U.S. FOOD & DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

Office of Translational Sciences

2023 Annual Report

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From the Director

Welcome to the 2023 Annual Report for the Office of Translational Sciences (OTS). This report highlights some of the office's achievements by its core activities in the areas of drug regulatory review; inspections; science and research; advancing tools, technologies, and innovation; administrative operations; and outreach and communication efforts. These distinct activities are performed by a multidisciplinary team of collaborative and highly qualified professionals who are housed in OTS's five suboffices and the Immediate Office. These activities include:

- Promoting scientific collaboration and innovation in drug regulatory review across the Center for Drug Evaluation and Research (CDER).
- Assuring the validity of clinical trial design and analysis in regulatory decision-making.
- Developing and applying quantitative and statistical approaches to decision-making in the regulatory review process.
- Overseeing bioavailability/bioequivalence and nonclinical inspections to help ensure that safe and effective new and generic drugs are available.
- Aligning the research at CDER with the Center's goals.
- Facilitating the establishment of technology transfer agreements for collaboration with the broader scientific community.
- Maintaining knowledge management databases for improvements in the regulatory review process.

The pages that follow highlight some of our important efforts in 2023. We include hyperlinks, where possible, to encourage further reading. As evidenced by the breadth of accomplishments shared in this report, the professionals at OTS work together in diverse, multidisciplinary teams to help drive advancements in human health through scientific and regulatory innovation.

ShaAvhrée Buckman-Garner MD, PhD
Director

Core Functions of OTS

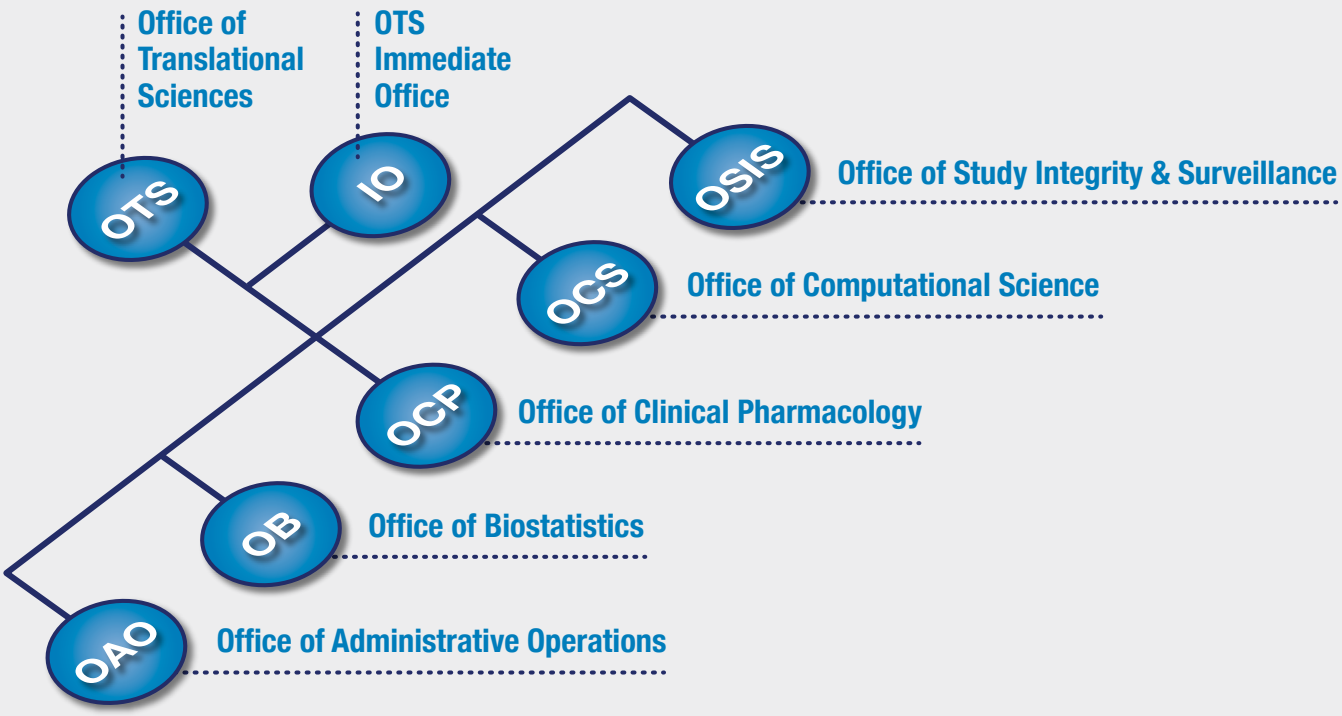
The Office of Translational Sciences (OTS) supports the mission of the U.S. Food and Drug Administration (FDA) through a variety of efforts that include contributing directly to drug evaluation and supporting the advancement of science by facilitating the conduct of research throughout the medical product life cycle. We perform core regulatory review efforts and applied regulatory research, facilitate scientific collaborations, and manage intramural and extramural research programs. We engage directly with government and nongovernment entities to develop methods, approaches, tools, and standards to streamline drug development. In addition, OTS helps other offices in the Center for Drug Evaluation and Research (CDER) develop collaborations with non-FDA researchers to stimulate innovation in the development, manufacture, and safe use of drugs.

OTS is guided by its vision, mission, and core values:

We empower a diverse, collaborative, and high performing workforce to champion innovation and advance global human drug development.

Driving advancements in human health through scientific and regulatory innovation.

Accountability
Civility
Collaboration
Communication
Creativity & Innovation
Leadership



OTS Organizational Chart

OAO provides internal customer service support to enable the OTS scientific, medical, and technical staff to focus on our mission with fewer administrative burdens.

OB plays a central role in promoting innovative, science-based, quantitative decision-making throughout the drug development life cycle. To support CDER's mission, OB provides statistical leadership, expertise, and advice to ensure that safe and effective drugs are available to the American people.

