U.S. FOOD & DRUG ADMINISTRATION

Center for Drug Evaluation and Research

OFFICE OF MEDICAL POLICY

Annual Report

Calendar Year 2023

Promoting and protecting public health by providing scientific and regulatory leadership in the development of medical policy



August 2024

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Director's Message

I am pleased to present the 2023 Annual Report for the Office of Medical Policy (OMP).

In 2023, OMP continued working with colleagues across FDA's Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), and Center for Devices and Radiological Health (CDRH) to advance cross-cutting policy priorities, including the use of real-world evidence (RWE) and artificial intelligence (AI) in regulatory decision-making. OMP also continued to encourage the use of innovative trial designs such as decentralized clinical trials and fit-for-use digital health technologies (DHTs). In addition, OMP advanced regulatory policies and activities promoting efficiencies, innovations, and transparency across the medical product lifecycle and made significant strides in addressing misinformation and disinformation.

Our Office of Prescription Drug Promotion (OPDP) issued guidances on communications from firms to health care providers regarding scientific information on unapproved uses of approved/cleared medical products and presenting quantitative efficacy and risk information in direct-to-consumer (DTC) promotional labeling and advertisements. OPDP also published a guidance and final rule on presenting the major statement in DTC prescription drug advertisements in a clear, conspicuous, and neutral manner. In addition, OPDP convened a workshop on the future of prescription drug promotion and digital marketing, issued 5 compliance letters, and authored 11 regulatory publications.

The Office of Medical Policy Initiatives (OMPI) convened a public workshop to enhance clinical study diversity and a public meeting on mitigating clinical study disruptions during disasters and public health emergencies as required by the Food and Drug Omnibus Reform Act of 2022 (FDORA). OMPI also issued guidances on labeling for dosing based on weight or body surface area ("dose banding") for ready-to-use containers, regulatory considerations for prescription drug-use-related software, a risk-based approach to monitoring of clinical investigations, and institutional review board review of individual patient expanded access requests. In addition, OMPI co-facilitated the diversity plans implementation committee, published a proposed rule on medication guides and patient medication information, and addressed issues regarding investigational new drug safety reporting.

Our RWE group published guidances for drugs and biological products on the topics of data standards (with the Office of Strategic Programs as technical lead), registries, and regulatory considerations. The group also published guidance on the design and conduct of externally controlled trials, including the use of real-world data (RWD) for drugs and biological products, and participated in more than 30 presentations or interviews to discuss CDER's perspective on RWD and RWE.

Our AI group led analysis efforts of a CDER, CBER, and CDRH/Digital Health Center of Excellence (DHCoE) collaborative discussion paper on the use of AI and machine learning in

the development of drug and biological products that was published in May 2023 and received over 800 comments from 65 organizations. The group also published a book chapter on AI in regulatory decision-making for drug and biological products and participated in 25 interviews and presentations related to the use of AI in drug development.

Our Clinical Methodology group issued guidance on the use of DHTs for remote data acquisition in clinical investigations; decentralized clinical trials for drugs, biological products, and devices; and electronic systems, electronic records, and electronic signatures in clinical investigations. The group also issued a technical amendment for non-repudiation letters.

In 2024, we continue to address cross-cutting policy issues and identify policy needs for our ever-changing regulatory environment, including needs for rapidly evolving technologies, such as AI. We also continue to engage interested parties and develop policy in support of our public health mission.

M. Khair ElZarrad, PhD, MPH
Director, Office of Medical Policy

OMP By the Numbers

January 1, 2023 – December 31, 2023

Policy Activities

- **16** Guidances
- **3** Frameworks, Discussion Papers, and Public Reports
- **2** Rules
- **16** Briefings
- **27** Responses to Congressional Requests

Outreach

- **9** Public Meetings, Workshops, Webinars, and Trainings
- **24** Demonstration and Research Projects
- **12** Meetings with External Interested Parties
- **837** Responses to Mailbox Inquiries
- **136** Publications, Presentations, and Posters

Consulting & Other Activities

- **5** Compliance Letters
- **318** Advisory Comments*
- **425** Patient Labeling Reviews
- **4** Innovative Initiatives

* The term Advisory Comments refers to OMP/OPDP's responses to voluntary requests for comments on draft (unpublished) prescription drug promotional communications

Who We Are

FDA's Center for Drug Evaluation and Research (CDER) **Office of Medical Policy** (OMP) is led by **Director M. Khair ElZarrad** and **Deputy Director Karen Hicks**. Also in the OMP Immediate Office (IO) are **John Concato, Associate Director for Real-World Evidence Analytics**, **Leonard Sacks, Associate Director for Clinical Methodology**, **Capt. Dianne Paraoan, Associate Director for Regulatory Affairs,** and **Juanita Marner, Senior Policy Coordinator**. OMP promotes and protects public health by providing scientific and regulatory leadership in the development of medical policy by:

- Providing Center oversight and leadership in the development of medical policy, procedures, and policy initiatives pertaining to drug development, drug approval, bioresearch monitoring, human subject protection, postmarket surveillance processes, and the science and efficiency of clinical trials.
- Providing scientific and regulatory leadership in ensuring accurate and effective communication of medical information to health care professionals and patients, in compliance with applicable regulations.
- Fostering an interdisciplinary approach to medical policy development, implementation, and coordination, through collaboration with other disciplines, program areas, FDA Centers, and interested parties in a manner that enhances integration of evolving science and policy into drug development, regulatory review, and postmarket surveillance processes.
- Providing guidance and policy development regarding prescription drug promotion and helping ensure prescription drug advertising and promotional labeling (promotional communications) are truthful, accurate, and not misleading.

