U.S. FOOD & DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

Office of New Drugs Extramural Research Outcomes Report (FY2021)

January 2023

Table of Contents

Background

How does OND use regulatory science research (RSR) to stimulate new drug development?

The Office of New Drugs Research Program (OND-RP) was created in 2019 to foster regulatory science research (RSR). OND plays a proactive role in stimulating drug development by investing in RSR that will address targeted knowledge gaps identified during regulatory review. External stakeholders benefit from OND's RSR activity as project outcomes are used by OND staff to develop or clarify regulatory pathways in areas of unmet need.

Why does OND conduct extramural research?

Although OND staff take the lead on identifying RSR knowledge gaps, the Officee doesn't always have the expertise, equipment, or capabilities needed to perform the research. When this occurs, OND conducts extramural research (EMR), a collaborative type of RSR that OND initiates together with an external partner(s). OND uses several FDA programs to engage with collaborators. They are described in detail at our OND-RP webpage.

Purpose and scope of this report

The purpose of this report is to summarize OND-funded EMR outcomes that have been used to facilitate new drug review. Outcomes were generated in fiscal year 2021 (FY21).

FY21 EMR Outcomes Summary Table

# of OND funded EMR Projects	Industry Guidance	Drug Development Tool	External Publications	External Presentations
5	1	1	10	2

Detailed Project Perspectives

This report features five EMR projects OND funded in FY21. Many of these efforts are still ongoing, so the report highlights both intermediate and final RSR outcomes.

Natural History of Adenovirus Infections Among Pediatric Hematopoietic Stem Cell Transplant Patients in the United States

Adenoviruses are common viruses that cause a broad spectrum of clinical symptoms in all age groups, but children with profound immunodeficiency are at risk for severe disease, including death. There are currently no drugs approved to treat this virus. OND leveraged FDA's Broad Agency Announcement (BAA) Program to fund an RSR project that would help generate the information needed to support a regulatory pathway for new drug approval for this rare pediatric illness. This collaboration between OND's Division of Antivirals (DAV) and Children's Hospital of Philadelphia is leveraging patient data from electronic health records at multiple clinical centers. The population under study is pediatric patients who underwent hematopoietic stem cell transplantation (HSCT) and were diagnosed with adenovirus infection. DAV is planning to use these real-world data to inform study design for novel antiviral drugs, including selection of comparator groups, endpoints, and statistical analysis strategies. FDA believes these data are needed to advance development in this area of unmet need.

Outcomes:

Data collection for this study is ongoing at 10 pediatric transplant centers. Once the study is complete and the data are analyzed, findings will be communicated to key stakeholders through publications and presentations. FDA will use the results to inform trial design considerations for this population and indication, which may be shared in an FDA Guidance for Industry.

Cardiac Safety Research Consortium Prevention of Sudden Cardiac Death in the Young: National Cardiac Screening Warehouse Pilot Study

Electrocardiograms (ECGs) are used to assess for and mitigate against the risk for serious and life-threatening heart rhythm abnormalities, especially in early phases of drug development. Interpretation of ECGs in children can be challenging due to differences from adults in certain ECG parameters because of normal developmental changes from birth to adolescence. OND leveraged the BAA Program to fund a RSR collaboration between the Division of Cardiology and Nephrology (DCN), the Cardiac Safety Research Consortium, and Duke Health. The project team is collecting real world ECG data from public groups that screen children for heart rhythm abnormalities that may result in sudden cardiac death at various venues, including schools. DCN will use this information to better understand how to interpret screening and follow up pediatric ECG readings and how exposure to therapeutic products might impact ECG parameters in children. OND funded this RSR because addressing this knowledge gap will allow FDA to conduct better pre- and post-market cardiac safety evaluations in children.

Outcomes:

Over 100,000 ECGs are included in the ECG dataset with over 37,000 pediatric ECGs in a digital data format for the pediatric ECG warehouse. This drug development tool is still under development with recruitment of additional public screening groups to provide more ECG data from their respective screening events. The current iteration of the ECG database is now available to support CSRC-approved research and development studies with the final iteration of the ECG database expected to support investigator- and sponsor-initiated pediatric therapeutic product development. This project was featured as a CDER Impact Story that was later reported on in Regulatory Focus.