OCP advances development of innovative new medicines by applying state-of-the-art regulatory science and clinical pharmacology principles. We promote therapeutic optimization and individualization through best practices in research, policy development, and drug evaluation throughout the product life cycle.[1]

OCS provides CDER reviewers with innovative, reliable solutions to improve and strengthen the scientific review process by integrating data, tools, and training.

OSIS ensures that data supporting regulatory decisions are reliable by conducting and directing inspections of bioavailability/bioequivalence and nonclinical good laboratory practice studies submitted to FDA.

The IO supports five suboffices in OTS and engages in activities that focus on business transformation strategy; data analytics and technology assistance; guidance, policy, and communications; health information technology; knowledge management; strategic partnerships and technology transfer; science and research oversight; scientific collaborations; and training and career development.

[1] Learn more about OCP through its annual report and the annual report of its Division of Applied Regulatory Science.

OTS Senior Leadership Team

ShaAvhrée Buckman-Garner
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Director

Mitra Ahadpour
MD, DABAM
Principal Deputy Director

Raya McCree
Director,
OAO

Malcolm Dennis
MA
Deputy Director,
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Sylva Collins
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Dionne Price
MS, PhD
Deputy Director,
OB

In Memoriam

Issam Zineh
PharmD, MPH, FCCP
Director, OCP

Shiew-Mei Huang
PhD
Deputy Director,
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Brian Folian
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Chekesha Clingman-Henry
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Deputy Director for Science & Associate Director for Strategic Partnerships

Mary Doi
MD, MS
Associate Director for Knowledge Management

Elizabeth Ford
RN
Associate Director for Regulatory Affairs

Nisha Bruce
Special Assistant for Strategic Innovation

2023 Achievements

Substance Use Disorders

OTS continues to address the substance use disorder crisis and foster development of evidence-based treatments through its efforts in regulatory science research and collaboration. Described below are OTS's notable accomplishments.

OTS used novel, structure-based computational tools to predict the biological function of newly identified opioids and binding kinetics of opioids and opioid-reversal agents.

- Provided ongoing review and support for the development of evidence-based clinical practice guidelines (CPGs). In this effort, OTS collaborated with FDA's Office of the Commissioner and CDER's Offices of the Center Director, New Drugs (OND), Surveillance and Epidemiology (OSE), and Medical Policy. The CPGs address prescribing for acute dental pain, safe tapering of benzodiazepines, postoperative pain in pregnancy and childbirth, low back pain, and laparoscopic abdominal surgeries.
- Led the ongoing Acute Pain Pathways (APP) Study in collaboration with the Yale University-Mayo Clinic Center for Excellence in Regulatory Science and Innovation (CERSI), CDER OSE and OND, and the FDA Office of Minority Health and Health Equity. The APP Study provides real-world evidence (RWE) to support FDA's goal of facilitating the appropriate prescribing of opioid analgesics and to collect information on how people are treating their pain (including non-opioid pharmacologic and nonpharmacologic treatments) and functional and social outcomes.

  Data sources for the APP Study include patient surveys, wearable technologies, and electronic health records (EHRs) from pharmacies and medical systems. The study recruited patients from multiple health care systems, primary care and urgent care clinics, emergency departments, and dental practices. The APP Study is the first to examine variations in prescribing and opioid use for acute pain across diverse patient populations according to demographic, social, and health factors. The findings will inform guidelines for prescribing opioids for acute pain while limiting leftover supplies to reduce misuse, diversion, and accidental poisonings. In 2023, the Study:

  - Completed the enrollment of 1,709 subjects from 12 states.
  - Completed the 6-month follow-up period and commenced data analysis.
  - Monitored and completed the multicenter study, which included building in the flexibility needed to conduct remote and virtual monitoring visits while complying with local, state, and federal COVID-19 policies.
- Applied innovative pharmacodynamic modeling and simulation systems and well-designed clinical research studies to expand our understanding of opioids and opioid-like compounds:
  - Used novel, structure-based computational tools such as the Public Health Assessment via Structural Evaluation methodology and metadynamics simulation, as well as machine learning, to predict the biological function of newly identified opioids and binding kinetics of opioids and opioid-reversal agents.

- Designed clinical studies to examine the effects of opioids on respiratory function, giving insight on managing the respiratory depression that may occur when opioids are co-administered with other commonly prescribed medications.
- Created tools to accelerate the development of new opioid overdose reversal agents.
- Applied a translational opioid-effects model to provide support for the approval of the first intranasal nalmefene product.
- Studied the effects of opioids in pediatric subjects and alternative opioid-antagonist dosing strategies, demonstrating the need for a postmarketing pharmacokinetic (PK)/pharmacodynamic investigation of naloxone-opioid interaction to establish the minimal effective dose of naloxone hydrochloride required to reverse respiratory depression in pediatric patients from birth to less than 12 years of age.

- Developed a prototype of a novel artificial-intelligence-enabled software to identify adverse drug event safety signals from free-text discharge summaries in EHRs. This effort may enhance FDA activities related to opioid drug safety and research. The prototype improves the efficiency of harnessing real-world data (RWD) for opioid drug safety and increases the usability of data to support regulatory review.

Drug Regulatory Review

OTS supports drug regulatory review, an activity that occurs as part of a multidisciplinary team. In 2023, staff conducted over 10,000 regulatory reviews of drug marketing applications: Investigational New Drug (IND) Application, New Drug Application (NDA), Biologics License Application (BLA), and Abbreviated New Drug Application (ANDA). The effort also incorporated the review of drugs already on the market in the United States because sponsors sought expansion of treatment options for these drugs, which included new clinical indications, patient populations, and dosing regimens. Described below are highlights of OTS's accomplishments.

Collectively, OTS staff conducted over 10,000 drug regulatory reviews including INDs, NDAs, BLAs, and ANDAs.

