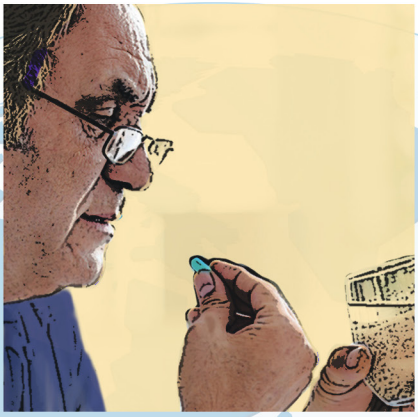
U.S. FOOD & DRUG ADMINISTRATION

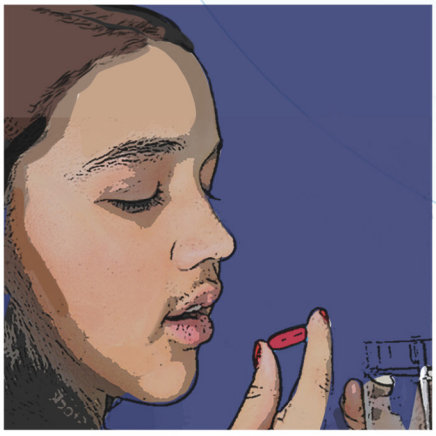
Office of Clinical Pharmacology

Office of Translational Sciences





2021 ANNUAL REPORT

Advancing Public Health Through Therapeutic Individualization

January 2022

www.fda.gov

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Director's MESSAGE

Given the challenges of the past 2 years, I cannot give enough praise to our staff in the U.S. Food and Drug Administration's (FDA's) Office of Clinical Pharmacology (OCP) for their tireless commitment to patients and public health. Applying rigorous scientific approaches and drug evaluation practices, our staff addressed multiple public health issues, including advancing therapeutics against COVID-19 and for people with unmet medical needs. We continued to expand model-informed approaches to accelerate the development of safe and effective drugs across the entire therapeutic landscape. We conducted groundbreaking research to ensure the safety and quality of certain commonly used over-the-counter products, in addition to addressing other important regulatory science issues. OCP also leveraged multiple engagement avenues to inform policy development, expand treatment options for diverse populations, and identify opportunities for further regulatory and scientific collaboration.

Our staff found creative ways to stay connected personally and professionally in a virtual world, and we implemented strategies to develop and recognize staff in meaningful ways. We are continually renewing our commitment to our core values of stewardship, leadership, excellence, connectedness, and diversity and respect to create a working environment that empowers and engages our staff to achieve our mission and vision.

Our staff have also recognized the importance of strategic visioning to ensure the continued excellence of our organization. In OCP's Roadmap to 2025, we will commit to focused, priority-driven decisions that will ultimately accelerate the science of clinical pharmacology and translational medicine and advance public health. As you will see in the pages that follow, we have completed the first phase in our strategic planning efforts and have identified three priorities. While moving forward in a challenging time is never easy, we are committed to sustained focus and growth in areas intended to advance science, ensure organizational health, elevate our people, and most importantly, benefit patients.

Herein, you will find a mere sampling of the incredible work of our inspiring staff. I am grateful for their perseverance, passion, and dedication, and for the opportunity to work with such talented colleagues who bring their entire selves daily in the hopes of benefiting others.

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

ORGANIZATION

OCP is a dynamic, purpose-driven organization dedicated to promoting and protecting global public health through the application of clinical pharmacology and translational medicine principles. OCP, an office within the FDA's Center for Drug Evaluation and Research (CDER) Office of Translational Sciences (OTS) super-office, is made up of over 260 pharmacologists, pharmacists, chemists, physicians, nurses, project and program managers, and administrative professionals. Our shared vision is to improve public health by building and translating knowledge of drug-response into patient-centered regulatory decisions of the highest quality.

Our mission is two-fold: 1) play a pivotal role in advancing the development of innovative new medicines by applying state-of-the-art scientific principles; and 2) promote therapeutic optimization and individualization through best practices in research, policy development, and drug evaluation throughout the product lifecycle. OCP fulfills its mission through its core functions of regulatory review, policy development and implementation, and research. Outcomes in these functional areas are enhanced by our expansive communication, stakeholder engagement, and outreach on national and international levels. We embrace our core values of stewardship, leadership, excellence, connectedness, and diversity and respect, which foster a culture that empowers our staff members to translate knowledge for the benefit of patients (See Figure 1).

Figure 1.

OCP Core Values

Over the past decade, OCP has seen transformational growth; we have almost doubled the number of staff and now have dedicated groups for project management, communications, guidance and policy, lifecycle management, regulatory science, and focused therapeutic areas (See Figure 2). We have successfully completed CDER's reorganization efforts, which realigned therapeutic areas and established leadership positions to enhance the robustness of the drug evaluation process. As the field of clinical pharmacology itself has evolved from a focus on biopharmaceutics to becoming a major contributor in evidence assessment, dose optimization, and therapeutic individualization, so has our organization.

Prompted by this unprecedented growth and expanded scope, OCP embarked on a Strategic Planning Initiative to provide clarity, focus, and direction for the Office for the next 5 years. This effort is critically necessary to set clear, evidence-based priorities to advance our mission and vision of public health. To achieve this goal, we are implementing a phased approach to developing our strategic priorities and goals, which engages stakeholders at all levels, both within and outside OCP, relies on rigorous data collection and analysis to inform our direction, and uses clear, timely communication of progress.

