U.S. FOOD & DRUG ADMINISTRATION

Office of New Drugs

2022 ANNUAL REPORT

Breaking Barriers to Advance Public Health

September 2023

www.fda.gov

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Director's Message

Peter Stein, M.D.
Director, Office of New Drugs

As you'll see from the OND Annual Report, 2022 was a very successful year. As we've seen the incidence of COVID-19 illnesses decline—even as this remains an important ongoing public health problem—OND staff in the Office of Infectious Disease and in the Office of Immunology and Inflammation, working with staff in the Office of New Drug Policy and the Office of Regulatory Operations, and in many other OND and CDER offices, can feel proud of the very key contributions they have made in supporting the development, authorization, and approval of treatments that reduced hospitalizations and helped save many lives. Beyond this important work on COVID-19, OND provided critical guidance across a very large range of IND development programs for diseases both rare and common, and conducted detailed reviews leading to approval of novel drugs to treat diseases across therapeutic areas. The increased proportion of rare disease applications, seen over the past years and continuing into 2022, often makes the assessment of these drug development programs challenging. Such programs typically have smaller randomized trials or use externally controlled studies and rely on clinical endpoints that may not have been previously employed and thus for which there may be limited prior experience. Despite these challenges, OND staff's detailed and thorough analyses in these settings led to robust assessments and well supported regulatory decisions.

Over the course of the year, OND staff conducted a very large number of meetings with drug sponsors to provide guidance on IND development programs, completed detailed assessments of NDA/BLA applications and supplements, and carefully tracked safety post- approval. Additionally, OND staff worked extensively—in collaboration with other CDER offices and FDA centers—to bring forward a wide range of essential guidances. These guidances ranged from those focused on general clinical development topics to guidances specific to drug development in particular diseases. Staff also organized and led or actively participated in numerous important workshops and meetings that advanced policy and thinking on critical areas in drug development. With the completion of PDUFA VII negotiations, and reauthorization of PDUFA with PDUFA VII, staff in OND were tasked with implementing the many new innovative programs—programs that will improve efficiency, such as the "STAR" program that may accelerate review, to those that will lead to innovation, such as the Rare Disease Endpoint program—and a number of other programs. Working collaboratively across OND, and closely with other CDER offices, OND staff led a number of working groups to ensure seamless implementation of PDUFA VII programs in OND.

In summary, 2022 was a very productive year for OND—and reflects the hard work and dedication to mission of our staff, their detailed and extensive scientific and clinical knowledge, and the wide-ranging experience they bring to bear on critical development issues. I hope you will take time to read about the many activities and the productivity and accomplishments of OND during 2022.

OND by the Numbers (CY2022)

OND, working hand-in-hand with other Center for Drug Evaluation and Research (CDER) super-offices, had a successful year for novel drug approvals and other drug development activities, such as industry meetings and guidances published during the calendar year 2022. Please see below for more information.

Investigational New Drugs (INDs) Received and INDs with Activity

Novel Drug Approvals (New Molecular Entity [NME] New Drug Applications [NDAs]/ Biologics License Applications [BLAs])

Non-NME NDA Approvals

Efficacy Supplement Approvals

Breakthrough Therapy Requests

Fast Track Requests

Expanded Access INDs Received and Expanded Access INDs Safe to Proceed

23
Published Guidances

6
Critical Path Innovation Meeting (CPIM) meetings with OND representation

22
Patient-Focused Drug Development (PFDD) meetings with OND representation

11
Patient Listening Sessions organized by OC/Office of Patient Affairs with OND representation

15
Patient Listening Sessions organized by Professional Affairs and Stakeholder Engagement (PASE) with OND representation

437
OND speaking engagements

OND Operations

In 2022, OND achieved a net hiring gain of **107** new staff. This important progress facilitated by OND operations helped OND manage increasing workload and public health priorities. OND operations also oversaw the implementation of **5** new PDUFA VII commitments/programs intended to benefit public health by enabling earlier patient access to important treatments, increasing feedback opportunities for new drug development programs, and improving consistency and predictability of the review process. These programs included the Split Real-time Application Review (STAR), new formal meetings (INTERACT and Type D), and Post marketing requirement communication timelines, just to name few.

In addition, to help maintain OND's internationally recognized standard of excellence for drug review and regulation, OND operations delivered **63** internal staff training courses for the equivalent of **8,500**+ attendees, to strengthen staff's scientific, regulatory, operational, and leadership skills and abilities. OND operations facilitated interactions with sponsors of new drug development programs via more than **3,400** formal meetings, and protected patient safety by overseeing the management of safety reviews for over **2,950** new INDs. OND operations also established a new internal advisory committee (AC) support team that provided review teams with necessary resources to enable better preparation and presentation for **17** public AC meetings during 2022, resulting in a more consistent and effective AC experience for the Agency, industry, and public. Finally, OND operations kept stakeholders such as Agency leadership, the public, media, and Congress informed of important new drug review program information by triaging and facilitating responses to more than **875** internal and external inquiries.

107 new staff

5 PDUFA VII commitments/ programs

63 internal staff training courses for 8,500+ attendees

3,400+ formal meetings

2,950+ new INDs

17 public Advisory Committee meetings

875+ internal and external inquiries

Office of Drug Evaluation Sciences

The Office of Drug Evaluation Sciences (ODES) supports OND's mission to foster advances in drug development by providing focused scientific expertise on the development and implementation of novel drug development tools (DDTs), facilitating the development of tools and practices for robust analysis and interpretation of data to support regulatory decisions, supporting regulatory research, and improving efforts to increase diversity in clinical trials. ODES consists of staff in two review divisions:

- Division of Clinical Outcome Assessment (DCOA)
- Division of Biomedical Informatics, Research, and Biomarker Development (DBIRBD)
- The ODES Immediate Office also has staff dedicated to:
- Developing the Drug Trials Snapshot, FDA's action plan in response to Section 907 of the Food and Drug Administration Safety and Innovation Act to report to Congress on certain information regarding clinical trial participation by demographic subgroups and subset analysis of the resulting data and to address the extent to which clinical trial participation and the inclusion of safety and effectiveness data by demographic subgroups is included in applications submitted to FDA.
- Digital health technologies (DHTs) to support CDER, Center for Biologics Evaluation and Research (CBER), Center for Devices for Radiological Health (CDRH), and FDA in fostering consistency with the use of DHTs in medical product development and ensuring Agency DHT-related activities are reflective of the perspective and input of OND.

Notable Advances in Drug Development Tools

DDTs are methods, materials, or measures that can aid drug development and regulatory review. In 2016, the 21st Century Cures Act (Cures Act) was signed into law. Section 3011 of the Cures Act added section 507 to the Federal Food, Drug, and Cosmetic Act, establishing a program for the qualification of DDTs. There are three DDT qualification programs at FDA: biomarker, clinical outcome assessment (COA), and animal model. In 2021, FDA established the Innovative Science and Technology Approaches for New Drugs (ISTAND) pilot program, another program intended for DDTs that are beyond the scope of the existing three qualification programs. The biomarker, COA, and ISTAND qualification programs are managed within ODES.

Qualification is a scientifically rigorous process and submissions are reviewed in three sequential stages (Letter of Intent [LOI], Qualification Plan, and Full Qualification Package), each providing and building on evidence to support a determination of whether the DDT can be qualified for its proposed context of use within any drug development program. From 2016-2021, the DDT program received 118 LOIs, and over half of these were accepted (29 in the COA program and 34 in the biomarker program). Some of these programs have progressed to later stages of qualification including the qualification of two biomarkers and four clinical outcome assessment measures. In 2022, the DDT qualification program continued to accept submissions for a variety of disease areas including alcohol use disorder, opioid use disorder, multiple sclerosis, and scleroderma. Two LOIs were accepted into the ISTAND pilot program in 2022.

"From 2016-2021, the DDT program received 118 LOIs, and over half of these were accepted."

Advances in Regulatory Science Research

The Office of New Drugs Research Program (OND-RP) fosters regulatory science research through the Oak Ridge Institute for Science and Education (ORISE) Fellowship Program and supporting extramural research projects. OND-led Regulatory Science Research projects address knowledge gaps identified during the regulatory review of investigational or new drug applications.

The OND ORISE Fellowship Program has grown in size and scope in the past decade, with initially only four to five ORISE fellows mentored in OND in 2013, the program expanded to 40-50 fellows in 2022. In addition to the full-year ORISE Fellowship Program, in 2022 OND hosted 27 summer students from STEM programs across the country. In response to Executive Order 14041, "White House Initiative on Advancing Educational Equity, Excellence, and Economic Opportunity Through Historically Black Colleges and Universities" (HBCUs), OND-RP has leveraged relationships with Agency partners to increase office participation in HBCU-specific career fairs and public recruitment opportunities to encourage HBCU students and alumni to apply for open fellowship opportunities within OND. OND's ORISE program

is a powerful workforce development tool. In 2022, twelve of OND's full-year ORISE Fellows converted to full-time Federal employees. Nine of them remained in OND.

The OND Extramural Research (OND-EMR) Program focuses on conducting outreach activities to educate review staff on leveraging EMR projects funded through Broad Agency Announcements, or through the Center of Excellence in Regulatory Science and Innovation (CERSI). An increase in staff participation within OND-EMR will generate new scientific information to inform OND's regulatory decision-making process. The program also conducts personalized quarterly check-in meetings with ongoing OND-EMR project owners to prepare them for upcoming data calls and to identify and resolve any project-related issues. In 2022, OND-EMR launched several newly designed tools to educate and support new project owners, including the OND-RP website at FDA.gov, and a CDER Impact Story on Applying the Non-Inferiority Paradigm to Assess Exposure-Response and Dosing Comparisons Between Pediatric and Adult Patients; August 2022.

Guidances and Publications

In collaboration with other offices in CDER including the Office of Oncologic Diseases (OOD), the Office of Strategic Programs (OSP), and the Office of Surveillance and Epidemiology (OSE), as well as CBER, ODES published Technical Specifications Documents; Final; March 2022, and Electronic IND Safety Reporting Technical Conformance Guide; Final; April 2022.

Biomarker Qualification at the European Medicines Agency: A Look Under the Hood; Clinical Pharmacology Therapeutics; Clinical Pharmacology & Therapeutics; May 2022.

MedDRA Labeling Groupings to Improve Safety Communication in Product Labels. Therapeutic Innovation & Regulatory Science; Therapeutic Innovation & Regulatory Science; August 2022.