- Conducted rigorous, multidisciplinary drug regulatory reviews using a patient-centric, issue-based strategy, thereby contributing to the FDA approval of 55 new drugs for use by patients.
- Used state-of-the-art quantitative approaches to maximize the utility, safety, and efficacy of drug products, both for the general patient population and patients with specific considerations (e.g., patients with renal or hepatic impairment, young children or neonates, patient groups with specific genetic mutations). In some cases, these approaches have allowed the regulatory approval of drugs for patients who are not specifically studied in clinical trials, thereby accelerating the delivery of innovative medicines to individuals who otherwise would not have been part of the indicated patient population.
- Promoted good review management principles and practices by modernizing clinical pharmacology review procedures for the review of IND applications, which is articulated in the updated *OCP Prioritization, Triage, and Review Process for INDs and Pre-INDs: MAPP 5100.3 Revision 1*. The document outlines good review management principles and practices to apply for IND submissions. The MAPP also promotes excellence in scientific reviews and a consistent approach for conducting the IND review process in conjunction with the policies of other stakeholders within CDER.
- Oversaw several key drug development meeting programs for FDA:
    - Complex Innovative Trial Design (CID) Meeting Program. The CID Meeting Program provides sponsors an opportunity for increased interaction with FDA to discuss their proposed innovative trial designs. Innovative trial designs help increase the efficiency of clinical trials. Over the course of the

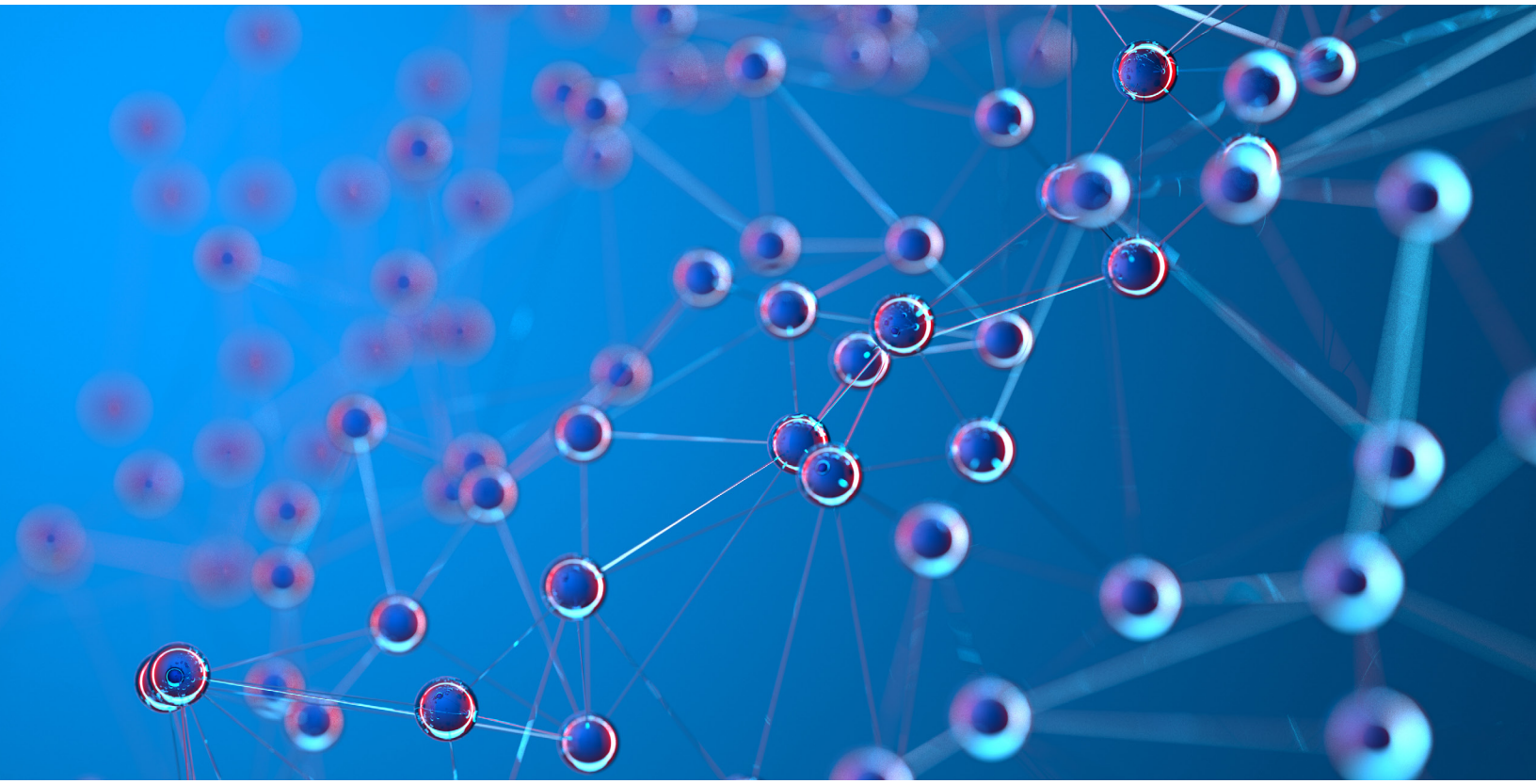
CID Meeting Program, a total of seven requests for meetings were accepted. Therapeutic areas discussed were neurology, analgesia, rheumatology, dermatology, and oncology. Trial designs were also for adult and pediatric rare disease drug development programs. Designs proposed incorporated Bayesian hierarchical modeling, the use of formal priors, and the formulation of a master protocol. In 2023, the CID Meeting Program:

- Added two case examples (Epilepsy with Myoclonic-Atonic Seizures Case Study and Multiple Sclerosis Case Study) to the FDA website.

