U.S. FOOD & DRUG ADMINISTRATION

OFFICE *of* CLINICAL PHARMACOLOGY
Office of Translational Sciences

# 2024 Annual Report

*Unlocking Doors to Better Health*

# Table of Contents



# Director's Message

Innovation can lead to better public health. Over the past several decades, transformational innovations have occurred at every step of the drug discovery and development processes. Our staff at the U.S. Food and Drug Administration's (FDA's) Office of Clinical Pharmacology (OCP) have advanced science to deliver on our mission of translating knowledge of drug response into patient-centered regulatory decisions of the highest quality. In other words, our staff are dedicated to improving *your* health by using the best scientific approaches available.

To achieve this goal, we continuously seek to develop and apply scientific and organizational innovation and excellence. We also highly value collaborations that enhance drug development and regulatory evaluation. I am pleased to report we have directed such efforts in several key areas this past year, perhaps most notably in the field of quantitative medicine (QM). This interdisciplinary approach leverages both quantitative data (from the molecular level to the population level) and mechanistic knowledge to inform drug discovery and development, regulatory decision-making, and patient care.

In early 2024, our Office played a pivotal role in establishing the Center for Drug Evaluation and Research (CDER) Quantitative Medicine Center of Excellence (QM CoE), an alliance of several CDER Offices dedicated to maximizing synergies in innovative methods and technologies that will advance drug development and improve public health. Early deliverables of the QM CoE include a collaborative workshop, the development and availability of educational resources on model-informed drug development (MIDD), and the initiation of a long-term planning effort to guide the Center's activities for years to come.

The QM CoE aligns with our OCP Priorities of: 1) advancing the science of translational clinical pharmacology for the benefit of patients; 2) bolstering patient-centered engagement; and 3) elevating our people. However, it is not the only area of which I am exceedingly proud. In this year's Annual Report, we also share how our highly committed OCP staff and partners continued to advance our science across all areas of scope: regulatory review, guidance development, research, and public engagement, only a fraction of which is presented in the pages that follow. It is my honor to serve alongside these dedicated individuals and teams daily to deliver safer, more effective, and more personalized medicines for patients. Together, we can unlock doors to better health for all.

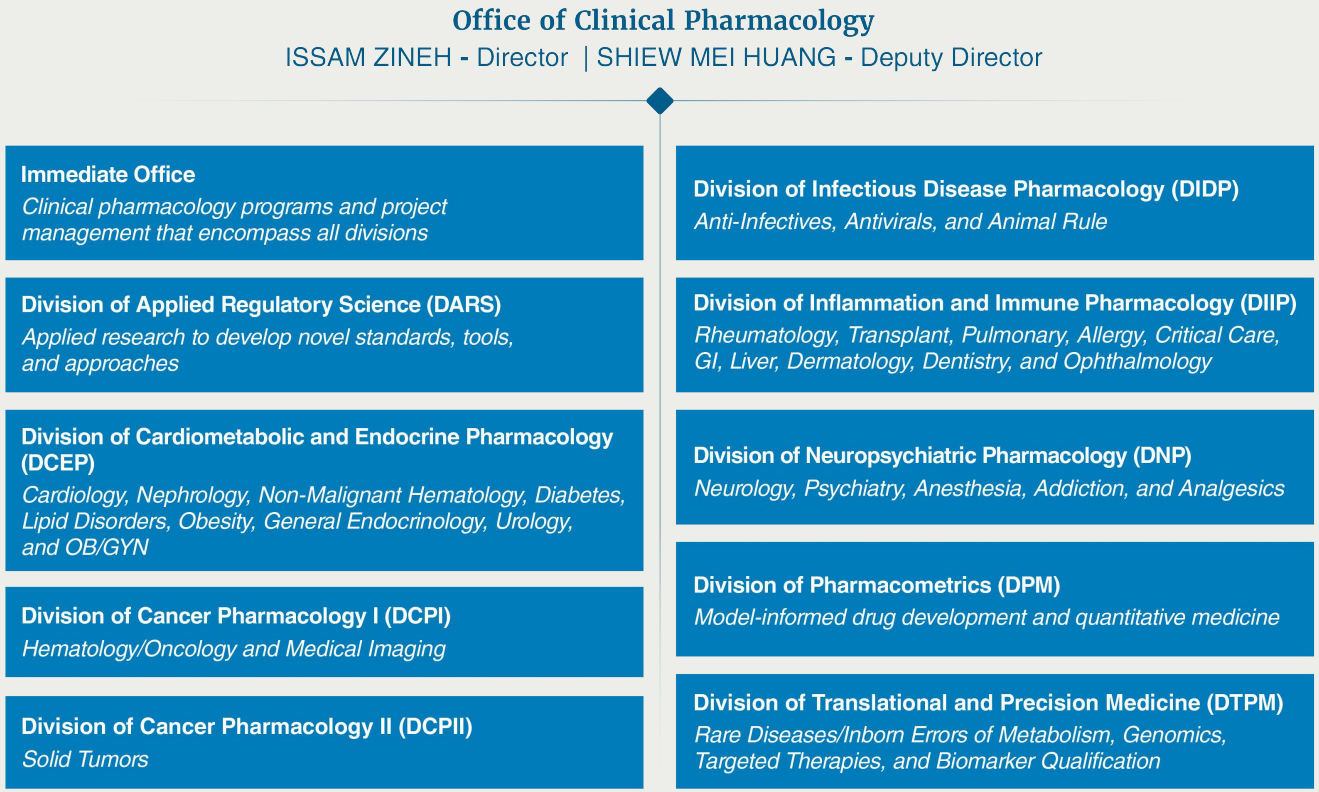
This report is dedicated to our cherished friend and colleague Dr. Joseph (Joe) Grillo. Joe was a passionate advocate for patients and had a generous and caring spirit. His commitment to clinical pharmacology, regulatory labeling, and patient care was unparalleled, leaving a lasting impact on everyone he worked with. Joe's devotion to those he served will continue to inspire us, and he is profoundly missed.

**Issam Zineh**
**PharmD, MPH, FCP, FCCP**
Director
Office of Clinical Pharmacology

# Organization

OCP is a dynamic, patient-focused organization dedicated to applying clinical pharmacology principles to ensure the safety, efficacy, and optimal use of human drugs and biological products. We are a multidisciplinary office within the FDA's CDER Office of Translational Sciences (OTS) super-office, comprised of over 270 pharmacologists, pharmacists, biologists, chemists, physicians, nurses, project and program managers, and administrative professionals (See Figure 1). Grounded in our core values – stewardship, leadership, excellence, connectedness, and respect – we promote and protect global public health by translating knowledge into patient-centered scientific advances and regulatory decisions. OCP builds relationships, drives progress, and shares scientific experience with our partners for the betterment of patient health.

**FIGURE 1** The Organization




## OUR MISSION

Advance the development of innovative new medicines by applying state-of-the-art scientific principles

Promote therapeutic optimization and individualization through best practices in research, guidance development, and drug evaluation throughout the product lifecycle

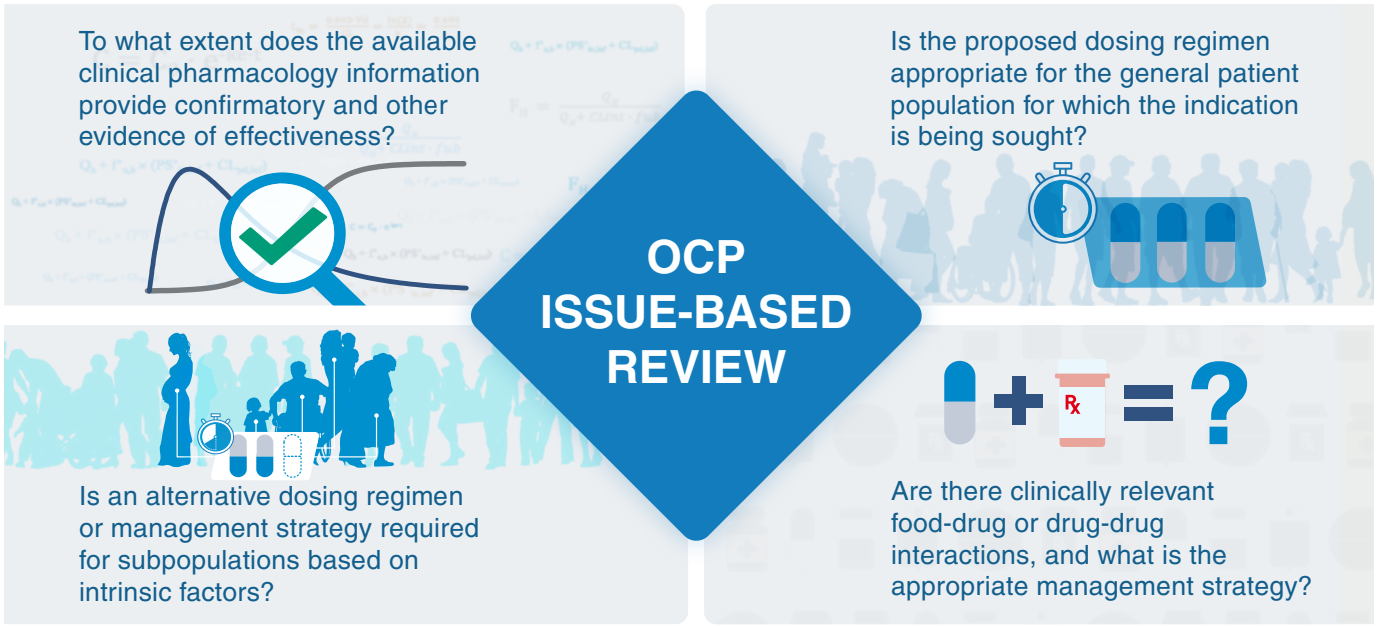
## OUR VISION

Improve public health by building and translating knowledge of drug-response into patient-centered regulatory decisions of the highest quality

# Regulatory Drug Evaluation

Clinical pharmacology is a multidisciplinary science. OCP's regulatory evaluations of drug marketing applications (i.e., "reviews") synthesize information from all relevant clinical pharmacology knowledge areas including drug disposition, pharmacology and biomarkers, quantitative methods, drug safety, pharmacotherapy, and clinical trial methods to inform regulatory decisions. OCP uses a patient-centric, issue-based strategy to assess information for investigational new drugs, new drug applications (NDA), and biologics license applications (BLA) to address issues of dose selection and optimization, therapeutic individualization, and benefit/risk balance (See Figure 2). Our reviews also identify critical gaps in the understanding of conditions for optimal therapeutic use and recommend studies that can practically address those gaps. OCP recommendations are guided by established and evolving regulatory policies and practices. In 2024, our review findings for NDAs and BLAs, including 351(k) applications (i.e., biosimilar biological products), were integrated into benefit/risk assessments, ultimately bringing 50 safe and effective new drugs and biological products to patients in 2024 (See Table 1).