External Engagement, Public-Private Partnerships, and Public Workshops

The FDA Center for Drug Evaluation and Research and the FDA Biomarker Working Group hosted a public workshop titled, Identification of Concepts and Terminology for Multi-Component Biomarkers; March 2022. During this workshop, attendees developed multi-component biomarker concepts and terminology to identify areas of conceptual language development through presentation of use cases and discussed gaps in terminology for concepts and approaches related to multi-component biomarkers. ODES collaborated with CBER to organize a meeting with the Chronic Obstructive Pulmonary Disease Foundation and the Chronic Lung Disease Biomarker and COA Qualification

Consortium to discuss biomarkers and COAs that could advance drug development for Chronic Obstructive Pulmonary Disease and other chronic lung diseases. The goal of the initiative is to establish a consortium of industry, academic organizations, patient advocacy groups, and regulatory agencies to pull together data from Alpha-1 anti-trypsin deficiency patients collected over many years in registries, clinical trials, and observational studies, to develop a disease progression model to evaluate the relationship between long-term outcomes and various measurements, including computed tomography (CT) scan densitometry, forced expiratory volume in one second, and other data collected for these patient groups, to inform the design of clinical trials for future therapeutics.

In 2022, FDA announced the initiation of pre-consortia at the Critical Path Institute for lysosomal diseases and alpha-1 antitrypsin deficiency. The goal of these public-private partnerships is to bring together FDA, academia, pharmaceutical industries, patient groups, and non-governmental organizations to address unmet drug development needs.

"The goal of these public-private partnerships is to bring together FDA, academia, pharmaceutical industries, patient groups, and non-governmental organizations to address unmet drug development needs."

Staff from the Biomedical Informatics and Regulatory Review Science team hosted a virtual public workshop titled Advancing Pre-Market Safety Analytics; September 2022. The objective of this meeting was to present FDA's efforts in recent years to improve the standardization of safety tables and figures used to present clinical trial data, address inconsistencies in definitions of safety-related terms, and to present a strategy developed by FDA for grouping adverse event terms in clinical trial data. These efforts produced two important documents, one on FDA Medical Queries, and the other on Standard Safety Tables and Figures. The first document presents a standardized approach to grouping adverse event terms to improve safety signal detection, and the second document presents standardized methods for visualization of clinical trial safety data in tables and figures. The conference was recorded for later viewership.

Advancing public health requires the breaking down of barriers that may inhibit innovative approaches to evaluating the safety and effectiveness of therapeutics, particularly in areas of unmet medical need. Staff in ODES supported this initiative with achievements including improvement of data analytics, advancement of programs exploring the use of novel tools and methodologies in drug development, and support of regulatory research.

Office of Infectious Diseases

OND's Office of Infectious Diseases (OID) consists of two review divisions:

- Division of Anti-Infectives (DAI)
- Division of Antivirals (DAV)

Notable Drug Approvals

In 2022, OID approved several groundbreaking treatments for new patient populations. This year, OID expanded the use of several important anti-infectives to treat children and adolescents. For example, in late March 2022, OID expanded the use of Cabenuva monthly regimen and bimonthly dosing regimen to treat HIV-1 infection in adolescents 12 years of age and older. Previously, use of Cabenuva was only approved for adults 18 years of age and older. In April 2022, OID approved a supplemental NDA for Veklury (remdesivir) that added a new treatment regimen for pediatric patients 28 days of age and older with COVID-19. Previously, the use of Veklury (remdesivir) was approved for patients 12 years of age and older, based on several randomized, controlled clinical trials which demonstrated that Veklury (remdesivir):

1. reduced the risk of hospitalization or death in certain patients with high risk for development of severe disease.
2. reduced the median time to recovery among hospitalized patients.

OID also approved Triumeq PD for treating HIV in pediatric patients weighing at least 10kg, Sunleca for treating HIV in patients who cannot be successfully treated with other available treatments due to resistance, intolerance, or safety considerations, and Solosec (secnidazole) oral granules for treating bacterial vaginosis in adolescents.

Other significant OID approvals included the supplemental approvals of TPOXX (tecovirimat) in a new dosage form (injection, 200mg/20mL) to treat smallpox, and Xofluza (baloxavir marboxil) tablets to treat or prevent influenza (post-exposure prophylaxis) in a new patient population. This supplement approval allows for the use of TPOXX (tecovirimat) as intravenous injection in adults and pediatric patients who are unable to take oral capsules. Formerly approved for patients 12 years of age and older, Xofluza (baloxavir marboxil) is now approved to treat patients as young as five years of age.

Guidances

In the past year, OID authored and revised guidances to promote drug development in areas of unmet need associated with many common disease areas.

For example, the revised guidance Antibacterial Therapies for Patients with an Unmet Need for the Treatment of Serious Bacterial Disease - Questions and Answers; Draft; May 2022, shares new options for development programs to treat serious bacterial diseases in patients with an unmet need, given the availability of some new therapeutic options. A new draft guidance, Clostridioides difficile Infection: Developing Drugs for Treatment, Reduction of Recurrence, and Prevention; Draft; October 2022, provides recommendations on clinical development of drugs to treat this infection categorized as an urgent antibiotic resistance threat by the Centers for Disease Control and Prevention. The revised guidance Human Immunodeficiency Virus-1 Infection: Developing Drug Products for Pre-Exposure Prophylaxis; Final; March 2019, providing new recommendations for trial design to facilitate the development of regimens that require infrequent administration with the goal of improved adherence. Updated guidance in areas of unmet need, such as antibacterial therapies and HIV-1, is critical to breaking barriers blocking advancement of drug development in these disease areas. The Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment; Final; April 2022, covers development starting with the initial investigation new drug application (IND), through the new drug application (NDA)/biologics license application (BLA), and the postmarketing period. The Pulmonary Tuberculosis: Developing Drugs for Treatment; Draft; December 2022, provides FDA's current recommendations regarding the overall development program and clinical trial designs for the overall development program and clinical trial designs for drugs to support an indication for the treatment of active pulmonary tuberculosis.

"Updated guidance in areas of unmet need, such as antibacterial therapies and HIV-1, is critical to breaking barriers blocking advancement of drug development in these disease areas."

Publications

Peer-reviewed scientific journals published innovative research articles from OID's DAV and DAI. Topics included analyses supporting dosing of recently approved antibacterial drugs such as plazomicin and cefiderocol in patients with renal impairment, publications focused on pediatric drug development for HIV-1 and COVID-19, a summary of a workshop focused on drug development for coccidioidomycosis (Valley Fever), and a New England Journal of Medicine perspective piece focused on development of therapeutics for monkeypox.

Below are the 2022 research articles by staff in OID, DAV and DAI:

- Cefiderocol Dosing for Patients Receiving Continuous Renal Replacement Therapy; Clinical Pharmacology Therapeutics; November 2022.
- FDA Public Workshop Summary-Coccidioidomycosis (Valley Fever): Considerations for Development of Antifungal Drugs; Clinical Infectious Diseases; June 2022.
- Application of Population Pharmacokinetic Modeling, Exposure-Response Analysis, and Classification and Regression Tree Analysis to Support Dosage Regimen and Therapeutic Drug Monitoring of Plazomicin in Complicated Urinary Tract Infection Patients with Renal Impairment; Antimicrobial Agents and Chemotherapy; April 2022.
- Considerations and Challenges in the Remdesivir COVID-19 Pediatric Development Program; Journal of Clinical Pharmacology; September 2022.
- What babies need: accelerating access to current and novel antiretroviral drugs in neonates through pharmacokinetic studies; The Lancet HIV; September 2022.
- Tecovirimat and the Treatment of Monkeypox - Past, Present, and Future Considerations; The New England Journal of Medicine; August 2022.
- Long-Acting Formulations for the Prevention and Treatment of Human Immunodeficiency Virus (HIV)-1 Infection: Strategic Leveraging and Integration of Multidisciplinary Knowledge to Advance Public Health; Clinical Infectious Diseases; November 2022.

External Engagement, Public-Private Partnerships, and Public Workshops

Through public workshops and forums, OID advanced drug development in areas of unmet need, including uncomplicated urinary tract infections (uUTI), and healthcare-associated infections.

To facilitate the development of antimicrobial drugs for the treatment of uUTIs, FDA held a workshop entitled, Considerations of Antimicrobial Drugs for the Treatment of Uncomplicated Urinary Tract Infections (UTI); June 2022, to discuss clinical trial design ideas in this space. The workshop focused on nonclinical and clinical considerations regarding antimicrobial drug development for uUTIs.

FDA co-sponsored a workshop with CDC, entitled, Drug Development Considerations for the Prevention of Healthcare-Associated Infections; August 30, 2022. This workshop focused on antimicrobial resistance threats as potential targets for decolonization and pathogen reduction as well as challenges and potential approaches to drug development and registration of products for the prevention of healthcare-associated infections.

FDA also collaborated with the European Medicines Agency (EMA) to host, Efficacy of Monoclonal Antibodies in the Context of Rapidly Evolving SARS-CoV-2 Variants; December 2022, bringing together scientists, clinicians, industry representatives and regulators to discuss alternative strategies to support the development of novel monoclonal antibody therapies

Office of Oncologic Diseases

The Office of Oncologic Diseases (OOD) is responsible for making safe and effective drugs for cancer available to the U.S. public. OND's OOD consists of six divisions:

- Division of Oncology I (DO I)
- Division of Oncology II (DO II)
- Division of Oncology III (DO III)
- Division of Hematologic Malignancies I (DHM I)
- Division of Hematologic Malignancies II (DHM II)
- Division of Hematology/Oncology Toxicology (DHOT)

Notable Drug Approvals

Throughout 2022, OOD broke barriers by approving new treatments for several forms of cancer. Many of these treatments are novel or the first approval for a particular indication.

For instance, in January 2022, OOD approved Kimmtrak (tebentafusp-tebn), an original biologic drug, to treat unresectable or metastatic uveal melanoma, a rare form of eye cancer. Kimmtrak is the first approval for this indication. Other notable OOD approvals this year included Enhertu (fam-trastuzumab deruxtecan-nxki) to treat patients with unresectable or metastatic HER2-low breast cancer. This is the first approved therapy for patients with the HER2-low breast cancer subtype, which is a newly defined subset of HER2-negative breast cancer. Elahere (mirvetuximab soravtansine-gynx). was approved for adult patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Mirvetuximab soravtansine-gynx is a folate receptor alpha (FRα)-directed antibody and microtubule inhibitor conjugate.