- Critical Path Innovation Meeting (CPIM). A CPIM is a forum for FDA and its stakeholders to discuss potential scientific advancements in drug development. Public health outcomes from CPIMs may take several years to realize. Described below are highlights of OTS's accomplishments:

  - Held five CPIMs on the following topics: precision psychiatry approaches to drug development, artificial intelligence for analyzing images to assess tumor response in oncology drug clinical trials, clinical outcome assessments (COAs) for primary Sjögren's syndrome, the use of computational modeling and microphysiological systems in preclinical and clinical drug development, and approaches to advance the development of approved drugs to treat primary sclerosing cholangitis.
  - Realized public health outcomes in 2023 from CPIMs held in 2017 and 2019 and in which FDA provided feedback:
    - The patient-reported outcome (PRO) instruments for alopecia areata, discussed during two CPIMs in 2017, were used during the evaluation of the drug ritlecitinib (Litfulo). FDA approved the drug in June 2023.
    - A CPIM in 2017 discussed pancreatic injury safety biomarkers (micro RNAs) to detect drug-induced pancreatic injury to better inform dosing-related decisions in clinical trials for new drug products. In 2023, FDA issued a Letter of Support for these pancreatic injury safety biomarkers.
    - At a 2019 CPIM, FDA provided feedback on a composite biomarker panel that now serves as a secondary efficacy endpoint for use in kidney transplant clinical trials. This composite biomarker, known as the iBox Scoring System, was evaluated internationally in 2023 and has become "the first qualified endpoint for any transplant indication and is now available for use in kidney transplant clinical trials."

- Model-Informed Drug Development (MIDD) Paired Meeting Program. The FDA MIDD Paired Meeting Program represents the application of a broad range of quantitative models to facilitate new drug development and regulatory decision-making. MIDD integrates data from pharmacology, disease biology, and patient characteristics to address critical questions in drug development. The seventh iteration of the Prescription Drug User Fee Act formalized this highly impactful program, which accelerates and optimizes drug development by providing an opportunity for sponsors and FDA to discuss MIDD approaches within a specific drug development program. In 2023, the MIDD Program:
  - Accepted seven meeting requests and conducted six meetings with drug sponsors.



Inspections

Decision-making in the drug regulatory review process requires FDA to have assurance in the quality and integrity of data it receives in support of new product approvals and marketing applications. To ensure the reliability of data supporting drug regulatory decisions, OTS conducts and directs inspections of bioavailability/bioequivalence (BA/BE) and nonclinical studies submitted to FDA through drug marketing applications. Listed below are highlights of OTS's accomplishments related to inspections.

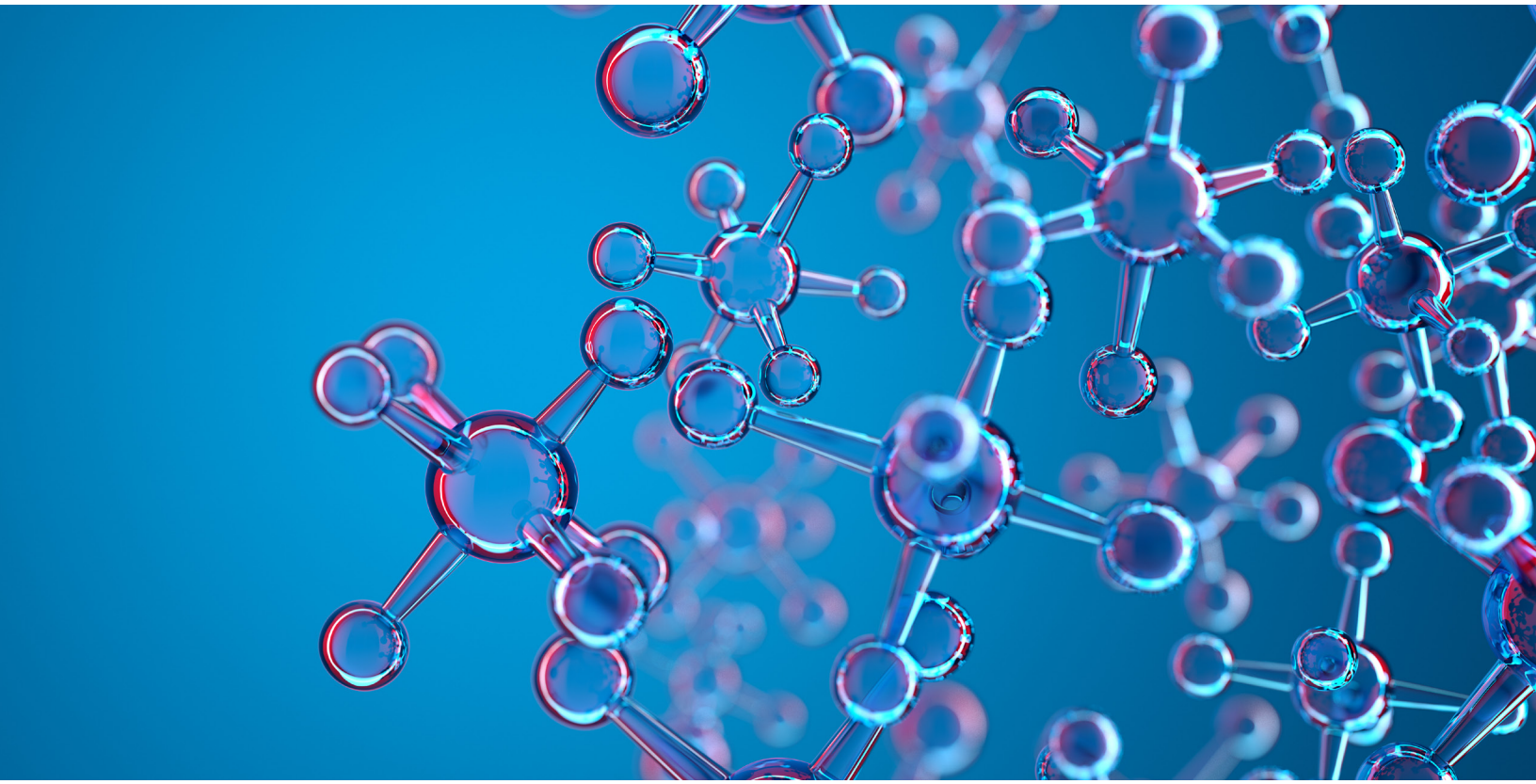
OTS conducted over 2,000 site assessments to determine the need for inspection to support drug marketing applications.