**FIGURE 2** OCP Issue-Based Approach to Drug Evaluation




**OCP AT-A-GLANCE REVIEW**

**Over 5400**
Investigational New Drug Reviews Conducted in 2024

**Over 3300**
Drug Development Meetings in 2024

**50**
Novel Drugs and Biological Products Approved in 2024

## TABLE 1. OCP Contributions to Novel Drug and Biological Product Approvals

| Drug Name | Indication | Primary Review Contribution | | | |
|---|---|---|---|---|---|
| | | Evaluated/proposed bridging or extrapolation strategies | Mitigated risk | Optimized dosing regimen | Provided evidence of effectiveness (confirmatory and other evidence)* |
| Anktiva | To treat bladder cancer | | | | ● |
| Aqneursa | To treat Niemann-Pick disease type C | ● | ● | ● | ● |
| Cobenfy | To treat schizophrenia | | ● | ● | |
| Duvyzat | To treat Duchenne muscular dystrophy in individuals aged 6 years and older | | ● | ● | ● |
| Ebglyss | To treat moderate-to-severe atopic dermatitis | | ● | ● | |
| Exblifep | To treat complicated urinary tract infections | | ● | ● | ● |
| Flyrcado | A radioactive diagnostic drug to evaluate for myocardial ischemia and infarction | | ● | ● | |
| Hympavzi | To prevent or reduce bleeding episodes related to hemophilia A or B | | ● | ● | |
| Imdelltra | To treat extensive stage small cell lung cancer | | ● | ● | |
| Iqirvo | To treat primary biliary cholangitis in combination with ursodeoxycholic acid | | ● | ● | ● |
| Itovebi | To treat locally advanced or metastatic breast cancer | | ● | ● | |
| Kisunla | To treat Alzheimer's disease | | ● | ● | ● |
| Lazcluze | To treat non-small cell lung cancer | | ● | ● | ● |
| Leqselvi | To treat severe alopecia areata | | ● | ● | ● |
| Letybo | To temporarily improve the appearance of moderate-to-severe glabellar lines | | ● | | |
| Livdelzi | To treat primary biliary cholangitis | | ● | ● | ● |
| Lumisight | To use as an optical imaging agent for the detection of cancerous tissue | | ● | ● | |
| Miplyffa | To treat Niemann-Pick disease type C | | ● | ● | ● |
| Nemluvio | To treat prurigo nodularis | | ● | ● | |
| Niktimvo | To treat chronic graft-versus-host disease | ● | ● | ● | ● |
| Ohtuvayre | To treat chronic obstructive pulmonary disease | | ● | ● | |
| Ojemda | To treat relapsed or refractory pediatric low-grade glioma | ● | ● | ● | |
| Orlynvah | To treat uncomplicated urinary tract infections | | ● | ● | |

** This criterion is only applicable if the review explicitly states that the clinical pharmacology program resulted in confirmatory or supportive evidence of effectiveness.*

| Drug Name | Indication | Primary Review Contribution | | | |
|---|---|---|---|---|---|
| | | Evaluated/proposed bridging or extrapolation strategies | Mitigated risk | Optimized dosing regimen | Provided evidence of effectiveness (confirmatory and other evidence)* |
| Piasky | To treat paroxysmal nocturnal hemoglobinuria | ● | ● | ● | ● |
| Rezdiffra | To treat noncirrhotic non-alcoholic steatohepatitis with moderate to advanced liver scarring | | ● | ● | ● |
| Rytelo | To treat low- to intermediate-1 risk myelodysplastic syndromes | | ● | ● | |
| Sofdra | To treat primary axillary hyperhidrosis | | ● | ● | |
| Tevimbra | To treat unresectable or metastatic esophageal squamous cell carcinoma | | ● | ● | |
| Tryvio | To treat hypertension | | ● | ● | |
| Vafseo | To treat anemia due to chronic kidney disease | | ● | ● | ● |
| Voranigo | To treat Grade 2 astrocytoma or oligodendroglioma | ● | ● | ● | |
| Voydeya | To treat extravascular hemolysis with paroxysmal nocturnal hemoglobinuria | | ● | ● | ● |
| Vyloy | To treat gastric or gastroesophageal junction adenocarcinoma | | ● | ● | |
| Winrevair | To treat pulmonary arterial hypertension | | ● | ● | |
| Xolremdi | To treat WHIM syndrome (warts, hypogammaglobulinemia, infections and myelokathexis) | | ● | ● | |
| Yorvipath | To treat hypoparathyroidism | | ● | ● | ● |
| Zelsuvmi | To treat molluscum contagiosum | | ● | | |
| Zevtera | To treat certain bloodstream infections, bacterial skin and associated tissue infections, and community-acquired bacterial pneumonia | ● | ● | ● | ● |

** This criterion is only applicable if the review explicitly states that the clinical pharmacology program resulted in confirmatory or supportive evidence of effectiveness.*

# Innovative Regulatory Approaches in OCP Review

For decades, CDER offices have been at the forefront of advancing regulatory innovations to inform pre-approval product review and post-approval product assessment. OCP plays a critical role in translating knowledge gained from approaches such as QM, model-informed methodologies, and drug development tools. In 2024, the CDER QM CoE was established to provide an organizational framework and operational structure to advance innovative QM approaches and support existing regulatory programs, including the MIDD Paired Meeting Program and FDA's Fit-for-Purpose (FFP) Initiative. Combining the most up-to-date science with efficient and effective regulatory review has accelerated drug development in several ways, including confirming the utility of novel biomarkers, refining dosing, improving safety, and validating efficacy for patients. Other programs on real-world evidence, treatments for rare diseases, and advanced data analytics have made significant strides as we continue to engage within the FDA and with the scientific, regulatory, and patient communities. Below, we provide more detail on how novel scientific methods integrated with effective regulatory programs and pathways contributed to evidence of effectiveness, optimized dosing, expanded indicated populations, and mitigated risk for novel drugs and biological products approved in 2024.

## OCP VOICE

**Rajanikanth Madabushi, PhD**
Director, FDA CDER Quantitative Medicine Center of Excellence

"OCP is a leader in advancing initiatives that spur innovation and promote integration of QM approaches. By incorporating QM methods into the drug development process, OCP and CDER help streamline the development pipeline, ensure better clinical trial design, and ultimately bring safe and effective drugs to patients faster.

I am fortunate to be a part of OCP at such an exciting time as we see the expanding application of QM to provide much-needed solutions. We have established a framework for meaningful, collaborative engagement to advance therapeutic medical product development and promote public health. I look forward to our continued progress integrating QM to maximize societal benefit and patient care."

# Quantitative Medicine in Action

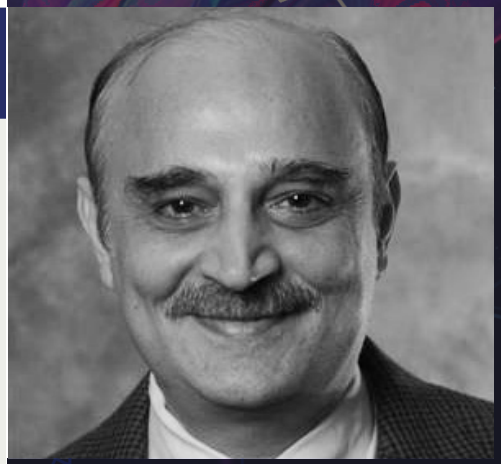
## PROVIDING CONFIRMATORY AND OTHER EVIDENCE OF EFFECTIVENESS

QM approaches including dose- and exposure-response analyses for pharmacodynamic biomarkers and pharmacokinetic modeling and simulation helped establish confirmatory and other evidence of effectiveness for numerous FDA-approved drugs in 2024 (See Table 1). These approaches were used to provide evidence of effectiveness for drugs across therapeutic areas, including oncology, dermatology, neurology, hematology, nephrology, infectious diseases, and inflammatory and endocrine disorders. QM approaches were also instrumental in establishing evidence of effectiveness for drugs intended to treat rare diseases, where it is often difficult to conduct more than one clinical efficacy trial.

## OCP VOICE

### Mehul Mehta, PhD

Director, Division of Neuropsychiatric Pharmacology



"As the Director of the Division of Neuropsychiatric Pharmacology, I have never been more excited to be a part of OCP. The fields of neurology, psychiatry, pain, and addiction are buzzing with groundbreaking research and applications. Our review contributions in evaluating mechanistic-based biomarkers and exposure-response analyses play a central role in providing confirmatory and other evidence towards approval of therapeutics for numerous important diseases (e.g., Alzheimer's disease, amyotrophic lateral sclerosis, also known as Lou Gehrig's disease, Duchenne muscular dystrophy, myasthenia gravis, post-traumatic stress disorder, Prader-Willi syndrome, and reversal agents for opioid overdose).

Our office is at the forefront of new transformational advances like quantitative systems pharmacology (QSP), real-world data and real-world evidence, artificial intelligence, etc., that are positively and fundamentally changing the conventional ways of drug development and evaluation. After 38 years at the FDA, I am continually amazed by the opportunity and ability of our science to protect and promote public health."

## EXTRAPOLATION OF EFFICACY TO YOUNG PATIENTS

Under the right circumstances, it may be possible to extrapolate efficacy from a well-studied population to populations not well-studied in demonstrative efficacy trials. For example, the pathophysiology and clinical manifestations of the disease may be similar, or there may be similar drug treatment paradigms and mechanisms of action between the studied and unstudied populations. For extrapolation to infants or neonates, it is important to understand the maturation status of metabolizing enzymes and the extent of renal and hepatic function. In 2024, OCP review staff were able to use QM methods to extrapolate efficacy to adolescents, younger children, infants, and patients weighing at least 40 kg regardless of age for nine new molecular entities. Seven of these FDA-approved drugs were for rare disease indications; as such, QM approaches allowed access to these medications far earlier than would be possible with traditional clinical investigations.