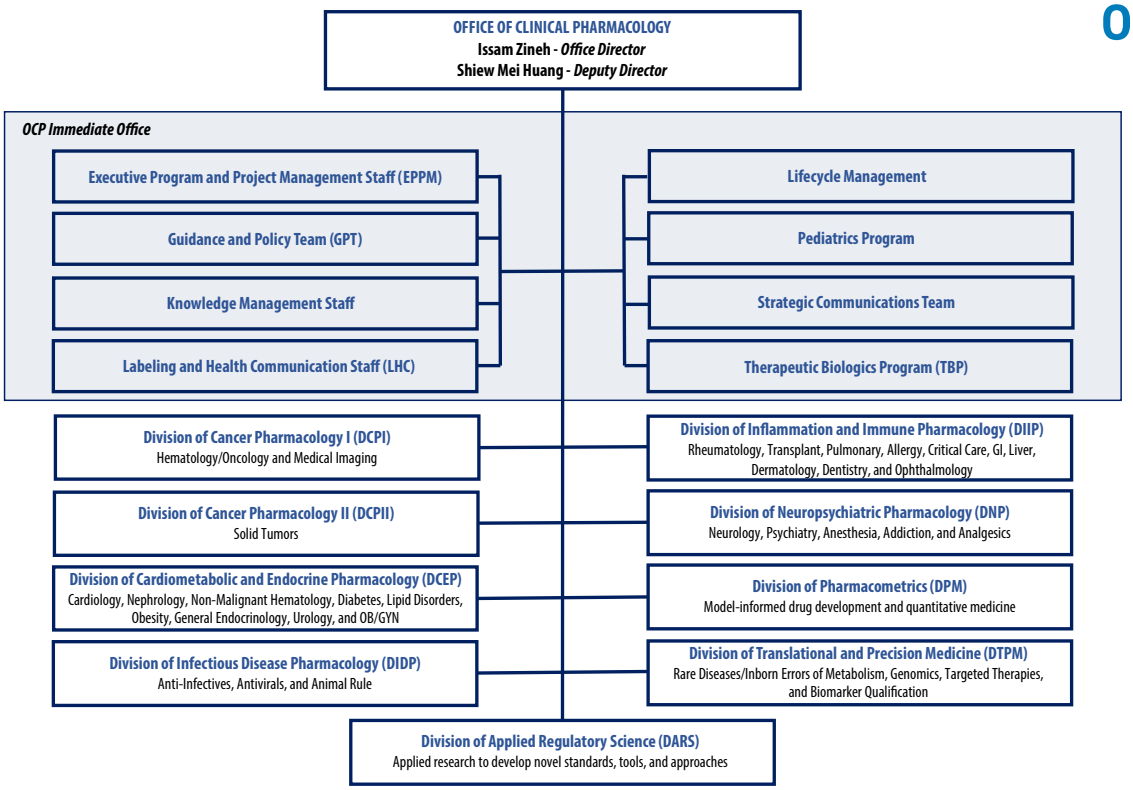
Over the past year, our dedicated staff have conducted surveys and interviews of internal and external stakeholders, assigned strategic themes, and thoroughly analyzed all data. As a result of their tireless efforts, we are proud to announce OCP's three strategic priorities for the next 5 years:

- Advance our science for the benefit of patients
- Bolster patient-centered engagement
- Elevate our people

We have engaged our staff to participate in working groups for these three focus areas and look forward to providing detailed implementation plans in the upcoming year.

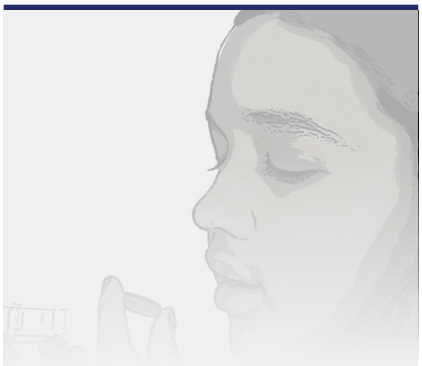
Figure 2.

OCP Organizational STRUCTURE



Regulatory REVIEW

OCP's regulatory evaluation ensures that approved drugs and biological products are administered at the right doses to the right patients at the right time in their disease process. Clinical pharmacology is a multidisciplinary science, and our 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. We use this evidence to inform our regulatory decisions (e.g., approvability, labeling, post-approval requirements, and product lifecycle management). From initial investigational new drug (IND) submission through new drug application or biologics license application (NDA/BLA) and the post-marketing phase, OCP's thoughtful analysis and integration of translational and clinical pharmacology knowledge of the products we evaluate allows us to directly improve patient health.



"Ultimately, we're all thinking about the patient and how to provide the best new therapies and the best care."

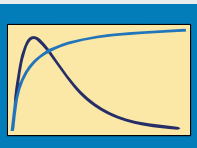
Dr. Issam Zineh
Director
OCP

The therapeutic challenges of 2021 were met with an efficient, multi-disciplinary, issue-based assessment strategy by our staff members (See Figure 3). OCP's drug evaluation assesses clinical pharmacology information in applicant submissions along with previously established knowledge to address issues of dose selection and optimization, therapeutic individualization, and benefit/risk balance across affected subpopulations of patients. Informed by current science and policy, our reviews identify any critical gaps in the understanding of conditions for optimal therapeutic use, and we recommend studies or leverage innovative scientific approaches that can practically address knowledge gaps. Additionally, OCP explored novel ways to increase the efficiency of drug evaluation through automation and analytics, as well as provide staff with enhanced experiences in other therapeutic areas.

OCP applied clinical pharmacology principles to proposed drug development plans for INDs, engaging drug developers and experts in multiple formats (face-to-face meetings, written responses as requested, advisory committee meetings, etc.). In 2021, we conducted 6985 reviews of IND submissions to facilitate product development, and our review findings for NDAs, NDA supplements, and BLAs, including 351(k) applications (i.e., biosimilars), were integrated into benefit-risk assessments, ultimately bringing 50 safe and effective new drugs and biological products to patients in 2021 (See Table 1 and Figure 4).

Figure 3.

OCP's Issue-Based Approach TO DRUG EVALUATION



To what extent does the available clinical pharmacology information provide pivotal or supportive evidence of effectiveness?

Is the proposed dosing regimen appropriate for the general patient population for which the indication is being sought?

Is an alternative dosing regimen or management strategy required for subpopulations based on intrinsic factors?

Are there clinically relevant food-drug or drug-drug interactions, and what is the appropriate management strategy?

Table 1.

OCP Contributions to NME and BLA APPROVALS

Therapeutic Areas	Drug name	Primary Review Contribution: Influenced Drug Development Plan Or Trial Design	Optimized Dosing Regimen	Evaluated/ Proposed Bridging or Extrapolation Strategies	Mitigated Risk	Assessed Genetic Factors	Other
Cardiology/ Nephrology	Leqvio				■		
	Verquvo	■			■		
Dermatology	Adbry		■		■		
	Korsuva				■		
Endocrinology	Voxzogo						■
Hematology	Besremi						■
	Cosela		■		■		
	Empaveli			■			
Hepatology/ Nutrition	Bylvay		■				
Immunology/ Inflammation	Livmarli						■
Infectious Disease	Brexafemme		■	■	■		
	Cabenuva		■		■		
	Livtencity						■
	fexinidazole		■		■		
Metabolic/ Endocrine	Evkeeza		■			■	
	Kerendia				■		
	Nextstellis				■		
	Skytrofa		■				
	Zegalogue						■
Neurology/ Psychology	Aduhelm						■
	Amondys 45			■	■	■	
	Azstarys			■	■		
	Lybalvi				■		
	Ponvory				■		
	Qelbree		■		■		
	Qulipta		■				
	Vyvgart		■				
Oncology	Cytalux		■				
	Exkivity						■
	Fotivda		■				
	Jemperli						■
	Lumakras		■		■		
	Pepaxto		■				
	Pylarify				■		
	Rezurock		■		■		
	Rybrevant		■			■	
	Rylaze	■	■		■		
	Scemblix						■
	Tepmetko		■		■		
	Tivdak		■				
	Truseltiq		■		■		
	Ukoniq		■		■		
	Welireg		■		■	■	
	Zynlonta		■		■		
Pulmonary	Tezspire				■		
Rare Diseases	Nexviazyme			■	■		
	Nulibry		■		■		
Rheumatology/ Transplant	Lupkynis		■		■		
	Saphnelo						■
	Tavneos				■		

Figure 4.