Site Evaluations (Inspections and Remote Regulatory Assessments)

- Improved the process for assigning and conducting regular, robust inspectional activities and advanced the use of alternative evaluation methods such as Remote Regulatory Assessments (RRAs). FDA conducted RRAs around the world.
- Conducted over 2,000 site assessments to determine the need for inspection to support drug applications (ANDAs, NDAs, BLAs, INDs). OTS reviews the applications and makes a risk-based decision to inspect the sites using criteria that include site history and study-specific details. Sites involved with marketing applications generate research data that are critical for the approval of new drugs and therapeutic biological products. Appropriate oversight of the research conduct provides confidence in the information provided. FDA and CDER provide annual Bioresearch Monitoring (BIMO) Inspection Metrics.
- Performed over 200 BA/BE (analytical, clinical, and clinical endpoint) and Good Laboratory Practice (GLP) site evaluations (inspections and RRAs). OTS conducts comprehensive, study-directed, and surveillance inspections of firms that conduct pharmacokinetic, BA/BE, GLP, and Animal Rule studies in support of human drug applications.

Inspection Tools

- Partnered with the CDER Office of Scientific Investigations to enhance the BIMO process workflows for regulatory reviewers. OTS built the BIMO database and is developing reports and dashboards that provide real-time information and improved metrics to regulatory reviewers for a more thorough analysis of BIMO data. OTS also supports site inspection needs with the Site Selection Tool platform to automate the site selection process across FDA, and the background package line-listing generator, to create the clinical inspectional background package to support the Office of Regulatory Affairs staff conducting inspections. The BIMO Evaluation Support Tools facilitate additional formats for the data comparison workflow, thereby making it faster for inspectors to locate, mark, and share data supporting their findings.



Science and Research

Regulatory science involves the development of new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products. CDER's regulatory science activities aim to enhance the development of new drugs while ensuring that the drugs are safe and effective when used as intended. To facilitate CDER's efforts in this area, OTS performs a variety of tasks that include promoting scientific collaboration and innovation in drug regulatory review across CDER, ensuring alignment of CDER research with CDER goals, and facilitating the establishment of technology transfer agreements that are vital to collaborations with the broader scientific community. Described below are highlights of OTS's accomplishments.

OTS provides oversight for CDER's engagement in PPPs and consortia with other government, academic, scientific, patient, and industry organizations to foster scientific collaborations to support the Critical Path Initiative and activities to advance regulatory science.

Advancing Regulatory Decision-Making

- Participated in the Collaborative Regulatory Review and Research Projects with FDA's National Center for Toxicological Research (NCTR) to develop methodologies, such as using artificial intelligence, machine learning, and natural language processing, to address inefficiencies in the regulatory review process. The research effort is evaluating technologies, developing new analytical approaches, and testing prototypes to understand what challenges exist and what strengths these technologies offer.
- Collaborated with NCTR and CDER on the Translating NCTR's Artificial Intelligence Models for Drug Safety Review program. The collaboration aims to apply the most advanced artificial intelligence methods to develop new tools to support FDA's regulatory science activities and strengthen the safety review of FDA-regulated products. The program consists of four initiatives: AnimalGAN, SafetAI, BERTox, and PathologAI. CDER leads the SafetAI Initiative to develop a suite of quantitative structure-activity relationship models, based on deep learning, for various safety endpoints critical to regulatory science and the IND review. The initiative has focused on three key safety endpoints—hepatotoxicity, carcinogenicity, and mutagenicity—and is developing a novel deep-learning-based precision system for toxicity, which is designed to optimize toxicity prediction for individual compounds based on their chemical characteristics.

Scientific Collaboration and Technology Transfer

- Facilitated and managed collaboration between CDER and the Critical Path (C-Path) Institute to advance drug development tools. The effort leveraged C-Path Institute's aggregated platform of patient-level data to supplement evidence for the approval of omaveloxolone for Friedreich's ataxia.
- Collaborated with the C-Path Institute to develop and launch the MIDD Training Course. The web-based training course is for scientists of all backgrounds interested in learning about quantitative tools and their applications in drug development and regulatory decisions. The course modules teach how MIDD approaches are applied across drug development, including in the first-in-human dose selection from preclinical data; in optimizing clinical trial design; in simulating different dosing regimens, formulations, and routes of administration; and in tailoring drug treatments for specific populations (e.g., pediatric population, patients with compromised organ functions).
- Continued to manage and oversee CDER's engagement in public-private partnerships (PPPs) and consortia with other government, academic, scientific, patient, and industry organizations to foster scientific collaborations to support the Critical Path Initiative and activities to advance regulatory science. These efforts encourage the development of new tools to facilitate innovation in medical product development. In 2023, OTS coordinated and participated in six PPPs:
    - Alcohol Clinical Trials Initiative (ACTIVE). ACTIVE aims to develop consensus reviews and recommendations to improve the design, execution and interpretation of trials of medications for the treatment of alcohol use disorder.
    - Setting International Standards of Quality of Life and Patient-Reported Outcomes Endpoints – Innovative Medicines Initiative (SISAQOL-IMI). SISAQOL-IMI addresses standardization in the conduct and reporting of PRO data in cancer clinical trials. OTS staff attended the SISAQOL-IMI 2023 consensus meeting that focused on several work packages related to randomized controlled trials, single arm studies, graphical presentation, and clinically meaningful change. The group produced the final list of new SISAQOL-IMI recommendations statements.
    - American Statistical Association (ASA) Biopharmaceutical RWE Scientific Working Group. This PPP advances the understanding of RWE research. It addresses significant methodological challenges with using RWE for regulatory purposes. The PPP is focused on (1) sensitivity analysis in real-world studies, (2) RWE for rare diseases, and (3) the intersection of RWE and digital health technologies (DHTs) and decentralized clinical trials.
    - Outcome Measures in Rheumatology (OMERACT) Proactive. OMERACT has the goal of sharing data and innovative thinking about the development of osteoarthritis (OA) outcome measures for clinical trials of therapies aimed at slowing OA progression. Several initial planning meetings identified objectives to develop novel potential outcome measures to

assess progression (pain and function) in both short-term and long-term clinical trials. FDA recommended the need for a new systematic literature review and the importance of early patient involvement.