## MITIGATING RISK

OCP review staff use QM tools to enhance their ability to reduce the likelihood and severity of drug-associated adverse events. For example, dose- and exposure-safety analyses help reviewers better understand the relationship between drug concentrations and toxicity, and when possible, optimize the dosage to reduce or prevent adverse events. When appropriate biomarkers are available, pharmacokinetic/pharmacodynamic analysis can help identify signals that an adverse event is occurring or likely to occur; population pharmacokinetic analyses can also assess the impact of patient-specific factors on drug safety. Polypharmacy is increasingly common, and OCP reviewers are dedicated to mitigating or preventing drug-drug interactions by providing actionable labeling instructions. These instructions are often informed by in vitro, in vivo, and in silico data (e.g., through physiologically based pharmacokinetic (PBPK) analyses). When gaps in the understanding of drug interactions were identified, OCP review teams issued postmarketing commitments and requirements to further ensure the safe use of approved drugs. For biological products, review staff used population pharmacokinetic analyses to assess the potential for immunogenicity and its impact on pharmacokinetics, efficacy, and safety. In addition, they used modeling approaches to help determine a drug's ability to prolong the QT interval, possibly leading to torsade de pointes, a potentially fatal arrhythmia.

## OPTIMIZING DOSING REGIMENS

Optimizing the dosing regimen of drugs submitted to the FDA for approval is one of the core functions of the multidisciplinary OCP review team. Our staff used multiple QM approaches to ensure that the right dose is given to the right patient at the right time for FDA-approved drugs in 2024. Dose- and exposure-response analyses for safety and efficacy helped identify the safest and most effective dosage for the general population. In 2024, OCP staff identified safer and more effective dosages based on age, weight, renal and hepatic function, concomitant food and medication administration, and patient subsets with specific genetic mutations. Population pharmacokinetic models were used to identify potential sources of variable drug exposure and enabled pharmacokinetic simulations of dosage scenarios not studied in clinical trials, including different drug loading doses and dosing regimens. OCP review teams also helped ensure the continued refinement of drug dosages after approval, by issuing, when appropriate, post-approval study requests to assess safety and effectiveness in renal and hepatic impairment, explore additional dosing regimens, and address representational deficiencies in clinical investigations.

## OCP VOICE

### Kellie Reynolds, PharmD

Director, Division of Infectious Disease Pharmacology

"Staff in the Division of Infectious Disease Pharmacology (DIDP) support global public health in the areas of infectious diseases and biothreat preparedness. Over the past three decades, I have witnessed tremendous advances in the treatment of viral diseases, including HIV and hepatitis C, with recent contributions for COVID-19. Much of the current HIV work is related to the development of long-acting injectable products for prevention and treatment, areas where clinical pharmacology plays a pivotal role. DIDP contributes to regulatory research aimed to combat antimicrobial resistance, including drugs to treat drug-resistant bacterial infections and fungal infections. The Division reviews the majority of products developed as medical countermeasures to be used during public health emergencies. These drug development programs rely heavily on clinical pharmacology methods to provide evidence of effectiveness.

Every day in DIDP and OCP provides new opportunities to make a positive difference in the world. Throughout my 30-year career at FDA, I have participated in countless activities that demonstrate the essential contribution of clinical pharmacology to the development of drugs for life-threating conditions."

# Best Practices and Guidances

FDA published a total of eight clinical pharmacology guidances in 2024, providing recommendations on a range of topics including drug interactions, clinical pharmacology studies for antibody-drug conjugates and oligonucleotides, bioequivalence studies, dose optimization for oncology drugs, mass balance, and the impact of renal impairment (See Figure 3). OCP also welcomed input from the public on topics such as identifying priorities for MIDD and clinical pharmacology guidance development as well as assessing the immunogenicity risk of host cell proteins.

In 2024, OCP leadership was instrumental in finalizing two guidances developed under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). These final guidances on drug interaction studies and bioequivalence assessment will help to streamline global drug development through recommendations that are acceptable to many regulatory agencies worldwide. OCP representatives are also leaders in working groups for ICH M15 General Considerations for Model-Informed Drug Development.

**FIGURE 3** OCP Guidances Published in 2024

**DOSE OPTIMIZATION**

- Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases (Final guidance)

**DRUG INTERACTIONS**

- Drug Interaction Information in Human Prescription Drug and Biological Product Labeling (Draft guidance)
- M12 Drug Interaction Studies (Final guidance)*

**DRUG PRODUCT DEVELOPMENT**

- Clinical Pharmacology Considerations for Antibody-Drug Conjugates (Final guidance)
- Clinical Pharmacology Considerations for the Development of Oligonucleotide Therapeutics (Final guidance)

**PHARMACOKINETICS**

- Clinical Pharmacology Considerations for Human Radiolabeled Mass Balance Studies (Final guidance)
- Pharmacokinetics in Patients with Impaired Renal Function – Study Design, Data Analysis, and Impact on Dosing and Labeling (Final guidance)
- M13A Bioequivalence for Immediate-Release Solid Oral Dosage Forms (Final guidance)*

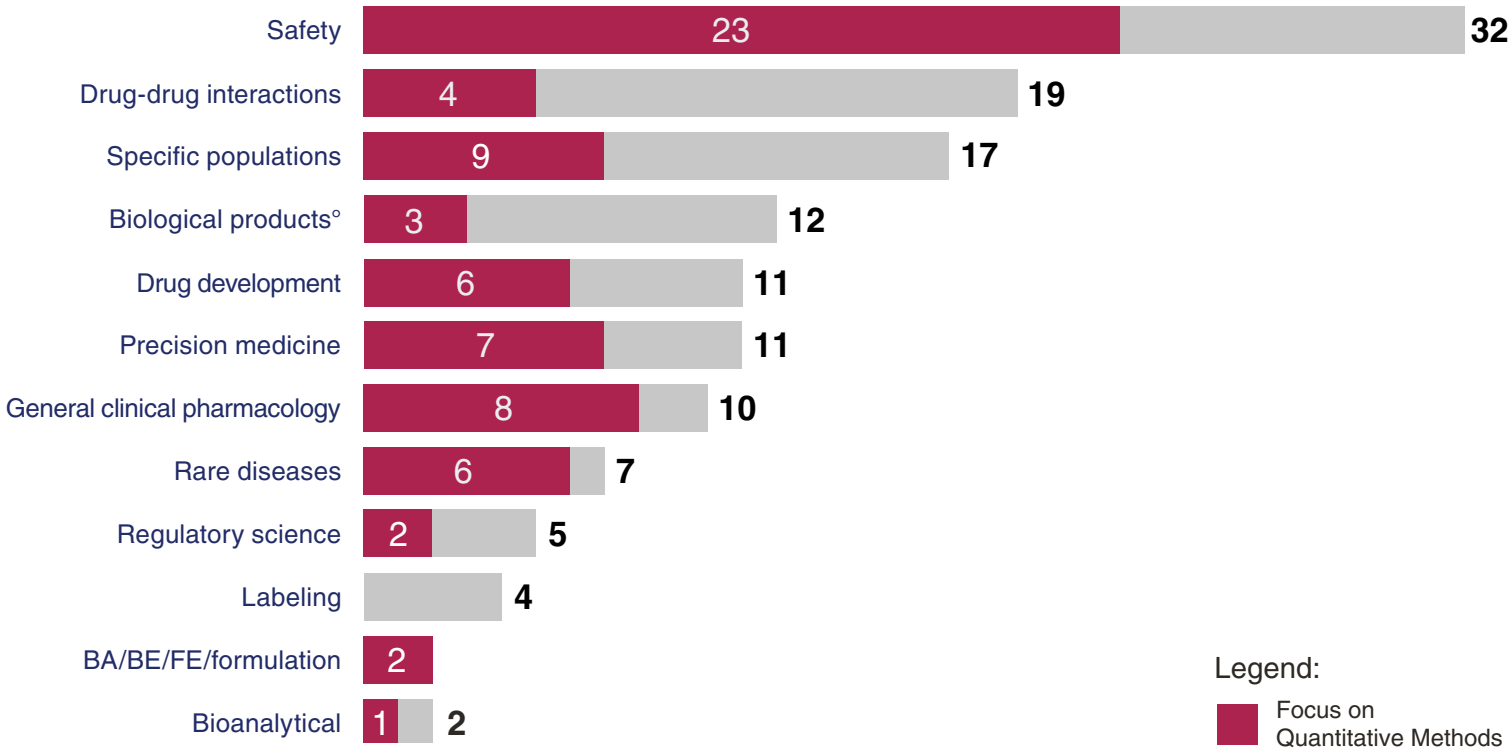
** This guidance was developed under the auspices of ICH.*

# Regulatory Science Research

Regulatory science research focuses on developing the tools, standards, and approaches needed to generate the data and information on which FDA assesses the safety, efficacy, quality, and performance of FDA-regulated products. Advances in regulatory science support evidence-based decision-making and enable the translation of discoveries in science and technology into safe and effective medical products.

With these objectives in mind, the OCP regulatory science research program uses state-of-the-art analytical, laboratory, and quantitative methods to address the multifaceted regulatory challenges we face in contemporary drug development. In 2024, our research portfolio consisted of 103 projects focused on a range of focus areas to address public health needs (See Figure 4).

**FIGURE 4** OCP Research Focus Areas in 2024




*A research project may cover multiple focus areas or use more than one quantitative method.*
*BA/BE/FE: bioavailability/bioequivalence/food effect; °includes biosimilar biological products*

**OCP AT-A-GLANCE RESEARCH**

**103**
Total Research Projects

**10**
Focused on Pediatric and Maternal Health Pharmacology

**71**
Focused on Quantitative Medicine

## INNOVATIVE RESEARCH METHODS

OCP researchers employed in vitro systems, modeling approaches, and clinical studies to characterize mechanisms of drug interactions (including the impact of rare drug metabolizing enzyme variants), better predict transporter-based interactions, and elucidate the combined pharmacodynamic effects of common drug combinations, such as sedative psychotropics, serotonin reuptake inhibitors, and opioids. Mechanistic pharmacodynamic models allowed our researchers to simulate a range of overdose scenarios, and the predictions from these models will provide more scientific evidence for recommending adequate doses of opioid antagonists to reverse toxicities from opioid overdose. PBPK modeling techniques were leveraged to advance maternal and fetal health research by describing clinical pharmacology characteristics during lactation and predict fetal exposure to drugs used during pregnancy. In addition, QSP models were explored for pediatric developmental safety prediction. Our staff also investigated an array of pharmacodynamic biomarkers for their utility in risk mitigation, precision medicine, oncology, and rare diseases, while artificial intelligence/machine learning technologies were used to explore clinical trial enrichment strategies and identify risk factors for immunogenicity. In 2024, our research activities informed regulatory best practices and global harmonization in the areas of proarrhythmia risk assessment and cardiac safety endpoints, control of nitrosamine impurities in human drugs, and immunogenicity assessment for therapeutic proteins.

