Assessment of Toxicity and Risk of Inhaled Environmental PCB Mixtures

Prior to Project 7's studies, little was known about the toxicity of inhaled semi-volatile PCBs. Over the past 5 years, the research team has developed a PCB vapor generation apparatus, nose-only and whole-body exposure systems, and methodology for quantifying exposures to all 209 congeners and measurement of those congeners plus OH-PCB and PCB sulfate metabolites in tissues and excreta.

Project 7 will carry out experiments to address three specific aims:

**Aim 1: Conduct inhalation studies using their Chicago Air Mixture (CAM+) to identify adverse outcome pathways and derive in vivo data for an integrated risk assessment.** Researchers have performed a 4-week inhalation rat study of PCB mixture that simulated PCB profile found in the indoor air of an East Chicago school (enrolled in AESOP study, Project 6). A wide array of adverse health outcomes were measured that focused on general health status (weight gain, body condition), organ histopathology, cytotoxicity, inflammation, immunotoxicity, oxidative stress, antioxidant status, thyroid hormone and reproductive hormone dysregulations, genotoxicity, neurobehavioral changes and neurotoxicity. The analyses of collected specimen is still ongoing.

**Aim 2: Conduct Absorption, Distribution, Metabolism, and Excretion (ADME) toxicology studies with lung exposure to radiolabeled tetra- and penta-chlorobiphenyls to provide data for toxicokinetic modeling.** Researchers have performed a mass balance study of radiolabeled [14C] PCB28 following our previous approach used in 14C-labeled PCB11 (5). Researchers found that the absorption of PCB28 by the lung was nearly complete, and PCB28 was distributed rapidly to all tissues of the body within minutes following pulmonary exposure. The majority initially went to the muscle and liver, and then shifted to the skin and adipose tissue, where it accumulated. Elimination was biphasic in most tissues, with an initial fast phase followed by a subsequent slower phase. In contrast to our findings with PCB11, the metabolism of PCB28 was limited, with the parent compound as the major stored or excreted radiolabeled material. With these two studies, researchers are filling up the gap in biological fate of inhaled individual PCB congeners.
Aim 3: Investigate developmental, immune, and neurologic toxicity after prenatal inhalation exposure to airborne PCBs. Researchers set up a Morris Water Maze (MWM) system in the laboratory to expand on proposed neurobehavioral testing. To be able to compare their neurobehavioral data obtained using MWM from animals exposed to PCBs, they have established a positive control. Researchers tested two compounds: scopolamine hydrobromide (1-4 mg/kg in saline by i. p. injection 30 min before each block of testing using MWM) and 1-bromopropane (800 mg/kg dissolved in corn oil by gavage daily for 12 consecutive days). The treatment with 1-bromopropane (1-BP) was shown to cause significant and consistent effects in our animals, thus they used this compound as their positive control.

Core Leader: Peter S. Thorne, PhD

Dr. Thorne is Professor and Head of the University of Iowa's Department of Occupational and Environmental Health with a secondary appointment in the Department of Civil and Environmental Engineering. He has over 23 years experience in toxicology research involving laboratory animals. He is the founder and director of the closely aligned Inhalation Toxicology Facility within the Environmental Health Sciences Research Center. Dr. Thorne served for many years on the Institutional Animal Care and Use Committee. He will have overall responsibility for the Core and will serve as the primary contact with other Project and Core Leaders in the isrp.

Andrea Adamcakova-Dodd, PhD.

Dr. Andrea Adamcakova-Dodd is an Assistant Research Scientist who has been involved in toxicology research of environmental pollutants since 1998. She has worked in the Pulmonary Toxicology Facility for 12 years. In her current position at the Pulmonary Toxicology Facility, she has led or collaborated on toxicity studies of inhaled particulate aerosols and vapors. In recent years she has been extensively involved in development of generation systems for inhalation exposures to PCBs vapors and toxicity assessment of PCBs using animal models.