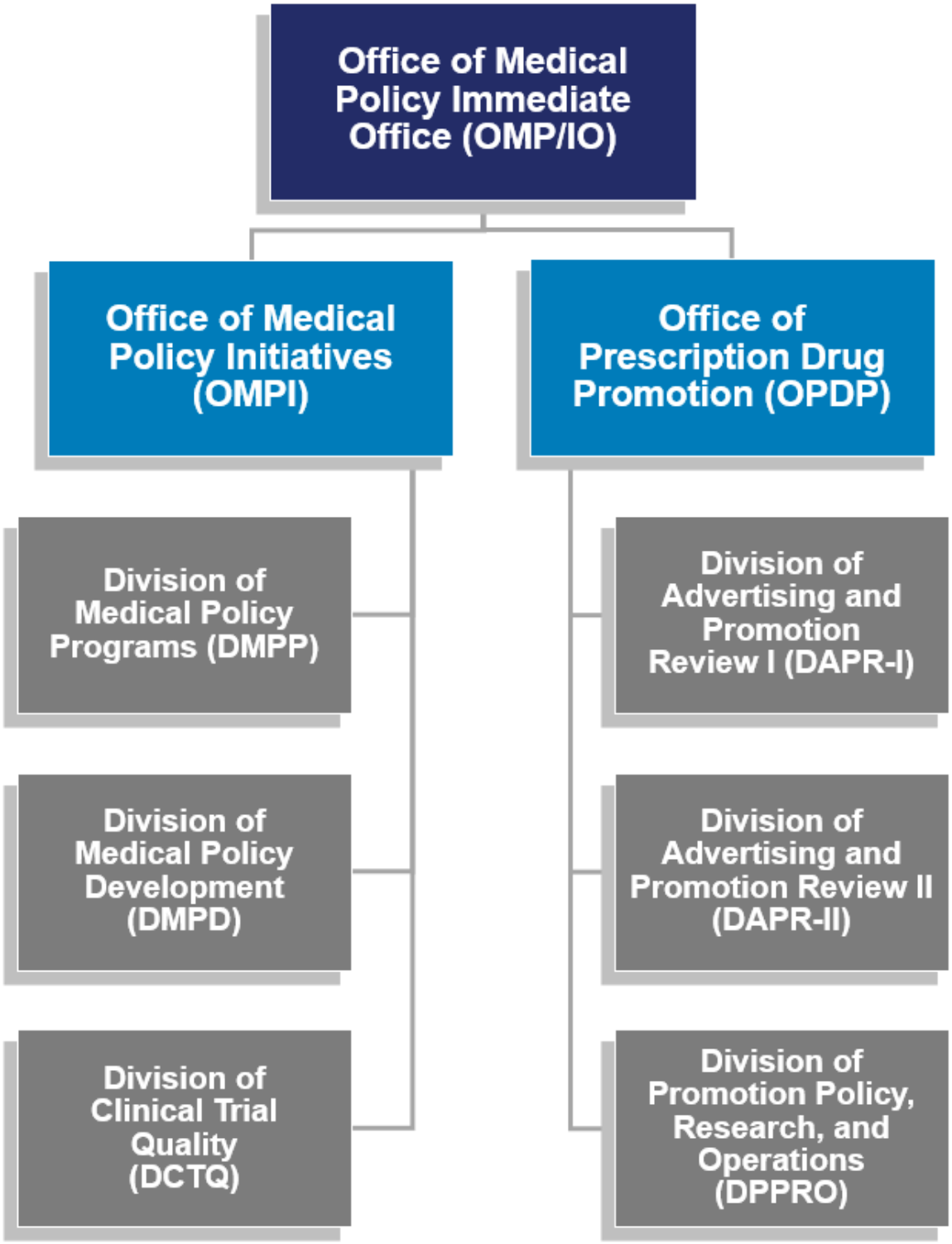
OMP's **Office of Prescription Drug Promotion** (OPDP) is led by **Director Catherine Gray** and **Deputy Director Mark Askine**. The office:

- Reviews prescription drug advertising and promotional labeling to ensure that the information contained in these promotional communications is not false or misleading.
- Provides consultation on draft labeling, cartons and product labels, Medication Guides, Patient Package Inserts (PPIs), Risk Evaluation and Mitigation Strategy (REMS) materials, Dear Health Care Provider letters, and proposed proprietary names.
- Runs an active research program designed to investigate applied and theoretical issues in the communication of risk and benefit information in direct-to-consumer (DTC) and health care provider-directed promotional prescription drug communications.
- Manages guidance and policy development regarding prescription drug promotion.
- Represents OMP on Center, Agency, and other cross-cutting working groups and collaborations relevant to prescription drug promotion activities and policy.

OMP's **Office of Medical Policy Initiatives** (OMPI) is led by **Director Victor Crentsil** and **Deputy Director Bryon Pearsall**. Also in the OMPI-IO are **Tala Fakhouri, Associate Director for Policy Analysis,** and **Capt. Janice Maniwang, Associate Director for Regulatory Affairs**. The office:

- Provides oversight and direction for the development of medical policies and procedures pertaining to the drug development and drug approval processes, bioresearch monitoring, and human subject protection.
- Provides oversight and direction for new and ongoing policy initiatives in broad-based medical and clinical policy areas, including initiatives to improve the science, efficiency, and quality of clinical trials, and collaboratively enhance professional and patient labeling.
- Provides leadership to effectively coordinate and collaborate with relevant program areas, FDA Centers, and interested parties to ensure optimal FDA scientific and technical input for medical policy development and ongoing policy initiatives.
- Represents OMP on Center, Agency, and other cross-cutting working groups and collaborations relevant to OMP programs and initiatives.
- Provides oversight and direction for research and other programs and initiatives to support and advance medical policy development.

Office of Medical Policy Organization Chart



Highlights of Accomplishments in 2023

Evaluating the use of real-world data and real-world evidence

Overview. OMP continues to have a leading role within CDER in evaluating the appropriate use of real-world data (RWD) and real-world evidence (RWE). RWD are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources, such as electronic health records (EHRs) and medical claims. RWE is the clinical evidence about the use and potential benefits or risks of a medical product derived from analysis of RWD. The 21st Century Cures Act instructed FDA to evaluate the potential use of RWE to help support the approval of new indications for approved drugs or to help support or satisfy post-approval study requirements. In addition, the seventh reauthorization of the Prescription Drug User Fee Act[1] (PDUFA VII) includes several commitments (see below) related to RWE.

OMP oversees FDA's RWE Program, working with colleagues in CDER (including through the Medical Policy and Program Review Council (MPPRC) and RWE Subcommittee), CBER, and other FDA Centers to coordinate activities involving the use of RWD to generate RWE for regulatory purposes. These activities include developing guidance, providing input (e.g., consults) to review divisions, soliciting input from external experts and other interested parties, and supporting demonstration (research) projects.

RWE Provisions under PDUFA VII. Led a cross-center team to design and publicly launch the Advancing RWE Program, which allows for "early" meetings between sponsors and FDA intended to improve the quality and acceptability of RWE-based approaches in support of new labeling claims, including approval of new indications of approved medical products or to satisfy post-approval study requirements. This effort includes managing and providing scientific leadership for semi-annual submission cycles and program meetings. ❖ Led a cross-center collaboration to improve processes for the identification and tracking of RWE submissions to CDER as well as to define the scope and key principles for the first public report on RWE submissions to CDER.

Ongoing activities. Fostered discussion and engagement with RWE-related issues with CDER colleagues ❖ Convened interested parties, including at public webinars and expert workshops, to discuss RWE-related guidance documents and other activities ❖ Participated in international engagements (including with the European Medicines Agency and Health Canada) - International Council for Harmonisation (ICH) reflection paper on "Pursuing Opportunities for Harmonisation in Using Real-World Data to Generate Real-World Evidence, with a Focus on

[1] PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 through 2027.

Effectiveness of Medicines" ❖ Responded to questions from external parties about RWE and RWD that were submitted to the CDER RWE email inbox ❖ Awarded four new 3-year RWE-focused cooperative agreements (U01s).