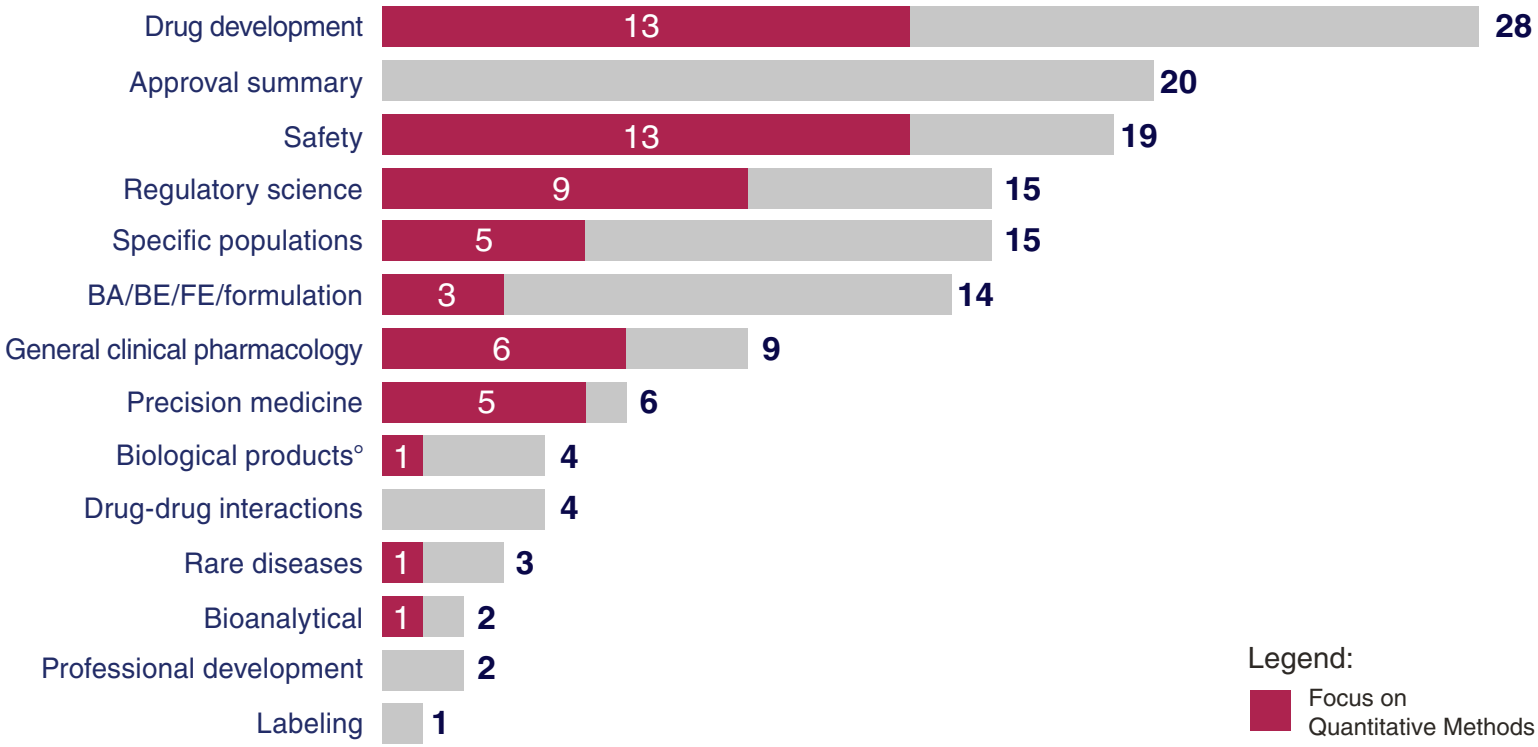
## COLLABORATIVE RESEARCH EFFORTS

Collaborative research efforts and partnerships were crucial in 2024, continuing to support problem-solving to address scientific and public health priorities. For example, our partnerships through the Centers of Excellence in Regulatory Science and Innovation (CERSIs) program addressed high-priority regulatory science needs including streamlining drug development for rare diseases, identifying and validating breast cancer resistance protein biomarkers, and prioritization for study of drugs in specific populations. The application of state-of-the-art methodologies to these challenges are enhanced by these partnerships and include using real-world administrative claims and electronic health records for risk assessment, humanized animal models, human disease-specific cell models, and PBPK modeling-informed frameworks. Project descriptions for these innovative research efforts can be found on the FDA CERSI Collaborative Research Projects website.

## OCP SCIENTIFIC PUBLICATIONS

Each year, OCP shares research findings and current regulatory perspectives through publication in the peer-reviewed literature. In 2024, our staff authored 120 journal articles across a range of clinical pharmacology focus areas (See Figure 5 and Appendix). Our publications summarize new drug approvals, present research findings and applications in alternative, mechanistic, and quantitative methods areas, and address timely drug development and clinical pharmacology topics. We promoted therapeutic optimization and individualization for patient groups, such as pediatric patients, older adults, pregnant women, and transplant recipients. Publications on urgent public health issues in 2024 included antimicrobial resistance, COVID-19, hand sanitizers, opioids and controlled substances, nitrosamines, and sunscreens. Collectively, our publication portfolio communicates our most up-to-date outcomes and conclusions of our investigative regulatory work to the community.

**FIGURE 5** OCP Publications Focus Areas in 2024




*A publication may cover multiple focus areas or use more than one quantitative method.*
*BA/BE/FE: bioavailability/bioequivalence/food effect; °includes biosimilar biological products*

### OCP AT-A-GLANCE PUBLICATIONS

**120**
Total Publications

**14**
Focused on Pediatric and Maternal Health Pharmacology

**51**
Focused on Quantitative Methods

# OCP Division of Applied Regulatory Science

In 2024, OCP's Division of Applied Regulatory Science (DARS) accelerated integration of new science into the drug review process and increased engagement to address emergent regulatory and public health questions for the Agency. DARS multidisciplinary teams and experts across translational research disciplines conduct mission-critical research and provide answers to scientific questions and solutions to regulatory challenges. DARS scientists engage key collaborators to address knowledge gaps and impediments to regulatory assessment to facilitate regulatory decision-making and impact critical public health issues. DARS capabilities include laboratory-based research specializing in omics, bioanalysis, microphysiological and cellular systems, immunology, and electrophysiology, as well as in silico research performed by informatics and computational modeling groups. In addition, DARS hosts a specialized unit that designs and executes small clinical studies.

DARS conducts clinical research focused on facilitating new and follow-on product development and assessing the safety of approved drugs. Using applied research, DARS investigates questions related to clinical pharmacology, medical toxicology, systems pharmacology, chemistry, and biology. Regulatory areas of research focus in DARS include assessing the systemic absorption of sunscreens, evaluating whether certain drugs convert to carcinogens in people, studying drug interactions with opioids, optimizing opioid antagonist dosing in community settings, facilitating biosimilar and generic drug development, and advancing therapeutic development for rare diseases. DARS embraces the study of wide-ranging issues in regulatory science, helping the FDA solve regulatory and scientific challenges.

For more details on our dedicated research division, visit the DARS website.

## OCP VOICE

### Rodney Rouse, PhD

Acting Director, Division of Applied Regulatory Science

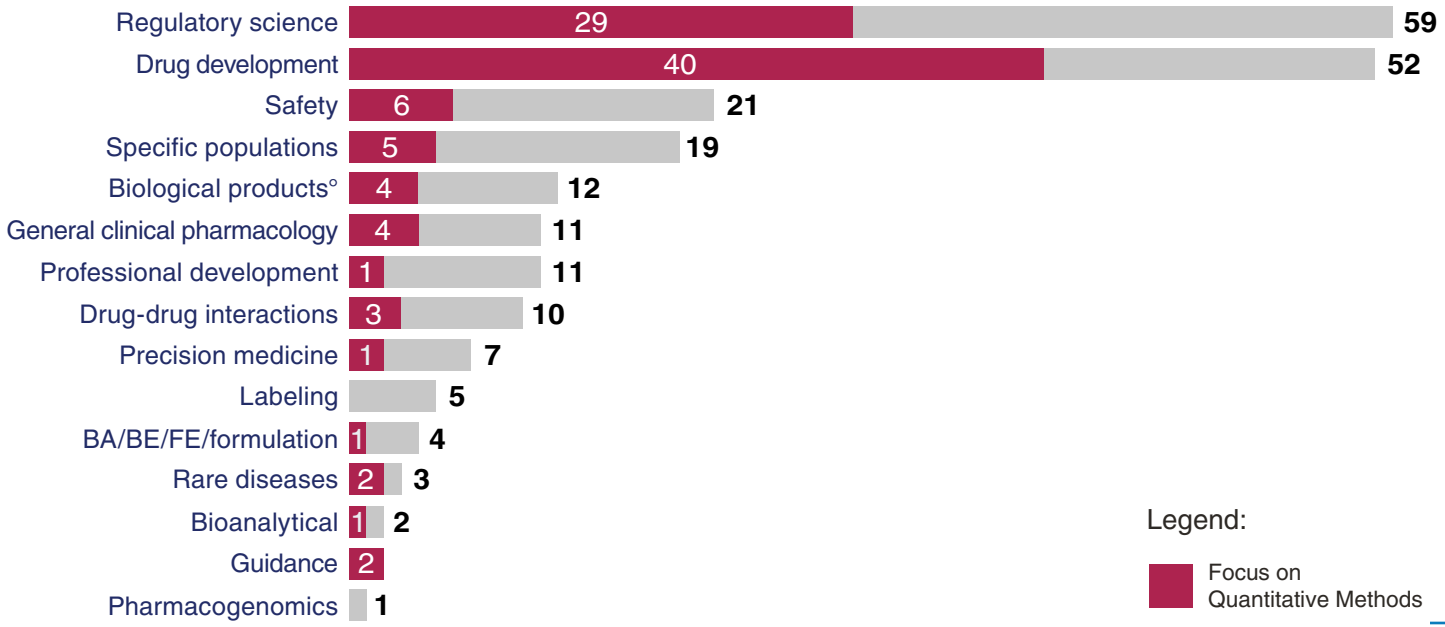
"Moving forward, DARS will build on its foundation of multiple successes in applied research by increasing alignment of our projects with regulatory review needs and collaborating to ensure better acceptance of new tools and approaches in the regulatory environment. DARS sits at a critical translational science intersection, having multiple computational, cell-based, and in vivo units as well as a clinical study unit that can synergize to solve problems. We see expansion of computational and clinical research within DARS as further enabling an essential and unique contribution to the mission of CDER and FDA.

