Opportunity Title: EPA Fellowship on Efforts to Refine and Expand In Vitro Toxicokinetic Data Use in Chemical Risk Evaluations
Opportunity Reference Code: EPA-ORD-CCTE-CCED-2022-07

Organization U.S. Environmental Protection Agency (EPA)

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How to Apply ***Connect with ORISE...on the GO!*** Download the new ORISE GO mobile app in the Apple App Store or Google Play Store to help you stay engaged, connected, and informed during your ORISE experience and beyond!

A complete application consists of:

- An application
- Transcript(s) – For this opportunity, an unofficial transcript or copy of the student academic records printed by the applicant or by academic advisors from internal institution systems may be submitted. All transcripts must be in English or include an official English translation. 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 recommendations. Click here for detailed information about recommendations.

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

Application Deadline 2/6/2023 3:00:00 PM Eastern Time Zone

Description ***Applications may be reviewed on a rolling-basis and this posting could close before the deadline.** Click **here** for information about the selection process.

EPA Office/Lab and Location: A research opportunity is available at the Environmental Protection Agency (EPA), Office of Research and Development (ORD), Center for Computational Toxicology and Exposure (CCTE), Chemical Characterization & Exposure Division (CCED) located in Research Triangle Park, North Carolina.

Research Project: This research opportunity will be located in the Office of Research and Development's (ORD's) Chemical Safety and Sustainability (CSS) Program. The research participant will collaborate with researchers within ORD who focus on the development of New Approach Methods (NAMs) to inform chemical assessments. NAMs represent methods and/or frameworks that incorporate in vitro experimental assays and in silico modeling to efficiently evaluate the large number of commercial chemicals in use in the United States (US) that lack hazard and/or exposure data. Such approaches are used to efficiently predict doses at which effects may be observed and parallel estimations of anticipated human exposures given expected use patterns. NAMs that incorporate high throughput toxicity screening data, toxicokinetics and exposure predictions have already been used to set chemical testing priorities in a process known as risk-based prioritization. The multidisciplinary nature of such efforts provides a valuable opportunity for an early career scientist to become familiar with a wide range of NAM tools and approaches associated with regulatory decision-making.

In vitro-in vivo extrapolation (IVIVE) is an approach that employs in vitro

data and modeling to predict either anticipated chemical concentrations in vivo given a certain exposure (toxicokinetics) or in vivo concentrations at which perturbations may be observed (toxicodynamics). Toxicokinetics provides critical information about chemical fate after uptake into a human or ecological system by consideration of absorption, distribution, metabolism and excretion (ADME). In NAMs, such information is critical in translating an in vitro effect concentration out to what would be an equivalent exposure in vivo to yield such bioactive concentrations internally. Another important aspect in refining IVIVE is understanding in vitro disposition of a chemical. Non-specific binding of a chemical in in vitro systems may significantly alter the chemical that is free to elicit an effect, leading to a potential underestimation of chemical potency in such assays. Despite concern over the impact of in vitro disposition on IVIVE, availability of empirical data to robustly evaluate these issues is currently inadequate.

The research participant will have the opportunity to develop and execute a range of in vitro toxicokinetic assays that measure plasma protein binding, hepatic clearance, metabolite formation and other aspects of ADME and in vitro disposition. This will provide expertise in the conduct of biochemical and cell-based assays. The research participant will also be trained in the use of analytical chemistry methods to detect and quantitate levels of commercial chemicals in toxicokinetic assay samples. These methods may include both targeted analyses but also non-targeted or suspect screening analyses to characterize metabolite formation. There will also be opportunities to perform data analysis, data integration, and in silico modeling as experimental data is incorporated into IVIVE approaches for dose estimation.

Learning Objectives: The research participant will gain expertise in the incorporation of in vitro toxicokinetics with NAM toxicity testing data to translate out to a "real world" exposure at which human health effects may be observed. The research participant will learn key considerations in the use of this IVIVE process and how toxicokinetic and in vitro disposition modeling is employed in dose estimation processes. The research participant will also learn how this approach is employed in regulatory decision-making to aid in risk-based priority setting, addressing the challenge of managing thousands of chemicals covered under the Toxic Substances Control Act yet lacking any type of toxicity data. The research participant will participate alongside a fast-paced multi-disciplinary research team and will have opportunities to interact with internationally recognized leaders, both within and outside the EPA. The research participant will have the opportunity to contribute to and/or publish original research in this effort and to present research at scientific meetings or during seminars.

Mentor(s): The mentor(s) for this opportunity is Barbara Wetmore (wetmore.barbara@epa.gov). If you have questions about the nature of the research please contact the mentor(s).

Anticipated Appointment Start Date: October 31, 2022. All start dates are flexible and vary depending on numerous factors. Click **here** for detailed information about start dates.

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Appointment Length: The appointment will initially be for one year and may be renewed up to three to four additional years upon EPA recommendation and subject to availability of funding.

Level of Participation: The appointment is full-time.

Participant Stipend: The participant will receive a monthly stipend commensurate with educational level and experience. Click **here** for detailed information about full-time stipends.

EPA Security Clearance: Completion of a successful background investigation by the Office of Personnel Management (OPM) is required for an applicant to be on-boarded at EPA.

ORISE Information: This program, administered by ORAU through its contract with the U.S. Department of Energy (DOE) to manage the Oak Ridge Institute for Science and Education (ORISE), was established through an interagency agreement between DOE and EPA. Participants do not become employees of EPA, DOE or the program administrator, and there are no employment-related benefits. Proof of health insurance is required for participation in this program. Health insurance can be obtained through ORISE.

ORISE offers all ORISE EPA graduate students and Postdocs a free 5 year membership to the National Postdoctoral Association (NPA).

The successful applicant(s) will be required to comply with Environmental, Safety and Health (ES&H) requirements of the hosting facility, including but not limited to, COVID-19 requirements (e.g. facial covering, physical distancing, testing, vaccination).

Questions: Please see the FAQ section of our website. After reading, if you have additional questions about the application process please email ORISE.EPA.ORD@orau.org and include the reference code for this opportunity.

Qualifications

The qualified candidate should have received a master's or doctoral degree in one of the relevant fields (e.g. Toxicology, Pharmacology, Biology, Chemistry, Cell Biology), or be currently pursuing a doctoral degree to be received by March 31, 2023. Degree must have been received within five years of the appointment start date.

Preferred Skills:

- Strong written, oral, and electronic communication skills, with proficiency in Microsoft Office applications (i.e., Excel, PowerPoint, Word, Outlook) and experience working with spreadsheets. Experience developing and giving oral PowerPoint presentations is preferred.
- Laboratory experience including: following written protocols, keeping accurate laboratory records, and proficiency performing basic chemistry calculations, solution preparation and pipetting
- Laboratory experience conducting in vitro experiments using a variety of methods and/or cell culture experience (i.e., experience in aseptic

technique) would be preferred
- Laboratory experience conducting targeted analytical chemistry techniques, such as method development, sample preparation, instrument usage (LC-MS/MS and/or GC-MS/MS), and data analysis would be highly valued
- Demonstrated ability to complete experiments in an organized and efficient manner with attention to detail and accurate recordkeeping
- Ability to work well with others in a laboratory environment and within a research team is preferred

Eligibility Requirements

- **Citizenship:** U.S. Citizen Only
- **Degree:** Master's Degree or Doctoral Degree received within the last 60 months or anticipated to be received by 3/31/2023 11:59:00 PM.
- **Discipline(s):**
  - **Chemistry and Materials Sciences** (2 👁)
  - **Life Health and Medical Sciences** (18 👁)
  - **Mathematics and Statistics** (1 👁)