Clinical Pharmacology Drug Evaluation IMPACT AREAS

Optimizing Dosing Regimens for Patients

- Examined bioanalytical, pharmacokinetic, pharmacodynamic, safety, and efficacy data to determine dosing regimens with an optimum benefit/risk profile
- Issued postmarketing requirements (PMRs)/postmarketing commitments (PMCs) to further evaluate and understand the safety and efficacy of therapeutics in racial and ethnic minorities and in patients with organ impairment
- Assessed whether drugs should be co-administered with food based on food's effect on pharmacokinetics and safety
- Evaluated the appropriateness of extended dosing schedules, body-weight dosing strategies, or dosing based on genetic alterations

Mitigating Risk to Patients

- Provided recommendations to mitigate or avoid drug-drug or food-drug interactions based on clinical studies and/or physiologically based pharmacokinetic (PBPK) analyses
- Ensured labeling language advised prescribers and patients on actions to take in the event of missed doses or drug discontinuation where appropriate
- Evaluated the likelihood of a therapeutic to prolong the QTc interval, increasing the potential for developing Torsades de Pointes
- Determined the potential for immunogenicity to alter the benefit/risk profile of a therapeutic

Evaluating Bridging or Extrapolation Strategies

- Used extrapolation principles, population pharmacokinetic analysis, exposure-response data, and modeling and simulation to expand indications to patients who were not studied in clinical trials (e.g., pediatric and adolescent patients)
- Performed a comprehensive, integrated assessment of data suitability to support extrapolation, including pathophysiology, mechanism of action, disease manifestations, pharmacokinetics, pharmacokinetic/pharmacodynamic relationships, safety, and immunogenicity

Influencing Drug Development or Trial Design

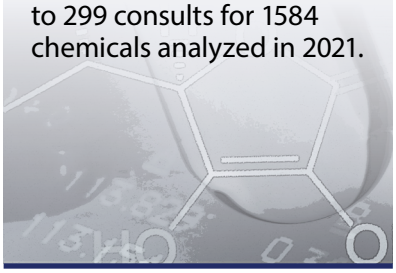
- Evaluated modeling and simulation data to inform dosing regimens for use in clinical trials during drug development
- Recommended comprehensive cardiac channel testing to elucidate drug effects on QT interval under worst case scenarios to inform mitigation strategies, if necessary

Assessing Genetic Factors

- Evaluated the appropriateness of expanding indications to patients with genetic profiles not studied in clinical trials (e.g., patients with ultra-rare mutations) by examining the mechanisms of disease pathogenesis and the safety profile of the therapeutic
- Examined genetic classification schemes for their relevance in determining safe and efficacious dosing regimens

OCP's Chemical Informatics Program

OCP's Chemical Informatics Program conducted structure-based safety assessments of non-clinical and clinical endpoints to inform regulatory decision-making, including genetic toxicity, carcinogenicity, hepatotoxicity, and cardiotoxicity, in response to 299 consults for 1584 chemicals analyzed in 2021.



Model-Informed
DRUG DEVELOPMENT

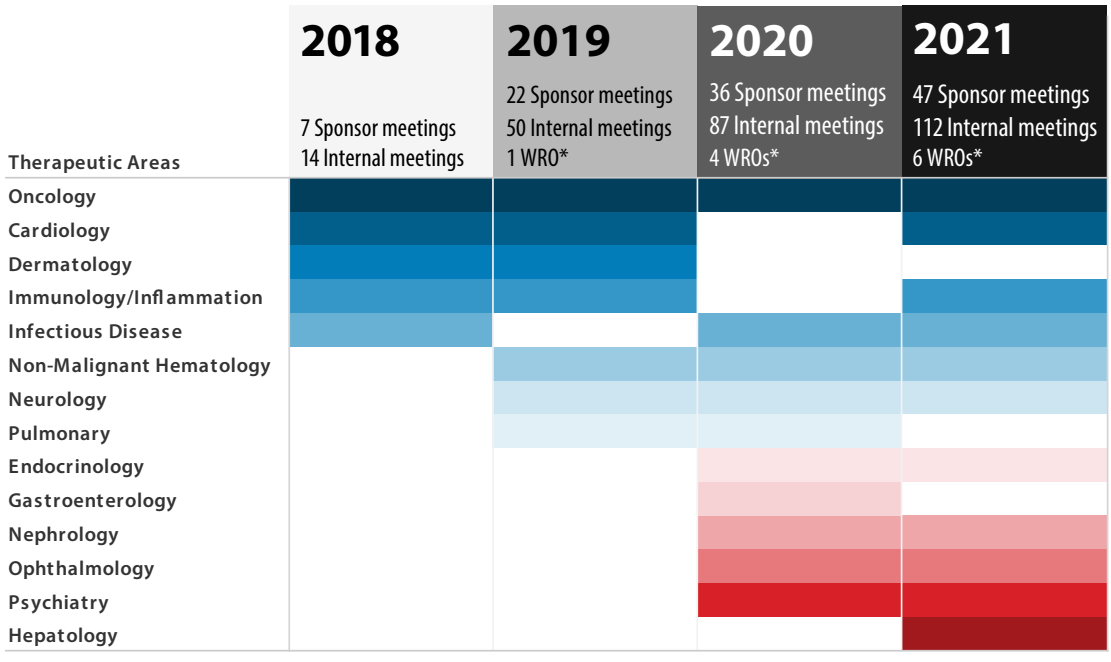
Model-informed drug development (MIDD) uses preclinical and clinical data with exposure-based, biological, and statistical models to help facilitate decision-making in the development of safe and effective drugs. MIDD leverages a range of quantitative approaches to inform decision-making and has been routinely used and successfully applied to provide supportive evidence for safety and effectiveness, optimize dosing, and inform clinical trial design.

