U.S. FOOD & DRUG ADMINISTRATION

Office of New Drugs (OND)

2023 ORISE on the Move

Diversity, Equity, Inclusion (DEI) Edition

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 2024 CDER ORISE summer fellowship program can be found here: https://www.zintellect.com/Opportunity/Details/FDA-CDER-2024-0000. Applications are now being accepted through April 15, 2024. It is strongly recommended that interested candidates apply early.

* ORISE: Oak Ridge Institute for Science and Education

PROJECT PERSPECTIVES

The perspectives below highlight some of OND's summer regulatory research projects that focus on diversity, equity and inclusion.

DIVERSITY

Representation in Clinical Trials Supporting Approvals in Breast Cancer

Mentor
Lola Fashoyin-Aje, MD, MPH

Fellow
Fudhah (Silver) Alkhafaji, PhD candidate

Major: Pharmacology

School: University of California, San Francisco

Project Collaborator
Jessica Boehmer, MBA

This project was designed to address important questions regarding study population representativeness as it pertains to demographics, for cancer trials that serve as the basis for FDA approval of breast cancer treatments. Over the years, we have received inquiries from the media, patient advocacy groups, policy makers, and researchers on this topic and our responses have predominantly been based on small scale analyses of trials evaluating new molecular entities (NMEs) in a given year, which can be limited. In this analysis, we sought to characterize the demographics of clinical trial participants for NME and supplemental approvals over a 10-year span. The demographic characteristics of interest were race, ethnicity, sex, and age and this information was abstracted directly for the application submissions and pooled for analysis. In addition to the demographic information, we also analyzed information pertaining to the geographic location of trial participants to explore the potential impact on participant demographics.

The outcomes in some ways, were not surprising- Blacks, older adults, and males were underrepresented relative to national statistics on disease incidence across these groups. But our understanding of breast cancer was enriched by unexpected observations that may inform future research and policy initiatives and this work will help provide a baseline for ongoing efforts to improve the diversity and representativeness of trial participants so that they better reflect the population with the disease and the intended use population. Dr. Alkhafaji's quick learning of our databases and Ms. Jessica Boehmer's support facilitated completion of this project in just a few weeks' time.

EQUITY

Use of Medicaid Databases in Pediatric Regulatory Decision Making

Mentor
Charlotte Jones, MD, PhD, MSPH

Fellow
Delara Rajabi Abhari, MPH candidate

School: University of Maryland at College Park

Co-mentor
Yeruk (Lily) Mulugeta, PharmD

Project Collaborators
Corrine Woods, RPh, MPH
Nicholas Miles, PharmD
Yuze Yang, PharmD

Sponsors, at times, submit justifications for waivers of pediatric studies under Pediatric Research Equity Act (PREA) using commercial databases to estimate the prevalence of diseases in the pediatric population and pediatric drug use. Unfortunately, commercial databases may exclude children receiving Medicaid. Medicaid covers 40% of children, both those who are low-income and those who have serious chronic diseases. In a recent consult, the Office of Surveillance and Epidemiology identified that for drugs used to treat severe forms of epilepsy, a failure to include children with Medicaid could underrepresent the population receiving treatment by up to 73%.

Based on our analysis of initial Pediatric Study Plans (iPSPs) reviewed by the Pediatric Review Committee (PeRC) between March 2022-January 2023 that included a plan to request a partial waiver of pediatric study requirements, approximately 16% iPSPs specifically referenced drug use or claims data to support a justification for the partial waiver. Of the iPSPs that referenced drug use or claims data, only 7/19 of the references clearly included the pediatric Medicaid population.

This research is an initial step in understanding the accuracy and relevance of disease prevalence and drug use estimates from commercial databases when assessing justifications for waivers to conduct pediatric studies. It is critical that these estimates supporting pediatric regulatory decisions are representative of the entire population including vulnerable pediatric populations including those who are financially disadvantaged, facing serious health care challenges, and at increased risk of being from marginalized communities.

This work is a collaborative project across multiple offices at the FDA including the Office of New Drugs Division of Pediatrics and Maternal Health (DPMH) and Division of Cardiology and Nephrology (DCN) (DPMH and DCN), Office of Surveillance and Epidemiology and the Office of Pediatric Therapeutics.

