U.S. FOOD & DRUG ADMINISTRATION

Office of New Drugs (OND)

2024 ORISE on the Move

What is OND's Summer ORISE Program?

The Office of New Drugs (OND) is located within Food and Drug Administration (FDA)'s Center for Drug Evaluation and Research (CDER). OND is responsible for the clinical and nonclinical review of all new drugs and biologics that FDA approves for the American people. OND participates in FDA's ORISE* Fellowship program to contribute to the development of FDA's future workforce.

The ORISE Research Participation Program at the U.S. Food and Drug Administration (FDA) is a training program for college students and recent graduates in the STEM field. ORISE Fellows participate in mentor-led research projects to gain hands-on experience in the field of regulatory science.

OND's Summer ORISE Program is a mini-version of the full-year fellowship. Candidates who are accepted into the program onboard at the beginning of the summer and participate in research from May through September.

The advertisement for the 2025 CDER ORISE summer fellowship program can be found here: https://www.zintellect.com/Opportunity/Details/FDA-CDER-2025-0000. Applications will be accepted through April 18, 2025.

* ORISE: Oak Ridge Institute for Science and Education

FDA CDER ORISE Indigenous Knowledge Initiative Summer Fellowship Program

In response to the White House Executive Order focused on Advancing Educational Equity, Excellence, and Economic Opportunity for Native Americans, CDER ORISE stood up the first of its kind pilot summer program which encouraged applications from American Indian and Alaska Native researchers (undergraduate, graduate, doctoral, or post-doctoral) from a federal or state recognized tribe or a descendant of an enrolled member. Applicants also needed to demonstrate a commitment to improving public health and Native healthcare policy and research.

The OND ORISE program took the lead on recruiting mentors and identifying appropriate regulatory research projects for the fellows that would allow them to contribute their Indigenous knowledge to the FDA's public health mission. Outreach regarding this opportunity was conducted by the OND ORISE program lead to various tribal colleges and universities as well as tribal STEM organizations such as AISES (American Indian Science and Engineering Society). As a result of the outreach, there were eight Indigenous students who were selected for the opportunity and their ORISE projects are highlighted on the next page.

To ensure that these students were fully supported throughout their fellowship, selected fellows were matched with a peer mentor to help them acclimate to the Agency. The peer mentor was an ORISE fellow who has been in the program at least one year or more. Additionally, monthly networking hours were held via Zoom with 3 FDA Indigenous staff to help support the fellows throughout their summer fellowship. All fellows had the opportunity to participate in two internal summer drug development regulatory courses taught by OND staff. Fellows concluded their fellowship with an internal presentation summarizing their summer research at the FDA Tribal Affairs Lecture Series which was held on August 9, 2024.

Project Perspectives

Indigenous Participation in Pivotal Breast Cancer Clinical Trials, 2014–2023

Fellow
Victoria Faith Hough

Tribal Affiliation:
Mi'kmaq – Benoit First Nation

Year in College:
1st year Medical Student

College:
Mayo Clinic Alix School of Medicine

Major: B.S. Biology, 2024

Research Mentors:
Melanie Royce, MD, PhD
Kathryn Aikin, PhD

The purpose of this study is to analyze Indigenous representation in pivotal breast cancer clinical trials conducted between 2014 and 2023. Our goal is to conduct an exploratory study to provide a clearer picture of Indigenous representation in breast cancer clinical trials and contribute insights that researchers can utilize to enhance this representation.

We identified Food and Drug Administration (FDA) drug approvals in breast cancer from January 1, 2014, to December 31, 2023 and their associated trials. The studies were screened for inclusion and demographic data was sourced. We defined Indigenous as American Indian/Alaskan Native (AI/AN) participants and Native Hawaiian/Pacific Islanders (NH/PI). We also analyzed various trial characteristics to understand factors that may potentially influence indigenous participation.

Results reveal disparities with 19.2% of trials lacking any Indigenous participants. 46% of the trials had 0 AI/AN participants and 42% had 0 NH/PI participants. Successful recruitment strategies included trials near Indigenous populations, those with diverse recruitment sites, and inclusive criteria. By utilizing these strategies, researchers can improve the representativeness of their research to promote health equity and ensure that all populations are able to equally benefit from advancing oncology clinical research.

Improving Indigenous representation enhances trial generalizability and equitable access to cancer treatments. This study aims to inform future trial designs and promote health equity in breast cancer research.