OOD approved several other novel drugs this year, including: Pluvicto (lutetium Lu 177 vipivotide tetraxetan) to treat patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer who have received at least two specific lines of therapy, Opdualag (nivolumab and relatlimab-rmbw) for patients 12 years of age or older with unresectable or metastatic melanoma, and Tecvayli (teclistamab-cqyv) to treat relapsed or refractory multiple myeloma among adults who have received at least four specific lines of therapy. Pluvicto is the first PSMA-targeted radiopharmaceutical. Tecvayli is the first bispecific therapy directed at both the B-cell maturation antigen protein and cluster of differentiation

3 protein complex and T cell co-receptor. Imjudo in combination with durvalumab for adult patients with unresectable hepatocellular carcinoma also received approval.

Additionally, OOD approved Pedmark (sodium thiosulfate injection) to treat ototoxicity (hearing or balance problems) associated with the medication cisplatin in pediatric patients, Retevmo (selpercatinib) capsules for locally advanced or metastatic RET fusion-positive solid tumors, Imfinzi (durvalumab) injection for locally advanced or metastatic biliary tract cancer (cancer associated with the liver, gall bladder, and bile ducts), and dabrafenib Tafinlar (dabrafenib) in combination with trametinib Mekinist (trametinib) for the treatment of adult and pediatric patients six years of age or older with unresectable or metastatic solid tumors that have progressed following prior treatment and have no satisfactory alternative treatment options.

Guidances and Publications

OND's Office of Oncologic Diseases authored eleven guidances for industry.

- Inclusion of Older Adults in Cancer Clinical Trials; Final; March 2022, provides recommendations regarding the inclusion of older adult (65 years and older) patients in clinical trials of drugs for the treatment of cancer. This guidance is intended to assist stakeholders, including sponsors and institutional review boards, responsible for the development and oversight of clinical trials.
- Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics; Final; March 2022, provides advice to sponsors regarding the design and conduct of first-in-human clinical trials intended to efficiently expedite the clinical development of oncology drugs, including biological products, through multiple expansion cohort trial designs.
- Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics; Final; March 2022, provides recommendations to sponsors of drugs or biologics for the treatment of cancer regarding the design and conduct of clinical trials intended to simultaneously evaluate more than one investigational drug and/or more than one cancer type within the same overall trial structure (master protocols) in adult and pediatric cancers.
- Advanced Prostate Cancer: Developing Gonadotropin-Releasing Hormone Analogues Guidance for Industry; Final; May 2022, describes the FDA's current recommendations regarding the overall development program to establish the effectiveness and safety of gonadotropin-releasing hormone analogues for treating advanced prostate cancer.

- Use of Circulating Tumor Deoxyribonucleic Acid for Early-Stage Solid Tumor Drug Development; Draft; May 2022, is intended to help sponsors planning to use circulating cell-free plasma derived tumor deoxyribonucleic acid as a biomarker in cancer clinical trials conducted under an IND and/or to support marketing approval of drugs and biological products for treating solid tumor malignancies in the early-stage setting.
- Renal Cell Carcinoma: Developing Drugs and Biologics for Adjuvant Treatment; Final; June 2022, provides recommendations to sponsors regarding the development of drugs and biological products regulated by CDER and CBER for the adjuvant treatment of renal cell carcinoma.
- Bladder Cancer: Developing Drugs and Biologics for Adjuvant Treatment; Final; June 2022, provides recommendations to sponsors regarding the development of drugs and biological products regulated by CDER and CBER for the adjuvant treatment of muscle-invasive bladder cancer.
- Cancer Clinical Trial Eligibility Criteria: Available Therapy in Non-Curative Settings; Final; June 2022, provides recommendations to clinical investigators and sponsors regarding the inclusion of patients who have not received available therapy for their cancer in clinical trials of drugs and biological products for the treatment of cancer in the non-curative setting.
- Real-Time Oncology Review (RTOR); Draft; July 2022, provides recommendations to applicants on the process for submission of selected NDA and BLA with oncology indications for review under the RTOR. FDA's Oncology Center of Excellence (OCE), in collaboration with OOD, commenced the RTOR program in February 2018 to facilitate earlier submission of top-line results and datasets, after database lock, to support an earlier start to the FDA application review.
- Acute Myeloid Leukemia: Developing Drugs and Biological Products for Treatment; Final; October 2022, assists sponsors in the clinical development of drugs and biological products for the treatment of acute myeloid leukemia .
- Cross Labeling Oncology Drugs in Combination Regimens; Final; November 2022, describes FDA's current recommendations about including relevant information in labeling for oncology drugs approved for use in a combination regimen, including important considerations for cross labeling of these drugs.
- Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Guidance for Industry; Draft; April 2022, provides recommendations to sponsors developing medical products on the approach for developing a Race and Ethnicity Diversity Plan to enroll representative numbers

of participants from underrepresented racial and ethnic populations in the United States, such as Black or African American, Hispanic/Latino, Indigenous and Native American, Asian, Native Hawaiian and Other Pacific Islanders, and other persons of color, in clinical trials.

Public Meetings

OOD participated in many ground-breaking public-meetings over the course of the year.

- The Oncologic Drugs Advisory Committee; April 2022, met to discuss the appropriate approach for phosphatidylinositol-3-kinase inhibitors currently under development in patients with hematologic malignancies, and whether randomized data should be required to support a demonstration of substantial evidence of effectiveness, and that the drug is safe for its intended use in the proposed population.
- The 7th Annual Clinical Outcome Assessment in Cancer Clinical Trials Workshop; June 2022, provided a forum for collaborative and productive multidisciplinary discussions to advance understanding of the complex regulatory, health care policy, and scientific issues surrounding the use of patient-reported outcome (PRO) measures in cancer clinical trials. Attendees had the opportunity to attend three sessions on exploring the realities of open-label trials in oncology and use of PROs analysis and interpretation of PRO data from open-label cancer trials; and on efforts to advance PRO to inform tolerability regardless of blinding status in oncology.
- Getting the Dose Right: Optimizing Dose Selection Strategies in Oncology – An FDA-ASCO Virtual Workshop; May 2020, served as a follow-on workshop to the FDA-ASCO Virtual Workshop Defining a Research Agenda to Address Barriers and Solutions to Oral Anticancer Agent Adherence; February 2021. Attendees discussed research and clinical challenges for dose optimization, and highlighted strategies to improve dose optimization for anticancer agents.
- Moving on Equity: OCE Expands Diversity Initiative, a Cancer Moonshot Community Conversation; May 2022, is part of a series of coordinated Cancer Cabinet Community Conversations under President Biden's Cancer Moonshot Initiative. This roundtable discussion focused on the new draft guidance, Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials; April 2022.

Office of Neuroscience

OND's Office of Neuroscience (ON) consists of five divisions:

- Division of Neurology 1 (DN 1)
- Division of Neurology 2 (DN 2)
- Division of Psychiatry (DP)
- Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)
- Division of Pharmacology and Toxicology for Neuroscience (DPT-N)

Notable Drug Approvals

In 2022, ON approved treatments to address unmet medical needs and expanded drug approvals to new indications and patient populations. For example, in March 2022, ON approved Ztalmy (ganaxolone) to treat seizures associated with cyclin-dependent kinase-like 5 deficiency disorder (CDD) in patients two years of age and older. This is the first treatment specifically for CDD and seizures associated with CDD. ON also approved a new indication for Fintepla (fenfluramine), to treat seizures associated with Dravet syndrome in patients ages 2 and older. Dravet syndrome is a life-threatening, rare, and chronic form of epilepsy often characterized by severe and unrelenting seizures despite medical treatment. In September 2022, ON approved FDA approved Relyvrio (sodium phenylbutyrate/taurursodiol) for amyotrophic lateral sclerosis (ALS), creating additional treatment options for this neurodegenerative disease.

Amongst other notable ON approvals were the approval of an expanded indication for Zulresso (brexanolone) to include patients 15 years and older diagnosed with postpartum depression, the approval of an oral form

of Radicava ORS (edaravone) to treat ALS, and the approval of Quviviq (daridorexant) to treat adult patients with insomnia.

This year, ON also approved products that impacted the Department of Defense (DoD) and American military personnel. In February 2022, the FDA approved naloxone hydrochloride autoinjector for use by military personnel and chemical incident responders for emergency treatment of patients 12 years of age and older where the use of high-potency opioids such as fentanyl analogues as a chemical weapon is suspected. August 2022 saw the approval of Midazolam Injection for the treatment of status epilepticus. DoD developed this product with Rafa Laboratories, Ltd.

Guidances and Publications

This past year, ON also contributed to guidances and strategies aimed at combating serious public health issues and rare neurodegenerative diseases.

For example, the guidance Development of Non-Opioid Analgesics for Acute Pain; Draft; February 2022, provides recommendations to companies developing non-opioid analgesics for acute pain lasting up to 30 days. The objective of this guidance is to help address challenges to developing non-addictive medical products to manage pain. The guidance covers considerations for trial designs, eligibility, efficacy endpoints, statistics, and safety considerations in Phase 3 studies.

Additionally, ON advanced the space of rare neurodegenerative diseases by contributing to the Action Plan for Rare Neurodegenerative Diseases including ALS; June 2022. This five-year strategy aims to improve and extend the lives of people living with rare neurodegenerative diseases by advancing the development of safe and effective medical products and facilitating patient access to novel treatments. Specific actions laid out in the strategy include regulatory science initiatives, enhancements to existing programs, and new policy initiatives.

"… by advancing the development of safe and effective medical products and facilitating patient access to novel treatments."

Public Meetings

ON convened meetings of the Peripheral and Central Nervous System Drugs Advisory Committee; March and September 2022, focused on evidence for the effectiveness of sodium phenylbutyrate/taurursodiol (AMX0035) to treat ALS. There is an urgent need for ALS treatments because the disease has no cure, and previously, there were only two products approved in the U.S. to treat the symptoms of ALS. The Advisory Committee members input was important to ON's considerations of the application.

Office of Nonprescription Drugs

The Office of Non-Prescription Drugs (ONPD) consists of two review divisions: The Division of Nonprescription Drugs I and Nonprescription Drugs II. The Immediate office oversees the development, review, and regulation of nonprescription products (marketed under Over-the-counter (OTC) monographs and under NDAs) reviewed in these divisions. OTC drugs play an increasingly vital role in America's health care system.