Transformative and adaptive technologies. Fully implemented the developed version of the Edge Tool, the automated EHR extraction tool leveraged by CURE ID ❖ Enabled collection of initial 14,000 cases of COVID-19 patients treated with repurposed drugs to be included in CURE ID (with ~120,000 additional cases making their way through the transfer process) ❖ Further developed the patient portal, allowing crowdsourcing of a patient's experience with repurposed drugs for diseases like Long COVID, RASopathies, and sarcomas. This information is of most value for conditions with prolonged treatment histories and many complicated symptoms, for which multiple clinicians have treated the patient ❖ Expanded the CURE ID platform to include non-infectious diseases, focusing on rare cancers (e.g., Angiosarcoma) and rare genetic disorders (e.g., Noonan Syndrome), which lack adequate approved therapies.

Demonstration projects and grants. Supported multiple demonstration (research) projects focused on understanding data reliability, improving RWE tools, and developing novel approaches to study design and analysis, including:

- Developing novel methods to facilitate hybrid externally controlled trials and trial external control arms using RWD through cooperative agreements with Genentech, University of North Carolina, Duke University, and Johnson & Johnson.
- Developing advanced technologies and approaches to maximize use of unstructured EHR data in RWE generation for effectiveness and safety of medical therapies through cooperative agreements with Verantos and the Harvard-MIT Center for Regulatory Science.
- Validating Centers for Medicare & Medicaid Services (CMS) Medicare Advantage data for use in studies generating RWE through linkage with a large national transcatheter valve therapies registry via a Broad Agency Announcement with Duke University.
- Improving outcome ascertainment in a simple pragmatic trial, the RELIANCE trial, evaluating efficacy of chronic obstructive pulmonary disease therapies by linking to CMS Medicare claims data through an FDA-Catalyst funded partnership with Harvard Pilgrim Healthcare and the RELIANCE trial team.
- Retrospectively replicating 30 randomized trials using health care claims data (RCT-DUPLICATE) to understand and improve the validity of studies using RWD to support regulatory decision-making. The main results were published in the *Journal of the American Medical Association* in April 2023.
- Engaging in other cooperative agreements to support research, such as with the Critical Path Institute and with Brigham & Women's Hospital.

Advancing emerging and evolving policy areas

Overview. In 2023, OMP continued to address cross-cutting policy issues and emerging needs for rapidly evolving technologies.

Artificial intelligence

In the past decade, technological advances and the rise of "big data" have greatly increased the potential of artificial intelligence (AI), and specifically, machine learning (ML), to transform the health care industry. In 2019, OMP began to engage with partners at FDA, academia, industry, and the international community to explore ways in which AI and ML can be used to safely promote drug development, from drug discovery to postmarketing surveillance. OMP's 2023 highlights include:

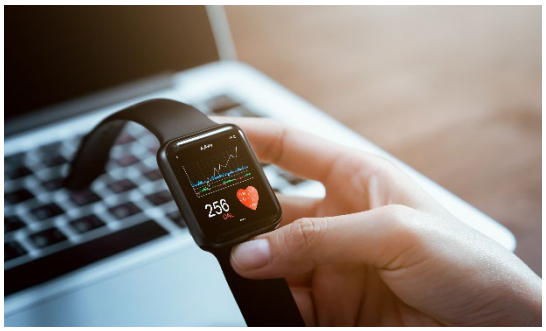
- Participated in and represented a regulatory perspective on the International Telecommunication Union (ITU)/World Health Organization's (WHO) Focus Group on Artificial Intelligence for Health (FG-AI4H).
- Contributed to the deliverable of the FG-AI4H's Working Group on Regulatory Considerations on AI for Health; the deliverable is a high-level overview of regulatory considerations for the use of AI in health.
- Worked with multiple parties on exploring the potential role and uses of AI tools to support the full spectrum of therapeutic development. Engaged with academic centers and non-profit organizations to determine possible regulatory and ethical implications for the use of AI in clinical trials.
- Represented CDER's perspective on the use of AI in drug development at 25 meetings, national conferences, and interviews.

Digital health technologies

A digital health technology (DHT) is a system that uses computing platforms, connectivity, software, and/or sensors, for health care and related uses. Examples include but are not limited to portable sensors and mobile applications (mobile apps) such as activity trackers and smart watches. DHTs provide opportunities to record data directly from trial participants (e.g., performance of activities of daily living, sleep) wherever the participants may be (e.g., home, school, work, outdoors).

2023 highlights include:

- PDUFA VII required FDA to establish a committee including members from CDER and CBER to support implementation of PDUFA VII commitments, including the design and implementation of a DHT Framework. OMP launched and chairs the Digital Health Technologies Steering Committee (DHT SC) to promote consistency across centers regarding DHT-based policies and procedures.
- The DHT SC hosted listening sessions with external stakeholders on DHT-related issues.
- PDUFA VII also charged FDA with enhancing its information technology capabilities to support the review of DHT-generated data. To this end, OMP facilitated the revision to FDA standard forms 1571 and 356H to track incoming DHT-related submissions. OMP continues to assess the data coming in to understand which submissions included DHT-derived data.



In addition, OMP:

- Published the webpage *DHTs for Drug Development*[2]
- Completed two demonstration projects with Centers of Excellence in Regulatory Science and Innovation (CERSI) collaborators using DHTs to measure treatment responses in heart failure and in mood disorders in adolescents.
- Identified two new DHT demonstration projects to explore DHT-derived endpoints in pediatric populations.
- In March 2023, hosted the public workshop "Understanding Priorities for the Use of Digital Health Technologies to Support Clinical Trials for Drug Development and Review," bringing collaborators together to discuss the adoption of DHTs in clinical trials, the impact of DHTs on the diversity of patient populations, and the use of actigraphy and other DHTs in clinical trials.
- Presented publicly on DHTs at the following meetings: REdI webinar on Modern Clinical Trials, DTx West, and Regulatory Affairs Professional Society Convergence 2023.

Decentralized clinical trial procedures

Decentralized Clinical Trials (DCTs) may enhance convenience for trial participants by enabling remote participation, reducing the burden on caregivers, and facilitating research on rare diseases and diseases affecting populations with limited mobility. Procedures to promote DCTs include telehealth visits, use of local health care providers (HCPs), sending trial staff to participants' homes, mailing investigational products directly to participants' homes, and promoting use of electronic informed consent and the use of DHTs to acquire data remotely.

[2] https://www.fda.gov/science-research/science-and-research-special-topics/digital-health-technologies-dhts-drug-development

Accomplishments include public presentations on DCTs at the following meetings: Fierce biotech conference, FDA Clinical Investigator Training Course, Office of Women's Health Regulatory Series, Decentralized Trials and Research Alliance, and National Academies of Sciences, Engineering, and Medicine (NASEM) Neuroscience Annual Meeting.

Integration of randomized controlled trials for drug and biological products into routine clinical practice

There is growing interest in the medical community in the conduct of randomized controlled drug trials with streamlined protocols and procedures that focus on essential data collection, allowing integration of research into routine clinical practice. Such trials, sometimes referred to as point-of-care trials, may range from those that are almost completely reliant on data acquired by the participant's local HCPs during routine clinical practice visits to those that require significant supplementation with dedicated, research-specific activities for data collection conducted by trial staff. Engaging health maintenance organizations, hospital systems, clinical networks of HCPs, and national health systems in the research enterprise provides novel opportunities to facilitate the enrollment of sizable trial populations in a short period of time by improving convenience and accessibility for participants. HCPs in these institutions may contribute to clinical trials valuable data that they obtain in the course of providing clinical care. OMP has led an FDA working group on this topic and intends to publish guidance on integrating randomized controlled trials into routine clinical practice in 2024.