We come to work at FDA from many other places and for many different reasons, but a common thread is the desire to advance public health. Working in DARS quickly demonstrated that good science truly makes a difference, contributing to improved regulatory decision-making, guidance creation, and drug development programs, and can influence key leaders to improve public health."

# Communication, Outreach, and Engagement

Accurate, user-friendly scientific information in the hands of health care providers, patients, and fellow scientists is the foundation of optimal drug therapy. Our connection with internal and external partners is multifaceted to ensure they have the necessary information for efficient drug development and effective patient care. OCP uses a variety of in-person, virtual, and direct communication channels to share regulatory perspectives, information on approved drug therapies, and scientific advances. We value opportunities to share knowledge in national and international forums and professional society meetings, collaborative workshops, and through web-based channels and media (See Figure 6 and Figure 7). OCP's direct email subscription services *Clinical Pharmacology Corner* and *Quantitative Medicine* reach over 160,000 subscribers collectively, providing reliable and timely information on application of novel quantitative methods in drug development, recent NDA/BLA approvals, guidance publications, FDA-sponsored events, and other notable topics. In 2024, OCP appreciated unique opportunities to convene with stakeholders, such as cross-Center collaborative communities, forums in which patients, health care providers, industry scientists, and regulators work together on medical device challenges to achieve common objectives and outcomes (e.g., to optimize standards, practices, and resources related to pharmacogenetic testing).

**FIGURE 6** OCP Presentations Focus Areas in 2024




*A presentation may cover multiple focus areas or use more than one quantitative method.*
*BA/BE/FE: bioavailability/bioequivalence/food effect; °includes biosimilar biological products*

**OCP AT-A-GLANCE**
**COMMUNICATION ACTIVITIES**

**Over 106,000**
*Clinical Pharmacology Corner* Subscribers

**Over 54,000**
*Quantitative Medicine* Subscribers

**200**
Presentations

# Engagement Through Workshops, Conferences, and Webinars

OCP engages the public through workshops, conferences, and webinars which provide opportunities for information exchange and sharing of perspectives. Among our many partnerships, we continued collaboratives with the Critical Path Institute (C-Path) and Health and Environmental Sciences Institute (HESI) for events focusing on alternative methods in drug development. Along with the Duke Margolis Institute for Health Policy, we convened a roundtable to gather insights from a multidisciplinary group of health care providers, drug information experts, industry representatives, medical toxicologists, health literacy experts, and labeling specialists to understand their needs and preferences for overdose information in the prescription drug labeling and to help inform future best practices. In 2024, OCP participated in several events sponsored by the FDA with external partner organizations, and engaged in discussions on dose optimization, guidance, novel therapeutic modalities, precision medicine, QM, rare diseases, and risk mitigation (See Figure 7).

**FIGURE 7** OCP Workshops, Conferences, and Webinars in 2024

### WORKSHOPS AND CONFERENCES

- 2024 DIA/FDA Oligonucleotide-Based Therapeutics Conference
- Clinical Pharmacology Guidances Advancing Drug Development and Regulatory Assessment: Role and Opportunities
- Duke Margolis Institute for Health Policy: Opportunities to Improve Dose-Finding and Optimization for Rare Disease Drug Development
- Evaluating Immunosuppressive Effects of In Utero Exposure to Drug and Biologic Products
- FDA Omics Days 2024
- FDA/CDER Office of Clinical Pharmacology and American Association for Cancer Research (AACR) Public Workshop: Quantitative Approaches to Select Dosages for Clinical Trials
- Product Quality Research Institute (PQRI) Workshop: MIDD Approaches in Pediatric Formulation Development
- Therapeutic Drug Monitoring of Biologics: Current Practice, Challenges and Opportunities
- Streamlining Drug Development and Improving Public Health through Quantitative Medicine: An Introduction to the CDER Quantitative Medicine Center of Excellence

### WEBINARS

- Clinical Pharmacology Considerations for Novel Therapeutic Modalities
- Clinical Pharmacology Considerations for Radiolabeled Mass Balance Studies
- ICH M12 Drug-Drug Interaction Studies Final Guidance

# Web Resources

We expanded our web presence to make clinical pharmacology and QM content more accessible. Together with our colleagues in FDA CDER's Office of Communications, we used website analytics to inform our digital strategy and grow our audience to ensure accurate and timely information reaches the public. Valuable resources have been made available on our websites with examples below.

## CDER QM CoE WEBPAGES

Established in 2024, the QM CoE facilitates and coordinates the continuous evolution and consistent application of QM for drug development and regulatory decision-making across CDER. The QM CoE webpages provide an overview of CoE activities, details on CoE organizational structure and members, helpful frequently asked questions and a fact sheet, and links to educational resources on QM.

## CLINICAL PHARMACOLOGY PEDIATRICS PROGRAM WEBSITE

The Clinical Pharmacology Pediatrics Program within OCP brings together multidisciplinary experts to promote the application of fundamental clinical pharmacology principles and tools to advance the development of new therapies for the pediatric population. Focus areas of the program include outreach and education, regulatory reviews and best practices, and regulatory science research. The Clinical Pharmacology Pediatrics Program website offers further details on this program and FDA's work in the pediatric space.

## FDA/C-PATH INSTITUTE MIDD WEB-BASED TRAINING

QM involves the development and application of exposure-based, biological, and quantitative modeling and simulation approaches derived from nonclinical, clinical, and real-world sources to inform drug development, regulatory decision-making, and patient care. MIDD is a fundamental QM activity, and in 2024, the QM CoE, in collaboration with CDER's OTS and the C-Path Institute, released a series of free, web-based training modules on MIDD for scientists of all backgrounds. This educational series was developed by experts in the field and teaches applications of MIDD approaches in development of drugs and biological products.

## THERAPEUTIC BIOLOGICS PROGRAM WEBSITE

TBP within OCP consists of scientists with broad clinical pharmacology knowledge and specialized experience in biological products. The program seeks to facilitate the development and approval of novel biological products and biosimilar biological products (biosimilars) through guidance development, regulatory review, research to address review issues and knowledge gaps, and collaboration to enhance communication and advance science. The TBP website highlights notable publications on novel therapeutic modalities and clinical pharmacology of biological products, relevant guidances, and collaboration and outreach resources.

## OCP VOICE

### Yow-Ming Wang, PhD

Associate Director for Biosimilars and Therapeutic Biologics

"OCP staff in the Therapeutics Biologics Program (TBP) are privileged and excited to serve as subject matter experts on therapeutic proteins and contribute to the FDA's public health mission. The innovations in therapeutic biological products present enormous potential to benefit patients with unmet medical needs and enhance the patient experience with treatments. Similarly, the rapidly expanding development pipeline of biosimilars promises to increase the availability of affordable therapeutic proteins.

In 2024, TBP addressed a wide range of exciting topics such as novel therapeutic modalities, bridging strategies, biomarkers in rare disease drug development, therapeutic drug monitoring, immunosuppressive effect of in utero exposure, and promoting evidence-based approaches to streamlining biosimilar development. The scientific and technical challenges we face demand rapid professional growth. Beyond the intellectual growth, I cherish the prospect that my daily work increases the availability of safe and effective medications for patients."

# 2025 Outlook

We will continue to bolster an already robust strategy that not only meets current public health needs, but also responds to any emerging public health crises. In 2025, we will begin implementation of our long-term goals to innovate and streamline the use of QM approaches in drug development and regulatory decision-making. We will execute our OCP Priorities, which will engage patients and health care providers, modernize our review processes, and ensure our staff have access to the most up-to-date science, education, and tools. Our research capabilities are poised to continue our work across the entirety of the translational science spectrum, with special emphasis on addressing complex regulatory and scientific questions. OCP will integrate learnings from research and review into guidances and best practices that can advance and enhance drug development.

We will also seek new ways to connect with our health care partners and professional societies, recognizing that we are part of a larger like-minded community interested in improving the health of individuals and society. In 2025, OCP will hold public workshops on topics including drug safety and the development of anti-infectives for pediatric patients, mechanistic modeling approaches in drug development, and model-based approaches to help optimize drug dosages for patients with cancer. We will provide timely, transparent, and meaningful communications through our recently expanded subscription services that now reach over 160,000 community members and continue to broaden our outreach and engagement channels to empower scientific, regulatory, and patient communities with reliable information.

Meeting the needs of patients, their families, and caregivers is at the forefront of our work. To that end, we reaffirm our commitment to tackling scientific, regulatory, and systems challenges to effective and efficient drug development. Our focus will be on translational science in its broadest sense. We wholeheartedly believe in the translational science principles of: 1) focusing on unmet medical need; 2) developing generalizable and scalable solutions; 3) encouraging creativity and innovation; 4) leveraging cross-disciplinary expertise; 5) developing efficiencies; 6) cultivating broad partnerships across organizational boundaries; and 7) being bold and rigorous. Our future direction is guided by these principles coupled with our core values. Our passionate and dedicated staff looks forward to continuing our pursuit of improving lives and the betterment of health for all.

*Examples presented in this Annual Report are illustrative and are not a comprehensive representation of our 2024 activities and accomplishments. For comments or questions, please contact* ocp@fda.hhs.gov.

