



**Karolinska  
Institutet**

**Institute of Environmental Medicine (IMM), Unit of  
Environmental Health Risk Assessment**

## **Tissue Distribution Studies and Risk Assessment of Perfluoroalkylated and Polyfluoroalkylated Substances (PFASs)**

**AKADEMISK AVHANDLING**

som för avläggande av medicine doktorsexamen vid Karolinska  
Institutet offentligen försvaras i sal Atrium, Nobels Väg 12B,  
Karolinska Institutet.

**Onsdagen den 5 juni, 2013, kl. 09.15.**

av

**Daniel Borg**

*Huvudhandledare:*

Professor Helen Håkansson  
Karolinska Institutet  
Institutet för Miljömedicin (IMM)  
Enheten för Miljömedicinsk Riskbedömning

*Bihandledare:*

Doktor Krister Halldin  
Karolinska Institutet  
Institutet för Miljömedicin (IMM)  
Enheten för Miljömedicinsk Riskbedömning

Doktor Ulrika Bergström  
Totalförsvarets Forskningsinstitut (FOI)  
Avdelningen för CBRN-skydd och säkerhet

*Fakultetsopponent:*

Dr. David Bell  
European Chemicals Agency (ECHA)  
Helsinki, Finland

*Betygsnämnd:*

Docent Magnus Breitholtz  
Stockholms Universitet  
Institutet för Tillämpad Miljövetenskap (ITM)

Professor Gunnar Johansson  
Karolinska Institutet  
Institutet för Miljömedicin (IMM)  
Enheten för Arbetmiljötoxikologi

Docent Anna Kärrman  
Örebro Universitet  
Institutionen för Naturvetenskap och Teknik

**Stockholm 2013**

## Abstract

Perfluoroalkylated and polyfluoroalkylated substances (PFASs) represent a large class of man-made chemicals. These substances have emerged as environmental contaminants due to their extraordinary resistance to degradation, potential for bioaccumulation, toxicity and a global presence in humans, wildlife and the environment. In the Swedish population 17 PFASs have so far been analyzed in blood. In animal studies, PFASs cause liver toxicity and reproductive/developmental toxicity as well as a range of other toxic effects. Detailed data on the tissue distribution of PFASs, which could contribute to better understanding of their toxicity, are limited. Also, health risk assessment information has been lacking for all PFASs except the most studied, perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA).

The aims of this thesis were to 1) generate detailed tissue distribution data on PFOS in perinatal and adult mice and on its replacement chemical perfluorobutane sulfonate (PFBS) in adult mice; and 2) and assess potential risks to human health associated with exposure to the 17 PFASs analyzed in the general Swedish population and occupationally exposed ski waxers, for all PFASs individually and in combination.

The results of the experiments showed that following exposure of pregnant dams PFOS was readily transferred to mouse fetuses resulting in tissue levels similar to or higher than maternal blood levels. PFOS was markedly distributed to the perinatal and maternal lungs; showing the highest levels of the tissues analyzed in fetuses/pups on gestational day 20 and postnatal day 1. This finding may help to explain the respiratory distress seen in neonatal and adult rodents following exposure to PFOS. Further, in adult male mice after short-term dietary exposure to one environmentally relevant low dose and one experimentally relevant high dose, PFOS was recovered in all 19 examined tissues, with similar tissue distribution profiles at both doses though with a higher tissue:blood ratio at the higher dose. The highest concentrations of PFOS were found in liver, lung, blood, kidney and whole bone and the major body compartments were liver, bone, blood, skin and muscle. Blood hemoglobin levels were markedly increased at the high dose which could be connected to the localization of PFOS in bone marrow. In a similar experiment PFBS was recovered in all 20 examined tissues in adult male mice after short-term dietary exposure to the same molar concentration as the high dose of PFOS. The distribution and compartment profiles were similar to those of PFOS with the exception of a remarkably high concentration in cartilage. Also, PFBS displayed significantly lower tissue concentrations and tissue: blood ratios than PFOS and a less marked erythropoietic effect.

The risk assessment of PFASs showed that hepatotoxicity and reproductive/developmental toxicity may be of concern for high local exposure and occupational exposure but indicated no risk for the general population. Concern for the less studied endpoints immunotoxicity and altered mammary gland development was identified for the general population and the occupationally exposed. A need of additional toxicological data for all investigated toxicological endpoints was recognized.

Altogether, the work included in this thesis has generated experimental data that can be used to improve risk assessment of PFASs. It has also assessed the risks associated with current exposures to PFASs in Sweden and identified data needs.