Electronic records and signatures (21 CFR Part 11)

OMP responded to more than 90 external stakeholder inquiries regarding FDA's policies pertaining to compliance with 21 CFR part 11, particularly regarding certified copies and electronic signatures.

Cloud-based computing

OMP has partnered with CDER's Office of Strategic Programs (OSP) to explore the potential use of cloud-based computing technologies to transform how sponsors and regulators may communicate, exchange, and analyze data. OMP is developing and evaluating the policy and regulatory considerations of moving some parts of the regulatory review collaboration process into the cloud using specific use cases as examples.

2023 highlights include:

- Along with OSP, OMP:
  - Worked with external interested parties through a Public Private Partnership to develop a new way for biopharmaceutical sponsors to communicate with health authorities.
  - Identified and developed potential use cases and cloud demonstration projects to meet the requirements laid out in the PDUFA VII commitment letter.
- Worked closely with external interested parties and the Oncology Center of Excellence (OCE) to develop a prototype solution for the Collaborative Review Use Case, a use case modeled on the OCE Project Orbis initiative that enables concurrent review of Applications with other global health authorities using an Assessment Aid template.

Prescription drug use-related software

Sponsors are increasingly seeking to include software in their prescription drug applications or to disseminate software to use with their prescription drugs. In 2023, OMP communicated with interested parties about the proposed Prescription Drug Use-Related Software (PDURS) framework and also requested involvement from review staff to ensure a consistent approach across CDER when software is proposed or introduced for use with drug products.

Promoting responsible marketing and advertising

Overview. OMP staff in the Office of Prescription Drug Promotion (OPDP) protect public health by helping to ensure that prescription drug information is truthful, balanced, and accurately communicated. They accomplish this through comprehensive surveillance, compliance, education, and research programs, and by fostering better communication of labeling and promotional information to both health care professionals and consumers.

OPDP staff review prescription drug advertising and promotional labeling to ensure that the information contained in these promotional materials is not false or misleading. They engage in a variety of tasks to perform this responsibility, including:

- Providing responsive written comments to voluntary requests from pharmaceutical sponsors regarding their proposed promotional materials to facilitate compliance with the laws and regulations relating to prescription drug promotion;
- Reviewing complaints about alleged violations in prescription drug promotional communications;
- Issuing compliance letters on promotional communications that are false or misleading;

- Comparing the product labeling and promotional materials of various closely related products to ensure that the regulatory requirements are consistently and equitably applied;
- Reviewing proposed draft prescribing information, patient package inserts, medication guides, carton and container labels, and risk evaluation and mitigation strategy (REMS) materials to ensure they are not promotional in tone;
- Attending major medical meetings and pharmaceutical conventions to monitor promotional exhibits and activities;
- Acting as a liaison between OPDP and other divisions within FDA on promotional issues; and
- Launching four research projects to investigate pertinent developments in prescription drug promotion.

Engagement with interested parties. Presented on OPDP and its policy, compliance, and research work at meetings of the following groups: Drug Information Association (DIA), Pharmaceutical Compliance Congress, International Field Directors and Technologies, FDA Science Forum, Food and Drug Law Institute (FDLI), and the American Society of Hematology Committee on Government Affairs ❖ Issued five compliance letters for violative promotional communications ❖ Published a new webpage consolidating all OPDP Untitled Letters issued since 2017 onto a single webpage ❖ Featured OPDP social science research in CDER Regulatory Science newsletter and Spotlight on CDER Science ❖ Updated webpage with new frequently asked questions (FAQ) information specific to the final rule on presenting major statements in a clear, conspicuous, and neutral manner.

Thought leadership. Co-hosted Duke-Margolis Public Meeting "The Future of Prescription Drug Promotion and Digital Marketing" ❖ Led discussion of responsive search advertisements best practices and recommendations at a DIA roundtable webinar ❖ Provided briefings on two draft guidances and one final rule ❖ Collaborated closely with internal and external parties to consider unique circumstances concerning prescription drug promotion.

Other accomplishments. Expanded distribution of *The Brief Summary*—OPDP's quarterly bulletin to interested parties—to over 65,000 subscribers ❖ The OPDP Digital Marketing Team (DMT)—a collaborative team of OPDP staff focused on developing resources and institutional knowledge of emerging marketing strategies in the digital space—built out a consolidated library of relevant information to serve as a reference for OMP ❖ Reviewed 127 Emergency Use Authorization (EUA) Promotional Submissions containing 181 promotional communications for Authorized Products ❖ Obtained OMB approval for four generic information collections ❖ Precepted seven pharmacy students.

Ensuring consistent communication in patient drug labeling

Overview. OMP staff promote the safe and effective use of prescription medications by collaborating with offices within CDER and throughout FDA to deliver effective and consistent patient labeling. A team of OMP staff reviews patient labeling, including:

- ***Patient Package Inserts (PPI).*** PPIs are written prescription drug product information for patients that applicants develop. FDA regulations require that applicants develop PPIs for oral contraceptives and estrogen-containing products. Applicants must submit the required PPIs to FDA for approval and provide FDA-approved PPIs with each package of the drug product that the manufacturer or distributor intends to dispense to a patient. Applicants can also voluntarily create PPIs for other prescription drug products and may submit them to FDA for review and approval as part of a prescription drug product's labeling. However, distribution of a voluntarily submitted PPI is not required.
- ***Medication Guides (MGs).*** MGs are written prescription drug product information that applicants develop, and FDA approves. They are required to be distributed when a relevant prescription drug product is dispensed to a patient. A MG is required when FDA determines that a prescription drug product poses a serious and significant public health concern that requires distribution of FDA-approved patient information (21 CFR 208). A MG contains information necessary to a patient's safe and effective use of a prescription drug product.
- ***Instructions for Use (IFU).*** IFUs are written prescription drug product information that applicants develop, and FDA approves. IFUs are part of the FDA-approved prescription drug labeling. IFUs are developed for drug products that have complicated or detailed patient-use instructions. The IFU provides guidance on how to use a prescription drug product (for example, devices patients must use to self-administer a drug).

Engagement with interested parties. Educated CDER colleagues through road show presentations on patient labeling activities.

Safety Labeling Changes (SLC). When FDA requires certain drug and biological product application holders to make safety-related labeling changes based on new safety information that becomes available after approval of the drug or biological product, OMP staff provide edits and recommendations to MGs and PPIs to reflect labeling changes based on the safety-related issue(s).