Inclusion of Adolescents in Adult Asthma Trials: Sample Size Considerations, Differential Efficacy Findings, and Regulatory Consideration in the Approval of Products

Mentor
Yeruk (Lily) Mulugeta, PharmD

Fellow
Sabrina Rahman Archie, PhD

Co-mentors
Kelly D Stone, MD, PhD;
James Travis, PhD;
Robert Abugov, PhD;
Yongman Kim, PhD

Traditionally, FDA has approved asthma products for adolescents by extrapolating efficacy results from adults to adolescents, based on the assumption that the course of disease and response to treatment is similar in adults and adolescents. Adolescents have usually been included with adults in pivotal trials; FDA has generally not required that the adolescent population be powered for the primary endpoint; as a result, small adolescent populations have been enrolled in pivotal trials and efficacy results in the adolescent subgroup have been variable with wide confidence intervals. Although trends favoring efficacy in the adolescent population have been viewed as supportive, the primary efficacy analyses have been performed on the overall study population, combining adults and adolescents.

In 2015, however, Breo Ellipta (fluticasone furoate/vilanterol) was approved for adults, but not for adolescents, despite the inclusion of adolescents in the pivotal trials. This decision was based on subgroup analyses that demonstrated that the primary endpoint of asthma exacerbations favored the control arm over the treatment arm, with wide confidence intervals that crossed 1, and that more hospitalizations occurred in the treatment arm than in the control arm. This decision to approve Breo Ellipta for only adults was noted to mark a change in expectations for adolescent data for asthma drug approval. Differential efficacy findings have been reported in other programs as well, with variable justification, for programs submitted to FDA that included combined adult-adolescent pivotal trial populations. For example, Airsupra (albuterol sulfate/budesonide), which is a new combination of short-acting beta2-adrenergic agonist and inhaled corticosteroid for reliever treatment of asthma, was recently approved only in adults, despite a primary analysis population that included adolescents and adults. Subgroup analyses in the adolescent population noted point estimates for time to first asthma exacerbation that favored control over treatment; factors contributing to this result included small numbers of adolescent patients enrolled and a small number of exacerbations in this subgroup over the treatment period. As a result, almost complete extrapolation (>95%) of efficacy from adult data was required to

demonstrate efficacy in adolescent subjects. The appropriateness of and justification for such a high degree of extrapolation was discussed at an FDA Pulmonary-Allergy Drugs Advisory Committee meeting. Due to limited efficacy data and the proposed novel indication for as needed inhaled corticosteroids to prevent severe asthma exacerbations, the advisory committee was evenly divided on whether there was sufficient efficacy data to support approval in adolescents.

Our project aims to perform retrospective analyses of prior approvals of asthma products for adolescents, including inclusion of adolescents in pivotal trials for asthma drugs, sample size considerations, differential efficacy and safety findings, and the bases for regulatory actions in the approval of these products. The role of extrapolation of efficacy data from adults to pediatric patients was also included. This is a collaborative project across offices and disciplines at FDA, including the Division of Pediatrics and Maternal Health (DPMH), the Division of Pulmonology, Allergy and Critical Care (DPACC), and the Division of Biometrics (DB). These findings will enable our offices to develop a prospective framework for asthma drug approval for adolescents and will incorporate recommendations from the FDA E11A Pediatric Extrapolation Guidance.

Additional Project Perspectives

BRITTNEY THOMPSON

School: Louisiana State University
Major: Inorganic Chemistry, 1st year (Doctoral)
Project Mentor: Margaret VanHeusen, MS
Project Title: Qualitative and Quantitative Review of the Development of the Competing and Affected Products (C/AP) List and the Use of the CAP Tool

Brittney's Perspective:
This fellowship enhanced my research skills and provided me with the opportunity to expand my depth of knowledge of the regulatory approach and the significance of drug regulation in product development. My research surrounded the process of how competing and affected products are appraised.

What advice do you have for other Historically Black Colleges and Universities (HBCU) students who may be interested in pursuing a summer fellowship at the FDA?
I have had the pleasure to complete a research fellowship with the FDA, CDER in the Office of New Drugs. I would like to say to my fellow HBCU students that you will be entering the world, and you need to be fully prepared. I hope what I share will encourage others to take advantage of this opportunity. Beyond my specific research project, this experience helped me by connecting me with

people who showed me what life would be like in various professions. This not only inspires me to grow and thrive, but also supports my growth through related opportunities. Through research, the environment, people, and other factors, I've had the opportunity to get an overview of what working life would be like as a part of the FDA.

MARK SMITH JR.

School: The University of Maryland at Baltimore County
Major: Biology, Senior
Project Mentors: Yeruk (Lily) Mulugeta, PharmD; Amy Taylor, MD, MHS
Project Collaborators: Martine Solages, MD; James Travis, PhD; Bob Abugov, PhD
Project Title: Inclusion of Under-represented Populations in Pediatric ADHD Trials

Mark's Perspective:
Training as a summer ORISE fellow has been an incredible experience. Working with professional mentors, meeting other ORISE fellows, and gaining knowledge in ADHD treatment has been unparallel. During this summer fellowship, I've also learned how to analyze data, statistical reviews, and clinical studies. This project has given me new insight into drug development.