# Appendix: OCP Publications in 2024

| PUBLICATION | CITATION |
|---|---|
| 2023 white paper on recent issues in bioanalysis: ISR for ADA assays, the rise of dPCR vs qPCR, international reference standards for vaccine assays, anti-AAV TAb post-dose assessment, NanoString validation, ELISpot as gold standard (part 3 - recommendations on gene therapy, cell therapy, vaccines immunogenicity & technologies; biotherapeutics immunogenicity & risk assessment; ADA/NAb assay/reporting harmonization). | Bioanalysis. 2024 Apr;16(7):77-119. doi: 10.4155/bio-2024-0024. Epub 2024 Feb 22. PMID: 38389403. |
| A meta-analysis of the safety and immunogenicity of pharmacokinetic similarity studies and comparative clinical studies. | J Clin Pharmacol. 2024 Nov 27. doi: 10.1002/jcph.6165. Epub ahead of print. PMID: 39604041. |
| A modified delphi study to establish essential clinical pharmacology competencies. | Ther Innov Regul Sci. 2024 May;58(3):473-482. doi: 10.1007/s43441-023-00609-y. Epub 2024 Feb 6. PMID: 38319585. |
| Accuracy of left ventricular mechanical dyssynchrony indices for mechanical characteristics of left bundle branch block using cardiovascular magnetic resonance feature tracking. | Eur Heart J Cardiovasc Imaging. 2024 Nov 22:jeae301. doi: 10.1093/ehjci/jeae301. Epub ahead of print. PMID: 39576753. |
| Addressing drug-drug interaction knowledge gaps at the time of approval: an analysis of FDA postmarketing requirements and commitments from 2009 to 2023. | J Clin Pharmacol. 2024 Oct 3. doi: 10.1002/jcph.6142. Epub ahead of print. PMID: 39363538. |
| Advancing alternative methods to reduce animal testing. | Science. 2024 Nov 15;386(6723):724-726. doi: 10.1126/science.adg6228. Epub 2024 Nov 14. PMID: 39541448. |
| Advanced smart biomaterials for regenerative medicine and drug delivery based on phosphoramidite chemistry: from oligonucleotides to precision polymers. | Biomacromolecules. 2024 May 13;25(5):2701-2714. doi: 10.1021/acs.biomac.4c00259. Epub 2024 Apr 12. PMID: 38608139. |
| Advancing the utilization of real-world data and real-world evidence in clinical pharmacology and translational research-proceedings from the ASCPT 2023 preconference workshop. | Clin Transl Sci. 2024 Apr;17(4):e13785. doi: 10.1111/cts.13785. PMID: 38572980. |
| Algorithmic identification of treatment-emergent adverse events from clinical notes using large language models: a pilot study in inflammatory bowel disease. | medRxiv [Preprint]. 2023 Sep 8:2023.09.06.23295149. doi: 10.1101/2023.09.06.23295149. Update in: Clin Pharmacol Ther. 2024 Jun;115(6):1391-1399. doi: 10.1002/cpt.3226. PMID: 37732220. |
| An evaluation of first-in-human studies for RNA oligonucleotides. | Nucleic Acid Ther. 2024 Dec;34(6):276-284. doi: 10.1089/nat.2024.0036. Epub 2024 Sep 23. PMID: 39311689. |
| Antioxidants had no effects on the in-vitro permeability of BCS III model drug substances. | J Pharm Sci. 2024 Sep;113(9):2708-2714. doi: 10.1016/j.xphs.2024.05.033. Epub 2024 Jun 9. PMID: 38862090. |
| Application of advanced modeling approaches supporting generic product development under GDUFA for fiscal year 2023. | AAPS J. 2024 Apr 24;26(3):55. doi: 10.1208/s12248-024-00924-8. PMID: 38658449. |
| Application of model-informed drug development in dose selection and optimization for siRNA therapies. | J Clin Pharmacol. 2024 Jul;64(7):799-809. doi: 10.1002/jcph.2418. Epub 2024 Mar 1. PMID: 38426370. |
| Application of transporter assays for drug discovery and development: an update of the literature. | Expert Opin Drug Discov. 2024 Oct;19(10):1247-1257. doi: 10.1080/17460441.2024.2387790. Epub 2024 Aug 6. PMID: 39105537. |
| Approval of mycophenolate mofetil for prophylaxis of organ rejection in pediatric recipients of heart or liver transplants: a regulatory perspective. | Clin Pharmacol Ther. 2024 Sep;116(3):807-813. doi: 10.1002/cpt.3288. Epub 2024 May 2. PMID: 38695530. |
| Assessing the immunogenicity risk of salmon calcitonin peptide impurities using in silico and in vitro methods. | Front Pharmacol. 2024 Aug 9;15:1363139. doi: 10.3389/fphar.2024.1363139. PMID: 39185315. |

| PUBLICATION | CITATION |
|---|---|
| Assessment of dosing strategies for pediatric drug products. | Clin Pharmacol Ther. doi: 10.1002/cpt.3250, 116, 3, (479-874), Epub 2024 Mar 17. |
| Biowaiver monograph for immediate-release solid oral dosage forms: fexofenadine. | J Pharm Sci. 2024 Sep;113(9):2981-2993. doi: 10.1016/j.xphs.2024.06.002. Epub 2024 Jun 8. PMID: 38857646. |
| Biowaiver monographs for immediate-release solid oral dosage forms: lemborexant. | J Pharm Sci. 2024 Oct 23:S0022-3549(24)00480-5. doi: 10.1016/j.xphs.2024.10.030. Epub ahead of print. PMID: 39454947. |
| Biowaiver monograph for immediate-release solid oral dosage forms: raltegravir potassium. | J Pharm Sci. 2024 Nov;113(11):3137-3144. doi: 10.1016/j.xphs.2024.08.006. Epub 2024 Aug 16. PMID: 39154736. |
| Changes in drug crystallinity in a commercial tacrolimus amorphous formulation result in variable pharmacokinetics. | J Pharm Sci. 2025 Jan;114(1):313-322. doi: 10.1016/j.xphs.2024.09.025. Epub 2024 Oct 15. PMID: 39414078. |
| Clinical pharmacology approaches to support approval of new routes of administration for therapeutic proteins. | Clin Pharmacol Ther. 2024 Mar;115(3):440-451. doi: 10.1002/cpt.3178. Epub 2024 Jan 18. PMID: 38235832. |
| Clinical pharmacology considerations for first-in-human clinical trials for enzyme replacement therapy. | J Inherit Metab Dis. 2024 May 13. doi: 10.1002/jimd.12746. Epub ahead of print. PMID: 38740427. |
| Clinical pharmacology of glucagon. | Clin Pharmacol Ther. 2024 Oct;116(4):976-979. doi: 10.1002/cpt.3340. Epub 2024 Jun 7. PMID: 38847591. |
| Closing the gap: a United States perspective on enhancing drug evaluation in older adults. | J Am Geriatr Soc. 2024 Sep;72(9):2903-2906. doi: 10.1111/jgs.18903. Epub 2024 Apr 3. PMID: 38567777. |
| Clustering plasma concentration-time curves: applications of unsupervised learning in pharmacogenomics. | J Biopharm Stat. 2024 Jun 18:1-19. doi: 10.1080/10543406.2024.2365389. Epub ahead of print. PMID: 38888431. |
| Collaborative science in action: a 20 year perspective from the Health and Environmental Sciences Institute (HESI) cardiac safety committee. | J Pharmacol Toxicol Methods. 2024 May-Jun;127:107511. doi: 10.1016/j.vascn.2024.107511. Epub 2024 May 6. PMID: 38710237. |
| Commentary on 'exploration of suitable pharmacodynamic parameters for acarbose bioequivalence evaluation: a series of clinical trials with branded acarbose' by Jie Huang et al. | Br J Clin Pharmacol. 2024 Sep;90(9):2320-2322. doi: 10.1111/bcp.16148. Epub 2024 Jun 25. PMID: 38922996. |
| Contractility assessment using aligned human iPSC-derived cardiomyocytes. | J Pharmacol Toxicol Methods. 2024 Jul-Aug;128:107530. doi: 10.1016/j.vascn.2024.107530. Epub 2024 Jun 24. PMID: 38917571. |
| Covariate modeling in pharmacometrics: general points for consideration. | CPT Pharmacometrics Syst Pharmacol. 2024 May;13(5):710-728. doi: 10.1002/psp4.13115. Epub 2024 Apr 2. PMID: 38566433. |
| Current state and new horizons in applications of physiologically based biopharmaceutics modeling (PBBM): a workshop report. | Mol Pharm. 2025 Jan 6;22(1):5-27. doi: 10.1021/acs.molpharmaceut.4c01148. Epub 2024 Dec 16. PMID: 39680866. |
| Current status and future directions: the application of artificial intelligence/machine learning for precision medicine. | Clin Pharmacol Ther. 2024 Apr;115(4):673-686. doi: 10.1002/cpt.3152. Epub 2024 Jan 3. PMID: 38103204. |
| Determining recommended acceptable intake limits for n-nitrosamine impurities in pharmaceuticals: development and application of the carcinogenic potency categorization approach (CPCA). | Regul Toxicol Pharmacol. 2024 Jun;150:105640. doi: 10.1016/j.yrtph.2024.105640. Epub 2024 May 14. PMID: 38754805. |
| Development of quantitative comparative approaches to support complex generic drug development. | AAPS J 26, 15 (2024). https://doi.org/10.1208/s12248-024-00885-y. |