Medication Guides: Patient Medication Information, Proposed Rule. OMP's Office of Medical Policy Initiatives (OMPI) staff continue to work to ensure that patients are provided accurate and understandable information about their prescription drug products. Currently, patients may receive information from several sources regarding their prescription medication. After years of research, FDA determined that existing documents (Consumer Medication Information) do not consistently provide patients with

clear, easily understood information about their prescription medications. Communications that do not provide clarity regarding prescription medications may lead to patient nonadherence, which may, in turn, be responsible for increased hospitalizations, treatment failures, and even increased death rates in the United States each year.

To address this issue, in May 2023, FDA proposed to amend its human prescription drug product labeling regulations for MGs that, if finalized, will require a new type of information known as Patient Medication Information (PMI). PMI is a new type of MG proposed by FDA, designed to provide concise, easy-to-understand information about a prescription medicine for patients. In most cases, PMI will be a one-page written document approved by FDA and provided to patients when receiving outpatient prescription drug products.

Promoting clinical trial science, efficiency, and quality

Overview. CDER relies on the results of high-quality clinical trials to inform regulatory decisions. At the core of every clinical trial is the necessity for human subject protection and data integrity, as key components of clinical trial quality. In 2023, OMP developed, initiated, and supported initiatives focused on promoting clinical trial quality, often with extensive engagement of interested parties.

Representation in clinical trials. During 2023, OMP led cross-cutting policy development, initiatives, requests from various interested parties, and public engagements addressing inclusion and diversity in clinical trials to better reflect the demographics of clinically relevant populations. These activities aim to ensure that future trials better represent the demographics of relevant populations, including factors such as sex, gender, age, race, and ethnicity and help reduce barriers that may prevent the enrollment and retention of a diverse population. OMP's efforts are part of the FDA's ongoing commitment to promoting diversity in research and enhancing the applicability of study findings to the broader population.

Demographic, non-demographic, and disease-related factors can influence individual responses to a given therapeutic product. Thus, enrolling participants with diverse baseline characteristics in clinical trials can more accurately reflect the broader population likely to use these products, if approved. The factors and barriers contributing to the underrepresentation of certain groups in clinical studies are complex and extend beyond the trial designs themselves.

OMP leads cross-agency collaborations and committees focusing on discussions, recommendations, and coordination of the implementation of the requirement for diversity action plans in medical product development programs. These action plans align with FDA's continuous commitment to foster diverse participation in clinical trials. In December 2022, the Agency received new authorities through FDORA. As part of this mandate, OMP organized one public meeting and one public workshop in collaboration with CDER, CBER, CDRH, the OCE, and the Clinical Trials Transformation Initiative (CTTI), involving relevant industry and organizations such as drug and medical device sponsors, clinical research organizations, academia, patients, and others. The public meeting, "Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies," was convened on October 18–19, 2023, and discussed strategies sponsors use to mitigate clinical study disruptions during public health emergencies, including flexibilities such as advanced modalities, innovative technologies, and study designs with decentralized elements to reduce burden and enhance the inclusion of diverse patients as partners in clinical studies. The "Public Workshop to Enhance Clinical Study Diversity" was convened on November 29–30, 2023, and solicited input from various parties on increasing the enrollment of historically underrepresented populations in clinical studies, helping to reduce barriers to enrollment and retention, and encouraging clinical study participation that reflects the prevalence of the disease or condition among demographic subgroups.

OMP also provided two guidance snapshots and two podcasts for patients and industry to raise public awareness and increase communication regarding FDA's guidance *Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices and Trial Designs* (November 2020). In addition, at the Regulatory Affairs Professional Society Convergence 2023, OMP discussed actions FDA has taken to encourage participation of a diverse population in clinical trials on the panel "Actionable Steps to Meeting Regulatory and Ethical Considerations in Clinical Trial Diversity." OMP published a manuscript in the *Journal of Clinical Pharmacology* titled "Demographic Diversity of Clinical Trials for Therapeutic Drug Products: A Systematic Review of Recently Published Articles, 2017–2022" (December 2023) to assess recent literature on the demographic diversity of clinical trial participants, describe the historical methods used in defining clinical trial diversity, and address knowledge gaps to enhance clinical trial diversity.

Thought leadership and convening role within FDA/HHS. Managed Agency engagement with external parties on topics including statistical analytic approaches, pharmacovigilance, enabling translational safety capabilities, and embedded pragmatic trials ❖ Participated in the development of the ICH of Technical Requirements for Pharmaceuticals for Human Use documents:

- Led the multi-national efforts to revise the ICH document, E6(R3) Good Clinical Practice.
- Co-led the efforts on ICH M11 to develop a harmonized guideline that specifies comprehensive clinical protocol organization with standardized content. This includes the development of the Clinical electronic Structured Harmonised Protocol (CeSHarP) template and a technical specification to use an open, nonproprietary standard to enable electronic exchange of clinical protocol information. Presented a Progress Update on ICH M11 at the January 2023 CTTI webinar.

Training of clinical investigators. FDA's annual clinical investigator training course has been an institution led by OMP for more than 10 years. With the goal of improving trial quality, it typically attracts registrants from around the world and has provided three days of intense training by FDA experts on all aspects of clinical trials. In 2023, OMP collaborated with CDER Small Business & Industry Assistance (SBIA) to provide a virtual course over two days on

selected current topics of importance to clinical investigators, including trial design, study populations, safety, statistical analysis, and compliance. The course also addressed nonclinical data to support clinical trials and current initiatives to modernize the trial enterprise such as the use of RWD, DHTs, and decentralized trial approaches. More than 11,000 participants registered for the event, and 3,911 individuals from 141 countries participated in the course over two days. Ninety-eight percent of those who participated in evaluation of the course found it valuable, new, and timely. Participants also provided enthusiastic reviews about the quality of the program.

Providing stewardship of FDA policies

Overview. OMP provides oversight and direction to develop medical policies and procedures pertaining to drug development and drug approval processes, bioresearch monitoring, and human subject protection and for new and ongoing policy initiatives in broad-based medical and clinical policy areas. These efforts include initiatives to improve the science and efficiency of clinical trials, promote clinical trial quality, and collaboratively enhance professional and patient labeling. OMP provides leadership to effectively coordinate and collaborate with relevant program areas, FDA Centers, and interested parties to promote optimal FDA scientific and technical input for medical policy development and ongoing policy initiatives.

Engagement with interested parties. CDER's OMP Mailbox managed over 660 inquiries/responses, including the review of 78 guidance documents, 5 regulations, Compliance Programs, and other policy documents.

Promoting patient access to drugs

Overview. OMP and FDA colleagues continue to expedite the development and review of drugs for serious conditions through programs such as:

- ***Expedited Development Programs for Serious Conditions.*** Expedited development programs are intended to help ensure that therapies for serious conditions are approved and available to patients as soon as it can be concluded that the benefits justify their risks. The four programs that support these principles are fast track designation, breakthrough therapy designation, accelerated approval, and priority review designation.
- ***Promoting Clinical Trial Efficiency to Enhance Drug Development.*** OMP and FDA colleagues continue to increase speed and efficiency in several areas of the clinical trial phase of drug development, including:
    - Assisting with establishing flexible clinical development designs and accepting such designs when they support the high standards for demonstrating safety and efficacy.
    - Meeting frequently and working closely with industry sponsors throughout the development process to plan efficient clinical trial programs and agree on needed data.