- C-Path Institute PRO Consortium. OTS participated in the 14th Annual PRO Consortium Workshop and provided overarching FDA recommendations relevant to the PPP and updates on FDA initiatives. OTS staff provided comments from a regulatory and scientific perspective after participants presented their work.
- ASA Biopharm Safety Working Group. This PPP initiated different workstreams that focused on aggregated safety assessment planning, benefit-risk planning, safety graphics, and safety estimands. The group held quarterly scientific webinars on topics in these areas to increase communication and information sharing with the greater scientific community. Group members presented their work at several international venues, provided a short course, and led authorship of multiple published papers. The safety graphics workstream published tools on CRAN. Midyear and end-of-year summary presentations were provided to FDA liaisons to foster engagement and feedback.

- Executed 63 technology transfer agreements and other collaborations that allowed for the transfer of data and materials and research collaborations between CDER and industry, nonprofit, government, and domestic and international partners related to several cutting-edge scientific areas. Among these collaborations, OTS:
  - Established a Research Collaboration Agreement (RCA) between CDER and Pennsylvania State University. The RCA is evaluating novel analytic approaches, such as machine learning, to characterize the natural history of rare diseases, discover predictive and prognostic biomarkers, and identify new therapeutic targets.
  - Conducted research under 14 memoranda of understanding to promote partnerships and scientific progress with academic, domestic, and nonprofit entities on shared interests such as education and research programs.
  - Was involved in several research agreements/collaborations (CERSIs, Cooperative Research & Development Agreements, RCAs, Material Transfer Agreements, and Broad Agency Announcements [BAAs]) on topics addressing patient factors, novel modeling applications and alternative methods, rare diseases, biomarkers, pharmacogenetics, treatment disparities, drug metabolism and toxicity, and urgent public health crises.

- Provided technical and scientific support for the FDALabel Database research effort. OTS implemented enhancements to improve search capabilities to help users find the drug label of interest. This web-based database performs customizable searches of over 140,000 labels of human and animal prescription, biological, and over-the-counter drug products—as well as medical devices and vaccines. The information in the FDALabel Database can be used for many cases, including by health care providers

for quick access to drug indications and warnings, pharmaceutical companies for drug development, or by researchers for studying drug safety.

- Participated in the following regulatory science and research activities:
  - C-Path Institute Rare Disease Cures Accelerator. OTS conducted pilot analyses of Friedreich's ataxia study data to evaluate factors that influence natural history.
  - Clinical Trial Transformation Initiative. OTS provided executive leadership and engaged stakeholders on the development and adoption of disease progression models.
- Supported intramural (i.e., within CDER) and extramural regulatory science research activities:
  - Led and managed the review of over 40 intramural proposals to explore cutting-edge technologies and scientific methods and approaches that can advance regulatory review and make new methods and tools available to the drug development community.
  - Coordinated and facilitated the use of extramural research mechanisms.
    - Supported 17 projects at various CERSIs (Johns Hopkins University; Yale University-Mayo Clinic; the University of North Carolina at Chapel Hill-Duke University; the University of California, San Francisco-Stanford University; and the University of Maryland).
    - Supported 23 BAA projects with universities and companies.

Research Fellowships

- Hosted numerous fellows in the field of science, technology, engineering, and mathematics (STEM) through the Oak Ridge Institute for Science and Education (ORISE) Program. The ORISE Program at FDA is an educational and training program designed to provide college students, recent graduates, and university faculty opportunities to connect with the unique resources of FDA. With the support of an assigned mentor, participants have authentic research experiences using equipment not found on most college campuses. These research experiences complement the educational nature of the programs and make participants aware of potential STEM employment opportunities at the sponsoring agency. Participants have access to unique research and training opportunities, top scientists and engineers, and state-of-the-art facilities and equipment.

Advancing Tools, Technologies, and Innovation

OTS actively seeks to advance the utilization of data, tools, and technologies that yield innovations to enhance regulatory review and regulatory science research. Below are highlights of the office's accomplishments.

OTS supports the development of analytical data standards for COAs and DHTs.

Enhancing the Efficiency of Drug Regulatory Review

- Oversaw the CDER Innovation Board and its project portfolio, providing access to reusable resources that facilitate concept development, prototyping, and piloting. The effort created a network of subject matter experts and facilitated knowledge management to inform future innovations.
- Developed and delivered new projects in CDER's cloud-enabled infrastructure, providing reviewers and technologists with a platform to quickly test concepts, build prototypes, and demonstrate scalability. This research and development space enables CDER to test solutions on a smaller scale before moving into production, thereby minimizing the cost and risk associated with enterprise release.
- Delivered innovative services and solutions to advance, automate, and streamline CDER's regulatory review as part of its ongoing effort to identify, evaluate, and apply ready-to-use technologies that can optimize its core operations. As part of this effort, OTS:
  - Extended the footprint of CDER's regulatory review data preparation engine through an increasing number of automated system connections, making quality study data available to more users across CDER.
  - Enhanced data quality assessments with new findings, parameters, and validation rules to improve the scope and usability of standardized submission study data.
  - Streamlined and automated the delivery of data quality and safety analysis services, expanded service offerings to include standard tables and figures and custom analyses, and extended service offerings to new CDER communities.
- Supported the development of analytical data standards for COAs and DHTs. This development was part of OTS's effort to advance the utilization of data, tools, and technologies to enhance regulatory review and research:

- Developed technical specification documents to define the optimal or preferred analysis data requirements for COAs. The documents support the efficiency of regulatory reviews.
- Participated in the R Consortium working groups that successfully completed the R Submission Pilot 2 Project. The project tested the concept that a Shiny application created with R-language can be both successfully bundled into a submission package and transferred to FDA reviewers.