OTC Monograph Reform

In March 2020, Congress passed the CARES Act which included important statutory provisions that reform and modernize the way OTC monograph drugs are regulated in the United States. It replaced the rulemaking process with an administrative order process to establish, revise, or amend OTC monographs. An OTC monograph details conditions, such as active ingredients, uses (indications), doses, route of administration, labeling, and testing under which an OTC drug is generally recognized as safe and effective (GRASE). OTC monographs cover approximately 800 active ingredients for over 1,400 different uses, authorizing over 100,000 drugs.

Since March 2020, ONPD has been at the center of several monograph reform accomplishments including:

- Annual Forecast for Planned Monograph Activities: each year FDA will post a nonbinding list of OTC monograph issues FDA intends to address in the coming 3 years.
- Sunscreen Proposed Order posted September 24, 2021: FDA issued a proposed order to amend and revise the Deemed Final Order (DFO) for OTC sunscreen drugs that transitions FDA's ongoing consideration of the appropriate requirements for OTC sunscreen drugs marketed without approved applications from the previous rulemaking process to the administrative order process.

Guidances

- OTC Monograph Meetings; Draft; March 2022, specifies procedures and principles for formal meetings with FDA and sponsors or requestors of OTC monograph drugs.
- Electronic Submissions; Draft; September 2022, details the requirements needed to submit OTC Monographs in electronic format to the FDA.
- Assessing OMUFA User Fees; Draft; November 2022, informs manufacturers and stakeholders on the process for submitting OTC Monograph Drug User Fee Program (OMUFA) fees to the FDA, submission deadlines, and fee exceptions.

Office of Specialty Medicine

The Office of Specialty Medicine (OSM) consists of Pharmacy Compounding Review Team and two review divisions:

- Division of Imaging and Radiation Medicine (DIRM)
- Division of Ophthalmology (DO)

Notable Approvals

On March 23, 2022, the Division of Imaging and Radiation Medicine approved Locametz (kit for the preparation of gallium Ga 68 gozetotide injection), a radioactive diagnostic agent for positron emission tomography (PET) of PSMA-positive lesions in men with prostate cancer. Locametz is the first imaging drug to be FDA-approved with a specific indication to select patients for treatment with a therapeutic drug, namely Pluvicto. Pluvicto was approved by the Division of Oncology I on the same day as Locametz and is a radioligand therapeutic agent indicated for the treatment of adult patients with PSMA-positive metastatic castration-resistant prostate cancer who have been treated with androgen receptor pathway inhibition and taxane-based chemotherapy. Locametz and Pluvicto constitute the first FDA-approved pair of diagnostic and therapeutic drugs that target the same molecular marker of prostate cancer, also referred to as a theranostic drug pair.

In August, the Division of Ophthalmology approved Cimerli, a vascular endothelial growth factor inhibitor. It is intended to treat patients with Neovascular (Wet) Age-Related Macular Degeneration, Macular Edema Following Retinal Vein Occlusion, Diabetic Macular Edema, Diabetic Retinopathy, and Myopic Choroidal Neovascularization. Cimerli is the first biological product that is interchangeable with Lucentis (ranibizumab injection)

for all five indications. The reliance of Cimerli on its respective reference product provides both greater treatment access and choice for patients, payors and providers in the U.S. retinal disease community.

In December, DIRM approved an efficacy supplement for Cytalux (pafolocianine) as an adjunct for intraoperative identification of malignant and non-malignant pulmonary lesions in adult patients with known or suspected cancer in the lung. Cytalux is an optical imaging agent previously approved for intraoperative use in patient with ovarian cancer. DIRM also approved Xenoview (xenon Xe 129 hyperpolarized), a hyperpolarized contrast agent indicated for use with Magnetic Resonance Imaging (MRI) to evaluate lung ventilation in patients aged 12 years and older. Xenoview is the first inhaled imaging drug to be approved for use with MRI and is a component of a CDER-led combination product that includes devices used to prepare and deliver the drug to patients.

"Xenoview is the first inhaled imaging drug to be approved for use with MRI and is a component of a CDER-led combination product that includes devices used to prepare and deliver the drug to patients."

Publications

The Pharmacy Compounding Review team in the Office of Specialty Medicine in collaboration with the Office of Compounding Quality and Compliance and the Office of Pharmaceutical Quality evaluated several drug substances proposed to be used in compounding under section 503B of the Food Drug and Cosmetic Act, which led to the FDA's November 22, 2022, publication of a Federal Register notice. This notice identifies two bulk drug substances that FDA has considered and proposes to include on the 503B Bulks List to compound three categories of compounded drug products: arginine hydrochloride (HCl) for oral use, lysine HCl for oral use, and lysine HCl for intravenous use in combination with FDA-approved, single-ingredient arginine HCl for intravenous use. This notice also identifies three bulk drug substances that FDA has considered and proposes not to include on the 503B Bulks List: etomidate, furosemide, and rocuronium bromide.

External Engagement, Public-Private Partnerships, and Public Workshops

The Division of Imaging and Radiation Medicine and the FDA CDRH organized and hosted a workshop, Quantitative Brain Amyloid PET Imaging-Technical Considerations; November 2022, with co-sponsors, the Society of Nuclear Medicine and Molecular Imaging and the Medical Imaging and Technology Alliance. This full day workshop brought together FDA drug and device regulators, academic experts, industry representatives, and patient advocates for discussion of the state of the art of quantitative amyloid PET techniques.

The 2022 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI); June 2022, is a key conference for major academic and industry stakeholders. DIRM led an invited session where seven FDA speakers presented virtually on a variety of important topics regarding imaging drug regulation ranging from best practices in manufacturing and preclinical development to emerging concepts in clinical development of theragnostic drugs.

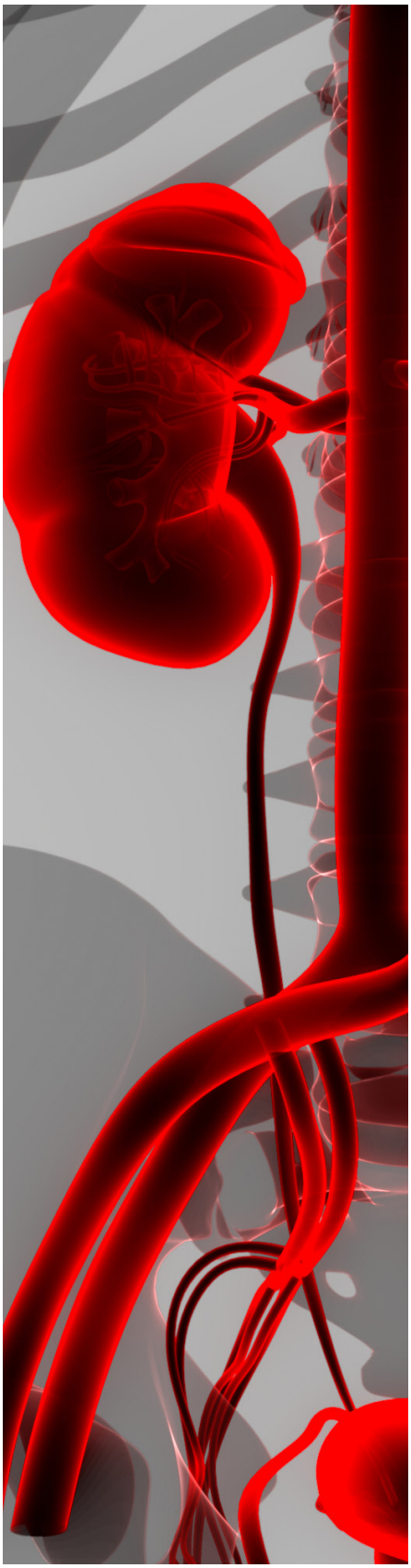
FDA held the Pharmacy Compounding Advisory Committee Meeting; June 2022, where OSM's Pharmacy Compounding Review Team presented four bulk drug substances nominated for inclusion on the 503A Bulks List: ammonium tetrathiomolybdate, enclomiphene citrate, ferric subsulfate, and glutathione, and one other substance, lorcaserin hydrochloride, proposed for addition to the Withdrawn or Removed List.

The Division of Ophthalmology participated in a patient-led listening session in June 2022. Patients and caregivers for pediatric patients shared their experiences living with and managing Stargardt Disease.

Office of Cardiology, Hematology, Endocrinology, and Nephrology

The Office of Cardiology, Hematology, Endocrinology and Nephrology (OCHEN) consists of five review divisions:

- Division of Cardiology and Nephrology (DCN)
- Division of General Endocrinology (DGE)
- Division of Nonmalignant Hematology (DNH)
- Division of Diabetes, Lipid Disorders and Obesity (DDLO)
- Division of Pharm/Tox for Cardiology, Hematology, Endocrinology and Nephrology (DPT-OCHEN)



Notable Drug Approvals

Several NMEs and supplement approval actions within OND's OCHEN in 2022 broke barriers as the first approved treatments for specific diseases and conditions.

For example, the Enjaymo (sutimlimab-jome) injection was approved as the first drug for cold agglutinin disease, a rare form of anemia. Pyrukynd (mitapivat) became the first drug to treat hemolytic anemia in adults with the rare genetic disease, pyruvate kinase deficiency. Terlivaz (terlipressin) injection was approved as the first treatment to improve kidney function in adults with hepatorenal syndrome with rapid reduction in kidney function. In addition, Tzield (teplizumab-mzwv) was approved later in the year as the first drug to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients aged eight years and older with Stage 2 T1D, and is the first approved disease-modifying therapy for T1D.

Other significant OCHEN approvals include Mounjaro (tirzepatide) injection to improve blood glucose control in adults with type 2 diabetes, as an addition to diet and exercise; and Vonjo (pacritinib), as an accelerated approval, to treat adults with intermediate or high-risk myelofibrosis. Vonjo (pacritinib) differs from other myelofibrosis treatments because patients with very low platelet levels can start treatment on the medication.

Regarding supplemental approvals within OCHEN, FDA approved Qsymia (phentermine and topiramate extended-release capsules) for chronic weight management in pediatric patients aged 12 years and older who are obese. With 20% of adolescents considered obese, it is important to have treatment options for this population. FDA also approved a new indication for Jardiance (empagliflozin) for a wider range of heart failure patients. Lastly, FDA approved a new indication for Cotellic (cobimetininb) for rare histiocytic neoplasms.

