in myriad industrial and commercial applications. PFASs have provided industries and the general public with products of convenience and safety, including oil- and water-repellent textiles and papers, coatings, and fire-retardants. However, the unintended presence of PFAS in environmental media, including biota, may have adverse effects on the health of exposed organisms. Reports of cancers of the liver, pancreas, and testes in rodents exposed to PFASs began appearing in the early 1990s; in the ensuing decades, the number of publications related to PFAS toxicity has increased dramatically, revealing that many of these substances are associated with toxicities in nearly every system studied. Although the potential health risks of these compounds have been assessed by governmental agencies and organizations in many countries and health advisories and recommendations have been established, many questions about PFAS toxicity remain. Therefore, one goal of this book is to highlight what is known about the toxicity of PFASs in experimental animal models and in exposed humans.

The chapters are organized by themes: human and wildlife exposure/body burdens, reviews of metabolism and toxicological effects by organ system/developmental stage, and aspects of PFAS toxicity that are driving PFAS research and regulatory oversight.

Human and wildlife exposure/body burdens: Chap. 1 provides an excellent and thorough summary of the major scientific advances related to PFASs research over the past several decades, including an overview of the major toxicological findings and considerations for evaluation of newly synthesized PFASs. Chapter 2 focuses on the current methods for the extraction and analysis of PFASs in biological matrixes as well as their analytical challenges and new developments.

Chapters 3 and 4 detail PFAS concentrations in human populations, mainly in the USA; Chap. 3 focuses on the general human population whereas Chap. 4 highlights highly exposed human populations. Finally, the section on PFAS exposure considerations concludes with concentrations in wildlife populations as well as some of the challenges associated with measuring such compounds in wildlife samples.

Reviews of metabolism and toxicological effects by organ system/developmental stage: While not every single toxicological effect published will be captured by these chapters, they cover the toxicological effects most commonly reported in human and experimental animal studies. This section starts with two chapters related to metabolism: Chap. 6 addresses the metabolism and pharmacokinetics of PFASs in biological organisms and Chap. 7 focuses on the effects of PFAS exposure on the metabolic processes themselves and how other effects may arise from toxicological changes in these metabolic processes. Chapter 8 captures the major outcomes that have been observed in studies of developmental exposure and Chaps. 9, 10, and 11 address toxicities to the three main controlling systems, neurotoxicity, immunotoxicity, and endocrine toxicity, respectively. The last two chapters of this section focus on broader toxicological issues. Chapter 12 details evidence of carcinogenicity in exposed organisms and Chap. 13 summarizes major epidemiological findings in human populations. Together, these eight chapters capture the major toxicological research associated with PFAS exposures.

Aspects of PFAS toxicity that are driving PFAS research and regulatory oversight: Chap. 14 synthesizes the data that were used to generate appropriate pharmacokinetic models to estimate human serum concentrations. Chapter 15 is actually a case study of the use of two PFAS compounds in literature-based evaluations of environmental contaminants and reflects an effort by the National Toxicology Program's Office of Health Assessment and Translation to increase its transparency in systematic review procedures of environmental contaminants. Chapter 16 is a thorough compendium of the human health risk assessment associated with these compounds and brings to light the need for effective communication among the many groups affected by such assessments. Chapter 17 focuses on the available toxicological data available for alternative fluorinated technologies that are being explored to replace longer chain PFASs that have been associated with toxicological effects. The final chapter summarizes the major points associated with PFAS toxicology and includes recommendations for future research.

I thank and gratefully acknowledge the chapter authors. In spite of enormous demands on his or her time, each author's expertise, dedication and willingness to participate in this project made this volume possible.

Greenville, NC, USA

Jamie C. DeWitt

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Editor Biography

Dr. Jamie C. DeWitt is an Assistant Professor in the Department of Pharmacology and Toxicology at the Brody School of Medicine at East Carolina University. She received BS degrees in Biology and Environmental Science from Michigan State University and PhD degrees in Environmental Science and Neural Science from Indiana University-Bloomington. Dr. DeWitt also completed postdoctoral training in Developmental Cardiotoxicity from Indiana University-Bloomington and in Immunotoxicology at the U.S. Environmental Protection Agency through a cooperative training agreement with the University of North Carolina at Chapel Hill. Dr. DeWitt is the immediate past-president of the North Carolina chapter of the Society of Toxicology and the Senior Councilor for the Immunotoxicology Specialty Section of the Society of Toxicology. She also was awarded the Outstanding Young Investigator Award from the Immunotoxicology Specialty Section in 2013. Dr. DeWitt's main research focus is on how toxicants found in the environment can lead to neurodevelopmental and neurodegenerative disorders via disruption of the developing immune system. She is especially interested in microglia, which are immune cells that reside in the central nervous system (CNS). These cells are often viewed as the interface between the CNS and the rest of the body and therefore are thought to be critical for proper neuronal development and homeostasis. Additionally, Dr. DeWitt and members of her lab work to understand how environmental toxicants impact both the adult and developing immune and nervous systems. Ultimately, she hopes that her work will not only improve our understanding of how exogenous chemicals alter these systems but also improve regulatory oversight and testing to reduce the number and amounts of potentially hazardous chemicals into the environment.