- Facilitating creation of clinical trial networks and “master protocols” to streamline and reduce the cost and duration of conducting clinical trials.

Thought leadership and convening role within FDA/HHS. Led the updates to the Form FDA 3926, Expanded Access (EA) Spanish webpage, and the EA webpages used by licensed physicians, patients, industry, and institutional review boards.

Engagement with interested parties. Helped maintain the Reagan-Udall Foundation for FDA’s Expanded Access Navigator, which provides resources for patients, families, and physicians interested in expanded access to investigational drugs ❖ Collaborated with the Reagan-Udall Foundation for FDA on improvements to and outreach for the Expanded Access eRequest site ❖ Presented at the Public Responsibility in Medicine and Research (PRIM&R) 2023 Annual Conference on the recent updates from the FDA guidance for institutional review boards and clinical investigators *Institutional Review Board (IRB) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products* (September 2023).

Transformative and adaptive technologies. Provided ongoing support for the Expanded Access eRequest site hosted by the Reagan-Udall Foundation for FDA. The site enables physicians to determine the appropriateness of single (individual) patient expanded access and electronically complete, sign, and submit an application for single patient, non-emergency, expanded access ❖ In 2023, released a new workflow on the Expanded Access eRequest site for requesting emergency access to the drug PAXLOVID (nirmatrelvir/ritonavir) to treat SARS-CoV-2 infection in severely immunocompromised individuals.

A Special Thank You to Our Collaborators

OMP is grateful to our colleagues in the following offices that help us to create innovative and cross-cutting policy:

- Center for Biologics Evaluation and Research
- Center for Devices and Radiological Health
- Center for Drug Evaluation and Research
  - Office of Communications
  - Office of Compliance
  - Office of Generic Drugs
  - Office of Management
  - Office of Medical Policy
  - Office of New Drugs
  - Office of Pharmaceutical Quality
  - Office of Regulatory Policy
  - Office of Strategic Programs
  - Office of Surveillance and Epidemiology
  - Office of Translational Sciences
- National Center for Toxicological Research
- Office of Combination Products
- Office of Minority Health and Health Equity
- Office of the Center Director
- Office of the Chief Counsel
- Office of the Chief Scientist
- Office of the Commissioner
- Office of Executive Programs
- Oncology Center of Excellence

OMP thanks our internal collaborators who contributed to our successes in 2023. We look forward to our future collaborations to promote and protect public health by providing scientific and regulatory leadership in the development of medical policy.

Appendix A: Regulatory Publications

Regulatory publications include guidance documents (draft and final), frameworks, discussion papers, rules (final and proposed), compliance letters, federal register notices, and meeting or workshop summaries.

Draft guidances

- Draft guidance for industry *Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products* (88 FR 6748, February 1, 2023)
- Draft guidance for industry *Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations – Questions and Answers* (88 FR 16268, March 16, 2023)
- Draft guidance for industry, investigators, and other stakeholders *Decentralized Clinical Trials for Drugs, Biological Products, and Devices* (88 FR 27900, May 3, 2023)
- Draft guidance for industry *Regulatory Considerations for Prescription Drug Use-Related Software* (88 FR 64443, September 19, 2023)
- Draft guidance for industry *Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers* (88 FR 73031, October 24, 2023)

Final guidances

- Guidance for industry *A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers* (88 FR 22038, April 12, 2023)
- Guidance for industry *Presenting Quantitative Efficacy and Risk Information in Direct-to-Consumer (DTC) Promotional Labeling and Advertisements* (88 FR 41966, June 28, 2023)
- Guidance for industry *Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products* (88 FR 60215, August 31, 2023)
- Guidance for institutional review boards and clinical investigators *Institutional Review Board (IRB) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products* (88 FR 62384, September 11, 2023)
- Guidance for institutional review boards and clinical investigators *Considerations for the Conduct of Clinical Trials of Medical Products During Disruptions Due to Major Disasters and Public Health Emergencies* (88 FR 65177, September 21, 2023)

- Guidance for industry *Human Prescription Drug and Biological Products—Labeling for Dosing Based on Weight or Body Surface Area for Ready-to-Use Containers—"Dose Banding"* (88 FR 67765, October 2, 2023)

- Guidance for industry *Presenting Quantitative Efficacy and Risk Information in Direct-to-Consumer (DTC) Promotional Labeling and Advertisements (Revision 1)* (88 FR 41966, revision published December 11, 2023)

- Guidance for industry, investigators, and clinical investigators *Digital Health Technologies for Remote Data Acquisition in Clinical Investigations* (88 FR 88629, December 22, 2023)

- Guidance for industry *Data Standards for Drug and Biological Product Submissions Containing Real-World Data* (88 FR 88633, December 22, 2023)

- Guidance for industry *Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products* (88 FR 88631, December 22, 2023)

- Guidance for industry *Direct-to-Consumer Prescription Drug Advertisements: Presentation of the Major Statement in a Clear, Conspicuous, and Neutral Manner in Advertisements in Television and Radio Format Final Rule: Questions and Answers* (88 FR 89303, December 27, 2023)

Frameworks

- Framework: Framework for the Use of Digital Health Technologies in Drug and Biological Product Development (88 FR 17852, March 24, 2023)

Discussion papers

- Discussion paper: Using Artificial Intelligence and Machine Learning in the Development of Drug and Biological Products (88 FR 30313, May 11, 2023)

Public reports

- Workshop report: "Understanding Artificial Intelligence and Machine Learning in the Drug Development Lifecycle" workshop summary prepared in collaboration with Duke Margolis (June 21, 2023)

Final rules

- Final rule: Direct-to-Consumer Prescription Drug Advertisements: Presentation of the Major Statement in a Clear, Conspicuous, and Neutral Manner in Advertisements in Television and Radio Format (88 FR 80958, November 21, 2023)

Proposed rules

- Proposed rule: Medication Guides: Patient Medication Information (88 FR 35694, May 31, 2023)

Compliance letters

- Recorlev Untitled Letter (June 6, 2023)
- Breztri Warning Letter (August 4, 2023)
- Slynd Untitled Letter (August 11, 2023)
- Phexxi Untitled Letter (October 31, 2023)
- Rexulti Untitled Letter (October 31, 2023)

Technical amendments

- Code of Federal Regulations Title 21: Technical Amendment for Non-Repudiation Letters 21 CFR 11.100 (c)(1) (88 FR 13018, March 2, 2023)

Additional *Federal Register* notices

- *Federal Register* notice "Agency Information Collection Activities; Proposed Collection; Comment Request; A Survey on Quantitative Claims in Direct-to- Consumer Prescription Drug Advertising" (88 FR 24997, April 25, 2023)
- *Federal Register* notice "Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Endorser Status and Actual Use in Direct-to-Consumer Television Ads" (88 FR 26316, April 28, 2023)
- *Federal Register* notice "Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Tradeoff Analysis of Prescription Drug Product Claims in Direct-to-Consumer and Healthcare Provider Promotion" (88 FR 26553, May 1, 2023)
- *Federal Register* notice "Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Perceptions of Prescription Drug Products With Medication Tracking Capabilities" (88 FR 27518, May 2, 2023)
- *Federal Register* notice "Agency Information Collection Activities; Proposed Collection; Comment Request; Adherence Potential and Patient Preference in Prescription Drug Promotion" (88 FR 70669, October 11, 2023)