Valganciclovir Use in Newborns with Congenital Cytomegalovirus

Congenital cytomegalovirus (cCMV) infection is a rare pediatric disease. Although it is the leading non-genetic cause of sensorineural hearing loss in children, there are currently no FDA-approved drugs for prevention or treatment of cCMV. Some experts recommend use of valganciclovir (vGCV) for newborns with symptomatic cCMV to improve or prevent progression of hearing loss, but safety and efficacy data are limited. OND's Division of Antivirals established a contract with the Sentinel Operations Center to gain access to administrative data and electronic health records from Sentinel data partners. DAV is using these data to understand prescribing practices, safety events, and the clinical course of cCMV in infants (treated and untreated with vGCV). FDA will use these findings to inform clinical study endpoints, comparator groups, and statistical analysis strategies for future studies.

Outcomes:

Although this project is still ongoing, DAV used the preliminary results of this study to frame a discussion in May 2021 at an internal mini-symposium on drug development considerations for cCMV. In turn, feedback from the mini-symposium was used to inform the next phase of data collection, which is nearing completion. Analysis of the administrative claims data were presented at two conferences: the 8th International Congenital CMV Conference (March 28-April 1, 2022, held virtually, Poster 1.10) and the International Conference on Pharmacoepidemiology (August 24-28, Copenhagen, Denmark, Spotlight Poster 1023). Additional results will be shared via future publications when data collection and analysis are complete. The goal is to use these data to inform clinical trial design for cCMV antiviral drug development, which may be shared in an FDA Guidance for Industry.

Developing Blood-Based Biomarkers for Traumatic Brain Injury

Every year, more than 1.7 million new cases of traumatic brain injury (TBI) occur in the United States. Developing drugs to treat TBI is challenging as patients present to the clinic with heterogenous symptoms and the tools available to determine prognosis rely on subjective interpretation (e.g., clinical assessments, neuroimaging). OND leveraged FDA's Centers for Excellence in Regulatory Science and Innovation (CERSI) Program to fund an RSR project that would generate the information to help qualify blood-based biomarkers for TBI. These biomarkers will stimulate new drug development for TBI by providing a sensitive, reproducible tool for patient stratification in clinical trials. The pre-clinical data generated from this collaboration between OND's Biomarker Qualification Program (BQP) and the University of Maryland CERSI was used to initiate internal discussions around submitting a Letter of Intent (LOI) for biomarker qualification and continuing the study of these biomarkers in human patients.

Outcomes:

After the LOI was submitted, feedback indicated that supportive human data was needed for the LOI to be accepted. This feedback was used to develop a study on clinical samples which confirmed that the biomarkers can help diagnose TBI and scale with the severity of TBI in humans. The currently ongoing study expands upon the pilot with additional clinical samples. A LOI will be resubmitted with the data from this larger human data set. Once the study is complete, the information generated will be shared publicly if the TBI biomarkers are qualified to support drug development under context of use.

Heart Failure Collaboratory

Despite the availability of FDA-approved therapies that reduce hospitalization and mortality, patients with heart failure still experience a high burden of symptoms and physical limitations. There remains an unmet need for new drugs to treat heart failure that can improve patient-driven outcomes such as quality of life, physical function, and symptoms. OND funded a public-private partnership (PPP) to bring together key stakeholders in the clinical trial community. The goal was to align on key endpoints that could be used to measure symptomatic and functional benefit in drug development for heart failure. This collaboration between OND's Division of Cardiology and Nephrology and Inova Heart and Vascular Institute facilitated several working-group style discussions between FDA and patients, clinical investigators, academic leaders, pharmaceutical and device industry representatives society representatives, third party payers, and government representatives from the National Institute of Health (NIH) and the Centers for Medicare and Medicaid Services (CMS).

Outcomes:

The Heart Failure Collaboratory (HFC) produced a large number of external publications (six). Many of these publications are available at the HFC website. The results of this project were also used to inform the draft FDA Guidance: *Treatment for Heart Failure: Endpoints for Drug Development*.

A Look Towards the Future

Our next report will feature fiscal year 2022 (FY22) outcomes from OND-funded EMR projects. It will be released in 2024.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Food and Drug Administration
www.fda.gov

Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993