Guidances and Publications

OCHEN led the development of guidances to facilitate drug safety and spur drug development. For example, the guidance for industry Assessment of Pressor Effects of Drugs; Draft; February 2022, advises sponsors on the premarket assessment of a drug's effect on blood pressure. Because of the risks associated with elevated blood pressure, the effect of a drug on blood pressure is an important consideration in risk assessment and product labeling.

OCHEN staff also co-authored over a dozen peer-review articles relevant to product development, such as the examples below in acute kidney injury, pulmonary hypertension in interstitial lung disease, and pediatrics:

- Optimizing the Design and Analysis of Future AKI [acute kidney injury] Trials; Journal of the American Society of Nephrology; August 2022.
- Clinical significance of pulmonary hypertension in interstitial lung disease: A consensus statement from the Pulmonary Vascular Research Institute's innovative drug development initiative—Group 3 pulmonary hypertension; Pulmonary Circulation; July 2022.
- Innovations in Pediatric Therapeutics Development: Principles for the Use of Bridging Biomarkers in Pediatric Extrapolation; Therapeutic Innovation & Regulatory Science; September 2022.

Conference Participation

OCHEN staff participated in numerous conferences and meetings aimed at fostering drug development. Several OCHEN leaders participated in the FDA-Duke Margolis workshop, Translational Science in Drug Development: Surrogate Endpoints, Biomarkers, and More; May 2022. This workshop focused on best practices and provided cases for successfully bringing forward evidence generated through translational science for regulatory submissions. Stakeholders discussed potential barriers to using translational science to support therapeutic development and strategies to overcome those barriers. Division specific conferences are shown below.

Some examples of conferences with OCHEN division participation are shown below:

- Duchenne Cardiac Consensus Meeting; March 2022, seeking better characterization of this disease.
- Stanford Digital Health Think Tank; March 2022, considering the use of wearable technology to assess activity and electrocardiograms.
- National Institute on Aging workshop, Development of Function Promoting Therapies: Public Health Need, Molecular Targets, and Drug Development; March 2022. This conference recognizes the public

health importance of the development and implementation of effective interventions to overcome or delay age-related muscle dysfunction and functional limitations. DNH participated in the National Human Genome Research Institute Intramural Research Program Project, Democratizing Education for Sickle Cell Disease Gene Therapy; September 2022. Attendees worked to develop high-quality patient educational materials about sickle cell gene therapies.

- Heart Failure Collaboratory Meetings; March 2022, April 2022, June 2022, August 2022, September 2022, and October 2022. The Heart Failure Collaboratory is a public-private partnership addressing myriad issues in development of new drug and device therapy for heart failure.
- DIA (Drug Information Association)/FDA Oligonucleotide-Based Therapeutics Conference; April 2022. The conference brought together leading experts to inform, educate, and share advancements in oligonucleotide-based therapeutic product development.
- Discussion on using continuous glucose monitors in clinical trials at the International Consensus Meeting on Continuous Glucose Monitoring in Clinical Trials; April 2022. The focus of this meeting was to seek consensus on standardization in the collection, analysis, and reporting of Continuous Glucose Monitoring data in clinical trials.
- American College of Cardiology Roundtable; June 2022, discussion of therapies for heart failure with preserved ejection fraction.
- Critical Care Clinical Trialists group; June 2022, addressing issues in critical care product development.
- Barth Syndrome Workshop; July 2022, intended to address barriers to conducting studies in this rare disease.
- Cardiac Safety Research Consortium think tank meeting; September 2022, to discuss centralized Institutional Review Boards.
- American Statistical Association Biopharmaceutical Scientific Working Group Webinar; September 2022. Safety planning for clinical trials and how aggregated safety assessment informs IND safety reporting decisions were amongst the topics discussed.
- Patient-focused drug development meeting September 2022, on cardiac consequences of oncologic therapy.
- International Heart Failure Guidelines Forum; October 2022 and November 2022.
- Joint meeting of the Society of Cardiac Angiography and Imaging and the Cardiac Safety Research Consortium; October 2022, seeking common approaches to development of treatments for cardiogenic shock.

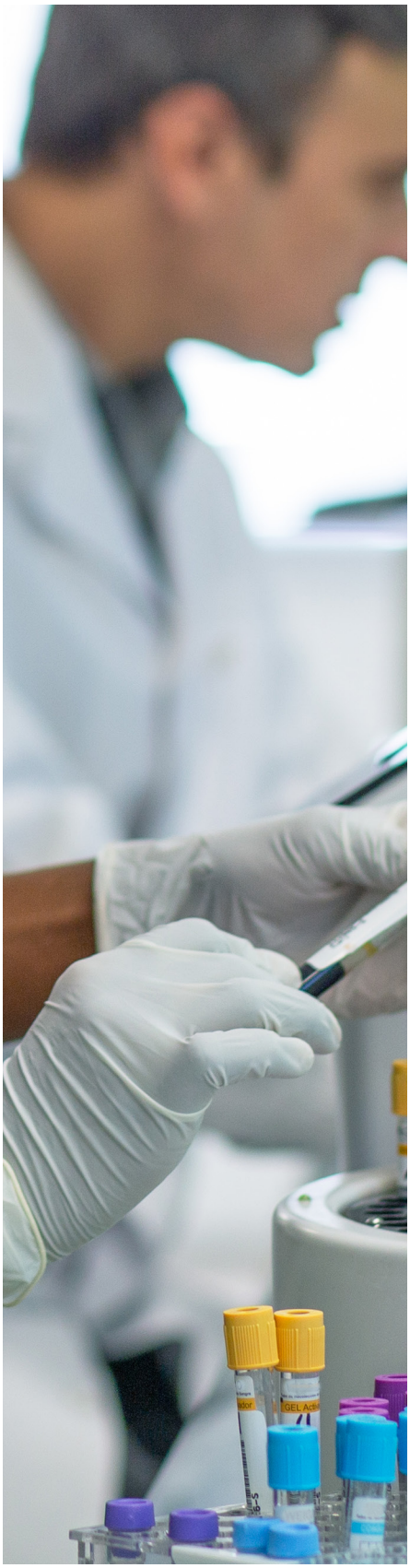
- 2nd Annual Rare Disease and Genetic Kidney Disease Drug Development Summit; October 2022, discussing earlier endpoint development to predict clinical outcomes in shorter clinical trials and the regulatory perspective on endpoint development.
- The director of DPT-CHEN attended the International Conference for Harmonisation (ICH) Biannual Meeting; November 2022, serving as the deputy topic leader on the ICH S1B addendum working group. This working group is focusing on changes to the testing paradigm for carcinogenicity testing of pharmaceuticals and ways to reduce animal testing when appropriate.43rd annual meeting of the American College of Toxicology; November 2022, which brings together scientists from industry, academia, and government to promote exchange of information and perspectives on safety assessment and share new developments related to applied toxicology.
- Patient-Reported Outcome Academic Research Consortium; November 2022, to discuss use of patient-reported outcome tools in heart failure studies.
- Amyloidosis Forum; November 2022.
- Cardiovascular Clinical Trialists Forum and Workshop; December 2022, addressing a variety of issues in medical product development for cardiovascular disease.
- Cardiovascular Clinical Trialists Forum and Workshop; December 2022, addressing Thrombosis Development.
- American Society of Hematology Research Collaborative DATA HUB for Sickle Cell Disease, which involves multiple working committees to develop the framework for using real world data to support applications for sickle cell disease.
- Sickle Cell Federal Interagency Working Group focusing on how to improve care for patients with sickle cell disease.

Office of Immunology and Inflammation

The Office of Immunology and Inflammation (OII) consists of six review divisions:

- Division of Dermatology and Dentistry (DDD)
- Division of Gastroenterology (DG)
- Division of Hepatology and Nutrition (DHN)
- Division of Pulmonology, Allergy and Critical Care (DPACC)
- Division of Rheumatology and Transplant Medicine (DRTM)
- Division of Pharm-Tox for Immunology and Inflammation (DPT-II)

This year OII broke barriers by overseeing the development, review, and regulation of drugs that were the first of their kind.



Notable Drug Approvals

In 2022, OII approved eight groundbreaking treatments for new patient populations:

- Olumiant (baricitinib) added two new uses: 1) treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO, the first immunosuppressant to be approved for this condition, and 2) treatment of adults with severe alopecia areata, the first FDA-approved treatment for this chronic inflammatory disorder.
- Cibinqo (abrocitinib) is an oral Janus Kinase inhibitor for treating adults with refractory, moderate-to-severe atopic dermatitis not adequately controlled with other systemic drug products. It is the first new Janus Kinase inhibitor to be approved since FDA required new safety labeling changes for the drug class.
- Opzelura (ruxolitinib) cream is a topical chronic treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older. It is the first FDA-approved treatment for this autoimmune disorder.
- Zoryve (roflumilast) cream 0.3% is a topical treatment of plaque psoriasis, including intertriginous areas, for patients 12 years of age and older. It is a new, non-steroidal option for the treatment of psoriasis.
- Spevigo (spesolimab-sbzo) is an interleukin-36 receptor antagonist indicated for the treatment of flares in adult patients with generalized pustular psoriasis. It is the first FDA-approved treatment for this serious, life-threatening autoimmune disorder.

- Sotyktu (deucravacitinib) is a tyrosine kinase 2 (TYK2) inhibitor indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. This is the first ever FDA approval of a tyrosine kinase 2 inhibitor.
- Skyrizi (risankizumab-rzaa), for the treatment of moderately to severely active Crohn's disease (CD) in adults, received approval as a 180 mg/1.2 mL prefilled cartridge. This presentation adds to the previously approved 360 mg/2.4 mL prefilled cartridge presentation, allowing patients to utilize a lower effective maintenance dose in managing their CD.
- Dupixent (dupilumab) added two new uses: 1) treatment of patients 12 years and older with eosinophilic esophagitis, and 2) treatment of adult patients with prurigo nodularis; this is the first FDA-approved treatment for these serious conditions.
- Nexobrid (anacaulase-bcdb), approved for eschar removal in adults with deep partial thickness and/or full thickness thermal burns. This is a novel proteolytic enzyme product indicated for this serious condition.
- Actemra (tocilizumab), approved for treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation or ECMO. This is the second FDA-approved immunosuppressant for this condition.

