Core A - Synthesis Core

The ISRP Synthesis Core is responsible for providing researchers with authenticated test compounds and analytical standards, such as PCB sulfates and other PCB metabolites, which are not available from commercial sources and need to be custom synthesized. These compounds enable ISRP researchers to address questions relevant to environmental public health and the mission of the Superfund Research Program that can only be studied with access to these compounds.

In addition to providing these compounds to individual research projects and the Analytical Core, the Synthesis Core also makes them available to other researchers, especially researchers from other Superfund Research Programs.

The Synthesis Core has four aims:

**Aim 1: Maintain and prepare PCB mixtures and pure PCB congeners.**

**Aim 2: Prepare hydroxylated PCB derivatives.**

**Aim 3: Synthesize PCB sulfate metabolites.**

**Aim 4: Prepare miscellaneous compounds, including diazomethane.**

The Synthesis Core in 2018/2019 supplied the following individual PCB congeners, PCB mixtures, hydroxylated PCB metabolites (OH-PCBs), PCB sulfates and miscellaneous PCB metabolites:

Compounds supplied to ISRP Projects and Cores:
Research Project 1: PCB 126 and PCB 52 were provided for toxicity studies in rats, including a recent study in AhR knockout rats.

Research Project 3: The Synthesis Core provided PCB77 and four hydroxylated PCB sulfates (i.e., 4'-OH-PCB12 sulfate, 4'-OH-PCB25 sulfate, 4-OH-PCB33 sulfate, and 4'-OH-PCB52 sulfate) as analytical standards to develop a GC/MS/MS-based method for the analysis of PCB sulfates in serum and urine samples from the AESOP study (Project #6).

Research Project 5: The Synthesis Core supported Project 5 with a large amount of 4'-MeO-PCB3 (over 60 mg) to study the biotransformation of this compound in poplar plants. In addition, a large number of PCB3 derivatives were provided as analytical standards. These analytical standards support studies investigating the interconversion of PCBs metabolites in plants.

Research Project 7: Gram quantities of PCB mixtures, including Aroclor 1254 and Aroclor 1221, were provided to Project 7 for a large inhalation toxicity study. Synthesis Core staff also assisted Project 7 researchers with the characterization of the exposure atmosphere for this study. These Synthesis Core efforts indirectly supported a range of ISRP activities because tissues from this animal study were provided to many ISRP researchers to measure toxicological endpoints of interest.

Analytical Core: The Synthesis Core continues the synthesis of diazomethane for the Analytical Core. Diazomethane is used to derivatize hydroxylated PCB metabolites for gas chromatographic analysis. These efforts indirectly supported over 350 OH-PCB analyses for Projects 3 and 5. In addition, a series of methoxylated PCB congeners were provided as standards to validate a method for the analysis of all 837 OH-PCB congeners. This method supports OH-PCB analyses performed by all ISRP Projects.

Compounds made available to researchers in the US and worldwide:

In addition to providing ISRP researchers with test compounds, the Synthesis Core has continued to make PCB congeners and PCB metabolites available to other researchers in the United States and abroad. PCBs and their metabolites were provided to:

- Dr. Keith J. Bein, University of California Davis
- Dr. Jonathan Doorn, University of Iowa
- Dr. Erika Holland, California State University-Long Beach
- Dr. Aloysius Klingelhutz, University of Iowa
- Dr. Hans-Joachim Lehmler, University of Iowa
- Dr. Palm Lein, University of California Davis
- Dr. Betsy Stone, University of Iowa
- Dr. Alicia Timme-Laragy, University of Massachusetts Amherst.

Recent Publications:


Core Leader: Hans-Joachim Lehmler, PhD

Dr. Lehmler is an experienced synthetic organic chemist with over twelve years of experience in the synthesis of polychlorinated biphenyls and their metabolites. He is currently a Professor in the University of Iowa Department of Occupational and Environmental Health. He has been involved in the NIEHS Superfund Program since 1998-first at the University of Kentucky and since 2003 at the University of Iowa. As Core Leader he will oversee and coordinate the chemical synthesis and the chemical characterization of synthetic compounds.

Larry W. Robertson, PhD, MPH

Dr. Robertson has over thirty years of experience in the synthesis of polychlorinated biphenyls, their metabolites and other environmental contaminants. His expertise in the synthesis of individual PCB congeners using the Cadogan and Ullmann coupling as well as the Sandmeyer reaction is an especially important asset for the Synthesis Core.

Contact

Please e-mail any inquiries relating to the Synthesis Core to Hans-Joachim Lehmler at hans-joachim-lehmler@uiowa.edu [12].

Attach files:  Standard Operating Procedure for the synthesis and handling of diazomethane [13]
National Institute of Environmental Health Sciences

Source URL (modified on 05/21/2019 - 10:04):
https://iowasuperfund.uiowa.edu/support-cores/synthesis

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[1] https://iowasuperfund.uiowa.edu/support-cores/synthesis
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[12] mailto:hans-joachim-lehmler@uiowa.edu