Development of Q&As about FDORA (Food and Drug Omnibus Reform Act) and New Approach Methodologies (NAMs)

Fellow
Marlena Robbins

Tribal Affiliation:
Diné/Navajo

Year in College:
3rd year Doctoral Student

College:
University of California, Berkeley

Major: Doctor of Public Health

Research Mentor:
Nakissa Sadrieh, PhD

The Food and Drug Omnibus Reform Act (FDORA) of 2022, also known as and the FDA Modernization Act 2.0, highlights the innovative technologies that can be used to support drug development, specifically, through the implementation of New Approach Methodologies (NAMs). This project seeks to understand and address the public interpretation of these legislative changes. The primary objective is to develop a comprehensive set of questions and answers (Q&As) to aid public and stakeholder understanding of FDORA's actual versus perceived impact. The Q&As developed will be used in CDER's public messaging about the status of NAMs implementation in current drug development.

The project is structured into three phases. The first phase involves describing the specific changes resulting from FDORA. The second phase involves an in-depth evaluation of documents from stakeholders such as Non-Governmental Organizations (NGOs), Congress, media, and industry, which report on or provide interpretations of FDORA. The final phase focuses on analyzing the findings and developing themes and Q&As for public and stakeholder inquiries.

Future steps include reviewing additional publications, analyzing nonclinical reviews, and generating additional Q&As about the nonclinical safety assessment paradigm current employed by CDER, in the evaluation of drug safety. Overall, this project aims to support the FDA's strategic direction towards reducing animal testing through validated alternative methods, ensuring scientific rigor, and promoting public health and safety.

Analysis of Patient Diversity in Clinical Trials for Liver Disease

Fellow

Samantha Grace Zottola Baguio

Tribal Affiliation:
Federated Indians of
Graton Rancheria

Year in College:
Senior Undergraduate

College:
Oregon State University

Major: Nutrition with a focus in
Dietetics and a Minor in
Public Health

Research Mentors:
Jinzhong Liu, PhD
Aaron Waddell, PhD

Clinical development programs aim to demonstrate that a treatment is safe and effective for its intended use through adequate and well-controlled Phase 3 trials. The study population in Phase 3 trials should closely resemble the racial and ethnic diversity of the U.S. population affected by a specific disease. Despite this, underrepresentation of minority groups in clinical trials remains an ongoing issue. As a result, the FDA recently published a draft guidance for Diversity Action Plans to improve diversity in trial enrollment.

Our ongoing project aims to assess whether Phase 3 trials from approved New Drug Applications (NDAs) for the treatment of liver disease have a demographic composition that reflects the U.S. population. Liver disease can disproportionally affect specific racial and ethnic groups and is a major cause of death globally. For our initial analysis, we analyzed Phase 3 trials from NDA 217785 and NDA 215498. Racial representation by percentage in both the analyzed trials and the U.S. population (data from the US 2020 Decennial Census) was calculated using the R programming language.

The U.S. population is approximately 61.6% White, 12.4% Black or African American, and 6.0% Asian. In comparison, the enrolled population in the pivotal Phase 3 trial from NDA 217785 was approximately 89.6% White, 2% Black or African American, and 2.7% Asian. Similar overrepresentation of White subjects was seen in NDA 215498. Therefore, our analysis showed potential racial representation differences between the U.S. and trial populations. Future work includes validating our results and expanding the analysis to include ethnicity.

Comparing and Contrasting Competing and Affected Products (C/AP) List Development for Advisory Committees Between CDER and CDRH

Fellow
Riley Williams

Tribal Affiliation:
Sisseton-Wahpeton Oyate

Year in College:
3rd year Pharmacy Student

College:
South Dakota University

Major: Pharmacy

Research Mentor:
Margaret VanHeusen, MS

This project aims to enhance the Office of New Drugs (OND) regulatory processes by learning the methods used by the Center for Devices and Radiological Health (CDRH) in creating Competing and Affected Products (C/AP) lists. This project seeks to identify best practices, unique challenges, and solutions to improve OND workflow. Key activities throughout this process include researching the OND Advisory Committee process, conducting interviews with CDRH, and encouraging adoption of their best practices. This project will also encourage interdepartmental communication and hopes to increase efficiency and expertise across all centers when creating C/AP lists.

Development and Validation of Insulin Bioassays

Fellow
Daniel White

Tribal Affiliation:
Chickasaw Nation

Year in College:
Senior Undergraduate

College:
University of Central Oklahoma

Major:
Chemistry-Health Science

Research Mentor:
Carole Sourbier, PhD

The Biologics Price Competition and Innovation Act was passed as part of the Affordable Care Act and under that law, insulins became regulated as biologics in March 2020 and are now regulated in the Office of Pharmaceutical Quality (OPQ) under section 351 for Biological Licensing Applications (BLAs). A key regulatory challenge in transitioning these products is to ensure the control of their biological activity (or potency) at release and during stability testing. With this project, our goal is to review known mechanisms of action of insulin products that could be monitored using a cell-based bioassay and to identify new potential bioassay endpoints to reflect these mechanisms of action.