Guidances and Publications

OND's Division of Gastroenterology authored three draft guidance documents:

- Crohn's Disease: Developing Drugs for Treatment; Draft; April 2022, addresses FDA's current thinking about necessary attributes of clinical trials for developing drugs for the treatment of Crohn's disease in adults, including recommendations for trial population, trial design, and efficacy and safety considerations.
- Ulcerative Colitis: Developing Drugs for Treatment; Draft; April 2022, addresses FDA's thinking about the necessary attributes of clinical trials for drugs developed for treating UC, including trial population, trial designs, efficacy considerations, and safety assessments.
- Celiac Disease: Developing Drugs for Adjunctive Treatment to a Gluten-Free Diet; Draft; April 2022, addresses FDA's recommendations regarding clinical trials for drugs developed for the treatment of celiac disease as an adjunct to a gluten-free diet in adults.

Divisions within the OII published groundbreaking research throughout the year:

- Measuring What Matters to Patients in Dermatology – Drug Development - A Regulatory Perspective; Dermatology Clinics; July

2022, highlights the importance of a patient's voice in the field, as treatment is determined based on the patient's experience.

- Dermatology Drugs for Children - U.S. Food and Drug Administration Perspective; Dermatology Clinics; July 2022, provides an overview of significant historical regulations affecting drug development in children, FDA regulatory authorities responsible for pediatric dermatology drugs, and recent trends in pediatric dermatology drug development.

External Engagement, Public-Private Partnerships, and Public Workshops

Divisions within OII assisted in workshop development throughout the year:

- The FDA Public workshop, Wound Healing; April 2022, discussed endpoints for clinical trials and gathered perspectives from patients living with chronic wounds.
- The FDA Public Workshop on the Role of Phytosterols in Patients with PNALD/IFALD; May 2022, discussed the evidence supporting phytosterols as liver toxins when present in intravenous peripheral nutrition products.
- The American College of Rheumatology/FDA Summit Meeting; May 2022, discussed various topics, notably the assessment of long-term safety of drugs intended to treat rheumatoid arthritis and psoriatic arthritis.
- FDA Workshop: Increasing the Efficiency of Biosimilar Development Programs; September 2022, focused on comparative clinical studies associated with biosimilar development programs and discussed possible innovative ideas that have the potential to streamline and improve the efficiency of biosimilar development.
- The American Gastroenterology Association Roundtable; September 2022, discussed challenges conducting clinical trials in inflammatory bowel disease.

Office of Rare Diseases, Pediatrics, Urologic, and Reproductive Medicine

The Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (ORPURM) consists of four review divisions:

- Division of Pediatric and Maternal Health (DPMH)
- Division of Rare Diseases and Medical Genetics (DRDMG)
- Division of Urology, Obstetrics and Gynecology (DUOG)
- Division of Pharmacology-Toxicology for Rare Diseases, Pediatrics, Urologic and Reproductive Medicine/Specialty Medicine (DPT-RPURM/SM)

Notable Drug Approvals

In August, the FDA approved Xenpozyme (Olipudase alfa), a hydrolytic lysosomal sphingomyelin-specific enzyme indicated for treating pediatric and adult patients with acid sphingomyelinase deficiency (ASMD), a rare genetic disease that causes premature death. Xenpozyme is the first approved medication to treat symptoms unrelated to the central nervous system in patients with ASMD.

In August, DUOG approved a new indication for Myfembree (relugolix, estradiol, and norethindrone acetate), an oral, once-daily product containing gonadotropin releasing hormone receptor agonist with hormonal addback, for the management of moderate to severe endometriosis-associated pain. Endometriosis is a chronic, debilitating disease that can significantly affect a woman's quality of life due to severe pain, infertility, and other associated

symptoms. Myfembree was first approved in 2021 for the management of heavy menstrual bleeding associated with uterine fibroids.

Workshops and Webinars

Divisions within the office attended and hosted workshops discussing rare diseases, pediatrics, women's health, and bridging the gap between academic investigation and the regulatory aspects of drug development.

The FDA and the Duke Margolis Center for Health Policy hosted a virtual public workshop Endpoint Considerations to Facilitate Drug Development for Niemann-Pick Type C (NPC); January 2022. This workshop focused on endpoint considerations in NPC, a rare genetic disease with no approved therapies in the United States. The workshop brought stakeholders together, including patients, patient advocates, academics, industry representatives, and other federal partners, to discuss clinical endpoints relevant to NPC clinical trials and innovative strategies to support developing therapies for patients with NPC. FDA and the Duke Margolis Center for Health Policy hosted a follow-up webinar, Endpoint Considerations to Facilitate Drug Development for NPC: Key Themes and Future Directions from the January 2022 Public Workshop; August 2022, that focused on key themes and future directions from the January 2022 public workshop.

"Advancing this field requires identifying key knowledge gaps, barriers to data collection, and potential innovative solutions to improve data generation and analysis."

In collaboration with the University of Maryland CERSI, the FDA hosted a two-day virtual public workshop entitled Pharmacokinetic Evaluation in Pregnancy; May 2022. The workshop included participants from DPMH and several other divisions and offices who engaged with stakeholders to assess available science and data gaps to advance the conduct of pharmacokinetic studies in pregnant persons. Further pharmacologic research and collection of pharmacokinetic data during pregnancy are needed to ensure that the appropriate dosing information is available for pregnant persons. Advancing this field requires identifying key knowledge gaps, barriers to data collection, and potential innovative solutions to improve data generation and analysis.

The National Academies of Sciences, Medicine, and Engineering convened a hybrid (in-person/virtual) public workshop entitled Inclusion of Pregnant and Lactating Persons in Clinical Trials; June 2022, to discuss the current landscape of evidence for medications used by pregnant and lactating persons and the challenges and opportunities for including these populations in clinical trials. Representatives from DPMH and DUOG participated in the workshop planning committee and served as session moderators and presenters.

FDA's Office of Women's Health (OWH) and Johns Hopkins -CERSI hosted a public webinar, Leveraging Real-World Data to Study Medication Use in Pregnancy and Lactation; May 2022. This three-session virtual workshop highlighted the potential role of real-world data in addressing gaps in knowledge, the opportunities, and challenges of collecting real-world data,

and current regulatory perspectives on the collection and potential use of real-world data. DPMH and DUOG participated in this webinar.

DPMH participated in two public webinars hosted by OWH: Pregnancy and Lactation Medication Information for the Healthcare Provider; May 2022, and Engaging Providers to Address Knowledge Gaps on Medication Use in Pregnancy and Lactation; October 2022. The first webinar helped learners examine how prescription drug labeling informs prescribing in pregnancy and lactation. The second webinar raised awareness of how healthcare providers can refer pregnant and lactating patients to participate in pregnancy registries and other studies, alongside other ways to get involved in research.

CDER's Rare Diseases Team and the National Institutes of Health's National Center for Advancing Translational Sciences developed and hosted Regulatory Fitness in Rare Disease Clinical Trials Workshop; May 2022, to inform external stakeholders of regulatory considerations in rare disease clinical trials. This workshop focused on academic investigators and those looking to learn how to bridge the gap between academic investigation and the regulatory aspects of rare disease drug development.

Publications

Divisions within the office published groundbreaking research throughout the year:

Scientific, Ethical and Legal Considerations for the Inclusion of Pregnant People in Clinical Trials; American Journal of Obstetrics and Gynecology; August 2022, summarizes the scientific, ethical, and legal considerations governing research conducted during pregnancy, as discussed during a recent subject matter expert convening held by the Duke-Margolis Center for Health Policy and the FDA on the topic.

DPMH and the Office of Pediatric Therapeutics co-authored The FDA Report to Congress on Best Pharmaceuticals for Children Act and Pediatric Research Equity Act. This report provides an assessment of the implementation of Best Pharmaceuticals for Children (BPCA) and the Pediatric Research Equity Act (PREA) including the impact of those statutes, highlights other successes stemming from these two statutes, and offers suggestions for advancing pediatric drug development by ensuring that the underlying objectives of BPCA and PREA are effectively and efficiently implemented. In addition to this report, DPMH staff authored numerous publications in peer-reviewed journals in 2022.

In the publication Accidental Flibanserin Ingestion in Children Causing Acute Respiratory and Central Nervous System Depression; Obstetrics & Gynecology; April 2022, ORPURM's staff collaborated with the Office of Surveillance and Epidemiology/ Division of Pharmacovigilance staff to raise awareness about

the potential risks of life-threatening injuries in toddlers who accidentally ingested their mothers' medications. Addyi (flibanserin) was approved in 2015 for the treatment of acquired, generalized hypoactive sexual desire disorder in premenopausal women.

Building Blocks for the Long-acting and Permanent Contraceptives Coordinated Registry Networks; BMJ Surgery, Interventions, & Health Technologies; November 2022, is part of a multistakeholder expert group consisting of representatives from professional societies, FDA, academia, industry and the patient community under the Women's Health Technology Coordinated Registry Network. The manuscript outlined a consensus-based core set of data elements in studies of contraceptives that influence patient and provider decisions about treatments and include important outcomes related to safety and effectiveness of these products.

Policy and Guidance Publications

In 2022, DPMH, in collaboration with other OND divisions, published two critical guidance documents including:

- ICH E11A Pediatric Extrapolation Guidance; Draft; August 2022.
- Measuring Growth and Evaluating Pubertal Development in Pediatric Clinical Trials; Draft; October 2022.

Presentations

DPMH participated in three separate Drug Information Association meetings in January, March and June's DIA Annual Global Meeting. This meeting brings industry, regulators, academics, and patients together to co-create, problem-solve, and discuss global and local challenges facing professionals in the life sciences community. DPMH spoke in the session entitled, "Post Approval Safety Studies: Approaches to Assessing Medication Exposure and Potential Safety Risks During Pregnancy." DPMH also participated in an interactive session with experts from the European Medicines Agency and FDA to address questions from their collaborative efforts in specific areas, including regulatory and scientific challenges and lessons learned in a COVID-19 environment. In addition to these presentations at DIA, DPMH was invited to give over 20 presentations at national and international meetings in 2022.

DPT-RPURM/SM participated in the Gastrointestinal Acute Radiation Syndrome Workshop; August 2002. The workshop was developed by Radiation and Nuclear Countermeasures Program, National Institute of Allergy and Infectious Disease, National Institutes of Health (NIH); Biomedical Advanced Research and Development Authority, United States Department of Health and Human Services (HHS); and FDA's CDER and CDRH centers. This meeting presented an overview of academic and

U.S. government efforts to expand scientific research to ensure medical preparedness in the wake of a radiation public health emergency with the development of medical counter-measures. DPT-RPURM/SM presented in the session on Regulatory Considerations for Gastrointestinal Acute Radiation Syndrome Product Development. DPT-RPURM/SM spoke at "Interpretation of DART in Regulatory Contexts and Frameworks"; HESI Developmental and Reproductive Toxicity (DART) Workshop; October 2022. The talk focused on the interpretation of nonclinical DART data to assess whether drugs under development may be safe for use in human pregnancy.