Under the Prescription Drug User Fee Act VI (PDUFA VI), OCP advanced the use of MIDD through policy and research, stakeholder engagement and outreach, and education. In 2021, OCP successfully completed the PDUFA-mandated public workshops on MIDD-related topics, conducted research, and published and presented findings in numerous forums, resulting in a significant impact on drug development and regulatory science (See Research and Publications pgs. 11-13 and Outreach and Engagement pgs. 15-16).

OCP also had a major role in the successful completion of the MIDD Pilot Program, a cross-center initiative enabling focused discussions between sponsors and FDA on modeling and simulation issues early in development. Since its inception in 2018, the pilot has met or exceeded its quarterly goals for granting meeting requests (See Figure 5). The FDA conducted 112 internal meetings and 47 sponsor meetings over the pilot period; in addition, the number of therapeutic areas significantly increased over the 4-year pilot period. The benefits of the MIDD pilot program in facilitating drug development were recognized in a recent publication by program participants (PMID: 34658027). As a result of the pilot's success, the MIDD program was recently made a permanent regulatory mechanism under PDUFA VII.

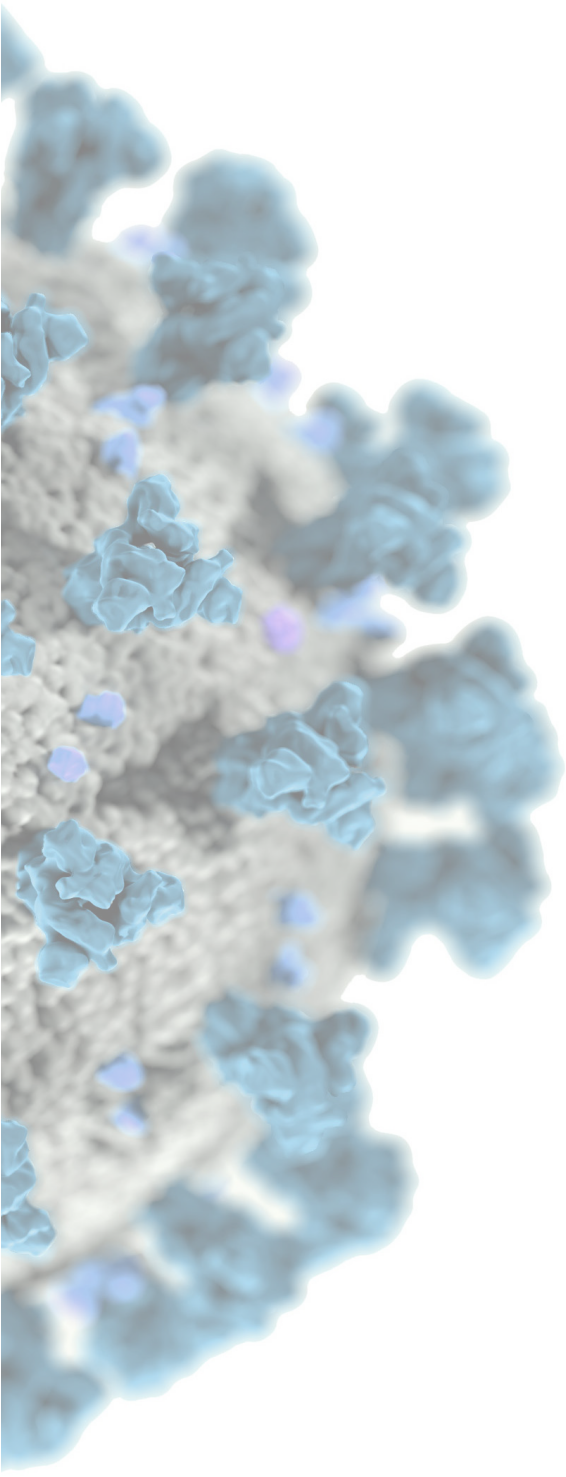
If you have any questions regarding MIDD, please email MIDD@fda.hhs.gov.

Figure 5.
MIDD Pilot Program
IN REVIEW



WRO: Written Response Only; Numbers presented by year are cumulative.

COVID-19



Since the COVID-19 National Public Health Emergency was declared in 2020, OCP drug evaluation activities have focused on ensuring the availability of treatments for patients fighting the devastating effects of SARS-CoV-2 infection. The pathogenesis of COVID-19 is complex and multifaceted, and effective management targets the unique stages of the disease as it progresses, from asymptomatic to critical disease and beyond (i.e., post-COVID conditions). Products developed for COVID-19 cover a wide range of mechanisms of action, including direct-acting antivirals, targeted monoclonal antibodies, anti-inflammatories, immunomodulators, and cardiovascular, pulmonary, and neurology agents. OCP teams in these therapeutic areas remain responsive to the constantly evolving pandemic treatment landscape.

In 2021, OCP contributions when evaluating products submitted for INDs, Emergency Use Authorization (EUA), and NDAs focused on translating pharmacokinetic, pharmacodynamic and exposure-response knowledge into sound dosing recommendations, expanding treatment options across diverse patient populations (e.g., pediatric patients), and formulating strategies to mitigate risk for patients with COVID-19 (See Figure 6). These contributions informed Fact Sheets for Healthcare Providers and Patients and Caregivers for authorized products, the principal mechanism for communicating clinical pharmacology aspects of COVID-19 treatments to the public. Our benefit-risk assessments also considered multidisciplinary perspectives and learnings from real-time data sources and surveillance for safety and variants, the developing treatment landscape and understanding of the virus, and recurring international exchanges.

Evaluating Safety/Toxicology of COVID-19 Treatments

In 2021, OCP was involved in a multidisciplinary effort to evaluate pharmacovigilance and surveillance data for COVID-19 treatments to inform practitioners and patients of risk. The American College of Medical Toxicology's (ACMT) Toxicology Investigators Consortium (ToxIC) is a unique multicenter pharmacovigilance and overdose surveillance and research network which tracks unlabeled adverse events in patients treated or self-medicated with approved and unapproved COVID-19 medications.

Figure 6.