| PUBLICATION | CITATION |
|---|---|
| Dosage optimization: a regulatory perspective for developing oncology drugs. | Clin Pharmacol Ther. 2024 Sep;116(3):577-591. doi: 10.1002/cpt.3373. Epub 2024 Jul 29. PMID: 39072758. |
| Dosing strategies and quantitative clinical pharmacology for bispecific T-cell engagers development in oncology. | Clin Pharmacol Ther. 2024 Sep;116(3):637-646. doi: 10.1002/cpt.3361. Epub 2024 Jul 4. PMID: 38962850. |
| Driving efficiency: leveraging model-informed approaches in 505(b)(2) regulatory actions. | J Clin Pharmacol. 2024 Aug 9. doi: 10.1002/jcph.6109. Epub ahead of print. PMID: 39120874. |
| Efflux transporters in drug disposition during pregnancy. | Drug Metabolism and Disposition May 29, 2024, DMD-MR-2023-001385; DOI: https://doi.org/10.1124/dmd.123.001385. |
| Enhancing pharmacogenomic data accessibility and drug safety with large language models: a case study with Llama3.1. | Exp Biol Med (Maywood). 2024 Dec 3;249:10393. doi: 10.3389/ebm.2024.10393. PMID: 39691764. |
| Evaluation of in vitro metabolism- and transporter-based drug interactions with sunscreen active ingredients. | Pharm Res. 2024 Aug;41(8):1613-1620. doi: 10.1007/s11095-024-03746-7. Epub 2024 Jul 24. PMID: 39044045. |
| Evaluation of the landscape of pharmacodynamic biomarkers in Niemann-Pick disease type c (NPC). | Orphanet J Rare Dis. 2024 Jul 26;19(1):280. doi: 10.1186/s13023-024-03233-7. PMID: 39061081. |
| Expanding role of endogenous biomarkers for assessment of transporter activity in drug development: current applications and future horizon. | Pharmaceutics. 2024 Jun 25;16(7):855. doi: 10.3390/pharmaceutics16070855. PMID: 39065552. |
| Experience learned and perspectives on using model-integrated evidence in the regulatory context for generic drug products-a meeting report. | AAPS J. 2024 Jan 10;26(1):14. doi: 10.1208/s12248-023-00884-5. PMID: 38200397. |
| Exploration of the potential impact of batch-to-batch variability on the establishment of pharmacokinetic bioequivalence for inhalation powder drug products. | CPT Pharmacometrics Syst Pharmacol. 2024 Nov 22. doi: 10.1002/psp4.13276. Epub ahead of print. PMID: 39575671. |
| FDA approval summary: alpelisib for PIK3CA-related overgrowth spectrum. | Clin Cancer Res. 2024 Jan 5;30(1):23-28. doi: 10.1158/1078-0432.CCR-23-1270. PMID: 37624421. |
| FDA approval summary: asciminib for pH+ CML in chronic phase treated with two or more tyrosine kinase inhibitors and for the T315I mutation. | Clin Cancer Res. 2024 Oct 1;30(19):4266-4271. doi: 10.1158/1078-0432.CCR-24-1086. PMID: 39088257. |
| FDA approval summary: capecitabine labeling update under Project Renewal. | Clin Cancer Res. 2024 Dec 16;30(24):5508-5514. doi: 10.1158/1078-0432.CCR-24-1708. PMID: 39377782. |
| FDA approval summary: dabrafenib in combination with trametinib for BRAFV600E mutation-positive low-grade glioma. | Clin Cancer Res. 2024 Jan 17;30(2):263-268. doi: 10.1158/1078-0432.CCR-23-1503. PMID: 37610803. |
| FDA approval summary: enfortumab vedotin plus pembrolizumab for cisplatin-ineligible locally advanced or metastatic urothelial carcinoma. | Clin Cancer Res. 2024 May 15;30(10):2011-2016. doi: 10.1158/1078-0432.CCR-23-3738. PMID: 38441576. |
| FDA approval summary: fam-trastuzumab deruxtecan-nxki for unresectable or metastatic non-small cell lung cancer with activating HER2 mutations. | Oncologist. 2024 Aug 5;29(8):667-671. doi: 10.1093/oncolo/oyae151. PMID: 38970465. |
| FDA approval summary: fruquintinib for the treatment of refractory metastatic colorectal cancer. | Clin Cancer Res. 2024 Aug 1;30(15):3100-3104. doi: 10.1158/1078-0432.CCR-24-0281. PMID: 38809262. |
| FDA approval summary: ivosidenib in combination with azacitidine for treatment of patients with newly diagnosed acute myeloid leukemia with an IDH1 mutation. | Clin Cancer Res. 2024 Apr 1;30(7):1226-1231. doi: 10.1158/1078-0432.CCR-23-2234. PMID: 38010220. |
| FDA approval summary: nalmefene nasal spray for the emergency treatment of known or suspected opioid overdose. | Clin Pharmacol Ther. 2024 Dec 8. doi: 10.1002/cpt.3514. Epub ahead of print. PMID: 39648641. |
| FDA approval summary: olutasidenib for adult patients with relapsed or refractory acute myeloid leukemia with an isocitrate dehydrogenase-1 mutation. | Clin Cancer Res. 2025 Jan 6;31(1):12-17. doi: 10.1158/1078-0432.CCR-24-2196. PMID: 39475462. |

| PUBLICATION | CITATION |
|---|---|
| FDA approval summary: pirtobrutinib for relapsed or refractory mantle cell lymphoma. | Clin Cancer Res. 2024 Jan 5;30(1):17-22. doi: 10.1158/1078-0432.CCR-23-1272. PMID: 37624619. |
| FDA approval summary: repotrectinib for locally advanced or metastatic ROS1-positive non-small cell lung cancer. | Clin Cancer Res. 2024 Aug 15;30(16):3364-3370. doi: 10.1158/1078-0432.CCR-24-0949. PMID: 38875108. |
| FDA approval summary: teclistamab-a bispecific CD3 T-cell engager for patients with relapsed or refractory multiple myeloma. | Clin Cancer Res. 2024 Dec 16;30(24):5515-5520. doi: 10.1158/1078-0432.CCR-24-1872. PMID: 39412823. |
| FDA approval summary: tremelimumab in combination with durvalumab for the treatment of patients with unresectable hepatocellular carcinoma. | Clin Cancer Res. 2024 Jan 17;30(2):269-273. doi: 10.1158/1078-0432.CCR-23-2124. PMID: 37676259. |
| FDA, CDC, and NIH co-sponsored public workshop summary-development considerations of antimicrobial drugs for the treatment of gonorrhea. | Clin Infect Dis. 2024 Jul 24:ciae386. doi: 10.1093/cid/ciae386. Epub ahead of print. PMID: 39045871. |
| Food and Drug Administration public workshop summary-addressing challenges in inhaled antifungal drug development. | Clin Infect Dis. 2024 Jun 14;78(6):1564-1570. doi: 10.1093/cid/ciad607. PMID: 37802928. |
| Food-drug effects and pediatric drug development studies submitted to the US Food and Drug Administration, 2012-2022. | J Clin Pharmacol. 2024 Jun;64(6):697-703. doi: 10.1002/jcph.2405. Epub 2024 Jan 31. PMID: 38294346. |
| Getting the dose right in drug development for rare diseases: barriers and enablers. | Clin Pharmacol Ther. 2024 Dec;116(6):1412-1432. doi: 10.1002/cpt.3407. Epub 2024 Aug 16. PMID: 39148459. |
| Healthcare providers' use of a concise summary to prescribe for lactating patients. | Res Social Adm Pharm. 2024 May;20(5):531-538. doi: 10.1016/j.sapharm.2024.02.004. Epub 2024 Feb 19. PMID: 38413289. |
| How debunking biases in research and development decisions could lead to more equitable healthcare? | Clin Transl Sci. 2024 Jul;17(7):e13880. doi: 10.1111/cts.13880. PMID: 39016187. |
| ICH M10 bioanalytical method validation guideline-1 year later. | AAPS J. 2024 Sep 12;26(5):103. doi: 10.1208/s12248-024-00974-y. PMID: 39266900. |
| In memoriam Arthur J. Atkinson, Jr. (1938-2024). | Clin Pharmacol Ther, 116: 20-21. https://doi.org/10.1002/cpt.3300 |
| In vitro assay development to study pulse field ablation outcome using *Solanum Tuberosum.* | Int. J. Mol. Sci. 2024, 25(16), 8967; https://doi.org/10.3390/ijms25168967 |
| Informing the risk assessment related to lactation and drug exposure: a physiologically based pharmacokinetic lactation model for pregabalin. | CPT Pharmacometrics Syst Pharmacol. 2024 Nov;13(11):1953-1966. doi: 10.1002/psp4.13266. Epub 2024 Oct 26. PMID: 39460526. |
| Intranasal naloxone repeat dosing strategies and fentanyl overdose: a simulation-based randomized clinical trial. | JAMA Netw Open. 2024 Jan 2;7(1):e2351839. doi: 10.1001/jamanetworkopen.2023.51839. PMID: 38261323. |
| Knockout transporter cell lines to assess substrate potential towards efflux transporters. | AAPS J 26, 79 (2024). https://doi.org/10.1208/s12248-024-00950-6. |
| Labetalol dosing in pregnancy: PBPK/PD and CYP2C19 polymorphisms. | J Clin Pharmacol. 2024 Nov;64(11):1443-1455. doi: 10.1002/jcph.2496. Epub 2024 Jul 8. PMID: 38973651. |
| Landscape of regulatory quantitative systems pharmacology submissions to the U.S. Food and Drug Administration: an update report. | CPT Pharmacometrics Syst Pharmacol. 2024 Dec;13(12):2102-2110. doi: 10.1002/psp4.13208. Epub 2024 Oct 18. PMID: 39423143. |
| Leveraging in vitro models for clinically relevant rare CYP2D6 variants in pharmacogenomics. | Drug Metab Dispos. 2024 Feb 14;52(3):159-170. doi: 10.1124/dmd.123.001512. PMID: 38167410. |