- *Federal Register* notice “Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; A Survey on Quantitative Claims in Direct-to-Consumer Prescription Drug Advertising” (88 FR 87431, December 18, 2023)

- *Federal Register* notice “Agency Information Collection Activities; Proposed Collection; Comment Request; Examination of Implied Claims in Direct-to-Consumer Prescription Drug Promotion” (88 FR 88398, December 21, 2023)

Appendix B: Public Meetings, Public Workshops, Trainings, and Webinars

Summary of OMP-organized conferences, public meetings, public workshops, trainings, and webinars:

Public meetings

- Mitigating Clinical Study Disruptions during Disasters and Public Health Emergencies Public Meeting (FDORA) (October 18–19, 2023) (88 FR 51323) (Report)

Public workshops

- Workshop on Draft Guidance on RWD: Electronic Health Records/ Medical Claims Data and Data Standards (February 27, 2023)
- The Future of Prescription Drug Promotion and Digital Marketing (September 14, 2023) (Report)
- Virtual Public Workshop to Enhance Clinical Study Diversity (FDORA) (November 29–30, 2023) (88 FR 57462) (Report)

Training

- FDA Clinical Investigator Training Course (December 6–7, 2023) (Materials)

Webinars

- Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products (April 13, 2023) (Materials)
- Electronic Systems, Electronic Records, and Electronic Signatures (April 25, 2023) (Materials)
- Decentralized Clinical Trials (DCT) Draft Guidance (June 20, 2023) (Materials)

Appendix C: Podcasts, Snapshots, and Webpages

Summary of OMP's podcasts, guidance snapshots, and webpages:

Podcasts

- Podcast for industry on FDA's guidance for industry *Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs* in collaboration with OTS and OCOMM (May 31, 2023)
- Podcast for patients on FDA's guidance for industry *Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs* in collaboration with OTS and OCOMM (May 31, 2023)
- "The FDA ponders whether artificial intelligence can help with drug approval" podcast interview on the Federal News Network (July 3, 2023)

Snapshots

- Guidance snapshot for industry on FDA's guidance for industry *Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs* in collaboration with OTS and OCOMM (May 31, 2023)
- Guidance snapshot for patients on FDA's guidance for industry *Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs* in collaboration with OTS and OCOMM (May 31, 2023)

Webpages

- Digital Health Technologies (DHTs) for Drug Development webpage
- Reagan-Udall Foundation's Expanded Access eRequest website; in 2023, added a new emergency IND request tool to enable physicians to request emergency use of PAXLOVID to treat patients with COVID-19

Appendix D: Non-regulatory Publications, Posters, and Selected Presentations

Summary of non-regulatory publications and posters that include one or more OMP authors. Not all are official OMP publications. Summary of selected presentations.

Non-regulatory publications

- Duong, LM, ABS Nono Djotsa, J Vahey, L Steele, R Quaden, KM Harrington, ST Ahmed, R Polimanti, E Streja, JM Gaziano, **J Concato**, H Zhao, K Radhakrishnan, ER Hauser, DA Helmer, M Aslan, and EJ Gifford, 2023, Association of Gulf War Illness with Characteristics in Deployed vs. Non-Deployed Gulf War Era Veterans in the Cooperative Studies Program 2006/Million Veteran Program 029 Cohort: A Cross-Sectional Analysis, Int J Environ Res Public Health, 20(1):258.

- **Fienkeng, M**, A Croker, Z Recinos-Vasquez, and M Carter, 2023, Enhancing Diversity in Clinical Trial Populations: An Agency-industry Perspective, Reg Focus, accessed August 2, 2024.

- **Aikin, KJ**, V Boudewyns, **KR Betts**, KC Giombi, RS Paquin, M Brewington, and R Malik, 2023, Implied Claims in Drug Advertising: A Review of Recent Literature and Regulatory Actions, Health Comm, 39(4):652–665.

- Gruber, S, RV Phillips, H Lee, M Ho, **J Concato**, and MJ van der Laan, 2023, Targeted Learning: Toward a Future Informed by Real- World Evidence, Statistics in Biopharm Res, 16(1):11–25.

- O'Lone, E, FS Apple, JO Burton, FJ Caskey, JC Craig, CR deFilippi, D Forfang, **KA Hicks**, V Jha, KW Mahaffey, PB Mark, P Rossignol, N Scholes-Robertson, A Jaure, AK Viecelli, AY Wang, DC Wheeler, D White, WC Winkelmayer, and CA Herzog, 2023, Defining Myocardial Infarction in Trials of People Receiving Hemodialysis: Consensus Report from the SONG-HD MI Expert Working Group, Kidney Internat, 103(6)1028–1037.

- Thompson, J, M Lynch, **HW Sullivan**, **KJ Aikin**, S Dolina, and M Brewington, 2023, Complexity of Data Displays in Prescription Drug Advertisements for Healthcare Providers, Ther Innov Regul Sci, 57:712–716.

- **Sullivan, HW**, **AC O'Donoghue**, V Boudewyns, RS Paquin, and K Ferriola-Bruckenstein, 2023, Patient Understanding of Oncology Clinical Trial Endpoints in Direct-to-Consumer Television Advertising, Oncologist, 28(7):e542–e553.

- Wang SV, S Schneeweiss, and **RCT-DUPLICATE Initiative**, 2023, Emulation of Randomized Clinical Trials With Nonrandomized Database Analyses: Results of 32 Clinical Trials, JAMA, 329(16):1376–1385.

- Giombi, K, J Thompson, C Wines, R Haughney, **HW Sullivan**, and **KR Betts**, 2023, A Scoping Review of Empirical Research on Prescription Drug Promotion, Res in Soc Admin Pharm, 19(6):859–872.

- Adhikari SD, S Chaudhuri, C Boodman, M Gupta, M Schito, **H Stone**, and N Gupta, 2023, Fosfomycin for Non-Urinary Tract Infections: A Systematic Review, Infez Med, 31(2):163-173.

- Igo, M, L Xu, A Krishna, S Stewart, L Xu, Z Li, JL Weaver, **H Stone**, **L Sacks**, T Bensman, J Florian, R Rouse, and X Han, 2023, A Metagenomic Analysis for Combination Therapy of Multiple Classes of Antibiotics on the Prevention of the Spread of Antibiotic-resistant Genes, Gut Microbes, 15(2).

- Lartey D, D Jateng, M Li, C Nguyen, **V Crentsil**, J Beitz, and B George, 2023, Quantification of Sertraline Maternal/Fetal Ratio and Amniotic Fluid Concentration Using a Pregnancy Physiologically Based Pharmacokinetic Model, Br J Clin Pharmacol, epub ahead of print, June 13, 2023, doi: 10.1111/bcp.15826.