OCP's Pandemic Response
IMPACT AREAS

Translate Knowledge Into Sound Dosing Recommendations

- Evaluated drug candidacy by comparing in vitro antiviral activity in relation to clinically achievable concentrations for repurposed drugs
- Explored relationships between drug exposure and disease severity to better understand effects of COVID-19 on pharmacokinetics to inform treatment regimens
- Integrated known pharmacokinetic and pharmacodynamic information, mechanism of action, in vitro activity, neutralization assays, viral dynamics, preclinical animal efficacy models, and prior clinical experience to predict safe and efficacious dosing regimens
- Used predictive modeling incorporating antiviral/neutralization activity against variants, duration of protection, and exposure targets to inform alternative routes of administration and dosing strategies for prevention

Expand Treatment Options For Diverse Populations

- Applied knowledge of pharmacodynamic response (interleukin levels and receptor saturation) in COVID-19 pneumonia to evaluate proposed dosing regimens in pediatric patients
- Evaluated weight-based dosing strategies in adult patients to ensure adequate exposure to COVID-19 treatments
- Recommended pharmacokinetic sampling strategies and integrated mechanism of action, pharmacokinetic, and exposure/response information to inform dosing in patients with renal impairment
- Used pharmacokinetic/pharmcodynamic knowledge and supportive modeling to understand the effect of patient factors, such as acute lung injury and conditions of high-risk disease, on treatment selection and dosing
- Utilized data from clinical studies, extrapolation, and model-informed methods to derive dosing recommendations for pediatric patients for treatment and prevention of COVID-19

Formulate Strategies To Mitigate Risk

- Encouraged comprehensive drug-drug interaction (DDI) evaluation strategies, model-informed methods, and protocol modifications to lessen drug interaction liability
- Evaluated alternative routes of administration using pharmacokinetic data, viral load reductions in patients, safety findings, and simulated dosing scenarios to ensure adequate exposure and reduce treatment delays
- Identified cardiac toxicity signals related to active metabolite concentrations and accumulation
- Optimized sampling approaches to assess the relationship between maximum concentration and unintended immunosuppressive effects
- Provided advice on ex vivo cardiac studies and clinical protocol design to characterize proarrhythmic potential and cardiac risk

Research & PUBLICATIONS

OCP's regulatory science research program is critical to advancing the science of clinical pharmacology and translational medicine and informs regulatory decision-making and contemporary policy development. OCP's comprehensive research portfolio is designed to address immediate and emerging regulatory science issues that impact the development, evaluation, and utilization of therapeutic products. We conducted 76 research projects employing a variety of translational methods, including experimental and analytical approaches, mechanistic and model-based methodologies, data-based tools and mining, and clinical studies (See Figures 7 through 9). OCP conveyed research outcomes and regulatory application of findings with the broader scientific community through 183 publications in peer-reviewed journals (See Figures 10 and 11).

OCP's dedicated research division, the Division of Applied Regulatory Science (DARS), specializes in the application of translational approaches such as in vitro and in vivo laboratory methods, experimental medicine, in silico computational modeling and informatics, and integrated clinical research to meet regulatory and public health challenges. OCP's regulatory research activities are further enhanced by our robust research fellowship program offered unique development opportunities to 119 new scientists in 2021.

For more details on our dedicated research division, visit the DARS website (https://go.usa.gov/xAH6Z).

"The work we do fills a gap that isn't being done elsewhere. What we try to do is come up with new tools and models and approaches that can be applied across the drug development spectrum in multiple different types of drugs to better predict safety and effectiveness, and it's really something that others aren't doing quite like we are."

David Strauss, M.D., Ph.D.,
Director
OCP DARS

Figure 7.

OCP Research AT A GLANCE

15
Average number of OCP publications per month in 2021

$18.7M
2021 research budget (approximate)

119
Research trainees in 2021

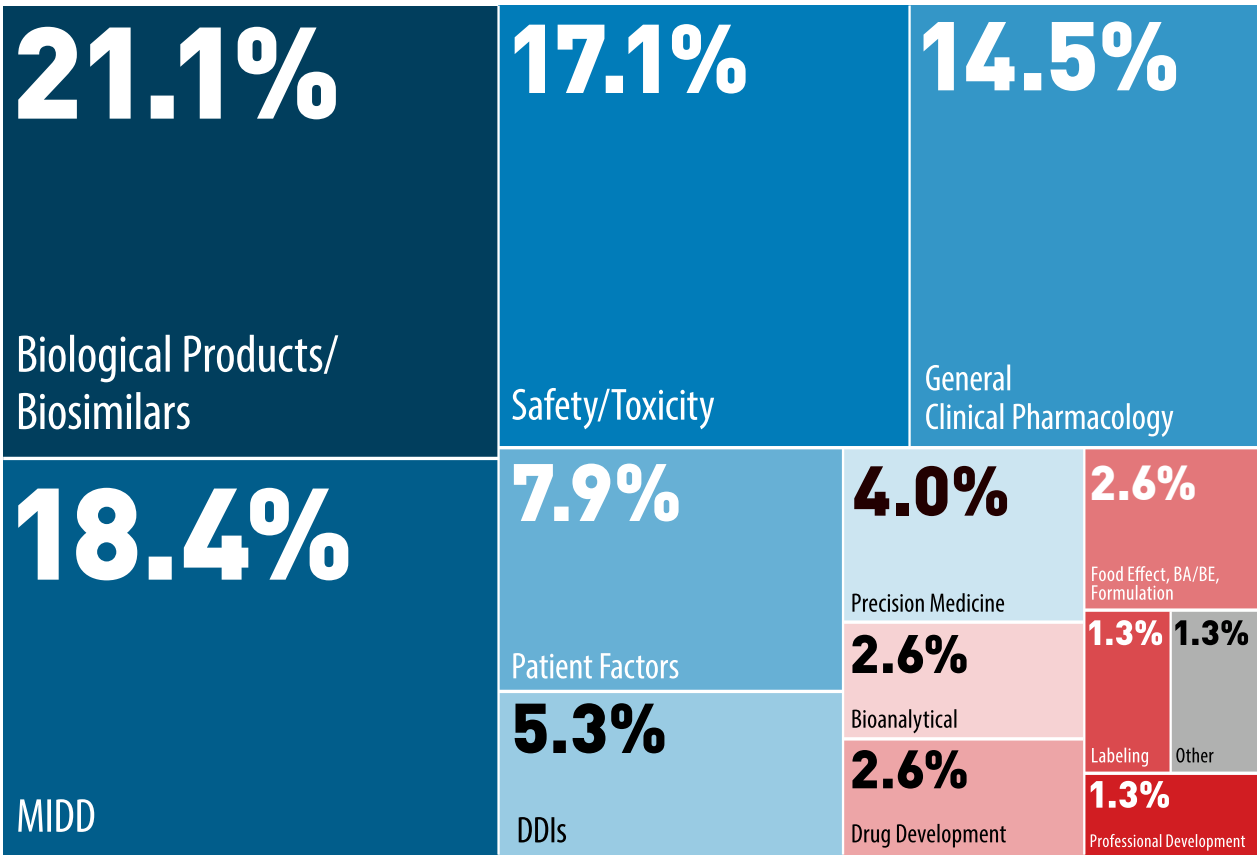


Figure 8.
OCP Research Focus Areas
IN 2021
(N=76)