DPT-RPURM/SM presented at the Korean American Professional Association in Life Sciences 6th annual conference in November 2022. The presentation discussed nonclinical testing recommendations for rare disease drug development from a regulatory perspective based on a conducting nonclinical review for DRDMG. This talk helped to facilitate collaborative learning experiences among attendees and insight regarding the FDA's drug review processes.

Programs

CDER launched the Accelerating Rare disease Cures (ARC) Program to provide strategic overview and coordination of CDER's rare disease activities. CDER's Rare Diseases Team manages the program, and ARC's leadership comprises those across CDER's Office of the Center Director, Office of New Drugs, and the Office of Translational Sciences.

Regulatory Science Research

DPMH's regulatory science research program continues to advance and inform regulatory decision-making and policy. DPMH's comprehensive research portfolio addresses regulatory issues impacting drug development for pediatric patients as well as pregnant and lactating persons.

In 2022, DPMH established the first Regulatory Pharmaceutical Fellowship in OND. The program is a two-year regulatory fellowship in collaboration with Rutgers University and Sanofi, designed to expose postdoctoral scholars to drug development and regulatory science through:

- Eight months in a clinical rotation experience at Rutgers.
- Eight months in regulatory affairs and strategy at Sanofi.
- Eight months in pediatric and maternal health regulatory science in DPMH.

The first Regulatory Pharmaceutical fellow has been selected and is expected to onboard in July 2023. The fellow will have the unique opportunity to work on a regulatory science project as part of the comprehensive training program.

DPMH also hosted its second fellow under the formal FDA/Children's National Hospital Collaboration. Through an Intergovernmental Personnel

Act assignment that was coordinated through ORPURM, the second physician began the program in January 2022 and is completing a 12-month fellowship in December 2022. This innovative program provides practical training in regulatory science to academic pediatricians so that clinical therapeutics research in children can be conducted more efficiently, and ultimately more successfully. The fellow conducted research on the natural history of IgA Nephropathy in pediatric patients to determine similarities between adult and pediatric patients, assessing the potential for extrapolation of adult data to children.

In 2022, DPMH conducted over 13 research projects ranging from an analysis of failure in pediatric trials to human data in the Pregnancy and Lactation Labeling Rule (PLLR). DPMH's robust training program offered summer internship opportunities to eight undergraduate and graduate scholars in 2022. Participants had an opportunity to gain research experience on a variety of regulatory research projects related to pediatric and maternal health. DPMH reviewers engaged with the participants and served as expert mentors to examine questions of interest related to the research projects. All participants presented their research projects at the OND ORISE Summer Fellow Research Presentation Day in August. Four of the participants continue to engage in research projects as part-time or full-time ORISE fellows. DPMH had two ORISE fellows who completed a research project and presentation at the OND ORISE Summer fellow Research Presentation Day on Analysis of Human Data in PLLR converted labeling and Pregnancy and lactation post-market reviews issued 2021-May 2022.

In October 2022, DPMH onboarded its third ORISE fellow to continue the ongoing research project "Antiretrovirals in Pregnancy: Physiologically-Based Pharmacokinetic Modeling," in collaboration with the Office of Clinical Pharmacology, Division of Antivirals, and the NIH-funded International Maternal Pediatric Adolescent AIDS Clinical Trial network P1026s clinical trial investigators.

DPMH provides subject matter expertise for the following ongoing extramural research projects in collaboration 1) with OWH and the Johns Hopkins University CERSI on Assessing Real-World Use of Pharmaceuticals Among Pregnant and Lactating Women, and 2) with OWH, DUOG, and the Yale-Mayo CERSI to Evaluate the Application of Machine Learning Algorithms to the Management of Postpartum Hemorrhage.

Additional ORPURM Publications

In addition to the publications noted above, DPMH authored eight important publications in 2022:

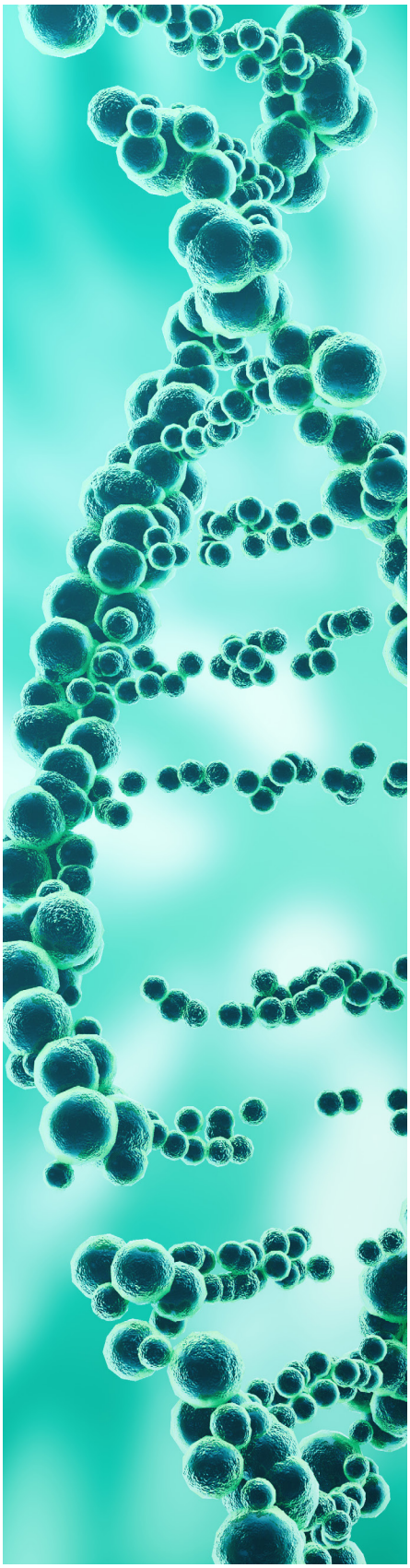
- A Review of Pregnancy and Lactation Postmarketing Studies Required by the FDA; Pharmacoepidemiology and Drug Safety; November 2022.
- Considerations and Challenges in the Remdesivir COVID-19 Pediatric Development Program; Journal of Clinical Pharmacology; September 2022.
- Innovations in Pediatric Therapeutics Development: Principles for the Use of Bridging Biomarkers in Pediatric Extrapolation; Therapeutic Innovation & Regulatory Science; September 2022.
- Pediatric Efficacy Extrapolation in Drug Development Submitted to the U.S. Food and Drug Administration 2015-2020; Journal of Clinical Pharmacology; September 2022.
- Surveillance of ARV safety in pregnancy and breastfeeding: towards a new framework; Journal of the International AIDS Society; July 2022.
- Risk of fetal or neonatal death or neonatal intensive care unit admission associated with gadolinium magnetic resonance imaging exposure during pregnancy; American Journal of Obstetrics and Gynecology; October 2022.
- Exploring the knowledge gaps in infant drug exposure from human milk: A clinical pharmacology perspective; Journal of Clinical Pharmacology; November 2022.

Additional DPMH Presentations

- DPMH presented at the ICH Health Canada Public Meeting Webinar; May 2022.
- DPMH presented at the World Health Organization's Pediatric Regulator's Network meeting; May 2022.
- DPMH presented on the history of statins and safety in pregnancy at the annual joint meeting of the Society for Birth Defects Research and Prevention and the Organization of Teratology Information Specialists; June 2022.
- DPMH participated in a symposium on Post-authorization Regulatory Strategies to Evaluate Drug Safety in Pregnancy and a symposium on Meeting the Needs for Research on Drug Safety During Lactation at the annual meeting of the International Society for Pharmacoepidemiology; August 2022.

- DPMH provided the keynote address for the New York Academy of Sciences Ethical Considerations in Research for Pediatric Populations; September 2022.
- DPMH spoke at the American Course on Drug Development and Regulatory Sciences on U.S. FDA Pediatric Development Requirements: FDARA and Other Updates; September 2022.
- DPMH presented on "Engaging Providers to Advance Research on the Safety of Medications used during Pregnancy and Lactation" at the U.S. Surgeon General's Maternal Morbidity and Mortality Webinar; September 2022.
- DPMH participated in the BioHealth Capital Regional Annual Forum 2022 on a panel titled, "The Role of the U.S. Food and Drug Administration in Supporting Innovations in New Drugs and Devices"; September 2022.
- DPMH gave a Congenital Heart Disease lecture at Howard University Medical School; October 2022.
- DPMH and DRDMG participated in the New Horizons in Pediatric Drug Development meeting; October 2022 in a session on pediatric extrapolation, a session on Clinical Trials in Pregnancy, and a session on rare diseases.
- DPMH presented at the Better Medicines for Children Pre-Conference Workshop on Pediatric Extrapolation; October 2022.
- DPMH spoke about safety considerations in pediatric antibacterial drug development at the REVIVE Global Antibiotic Research and Development Partnership Webinar; November 2022.
- DPMH presented at the Multi-regional Clinical Trials Center Meeting: Access to Medicines for Children: Using Pediatric Extrapolation in Regulatory and HTA Decision-Making; November 2022.
- DPMH spoke to the Ministry of Food and Drug Safety in the Republic of Korea regarding ICHE11A; November 2022.
- DPMH presented at the World Health Organization Global Accelerator for Pediatric Formulations Meeting; November 2022.
- DPMH provided the keynote presentation at the Annual Eli Lilly Pediatric Symposium; November 2022. The theme of the symposium was accelerating pediatric drug development.
- DPMH presented at the Ethical Considerations in Research for Pediatric Population Workshop on the future of pediatric research; September 2022.

- DPMH presented at the American Society of Pediatric Nephrology Therapeutics and Devices Committee; November 2022 regarding the FDA approval process.
- DPMH presented at the FDA Clinical Investigator Training Course; December 2022.
- DPMH participated in the BPCA Annual Stakeholder Meeting; December 2022.



Office of Therapeutic Biologics and Biosimilars

In 2022, the Office of Therapeutic Biologics and Biosimilars (OTBB) broke barriers through its coordination with and support of biosimilar and interchangeable product activities in the CDER.