- Determined that current nonclinical testing results under the *International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) S7B* do not predict QTc prolongation potential of proteins and peptides. As a result, FDA communicated in guidance and in publications to not recommend thorough QT studies for peptides.
- Used automated tools to complete standardized review reports for clinical pharmacology studies of selected new molecular entities, 351(k) (BLA), and 505(b)(2) (supplemental NDA) submissions. OTS continued to implement standardized applications for supporting clinical pharmacology data analyses.
- Conducted reviews of the impact of immunogenicity on the PK of biological products using an automated immunogenicity specimen assessment tool.
- Developed an artificial-intelligence-assisted analysis tool to provide regulatory review staff standardized, comprehensive, and customizable analyses in real time for NDA/BLA submissions.
- Implemented automated processes to streamline research-project life cycle tracking, standard operating procedures, knowledge management, and recordkeeping for over 50 research projects. The automated processes significantly reduced time spent on administrative tasks to maintain research projects and improved laboratory safety.
- Provided reliable and timely information on products regulated by CDER to support regulatory science research, policy development, and responses to inquiries from stakeholders.
  - Adjudicated data on novel drug approvals for CDER databases and for high-profile CDER reports. OTS used the tools it developed for the adjudication.
  - Developed and refined multiple dashboards to display various visuals for regulatory actions for novel drug products and submissions.

Health Information Technology

- Prepared detailed recommendations related to forthcoming regulations on enhancing health information technology systems to augment existing clinical trials data.
- Co-led the Code Map Services Project with CDER's Office of Strategic Programs, National Institutes of Health and the Office of the National Coordinator for Health Information Technology (ONC). The Code Map Services Project aims to create an automated set of code mapping services of common data models (CDMs) (e.g., Observational Medical Outcomes

Partnership [OMOP], Sentinel, Patient-Centered Outcomes Research Network [PCORnet], Informatics for Integrating Biology and the Bedside/ Accrual to Clinical Trials [2b2/ACT], TriNetX) and tools to support cross-network and cross-CDM data sharing for clinical research.

- Led the OneSource project in collaboration with the University of California San Francisco. This project is using EHRs as the electronic Source (eSource) in I-SPY 2.2 Breast Cancer Trial. This project is aiming to accomplish the following: 1) enhance the adverse event detection and reporting process by implementing standards-based electronic PROs; and 2) identify key data elements from electronic case report forms for breast cancer trials, focusing primarily on the I-SPY 2 family of trials, and provide the data elements to the ONC United States Core Data for Interoperability (USCDI). OneSource was implemented at 15 sites for eSource data capture of laboratory results and concomitant medications for the I-SPY COVID Trial.
- Reviewed and provided recommendations for the Health Level Seven draft standards that aim to make clinical research data more interoperable with health care data and improve FDA's ability to review RWD in regulatory submissions.

Outreach and Communication Efforts

The following accomplishments are highlights of OTS's outreach and communication efforts, and they include the publication of the inaugural guidance snapshot for the patient population.

OTS authored (or co-authored) 11 guidance documents and led their clearance for publication.

- Partnered with internal and external stakeholders—including NCTR, Pharmaceutical Users Software Exchange, and the Clinical Data International Standards Consortium—to drive innovation, share knowledge, and build subject matter expertise to develop solutions that address unmet computational science needs in health product development and regulatory review. Topics included data standards, delivering quality data/data quality assessments, and review tools and services to support reviewers.
- Continued to strengthen the office's coordination with international regulatory partners. The office shared important information and techniques and supported regulatory synergy by meeting regularly with the United Kingdom Medicines and Healthcare products Regulatory Agency, Health Canada, European Medicines Agency, and the World Health Organization.
- Collaborated with other international drug regulatory authorities to develop an approach to evaluate the predicted carcinogenic potency of nitrosamine drug impurities based on the structural features of these compounds.
- Continued to develop a relationship with the American Association of Colleges of Pharmacy. The office explored the development of, and participation in, a task force on future curricular development and needs.

Guidance and Policy Documents, Snapshots, and Podcasts

- Developed multiple guidance documents to communicate FDA's current thinking on a particular regulatory topic or process. These documents usually discuss more specific products or issues that relate to the design, production, labeling, promotion, manufacturing, and testing of regulated products. Guidance documents may also relate to the processing, content, and evaluation or approval of submissions as well as to inspection and enforcement policies.
    - Authored (or co-authored) the following 11 guidance documents and led their clearance for publication:

- Guidance for industry *Evaluation of Gastric pH-Dependent Drug Interactions with Acid-Reducing Agents: Study Design, Data Analysis, and Clinical Implications* (March 2023)
- Draft guidance for industry *Pharmacogenomic Data Submissions* (March 2023)
- Guidance for industry *Adjusting for Covariates in Randomized Clinical Trials for Drugs and Biological Products* (May 2023)
- Guidance for industry *Use of Whole Slide Imaging in Nonclinical Toxicology Studies: Questions and Answers* (May 2023)
- Guidance for industry *Clinical Drug Interaction Studies with Combined Oral Contraceptives* (June 2023)
- Guidance for industry *Drug-Drug Interaction Assessment for Therapeutic Proteins* (June 2023)
- Guidance for industry (technical specifications document) *Submitting Clinical Trial Datasets and Documentation for Clinical Outcome Assessments Using Item Response Theory* (November 2023)
- Guidance for industry (technical specifications document) *Submitting Patient-Reported Outcome Data in Cancer Clinical Trials* (November 2023)
- Draft guidance for industry *Translation of Good Laboratory Practice Study Reports: Questions and Answers* (November 2023)
- Draft guidance for industry *Clinical Pharmacology Considerations for Peptide Drug Products* (December 2023)
- Draft guidance for industry *Master Protocols for Drug and Biological Product Development* (December 2023)