BA/BE: Bioavailability/Bioequivalence

Figure 9.
OCP Research Highlights IN 2021

Opioids

- Developed mechanistic pharmacodynamic models to predict adequate naloxone doses to reverse opioid intoxication
- Evaluated opioids and chemicals with opioid-like properties using the Public Health Assessment via Structural Evaluation (PHASE) protocol, a computational-based approach using molecular dynamics for assessing the risk that a drug or compound may pose to public safety
- Identified a rat model to measure the effect of opioids alone and when co-administrated with sedative psychotropics on resting respiration, to further inform in vivo study design for these products
- Studied how fentanyl activates the mu-opioid receptor (mOR) at a molecular level, specifically by using X-ray crystal structure and several molecular simulation techniques to elucidate the detailed binding mechanism of fentanyl and calculating the fentanyl-mOR dissociation time by applying an enhanced sampling molecular dynamics technique

Ranitidine and N-Nitrosodimethyl-amine (NDMA)

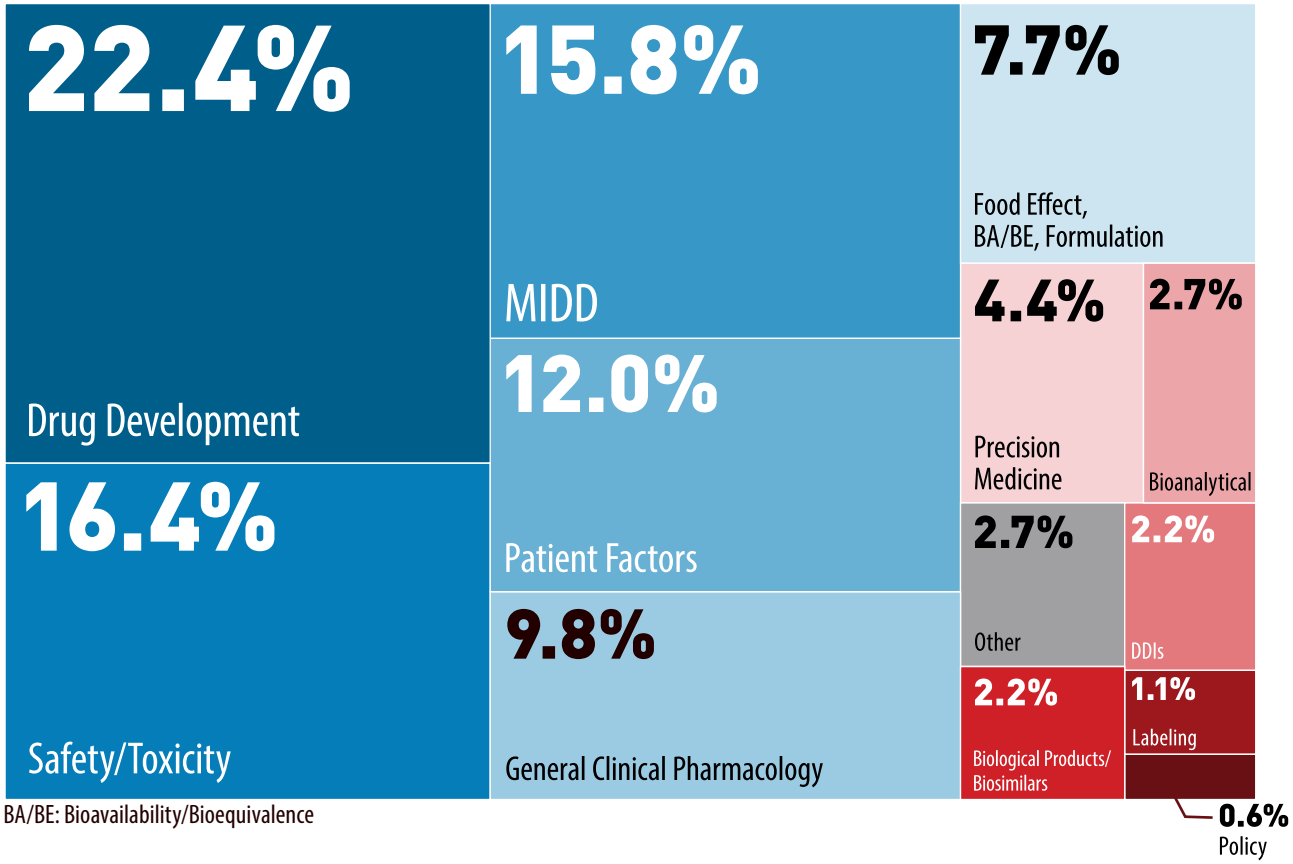
- Conducted a rigorous, randomized, double-blinded, placebo-controlled clinical trial to assess NDMA and dimethylamine (DMA) (proposed precursor to NDMA generated from ranitidine) content in plasma and urine after ranitidine administration
- Developed and validated low-temperature analytical methods to accurately determine the amounts of NDMA contained in ranitidine products
- Performed an in vitro assessment of the potential for ranitidine to convert to NDMA in simulated gastric fluid over a range of physiologic gastric nitrite concentrations

COVID-19

- Applied well-established mechanistic models for viral infections to SARS-CoV-2 to predict effective dosing regimens for combination and monotherapies to treat COVID-19
- Evaluated the potential for DDIs, liver toxicity, and the effect of patient factors for COVID-19 therapeutics using model-informed methodologies, such as a 3D human spheroid model and PBPK modeling
- Ensured the safety of drugs repurposed for COVID-19 by exploring in vitro and pharmacokinetic modeling to estimate QTc prolongation and inform risk assessment and performing ontogeny-based classification and analysis of adverse events

Figure 10.

OCP Publication Focus Areas
IN 2021
(N=183)



BA/BE: Bioavailability/Bioequivalence

Figure 11.