Notable Advances in Biosimilar and Interchangeable Product Development and Approval

Biosimilar and interchangeable product development and approval further strengthened in 2022 with seven approvals for a total of 40 approved biosimilars in the U.S. Approvals included including two interchangeable biosimilars: Rezvoglar (insulin glargine-aglr) which joined Semglee (insulin glargine-yfgn) as another interchangeable insulin glargine product in November 2022, and Cimerli (ranibizumab-eqrn), which was approved as the first interchangeable to Lucentis (ranibizumab) in August 2022. Additional approvals in 2022 included the fifth and sixth pegfilgrastim biosimilars, the third and fourth bevacizumab biosimilars, the third filgrastim biosimilar, and the eighth adalimumab biosimilar.

These approvals demonstrate continued growth in the biosimilar and interchangeable product development program and marketplace, providing additional treatment options for patients, which can help increase access for patients and potentially lower healthcare costs.

Notable Education and Public Engagement

OTBB helped support three public meetings and led one public meeting related to the Biosimilar User Fee Act (BsUFA) and the Biosimilar Product Development program. These included the BsUFA II Final Public Meeting; March 2022, and a related "Best Practices in Communication" meeting with industry stakeholders in May 2022. In April 2022, OTBB supported the Maryland-CERSI, and the Office of Clinical Pharmacology in planning for and conducting the workshop, Biosimilars: A Decade of Experience and Future Directions—Strategies for Improving Biosimilar Adoption and the Potential

Role of Clinical Pharmacology; April 2022. The presentations highlighted the successes, challenges, and opportunities for use of biosimilars in the clinic, strategies to improve biosimilar adoption, and the potential role of clinical pharmacology. OTBB led the planning and conduct of a public workshop, Increasing the Efficiency of Biosimilar Development Programs; September 2022. This workshop focused on innovative ideas for increasing the efficiency of comparative clinical studies associated with biosimilar development programs to reduce the costs and duration of comparative clinical studies, which can be a barrier to biosimilar development.

OTBB partnered with several important external stakeholders to reach priority audiences and deliver biosimilar and interchangeable product education in order to facilitate acceptance and uptake. One such partnership with The Council of State Governments led to an innovation classroom session, What is a Biosimilar?; May 2022. This session provided state leaders with information pertaining to biosimilars and how they can transform healthcare systems in the coming years. The Biosimilars Forum also hosted multiple stakeholder events that OTBB staff participated in, including Biosimilars 101 An Educational Webinar on Biosimilars; May 2022; and an Educational Webinar for the American Academy of Ophthalmology in June 2022. These events were comprehensive educational programs providing resources, information, and connections to interested parties throughout the United States. Additionally, OTBB staff provided education to the National Council for Prescription Drug Programs in August 2022.

In April 2022, OTBB began participating in collaboration meetings between the FDA, the Centers for Medicare & Medicaid Services (CMS), the Health Resource and Services Administration (HRSA), and the Agency for Healthcare Research and Quality in providing biosimilar education for their stakeholders and staff. Their outreach reached over 7.5 million CMS subscribers, including over 200 associations that represent all state hospital associations and medical societies and minority and rural health providers, and all 1400 HRSA funded health centers and their primary care associations and national training and technical assistance partners. They can promote additional resources as they become available.

Another successful collaboration was FDA's work with the United States Pharmacopeia (USP). FDA participated in several meetings with USP and their Biologics Sector and developed a joint education resource about biosimilars and quality that both FDA and USP distributed to multiple audiences.

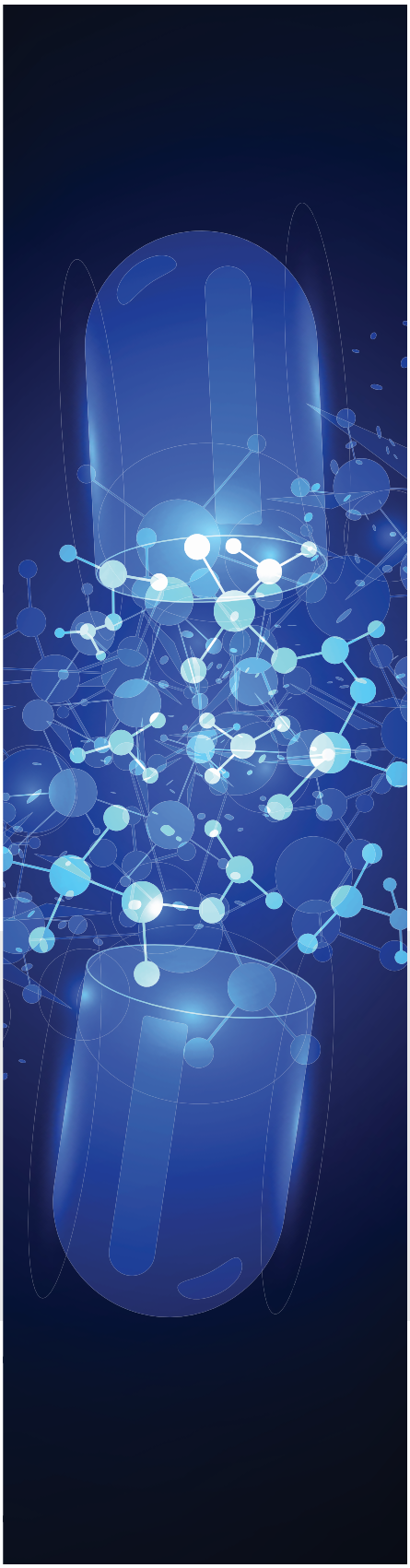
OTBB also contracted with Medscape to create and publish a suite of four Continuing Education materials to enhance understanding of biosimilars for healthcare providers, including doctors, pharmacists, and nurses. The first course went live in August 2022 and has reached almost 22,000 healthcare professional learners, including over 1700 physicians. We are excited about the potential for our courses to reach even more providers.

BsUFA III Preparation

Throughout the year, OTBB led multiple working groups to prepare to implement changes associated with BsUFA III, including establishing procedures for the categorization and review of the newly established BsUFA III supplement categories, and meeting management changes. Additionally, OTBB worked with CDER to implement a BsUFA Regulatory Science Pilot, including an initial BsUFA Regulatory Science Funding Opportunity Announcement; March 2022, and selection of five initial projects (Biosimilars | Science and Research | FDA) to enhance biosimilar and interchangeable biological product development and regulatory science.

OND Future Outlook

The OND Annual Report for 2022 reflects the wide-ranging efforts of the organization in supporting IND drug development, conducting extensive application reviews leading to important drug approvals, advancing policy through workshops and new guidances, and continuing to assure careful post-approval drug assessments. As a dynamic organization, 2022 also saw many new staff joining OND with a wide range of experience and disciplines—including clinicians, toxicologists, social scientists, clinical analysts, regulatory project managers, among many others—joining OND. Our organization is ready for the challenges that 2023 will bring.



Acronyms and Key Terms

Acronym	Definition
ALS	amyotrophic lateral sclerosis
ARC	Accelerating Rare disease Cures
ASMD	acid sphingomyelinase deficiency
BLA	Biologics License Applications
BPCA	Best Pharmaceuticals for Children
BsUFA	Biosimilar User Fee Act
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDD	cyclin-dependent kinase-like 5 Deficiency Disorder
CDRH	Center for Devices and Radiological Health
CERSI	Center of Excellence in Regulatory Science and Innovation
CMS	Centers for Medicare & Medicaid Services

Acronym	Definition
COA	clinical outcome assessment
CT	computer tomography
DAAP	Division of Anesthesiology, Addiction Medicine, and Pain Medicine
DAI	Division of Anti-Infectives
DART	Developmental and Reproductive Toxicity
DAV	Division of Antivirals
DCN	Division of Cardiology and Nephrology
DCOA	Division of Clinical Outcome Assessments
DDD	Division of Dermatology and Dentistry
DDLO	Division of Diabetes, Lipid Disorders, and Obesity
DDT	drug development tool
DG	Division of Gastroenterology
DHN	Division of Hepatology and Nutrition
DHT	Digital Health Technology

Acronyms and Key Terms (continued)

Acronym	Definition
DIA	Drug Information Association
DIRM	Division of Imaging and Radiation Medicine
DO	Division of Ophthalmology
DO I	Division of Oncology I
DO II	Division of Oncology II
DO III	Division of Oncology III
DoD	Department of Defense
DPACC	Division of Pulmonology, Allergy and Critical Care
DPMH	Division of Pediatrics and Maternal Health
DPT-II	Division of Pharm-Tox for Immunology and Inflammation
DRDMG	Division of Rare Diseases and Medical Genetics
DRTM	Division of Rheumatology and Transplant Medicine
DUOG	Division of Urology, Obstetrics, and Gynecology

Acronym	Definition
FDA	U.S. Food and Drug Administration
HBCU	Historically Black Colleges and Universities
HCl	hydrochloride
HHS	United States Department of Health and Human Services
HIV	Human Immunodeficiency Virus
HRSA	Health Resource and Services Administration
ICH	International Conference for Harmonisation
IND	Investigational New Drug Application
ISTAND	Innovative Science and Technology Approaches for New Drugs
LOI	Letter of Intent
NDA	New Drug Application
NIH	National Institutes of Health
NME	New Molecular Entity
NPC	Niemann-Pick Type C

Acronyms and Key Terms (continued)

Acronym	Definition
OCE	Oncology Center of Excellence
OCHEN	Office of Cardiology, Hematology, Endocrinology, and Nephrology
ODES	Office of Drug Evaluation Sciences
OID	Office of Infectious Diseases
OII	Office of Immunology and Inflammation
ON	Office of Neuroscience
OND	Office of New Drugs
OND-EMR	Office of New Drugs Extramural Research
OND-RP	OND Research Program
ONPD	Office of Nonprescription Drugs
OOD	Office of Oncologic Diseases
ORISE	Oak Ridge Institute for Science and Education
ORPURM	Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine
OSE	Office of Surveillance and Epidemiology

Acronym	Definition
OSM	Office of Specialty Medicine
OSP	Office of Strategic Programs
OTBB	Office of Therapeutic Biologics and Biosimilars
OTC	Over-the counter
OWH	Office of Women's Health
PET	positron emission tomography
PLLR	Pregnancy and Lactation Labeling Rule
PREA	Pediatric Research Equity Act
PRO	patient-reported outcome
PSMA	prostate-specific membrane antigen
RTOR	Real-Time Oncology Review
T1D	Type 1 Diabetes
USP	United States Pharmacopeia
uUTI	uncomplicated urinary tract infections

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