Developing Open-Source Software Tools for Cross-Study Analysis of Structured Toxicology Study Datasets via R Shiny Application

Fellow
Reese "Aak'inaa" Kayaani Jennings

Tribal Affiliation:
Tlingit tribe, Raven moiety, Táakw.aaneidi clan

Year in College:
Senior Undergraduate

College:
Washington University in St. Louis

Major: Biomedical Engineering with a minor in Materials Science

Research Mentors:
Kevin Snyder, PhD
Jose Vicente Ruiz, PhD

The Office of New Drugs (OND) is engaged in developing open-source software tools to facilitate cross-study analyses of CDISC-SEND-formatted standardized toxicology study datasets. The project seeks to improve the functionality of an R Shiny application that was developed to generate interactive visualizations with customizable data normalization and scoring procedures that enable users to easily compare and contrast the results of multiple repeat-dose toxicity studies. This application enables the user to produce visual comparisons of endpoints across multiple studies, providing an integrated representation of the toxicological profile of a given compound under various testing conditions, e.g. species, route of administration, dosing duration.

Concurrently, R code was developed to standardize the querying of these datasets, ensuring broad compatibility of the application with multiple different datasets. Despite technically adhering to SEND standards, submitted datasets often present inconsistencies in how the fields are populated; there are often multiple valid acronyms, capitalizations, and phrasings that can be used to express the same word or idea, which complicates both querying the data and cross-comparison. My role within the project involves troubleshooting and debugging in order to facilitate efficient and effective querying of the SEND datasets. Currently, the application is only compatible with a limited number of datasets, but the project seeks to expand the compatibility of the querying process in order to be able to work with all available datasets. This application will facilitate more efficient and reliable cross-comparison of current toxicology data, ultimately enhancing the OND's toxicology review program.

An Analysis of American Indian and Alaska Native Representation in Adult Type 2 Diabetes Drug Trials

Fellow
Lauren Elvrum

Tribal Affiliation:
Makah Tribe

College:
Boston College

Major: Bachelor of Arts in International Studies, Minor in Global Public Health, 2024

Research Mentors:
Aden Asefa, MPH
Ariel Armstrong, PhD
Lauren Wood Heickman, MD

The purpose of our study is to investigate the representation of American Indian and Alaska Native participants in clinical trials with the goal of forming recommendations to increase diversity in future drug trials. We compared the enrollment characteristics of subjects who participated in the key clinical trials that supported the original FDA approval for 4 drugs approved for the treatment of type 2 diabetes in adults between 2017 and 2023, available from the Drug Trial Snapshot (DTS) database, to the US prevalence of disease across racial demographics as a metric of representativeness. Our analysis revealed that the trials supporting the approval of tirzepatide and bexagliflozin had the highest enrollment of American Indian and Alaska Native participants amongst all key drug trials in the DTS database for the 4 approved drugs. The reported percentages of American Indian and Alaskan Native participants in these two development programs exceed the proportion of the US population affected by adult type 2 diabetes who are American Indian or Alaskan Native. The approaches to study enrollment resulting in the higher reported representation of American Indian and Alaskan Native participants in the tirzepatide and bexagliflozin programs deserve further study.

Additional Perspective

ALESIA NEZ

School: Washington State University
Tribal Affiliation: Diné-Navajo Nation Tribe
College: Washington State University
Major: BS Biology, 2024
Project Mentors: Yeruk Mulugeta, PharmD; Abigail Melake, PharmD

What motivated you to pursue a summer ORISE fellowship at FDA?
After graduating from Washington State University with my BS in Biology, I want to further my education journey with graduate school. I recently reevaluated my passion for education and reflected on my goals and how I can align my goals with a meaningful career path. I decided to take some time off to explore different fields and gain experience across various backgrounds. When I first learned about the ORISE fellowship at the FDA, I was excited about the opportunity to broaden my understanding of statistical data and project development.

What advice do you have for other Indigenous students or recent graduates who may be interested in pursuing a summer fellowship at the FDA?
Come in with an open mind. I initially thought I would continue pursuing a career in pharmacy but after working with the Division of Pediatrics and Maternal Health, I developed a strong interest in physician assistance. Through this experience, I realized that my passion lies in helping people and interacting with patients. Most importantly, I now see a clear path towards giving to my Indigenous community, which has always been one of my core goals.

What was the highlight of your summer ORISE fellowship?
The highlight for me was the collaboration with other professionals. It was incredibly rewarding to share my ideas with a group that valued my input equally, regardless of our titles. Everyone's perspectives were considered, which allowed us to collectively develop a project that addressed everyone's needs.