Notable OCP Publications IN 2021

MIDD

- 3D cell culture models: drug pharmacokinetics, safety assessment, and regulatory consideration (PMID: 33982436)
- Long short-term memory recurrent neural network for pharmacokinetic-pharmacodynamic modeling (PMID: 33210994)
- Regulatory considerations for the mother, fetus and neonate in fetal pharmacology modeling (PMID: 34381745)
- Use of model-informed drug development to streamline development of long-acting products: can these successes be translated to long-acting hormonal contraceptives? (PMID: 32997600)
- Whole body PBPK modeling of remdesivir and its metabolites to aid in estimating active metabolite exposure in the lung and liver in patients with organ dysfunction (PMID: 34656075)

Patient Factors

- Creatinine-based renal function assessment in pediatric drug development: an analysis using clinical data for renally eliminated drugs (PMID: 32696977)
- Effect of body weight and age on the pharma-cokinetics of dihydroartemisinin: FDA basis for dose determination of artesunate for injection in pediatric patients with severe malaria (PMID: 33605994)
- Extrapolation of efficacy and dose selection in pediatrics: a case example of atypical antipsychotics in adolescents with schizophrenia and bipolar I disorder (PMID: 34185904)
- Recommendations for dose selection for adolescent patients in relevant adult oncology clinical trials (PMID: 34714930)
- Roadmap to 2030 for drug evaluation in older adults (PMID: 34656074)

Safety/Toxicity

- Characterizing the reproducibility in using a liver microphysiological system for assaying drug toxicity, metabolism and accumulation (PMID: 33382907)
- Effect of oral ranitidine on urinary excretion of N-nitrosodimethylamine (NDMA): a randomized clinical trial (PMID: 34180947)
- Effects of sedative psychotropic drugs combined with oxycodone on respiratory depression in the rat (PMID: 34080766)
- In vitro analysis of N-nitrosodimethylamine (NDMA) formation from ranitidine under simulated gastrointestinal conditions (PMID: 34181009)
- Informing selection of drugs for COVID-19 treatment through adverse events analysis (PMID: 34234253)
- Translational models and tools to reduce clinical trials and improve regulatory decision-making for QTc and proarrhythmia risk (ICH E14/S7B updates) (PMID: 33332579)

POLICY

A lifecycle approach to guidance and policy development is critical to ensure that staff and drug developers have the most up-to-date and scientifically accurate information when developing and evaluating new drugs. There are multiple, robust mechanisms in place to identify areas that could benefit from the development or revision of guidances and policies, including but not limited to, collecting public comments using Federal Register notices and workshops.

OCP staff are highly committed to incorporating the most recent scientific advances into guidances and policies that can accelerate the safe and effective development of drugs, participating in a total of 64 working groups over the past year. 2021 saw the successful clearance and publication of a diverse set of guidances and policies, including three Federal Register notices, one Manual of Policies and Procedures, and one FDA guidance for industry (Figure 12). All guidances and policies are routinely evaluated for their relevance and scientific accuracy to maintain the lifecycle approach to policy development.

OCP also ensures that both new and existing staff receive training on the most up-to-date science, policies, and procedures through multiple education mechanisms, including an internal clinical pharmacology course, Lunch and Learn seminars, dedicated guidance trainings, and scientific interest groups.

Figure 12.
Policy Documents PUBLISHED IN 2021

GUIDANCES

Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1) Blocking Antibodies for Treatment of Patients with Cancer (Draft guidance)

MaPP

Scientific Interest Groups: Criteria and Policies

FRN

Request for Comments- Best Practices for Development and Application of Disease Progression Models; Public Workshop

FRN

Request for Information and Comments - Evaluating the Clinical Pharmacology of Peptides; Establishment of a Public Docket; Request for Information and Comments

FRN

Public Workshop Announcement - Best Practices for Development and Application of Disease Progression Models; Public Workshop

FRN: Federal Register notice

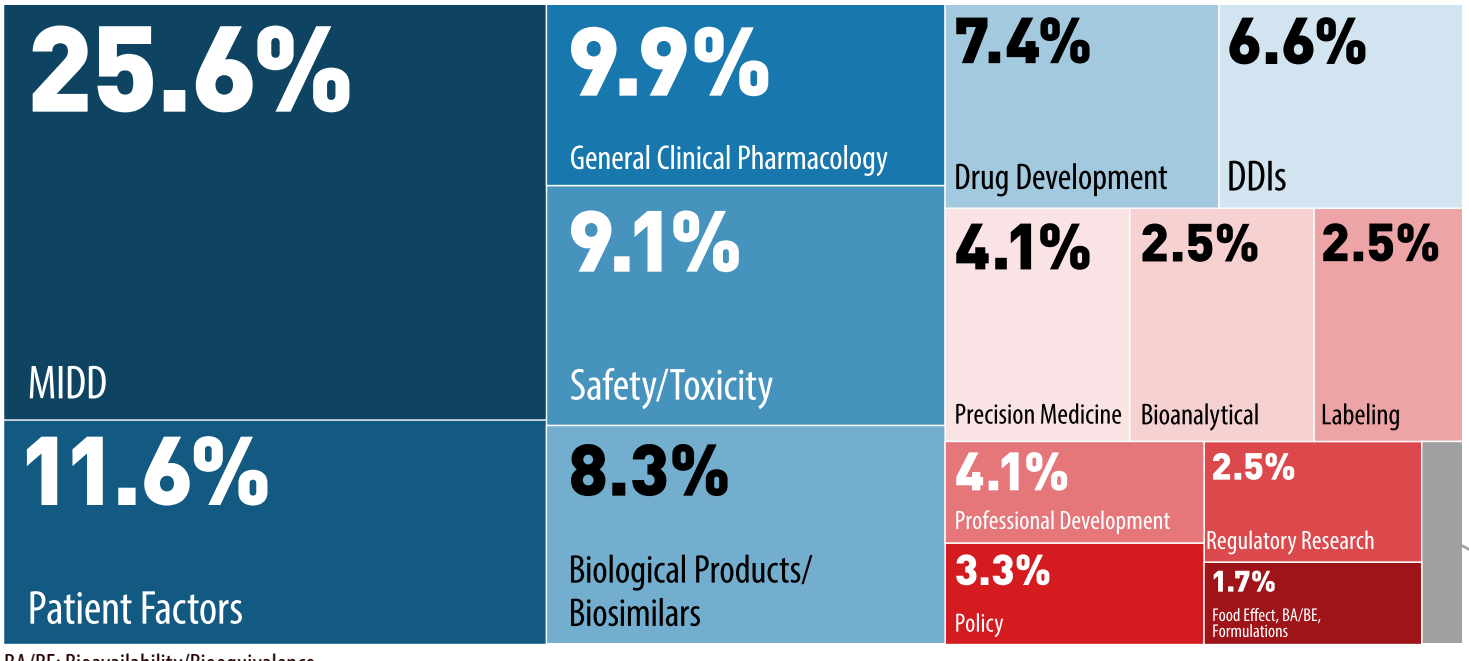
Outreach & ENGAGEMENT

In 2021, OCP staff shared current perspectives and innovative achievements in all areas of clinical pharmacology though presentations and webinars at internal, national, and international scientific virtual venues (See Figure 13 and 14). OCP's involvement in workshops was collaborative and multidimensional, as organizers, moderators, panelists, and presenters. The development topics discussed attracted new levels of interest and participation averaging over 1000 registrants per workshop. We fostered innovation and accelerated drug development through partnerships and collaborations with stakeholders, such as government agencies, global organizations, academia, and drug developers, on a variety of topics, including real-world data and evidence, machine learning, biological products and biosimilars, drug interactions, safety and toxicity, and more.

