Opportunity Title: FDA Fellowship in ALT and Predicting Hepatotoxicity in Clinical Trials
Opportunity Reference Code: FDA-CDER-2023-1350

Organization U.S. Food and Drug Administration (FDA)

Reference Code FDA-CDER-2023-1350

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

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

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

Application Deadline 3/29/2024 11:59:00 PM Eastern Time Zone

Description ***Applications will be reviewed on a rolling-basis.**

A research opportunity is currently available at the U.S. Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER), in the Office of New of Drugs/ Office of Immunology and Inflammation (OII) in Silver Spring, Maryland.

The Center for Drug Evaluation and Research (CDER) performs an essential public health task by making sure that safe and effective drugs are available to improve the health of people in the United States. As part of the U.S. Food and Drug Administration (FDA), CDER regulates over-the-counter and prescription drugs, including biological therapeutics and generic drugs. This research covers more than just medicines.

OII is pursuing quantitative systems toxicology (QST) approaches to better assess the liver safety of new drug candidates. A primary goal of this fellowship is to use QST approaches to more precisely assess the extent of liver injury caused by drugs. This will involve using laboratory databases from FDA archives and from other sources to estimate the extent of liver injury as assessed with the QST model DILIsym® and comparing the results to that determined by a recently proposed equation (P-ALT). Both traditional liver chemistries and more recently proposed biomarkers (e.g. GLDH) will be evaluated. Modification of software and a development of new mathematical approaches is anticipated. Once validated, improved methods to estimate the extent of liver injury could augment and/or potentially replace traditional methods of interpreting liver safety in clinical trials. Moreover, success in this endeavor would pave the way for improvement in assessments of injury to organs other than liver (e.g. kidney).

Under the guidance of the mentor, the participant will work with DILIsym®, a QST software which attempts to model drug metabolism and hepatotoxicity by integrating multiple data inputs including physiologically-based pharmacokinetics (PBPK), metabolite formation, and inter-individual variation in susceptibility. The studies will be performed in collaboration with Drs. Paul Watkins and Rachel Church at University of North Carolina (UNC), Chapel Hill. They have established a preliminary dataset supporting modeling approaches using serial measurements of serum alanine

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aminotransferase (ALT) to predict percent hepatocyte loss during drug-induced liver injury (DILI). Through learning and using DILIsym®, the participant will gain firsthand knowledge of the benefits and limitations of QST systems that are increasingly used to assess safety in drug development. The participant will be trained by QST experts at the FDA and UNC. The participant will also have the opportunity to participate in liver safety reviews and thereby learn about DILI in clinical trials, including how the FDA assesses DILI risk and the limitations in currently used tools.

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 FDA. **The initial appointment is for one year,** but may be renewed upon recommendation of FDA contingent on the availability of funds. The participant will receive a monthly stipend commensurate with educational level and experience. Proof of health insurance is required for participation in this program. The appointment is full-time at FDA in the Silver Spring, Maryland, area. Participants do not become employees of FDA, DOE or the program administrator, and there are no employment-related benefits.

Completion of a successful background investigation by the Office of Personnel Management is required for an applicant to be on-boarded at FDA. OPM can complete a background investigation only for individuals, including non-US Citizens, who have resided in the US for a total of three of the past five years.

FDA Ethics Requirements

If an ORISE Fellow, to include their spouse and minor children, reports what is identified as a Significantly Regulated Organization (SRO) or prohibited investment fund financial interest in any amount, or a relationship with an SRO, except for spousal employment with an SRO, and the individual will not voluntarily divest the financial interest or terminate the relationship, then the individual is not placed at FDA. For additional requirements, see FDA Ethics for Nonemployee Scientists.

FDA requires ORISE participants to read and sign their FDA Education and Training Agreement within 30 days of his/her start date, setting forth the conditions and expectations for his/her educational appointment at the agency. This agreement covers such topics as the following:

- Non-employee nature of the ORISE appointment;
- Prohibition on ORISE Fellows performing inherently governmental functions;
- Obligation of ORISE Fellows to convey all necessary rights to the FDA regarding intellectual property conceived or first reduced to practice during their fellowship;
- The fact that research materials and laboratory notebooks are the property of the FDA;
- ORISE fellow's obligation to protect and not to further disclose or use non-public information.

Qualifications

The qualified candidate should have received a doctoral degree in one of the relevant fields (e.g. Mathematics, Statistics, Computer, Information and Data Sciences, Biochemistry, Chemistry), or be currently pursuing the degree with completion before December 31, 2023. Degree must have been received within five years of the appointment start date.

Preferred Skills:

- Knowledge in computer programing is preferred.

Eligibility

- **Degree:** Doctoral Degree received within the last 60 months or

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Requirements

anticipated to be received by 12/31/2023 12:00:00 PM.

- **Discipline(s):**
  - **Chemistry and Materials Sciences** (1 👁)
  - **Computer, Information, and Data Sciences** (17 👁)
  - **Life Health and Medical Sciences** (1 👁)
  - **Mathematics and Statistics** (11 👁)

Affirmation

I have lived in the United States for at least 36 out of the past 60 months. (36 months do not have to be consecutive.)

and

I have read the FDA Ethics Requirements.