Workforce Recruitment Program

The Workforce Recruitment Program (WRP) is a recruitment and referral program that connects federal and private-sector employers nationwide with highly motivated college students and recent graduates with disabilities who are eager to demonstrate their abilities in the workplace through summer or permanent jobs. The OND ORISE program utilized the WRP database to find potential candidates looking for summer fellowship opportunities in public health. Two candidates were recruited and onboarded to participate in two different ORISE research projects within OND which are highlighted below.

Custom Medical Query Development – Symptom Extraction from FDA Documents

Fellow
Cole Wood

College:
Syracuse University

Major: MS in Applied Data Science, 2023

Research Mentors:
Linda Jeng, MD, PhD

Cole's project perspective:
Dr. Linda Jeng and I worked on creating a custom medical query (CMQ). In order to achieve the first steps, we successfully used both Dr. Jeng's clinical expertise and my Data Science background to develop a Python script to successfully extract symptoms from FDA labels to be reviewed for clinical relevance.

My experience working on the project for the FDA was exciting and rewarding at the same time. My mentor, Dr. Linda Jeng, was great, always there to help, develop ideas, trouble-shoot problems, network with others in the agency, and to point me in the right direction for questions that we collectively could not answer. Everyone I have encountered at the FDA has been enjoyable, eager to answer questions, and passionate about the work being done for the FDA.

Although I have a Data Science background, I had limited knowledge about Natural Language Processing (NLP). This project pushed the boundaries of my knowledge to obtain a better understanding of NLP, especially in the realm of Named Entity Recognition (NER), Regular Expressions (Regex), and utilizing other Python libraries I had not used in the past. This project allowed me the opportunity to work with real-world data, create an impactful project, collaborate with other disciplines, and communicate findings in an easy-to-understand way to stakeholders. This experience will allow me to add meaningful and unique experiences to my resume and help me achieve my goal of becoming a Data Scientist.

What advice do you have for recent graduates with a disability who may be interested in pursuing a summer fellowship at the FDA?

I would advise anyone who is a recent graduate looking to gain real-world experience to apply for an ORISE Fellowship with the FDA. The FDA in my experience has been an outstanding place to gain applicable domain knowledge. Everyone has been welcoming, helpful, and mission-driven to accomplish the goal of protecting the health of both Americans and people around the globe.

Any WRP participants who are interested in an ORISE Fellowship should inform themselves about the FDA's mission and tailor their resume to highlight their individual skills, their unique experiences, and showcase their passion for the agency's work. Even if you don't have a clinical background, I would still encourage anyone to apply. The FDA is always looking for qualified individuals with a STEM background and prides itself on supporting individuals with disabilities.

WRP participants who are awarded a fellowship should leverage their time at the FDA by actively participating in the classes offered to learn as much as possible and focus on skill building. I recommend networking with individuals both in and out of your perspective industries and leveraging any available resources to both aid in the project you are working on, as well as expanding your own network. Anyone participating in the ORISE Fellowship with the FDA should actively seek mentorship and explore long-term opportunities within the FDA.

Development of a Scoring Algorithm for Drug-Induced Liver Injury Diagnosis (DILI) in Clinical Trials

Fellow
Mark Gordon

College:
North Carolina State University

Major: MS Statistics, 2022

Research Mentors:
Paul Hayashi, MD, MPH

Mark's project perspective:

Drug-induced liver injury, DILI, is a clinical diagnosis by exclusion of other causes. There is no lab test to diagnose DILI. Several clinical causality assessment models have been published, but none are validated for clinical trial use. We aimed to create a model that would predict clinical diagnosis of DILI by FDA hepatologists. We ran a statistical analysis utilizing information from a patient level assessment DILI database which has over 1300 cases of liver injury assessed by FDA hepatologists. The dependent variable is the Drug-Induced Liver Injury Network, or DILIN, causality score FDA hepatologists use to score a case's probability that the liver injury is due to DILI. During data exploration we identified variables to model. These included the amount of time between injury onset and the drug start and/or stop. Due to the nature of the data, ordinal logistic regression made a strong contender for modeling. This preliminary model generated was able to correctly predict 61% of the cases. Even though the model generally performed well, it is not meant to replace clinician judgement because the bar for DILI diagnostic accuracy is high. Just one or two cases with high mortality risk, known as Hy's Law cases, could be the difference between a drug getting approved or not. However, our model could eventually be used to prioritize cases for review. For example, a more developed version may be able to accurately identify cases that have a high chance of being considered highly unlikely DILI by FDA hepatologists.

As a recent graduate who identifies as having a disability, can you describe the personal impact this project has had on your personal and professional growth within the public health field?

This project has helped my personal and professional growth tremendously. It has given me my first opportunity to apply my statistical skills in a professional setting and given me opportunities to learn new skills along the way as well.

Like what you see?

*The next edition of OND **ORISE on the Move** will be released in 2025!*