Opportunity Title: Developing in vitro-in vivo biotransformation extrapolation methods for fish
Opportunity Reference Code: EPA-ORD-NHEERL-MED-2016-06

Organization U.S. Environmental Protection Agency (EPA)

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How to Apply A complete application consists of:

- An application
- Transcripts – Click here for detailed information about acceptable transcripts
- A current resume/CV, including academic history, employment history, relevant experiences, and publication list
- Two educational or professional references

All documents must be in English or include an official English translation.

If you have questions, send an email to EPArpp@orau.org. Please include the reference code for this opportunity in your email.

Application Deadline 12/13/2016 3:41:00 AM Eastern Time Zone

Description A research opportunity is currently available at the U.S. Environmental Protection Agency's (EPA) Office of Research and Development (ORD)/National Health and Environmental Effects Research Laboratory (NHEERL). This appointment will be served with the Mid-Continent Ecology Division (MED), in Duluth MN.

Chemicals that accumulate in fish and other aquatic biota pose a threat to these organisms and the organisms that consume them, including humans. It is of interest, therefore, to develop *in vitro* and *in silico* methods that can be used to predict which chemicals are likely to accumulate in fish and which are not. Biotransformation (or metabolism) generally reduces the extent to which chemicals accumulate in fish. However, this activity cannot be predicted simply from chemical structure or physicochemical properties. For this reason, biotransformation (presence/absence and rate of activity) represents the largest source of uncertainty in many bioaccumulation assessments for fish. One promising approach to dealing with this challenge involves the use of *in vitro* systems (microsomes, S9 fractions, isolated cells) to measure intrinsic clearance of chemicals by liver tissue. Measured rates of metabolism are then extrapolated to the intact animal and used as an input to established mass-balance models for chemical bioaccumulation. Several "proof of concept" studies have shown that bioaccumulation predictions obtained in this way are much closer to measured values than predictions which assume no metabolism. Nevertheless, many important questions remain concerning the domain for applicability of these methods, metabolism occurring in extrahepatic tissues (e.g., gut), and mixture effects. The research participant will be provided with the opportunity to perform *in vitro* and *in vivo* studies that will explore these issues.

With guidance from the mentor, the research participant may be trained and involved in any or all of the following activities:

- Conducting *in vitro* substrate depletion assays with liver S9 fractions

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and isolated hepatocytes to measure intrinsic hepatic clearance in fish.
- Collecting biological material from fish (e.g., liver and gastrointestinal tract) and characterizing the metabolic activity of these samples using standard substrates for Phase I and II biotransformation enzymes.
- Performing *in vitro* mixture studies to examine mixture effects (e.g., competitive and non-competitive inhibition) on chemical biotransformation in fish.
- Analyzing extracted biological samples by high performance liquid chromatography (HPLC).
- Performing appropriate QA/QC procedures associated with toxicological research and chemical analysis.
- Conducting *in vivo* chemical exposures with fish as a means of evaluating the accuracy of *in vitro-in vivo* metabolism extrapolations.
- Conducting statistical analyses on experimental data.
- Compiling information from the literature and from on-line data sources relevant to the effects of biotransformation on chemical accumulation by fish.
- Contributing to the preparation of peer-reviewed journal articles and dissemination of research results.

The participant will have the opportunity to learn a diversity of laboratory techniques which can be applied across life sciences research fields. The participant will learn to operate and use a range of scientific equipment. The participant will learn to evaluate data quality, trouble shoot research results, apply statistical methods for data analysis and interpretation.

The participant will be integrated into a transdisciplinary research team and engaged in multiple aspects of project planning, communication and coordination, research implementation, and analysis. The research participant will be afforded an opportunity to interact with internationally recognized leaders, both within and outside EPA, in the area of aquatic toxicology and chemistry with a particular focus on chemical accumulation and biotransformation. It is expected that this training opportunity will provide an early career scientist with knowledge, skills, and abilities needed to apply new technologies and associated data to regulatory decision-making at the local, national, and/or international scale to pursue a professional career in life sciences research and/or additional graduate education.

This program, administered by ORAU through its contract with the U.S. Department of Energy to manage the Oak Ridge Institute for Science and Education, was established through an interagency agreement between DOE and EPA.

Qualifications Applicants must have received a master's degree in chemistry, biochemistry, analytical chemistry, environmental science, or relevant related field within five years of the desired starting date, or completion of all requirements for the degree should be expected prior to the start date. Previous research experience, beyond lab-oriented course work alone, would be beneficial for the research experience.

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The appointment is full for 9 months and may be renewed upon recommendation of EPA and contingent on the availability of funds. The participant will receive a monthly stipend. Funding may be available to reimburse the participant's travel expenses to present the results of his/her research at scientific conferences. No funding will be available to cover travel costs for pre-appointment visits, relocation costs, tuition and fees, or participant's health insurance. The participant must show proof of health and medical insurance. **The participant does not become an EPA employee**.

The mentor for this project is John W. Nichols (nichols.john@epa.gov). The desired start date is December 1, 2016.

Eligibility Requirements

- **Degree:** Master's Degree received within the last 60 month(s).
- **Academic Level(s):** Post-Master's.
- **Discipline(s):**
  - **Chemistry and Materials Sciences** (4)
  - **Environmental and Marine Sciences** (5)
  - **Life Health and Medical Sciences** (6)
  - **Mathematics and Statistics** (1)