As a person of color and a student attending an minority serving institution (MSI), can you describe the personal impact this project has had on your personal and professional growth within the public health field?
This project for me has reinforced the importance of having more minorities in healthcare and drug development. It has shown me the underrepresentation of racial and ethnic minority groups in medicine and has only encouraged me to continue to pursue a career in the medical/public health field. With the use of FDA resources and drug databases, constructing my final presentation gave me the opportunity to grow intellectually and professionally.

DEI Initiatives: 2023 CDER Summer ORISE Research Fellowship Program

The Center for Drug Evaluation and Research has been actively engaging in a strategy to enhance Diversity, Equity, Inclusion and Accessibility (DEIA) by incorporating these goals into our business units as well as improving targeted efforts in recruitment, advancement, retention, and education to increase awareness in our workplace. We are enthusiastic about making DEIA a part of our everyday conversation.

Various offices throughout the Center have attended recruitment events geared towards minority serving institutions. We have intentionally engaged in virtual, semivirtual, and in person opportunities.

Below is a snapshot of OND's contributions towards CDER's diversity plan:

OND Targeted HBCU Outreach

The OND Research Program created an OND HBCU advisory group comprised of staff that were HBCU alumni. The goal of the group was to focus on outreach efforts for recruiting STEM students and recent graduates for the 2023 CDER ORISE summer fellowship program. This initiative was stood up as a result of a 2021 White House Executive Order 14041, which focuses on Initiating and Advancing Educational Equity, Excellence, and Economic Opportunity Through Historically Black Colleges and Universities (HBCUs). This group conducted outreach to over 80 HBCUs with STEM programs over several months.

Additionally, the OND Research Program staff conducted external outreach to promote the CDER ORISE summer fellowship program that included a presentation on OND's ORISE Program at the Department of Education's annual Title III HBCU Project Directors Meeting this past spring.

CDER Fellow Diversity Ambassadors

The OND Research Program created a CDER ORISE fellow diversity ambassador group which is comprised of current fellows who are students or alumni from Historically Black Colleges and Universities (HBCUs) and Minority Serving Institutions (MSIs) and/or identify as Native American, Pacific Islander, Hispanic, or African American/Black. The group conducted outreach to the diversity clubs at their educational institutions and other affiliated professional organizations to spread awareness about the 2023 ORISE summer fellowship program.

CDER's DEIA efforts resulted in a significant increase in the number of students from underrepresented communities applying to the 2023 CDER ORISE summer fellowship in comparison to previous years as demonstrated in the tables below.

Table 1: Applicant MSI Designation Data:

CDER Summer ORISE Advertisement Year:	AANAPI SI	AANAPISI & ANNH	AANAPI SI & HSI	AANAPI SI & PBI	ANNH& NASNTI	HBCU	HSI	HSI & PBI	NASNTI	non- MSI	PBI	Grand Total
2020	26	1	10	1	1	12	11		1	259		322
2021	30		14	1		20	19	1		395	2	482
2022	23		16			15	25			408		487
2023	30		17	4		44	11		1	372	2	481
Grand Total	109	1	57	6	1	91	66	1	2	1434	4	1772

*Asian American and Pacific Islander Serving Institution (AAPISI)

*Alaskan Native-Serving or Native Hawaiian-Serving Institution (ANNH)

*Hispanic Serving Institution (HSI)

*Historically Black Colleges and Universities (HBCU)

*Native American-Serving Nontribal Institution (NASTNI)

*Predominately Black Institution (PBI)

Table 2: Applicant Race Demographic Data:

CDER Summer ORISE Advertisement Year:	Native Hawaiian or Other Pacific Islander	American Indian or Alaska Native	Asian	Black or African American	Decline to Answer	Other Race	White	Grand Total*
2020	1	3	10	57	15	6	136	341
2021		5	178	68	18	6	230	505
2022	4	2	210	69	22	12	203	512
2023	2	6	202	113	18	7	154	502
Grand Total	7	16	600	307	73	31	723	1860*

*Applicants may select multiple races, all responses included in Grand Total Counts.

Table 3: Applicant Ethnicity Demographic Data:

CDER Summer ORISE Advertisement Year:	I Choose Not to Respond	Not Hispanic or Latino	Hispanic or Latino	Grand Total
2020	13	280	29	322
2021	14	439	29	482
2022	15	442	30	487
2023	17	431	33	481
Grand Total	59	1592	121	1772

Like what you see?

*The next edition of OND **ORISE on the Move** will be released in 2024!*