Our direct communication mechanisms were valuable avenues for outreach, with our OCP Clinical Pharmacology Corner newsletter subscription service conveying timely information on NDA/BLA approvals, policy updates, events, and notable scientific topics reaching over 84,900 subscribers and OCP's PEDSCLIPS Pediatric Clinical Pharmacology Weekly Newsletter disseminated FDA-wide and to regulatory agencies across the globe.

Collectively, these mechanisms were an effective communication strategy in 2021, allowing OCP to share our science informed by the voice of our stakeholders.

Figure 13.
OCP Presentation Focus Areas
IN 2021
(N=121)



BA/BE: Bioavailability/Bioequivalence

Figure 14.

OCP Outreach Highlights IN 2021

Workshops

FDA creates a forum for scientific exchange on current scientific and regulatory topics through public workshops. OCP participated in eight collaborative public workshops in 2021, bringing together fellow regulators and experts from academia and industry to deliberate timely clinical pharmacology topics in areas such as specific populations and patient factors, biosimilars, MIDD, and biowaivers.

- Roadmap to 2030 for New Drug Evaluation in Older Adults
- Pharmacodynamic Biomarkers for Biosimilar Development and Approval
- Model Informed Drug Development Approaches for Immunogenicity Assessments
- Advancing the Development of Pediatric Therapeutics Complex Innovative Trial Design
- Analgesic Clinical Trial Designs, Extrapolation, and Endpoints in Patients from Birth to Less Than Two Years of Age
- Fetal Pharmacology and Therapeutics
- Best Practices for Development and Application of Disease Progression Models
- Drug Permeability: Best Practices for Biopharmaceutics Classification System-Based Biowaivers

Webinars

Webinars are an effective outreach and educational mechanism in a virtual world. OCP webinars targeted audiences from pharmaceutical industry, academic institutions, professional organizations, and other scientific sectors and were international in reach.

- Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment and Prevention of COVID-19
- FDA's Final DDI Guidances: What You Need to Know About Transporter DDIs
- Updates to the Final In Vitro and Clinical FDA DDI Guidance – Underlying Thoughts and Remaining Challenges
- Quantitative System Pharmacology Modeling for Model Informed Drug Development
- MIDD Approaches to Support New Drug Development and Regulatory Decision Making
- Assessing the Impact of Expert Knowledge on International Council for Harmonisation (ICH) M7 Quantitative Structure-Activity Relationship (QSAR) Predictions
- Application of PBPK Modeling and Simulation for Regulatory Decision Making and Its Impact on US Prescribing Information

Engagement

Direct engagement provides OCP an opportunity to learn the experiences, perspectives, needs, and priorities of our stakeholders, which we meaningfully incorporate into our organization's regulatory approach and strategy.

- **Clinical Pharmacology Without Borders:** Our organization held a two-day strategic planning session in 2021 in which external clinical pharmacology leaders and stakeholders from industry, academia, and internal FDA colleagues were invited to present on current and future trends in the field of clinical pharmacology. The perspectives and ideas shared are being used to inform strategic planning activities in 2021-2022.
- **Monthly Forum on Framework to Enable Pediatric Drug Development:** In a collaborative effort with pediatric drug development stakeholders, and the Best Pharmaceuticals for Children (BPCA) program under the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), OCP launched a new virtual public forum to discuss a generic framework to enable pediatric drug development studies. Topics covered in the forum: pharmacokinetic modeling to inform dosing, pediatric-friendly formulations, pharmacoepidemiology, biomarkers/developmental pharmacodynamics, systems pharmacology, and advancing clinical trial design.
- **The Pediatric Cluster:** In 2021, OCP actively participated in The Pediatric Cluster, monthly teleconferences with international regulators to identify gaps and harmonize approaches in pediatric development. These exchanges enhance the science of pediatric trials and to avoid exposing children to unnecessary trials, provides a robust ethical and scientific framework for pediatric studies, and benefits from the clinical pharmacology perspectives shared by our staff.

2022 OUTLOOK

Reflecting on 2021 and the accomplishments of our organization is an inspiring exercise. We continue to experience growth, and our programmatic enhancements allow us to be more responsive and dynamic. We've seen incredible advances in science and technology against a backdrop of major public health crises which have enhanced our mission-critical drug evaluation, policy, research, and engagement functions. OCP successfully addressed urgent public health needs through strategic visioning and leadership, high-quality drug evaluation, and a diligent regulatory science program.

As we embark on a new year, OCP remains committed to the patients we serve with a focus on a renewed strategy to improve public health with translational knowledge and sustaining our mission-critical activities. Using our vision, mission, and values as a guide, we will prioritize advances in clinical pharmacology and translational science to benefit patients, facilitate patient-centered decision-making, and empower our staff to achieve our goals and beyond. We advance our science through innovation, and as we recognize the progress we've made (e.g., enhanced organizational structure, streamlined and integrated drug evaluation, MIDD, applied research, novel tools and techniques), we enter this next phase ready to promote the translation of well-established and innovative new scientific approaches into clinical practice. The patient perspective will be key, and we will continue to strengthen and support patient-centered outreach mechanisms to facilitate meaningful exchange on how clinical pharmacology and translational medicine can best address patient, caregiver, and clinician needs. The foundation upon which this will be realized is our staff, and we aspire to offer a diverse range of opportunities, support staff development, provide meaningful recognition of staff contributions, and build a community where people are encouraged to be their authentic selves.

Challenges in an increasingly globalized society are certain, and we believe clinical pharmacology is the bridge to therapeutic individualization for all. We look forward to 2022 and the opportunities to demonstrate our invigorating commitment to the well-being of others.

Examples presented in this Annual Report are illustrative and are not a comprehensive representation of 2021 information. For detailed information on the content of this report or our Office's other activities, please contact *ocp@fda.hhs.gov*.

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