- Contributed to the review of 85 FDA guidance documents.
- Developed and published seven Guidance Snapshots and seven Guidance Recap Podcast episodes. A guidance snapshot is a communication tool that provides highlights from a guidance document using visuals and plain language. Each guidance snapshot accompanies a podcast episode that discusses highlights and background information on the guidance document through a conversation with its authors.
  - Launched the inaugural guidance snapshot for patients and its accompanying podcast episode.
  - Published three Manual of Policies and Procedures and 11 Federal Register Notices on topics including MIDD, dosing for oncology products, drug interactions, pharmacogenomic data submissions, and the IND application review.

Workshops, Meetings, and Publications

- Collaborated with internal and external stakeholders—including CDER's Small Business & Industry Assistance (SBIA), the Duke-Margolis Center for Health Policy, and the University of Maryland CERSI—to hold 14 public

workshops on topics including neonatal clinical pharmacology studies, biosimilar drug development, physiologically based biopharmaceutics modeling, food effect studies, rare disease drug development, and artificial intelligence for precision medicine.

- Participated in two ICH working groups to develop guidelines for drug interactions and general principles for MIDD.
- Contributed to the writing of over 200 manuscripts that were published in various peer-reviewed publications.
- Updated web resources for external stakeholders, including industry, clinicians, scientists, and patients. The resources included the Table of Pharmacogenetic Associations, Table of Pharmacogenomic Biomarkers in Drug Labeling, and the For Healthcare Professionals | FDA's Examples of Drugs that Interact with CYP Enzymes and Transporter Systems. The updates included less technical and more graphic, case-based approaches to enhance public comprehension.
- Gave over 400 presentations at national and international meetings.
- Shared up-to-date knowledge on clinical pharmacology regulatory science topics through 49 listserv communications to over 95,000 subscribers and through direct engagements with eight professional organizations.
- Communicated the scope and importance of CDER's regulatory science activities to its stakeholders by enhancing the Center's regulatory science newsletter, *What's New in Regulatory Science*. This publication is a compendium of news and updates about regulatory science activities to advance drug development and evaluation and reaches over 100,000 subscribers.

Regulatory Science Outreach

- Hosted nearly 50 students from the University of Maryland, Baltimore County (UMBC) Meyerhoff Scholars Program to a virtual event with scientific research presentations given by CDER scientists and a panel discussion where FDA staff shared information on their roles and responsibilities related to STEM.
- Presented on translational science and STEM career opportunities at FDA to UMBC undergraduate students as part of the course entitled Biotechnology Survey: Legal, Ethical, Regulatory, and Biosafety Issues.
- Participated in outreach efforts under the Accelerating Rare Disease Cures Program, including a workshop on addressing challenges in the design and analysis of rare disease clinical trials.
- Engaged in outreach at numerous conferences, including at the Eastern North American Region of the International Biometrics Society, Clinical Trial Transformation Initiative Spring Meeting, Drug Information Association (DIA) Annual Meeting, FDA/DIA Biostatistics Industry and Regulatory Forum, ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop, ASA New York City Metropolitan Area Chapter Statistical Innovation Community Summit, SBIA Regulatory Education for Industry Annual Conference, and the International Chinese Statistical Association Applied Statistics Symposium.

Abbreviations

ACTIVE	Alcohol Clinical Trials Initiative
ANDA	Abbreviated New Drug Application
APP	Acute Pain Pathways
ASA	American Statistical Association
BA	Bioavailability
BAA	Broad Agency Announcement
BE	Bioequivalence
BIMO	Bioresearch Monitoring
BLA	Biologics License Application
C-Path	Critical Path [Institute]
CDER	Center for Drug Evaluation and Research
CDM	Common Data Models
CERSI	Center of Excellence in Regulatory Science and Innovation
CID	Complex Innovative Trial Design
CPGs	Clinical Practice Guidelines
CPIM	Critical Path Innovation Meeting
COAs	Clinical Outcome Assessments
DHTs	Digital Health Technologies
DIA	Drug Information Association Meeting
EHRs	eSource Electronic Source
FDA	Food and Drug Administration
GLP	Good Laboratory Practice
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IND	Investigational New Drug
MIDD	Model-Informed Drug Development
NCTR	National Center for Toxicological Research
NDA	New Drug Application
OA	Osteoarthritis
OAO	Office of Administrative Operations
OB	Office of Biostatistics
OCP	Office of Clinical Pharmacology
OCS	Office of Computational Science
OMERACT	Outcome Measures in Rheumatology
ONC	Office of the National Coordinator for Health Information Technology
OND	Office of New Drugs
ORISE	Oak Ridge Institute for Science and Education
OSE	Office of Surveillance and Epidemiology
OSIS	Office of Study Integrity and Surveillance
OTS	Office of Translational Sciences
PK	Pharmacokinetic
PPP	Public-Private Partnership
PRO	Patient-Reported Outcome
RCA	Research Collaboration Agreement
RRA	Remote Regulatory Assessment
RWD	Real-World Data
RWE	Real-World Evidence
SBIA	Small Business & Industry Assistance
SISAQOL-IMI	Setting International Standards of Quality of Life and Patient-Reported Outcomes Endpoints – Innovative Medicines Initiative
STEM	Science, Technology, Engineering, And Mathematics
UMBC	University of Maryland, Baltimore County

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We dedicate this annual report to our friend and colleague Dionne Price, MS, PhD, the late Deputy Director of the Office of Biostatistics. She will be greatly missed.

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