| PUBLICATION | CITATION |
|---|---|
| Machine learned classification of ligand intrinsic activities at human $\mu$-opioid receptor. | bioRxiv [Preprint]. 2024 Jun 14:2024.04.07.588485. doi: 10.1101/2024.04.07.588485. Update in: ACS Chem Neurosci. 2024 Aug 7;15(15):2842-2852. doi: 10.1021/acschemneuro.4c00212. PMID: 38645122. |
| Mechanism-based organization of neural networks to emulate systems biology and pharmacology models. | Sci Rep. 2024 May 27;14(1):12082. doi: 10.1038/s41598-024-59378-9. PMID: 38802422. |
| Membrane transporters in drug development and as determinants of precision medicine. | Nat Rev Drug Discov. 2024 Apr;23(4):255-280. doi: 10.1038/s41573-023-00877-1. Epub 2024 Jan 24. PMID: 38267543. |
| Methanol poisonings from contaminated hand sanitizers identified by the United States Food and Drug Administration. | Clin Toxicol (Phila). 2023 Dec;61(12):1065-1067. doi: 10.1080/15563650.2023.2288809. Epub 2024 Jan 25. PMID: 38174554. |
| Methodology for good machine learning with multi-omics data. | Clin Pharmacol Ther. 2024 Apr;115(4):745-757. doi: 10.1002/cpt.3105. Epub 2024 Jan 31. PMID: 37965805. |
| Model-informed drug development-based approval of intravenous secukinumab for the treatment of adult patients with active psoriatic arthritis, active ankylosing spondylitis, and active non-radiographic axial spondyloarthritis. | Clin Pharmacol Ther. 2025 Feb;117(2):475-484. doi: 10.1002/cpt.3464. Epub 2024 Oct 16. PMID: 39411974. |
| Moving the needle for oncology dose optimization: a call for action. | Clin Pharmacol Ther. 2024 Jun;115(6):1187-1197. doi: 10.1002/cpt.3263. PMID: 38736240. |
| Narrow therapeutic index drugs: FDA experience, views, and operations. | Clin Pharmacol Ther. 2025 Jan;117(1):116-129. doi: 10.1002/cpt.3460. Epub 2024 Nov 11. PMID: 39529254. |
| Nonclinical evaluation of chronic cardiac contractility modulation on 3D human engineered cardiac tissues. | J Cardiovasc Electrophysiol. 2024 May;35(5):895-905. doi: 10.1111/jce.16222. Epub 2024 Mar 3. PMID: 38433304. |
| On placental and lactational transfer of IgG-based therapeutic proteins - Current understanding and knowledge gaps from a clinical pharmacology perspective. | Clin Transl Sci. 2024 Oct;17(10):e70049. doi: 10.1111/cts.70049. PMID: 39436322. |
| Optimizing dosage in pharmacotherapy-missing the forest for the trees. | Clin Pharmacol Ther. 2024 Sep;116(3):511-514. doi: 10.1002/cpt.3268. Epub 2024 Apr 15. PMID: 38618676. |
| Parameterization of physiologically based biopharmaceutics models: workshop summary report. | Mol Pharm. 2024 Aug 5;21(8):3697-3731. doi: 10.1021/acs.molpharmaceut.4c00526. Epub 2024 Jun 30. PMID: 38946085. |
| PBBM considerations for base models, model validation, and application steps: workshop summary report. | Mol Pharm. 2024 Nov 4;21(11):5353-5372. doi: 10.1021/acs.molpharmaceut.4c00758. Epub 2024 Sep 30. PMID: 39348508. |
| Pediatric cancer drug development: leveraging insights in cancer biology and the evolving regulatory landscape to address challenges and guide further progress. | Cold Spring Harb Perspect Med. 2024 Apr 1;14(4):a041656. doi: 10.1101/cshperspect.a041656. PMID: 38467448. |
| Pediatric extrapolation approach for U.S. Food and Drug Administration approval of brexpiprazole in patients aged 13 to 17 years with schizophrenia. | J Clin Pharmacol. 2024 Jul;64(7):771-778. doi: 10.1002/jcph.2429. Epub 2024 Mar 15. PMID: 38488344. |
| Perspectives on drug development for the treatment of chronic myeloid leukemia in pregnant patients and patients who are breastfeeding. | Clin Cancer Res. 2024 Sep 3;30(17):3658-3666. doi: 10.1158/1078-0432.CCR-24-0826. PMID: 38967550. |
| Pharmacokinetic models for inhaled fluticasone propionate and salmeterol xinafoate to quantify batch-to-batch variability. | AAPS J. 2024 Apr 26;26(3):56. doi: 10.1208/s12248-024-00913-x. PMID: 38671158. |
| Pharmacokinetics-bridging between autoinjectors and prefilled syringes for subcutaneous injection: case examples revealing a knowledge gap. | Clin Pharmacol Ther. 2024 Mar;115(3):404-407. doi: 10.1002/cpt.3145. Epub 2024 Jan 2. PMID: 38167787. |

| PUBLICATION | CITATION |
|---|---|
| Physiologically based biopharmaceutics modeling (PBBM): best practices for drug product quality, regulatory and industry perspectives: 2023 workshop summary report. | Mol Pharm. 2024 May 6;21(5):2065-2080. doi: 10.1021/acs.molpharmaceut.4c00202. Epub 2024 Apr 10. PMID: 38600804. |
| Physiologically based modeling reveals different risk of respiratory depression after fentanyl overdose between adults and children. | Clin Transl Sci. 2024 Apr;17(4):e13780. doi: 10.1111/cts.13780. PMID: 38618722. |
| Population pharmacokinetics (PopPK) support for pediatric dosing of biological products. | J Clin Pharmacol. 2024 Aug 16. doi: 10.1002/jcph.6116. Epub ahead of print. PMID: 39149895. |
| Potential value of animal microphysiological systems. | ALTEX. 2024 Aug 7. doi: 10.14573/altex.2311141. Epub ahead of print. PMID: 39133010. |
| Project Confirm: accelerated drug approvals for CML-response. | Clin Cancer Res. 2024 Jan 5;30(1):237-238. doi: 10.1158/1078-0432.CCR-23-3234. PMID: 38178776. |
| Pulsed electric field performance calculator tool based on an in vitro human cardiac model. | Front Physiol. 2024 Jun 7;15:1395923. doi: 10.3389/fphys.2024.1395923. PMID: 38911328. |
| Quantitative structure-activity relationship models to predict cardiac adverse effects. | Chem Res Toxicol. 2024 Dec 16;37(12):1924-1933. doi: 10.1021/acs.chemrestox.4c00186. Epub 2024 Nov 13. PMID: 39535830. |
| Realizing the promise of Project Optimus: challenges and emerging opportunities for dose optimization in oncology drug development. | CPT Pharmacometrics Syst Pharmacol. 2024 May;13(5):691-709. doi: 10.1002/psp4.13079. Epub 2024 Mar 21. PMID: 37969061. |
| Regulatory considerations in the approval of rezafungin (Rezzayo) for the treatment of candidemia and invasive candidiasis in adults. | J Infect Dis. 2024 Aug 16;230(2):505-513. doi: 10.1093/infdis/jiae146. PMID: 38502709. |
| Remdesivir discontinuation decisions based on thresholds of aminotransferase in an observational registry. | Drugs. 2024 Feb;84(2):209-217. doi: 10.1007/s40265-023-01981-7. Epub 2024 Jan 10. PMID: 38198063. |
| Statin drug-drug interactions: pharmacokinetic basis of FDA labeling recommendations and comparison across common tertiary clinical resources. | J Clin Pharmacol. 2024 Jun;64(6):704-712. doi: 10.1002/jcph.2406. Epub 2024 Feb 1. PMID: 38299698. |
| The incorporation of MALDI mass spectrometry imaging in studies to identify markers of toxicity following in utero opioid exposures in mouse fetuses. | Front Toxicol. 2024 Dec 3;6:1452974. doi: 10.3389/ftox.2024.1452974. PMID: 39691158. |
| The potential of disease progression modeling to advance clinical development and decision making. | Clin Pharmacol Ther. 2025 Feb;117(2):343-352. doi: 10.1002/cpt.3467. Epub 2024 Oct 15. PMID: 39410710. |
| The US Food and Drug Administration's model-informed drug development meeting program: from pilot to pathway. | Clin Pharmacol Ther. 2024 Aug;116(2):278-281. doi: 10.1002/cpt.3228. Epub 2024 Mar 6. PMID: 38445751. |
| The vision for expanding the visibility of the journal of clinical pharmacology: meet the new editor-in-chief and the 3 new associate editors! | J Clin Pharmacol. 2024 Jan;64(1):7-9. doi: 10.1002/jcph.2387. PMID: 38017359. |
| Therapeutic orphan no more: role for clinical pharmacology and translational science in developing therapeutics for rare and neglected diseases. | Clin Pharmacol Ther. 2024 Dec;116(6):1363-1368. doi: 10.1002/cpt.3474. PMID: 39543918. |
| Trust your gut: establishing confidence in gastrointestinal models - an overview of the state of the science and contexts of use. | ALTEX. 2024;41(3):402-424. doi: 10.14573/altex.2403261. Epub 2024 May 15. PMID: 38898799. |
| US Food and Drug Administration approval summary: capivasertib with fulvestrant for hormone receptor-positive, human epidermal growth factor receptor 2-negative locally advanced or metastatic breast cancer with *PIK3CA/AKT1/PTEN* alterations. | J Clin Oncol. 2024 Dec;42(34):4103-4113. doi: 10.1200/JCO.24.00427. Epub 2024 Aug 19. PMID: 39159418. |
| US Food and Drug Administration approval summary: eflornithine for high-risk neuroblastoma after prior multiagent, multimodality therapy. | J Clin Oncol. 2024 Sep 1;42(25):3047-3057. doi: 10.1200/JCO.24.00546. Epub 2024 Jun 25. PMID: 38917371. |

| PUBLICATION | CITATION |
|---|---|
| US Food and Drug Administration approval summary: elacestrant for estrogen receptor-positive, human epidermal growth factor receptor 2-negative, *ESR1*-mutated advanced or metastatic breast cancer. | J Clin Oncol. 2024 Apr 1;42(10):1193-1201. doi: 10.1200/JCO.23.02112. Epub 2024 Feb 21. PMID: 38381994. |
| US Food and Drug Administration approval summary: talazoparib in combination with enzalutamide for treatment of patients with homologous recombination repair gene-mutated metastatic castration-resistant prostate cancer. | J Clin Oncol. 2024 May 20;42(15):1851-1860. doi: 10.1200/JCO.23.02182. Epub 2024 Mar 7. PMID: 38452327. |
| Untargeted metabolomics and lipidomics in COVID-19 patient plasma reveals disease severity biomarkers. | Metabolomics. 2024 Dec 4;21(1):3. doi: 10.1007/s11306-024-02195-y. PMID: 39636373. |
| Use of the same model or modeling strategy across multiple submissions: focus on complex drug products. | AAPS J. 2024 Jan 4;26(1):12. doi: 10.1208/s12248-023-00879-2. PMID: 38177638. |
| Using machine learning to determine a suitable patient population for anakinra for the treatment of COVID-19 under the emergency use authorization. | Clin Pharmacol Ther. 2024 Apr;115(4):890-895. doi: 10.1002/cpt.3191. Epub 2024 Feb 13. PMID: 38348530. |
| Using mechanistic modeling approaches to support bioequivalence assessments for oral products. | AAPS J. 2024 Jan 24;26(1):19. doi: 10.1208/s12248-024-00886-x. PMID: 38267737. |

U.S. FOOD & DRUG
ADMINISTRATION

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

**Office of Clinical Pharmacology**
Office of Translational Sciences
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993