- Milani, B, DA Dagne, HL Choi, M Schito, and **HA Stone**, 2023, Diagnostic Capacities and Treatment Practices on Implantation Mycoses: Results from the 2022 WHO Global Online Survey, PLOS Neglected Trop Dis, 17(6):e0011443.

- Bloomfield-Clagett, B, **M Rahman**, **K Smith**, and **J Concato**, 2023, Use of Real-World Evidence in Neuroscience-Related New Drug and Biologics License Applications for Novel Therapeutics, Clin Pharmacol Ther, 114:1002–1005.

- Vasterling, JJ, MR Franz, LO Lee, AP Kaiser, SP Proctor, BP Marx, PP Schnurr, J Ko, **J Concato**, and M Aslan, 2023, Early Predictors of Chronic Posttraumatic Stress Disorder Symptom Trajectories in U.S. Army Soldiers Deployed to the Iraq War Zone, J Traumatic Stress, 36:955–967.

- **Fakhouri, TH**, Q Liu, and **MK ElZarrad**, 2023, Chapter 41: Artificial Intelligence in Regulatory Decision-making for Drug and Biological Products." In: Krittanawong, C, editor, Artificial Intelligence in Clinical Practice: How AI Technologies Impact Medical Research and Clinics, published online, Elsevier Inc., 373–375.

- **Rahman, M**, G Dal Pan, P Stein, M Levenson, S Kraus, A Chakravarty, DR Rivera, R Forshee, and **J Concato**, 2023, When Can Real-world Data Generate Real-world Evidence?, Pharmacoepidemiol Drug Saf, epub ahead of print October 19, 2023, doi:10.1002/pds.5715.

- Jonker, AH, S Day, M Gabaldo, **H Stone**, M de Kort, DJ O'Connor and AMG Pasmooij, 2023, IRDiRC Drug Repurposing Guidebook: Making Better Use of Existing Drugs to Tackle Rare Diseases, Nature Rev Drug Discov, 22:937–938.

- Singh, K, **J Concato**, and JM Davis, 2023, Real-World Evidence for Neonatal Drug Development: Challenges and Opportunities, J Peds, epub ahead of print October 31, 2023, https://doi.org/10.1016/j.jpeds.2023.113806.

- **Poddar, A**, M Raggio, and **J Concato**, 2023, Decisions on Non-oncology Breakthrough Therapy Designation Requests in 2017–2019, Ther Innov Regul Sci, epub ahead of print November 5, 2023, https://doi.org/10.1007/s43441-023-00589-z.

- Gulanski, BI, JL Goulet, K Radhakrishnan, J Ko, Y Li, N Rajeevan, KM Lee, K Heberer, JA Lynch, E Streja, P Mutalik, KH Cheung, **J Concato**, MC Shih, JS Lee, and M Aslan, 2023, Metformin Prescription for U.S. Veterans with Prediabetes, 2010–2019, J Investig Med, epub ahead of print November 20, 2023, doi:10.1177/10815589231201141.

- Yuan, L, **M Rahman**, and **J Concato**, 2023, Comparison of Two Assessments of Real-world Data and Real-world Evidence for Regulatory Decision-making, Clin Transl Sci, epub ahead of print December 13, 2023, https://doi.org/10.1111/cts.13702.

- Langman, CB, D Assimos, M Blank, J Calle, A Grauer, A Kausz, D Milliner, L Nazzal, **K Smith**, G Tasian, A Thompson, KD Wood, E Worcester, S Yang, MA Malley, F Knauf, JC Lieske; and Rare Kidney Stone Consortium (RKSC) Kidney Health Initiative (KHI) Oxalosis and Hyperoxaluria Foundation Enteric Hyperoxaluria Workgroup (OHF EH Workgroup), 2023, End Point Considerations for Clinical Trials in Enteric Hyperoxaluria, Clin J Am Soc Nephrol, 18(12)1637–1644.

- **Chege, W**, **A Poddar**, **ME Samson**, **C Almeida**, **R Miller**, **D Raafat**, **T Fakhouri**, **M Fienkeng**, **SO Omokaro**, and **V Crentsil**, 2023, Demographic Diversity of Clinical Trials for Therapeutic Drug Products: A Systematic Review of Recently Published Articles, 2017-2022, J Clin Pharm, epub ahead of print December 14, 2023, https://doi.org/10.1002/jcph.2398.

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Posters

- **Mignon Schley, Tomeka Arnett, Cecilia Almeida, and Stephanie Omokaro**. FDA COVID-19 Critical Care Drug Monitoring Survey Portal - Ongoing Surveillance of Critical Drugs Related to COVID-19 Supply Disruptions (2023 FDA Science Forum) (June 13, 2023)

- **Kevin Betts and Helen Sullivan**. An Assessment of Terms and Phrases Commonly Used in Prescription Drug Promotion (2023 FDA Science Forum) (June 13–14, 2023)

- **Heather Stone**. Landscape Analysis to Identify Effective Drug Repurposing Candidates for the Treatment of Implantation Mycoses: Comparison of World Health Organization Survey Treatment Data and Published Case Reports on CURE ID (IDWeek 2023) (October 11, 2023)

- **Heather Stone**. The Landscape of Infections Caused by Rare Bacterial Pathogens (IDWeek 2023) (October 11, 2023)

- **Kevin Betts**. A Content Analysis of Dosage Form Presentations in Prescription Drug TV Ads (National Conference on Health Communication, Marketing & Media) (July 19, 2023)

- **Kevin Betts and Helen Sullivan**. Using Nonmonetary Incentives to Increase Physician Participation in a Mail Survey (IFD&TC 56th Annual Conference) (June 25, 2023)

Selected presentations

- **John Concato**. Presentation. "FDA Draft Guidance on Real-World Evidence" at Bronx VAMC & Columbia University Grand Rounds (January 12, 2023)

- **Motiur Rahman**. Presentation. "FDA's Real-World Evidence Program" at Precision Medicine World Conference (PMWC) (January 26, 2023)

- **Alyson Karesh**. Presentation. "FDA draft guidance on Sponsor Responsibilities–Safety Reporting Requirements and Safety Assessment for IND and Bioavailability/Bioequivalence Studies (published June 2021)" at the DIA Global Pharmacovigilance and Risk Management Strategies Conference (February 6, 2023)

- **Kim Smith**. Presentation. "U.S. FDA and Real-World Evidence" at DIA Global Pharmacovigilance and Risk Management Strategies Conference (February 7, 2023)

- **John Concato**. Presentation. "FDA's Real-World Evidence Program" at the International Society for CNS Clinical Trials and Methodology (ISCTM) Annual Meeting (February 15, 2023)

- **Motiur Rahman**. Presentation. "Real-World Evidence: PDUFA VII Commitments and FDA Use Cases" at the International Society for CNS Clinical Trials and Methodology (ISCTM) Annual Meeting (February 15, 2023)

- **Katie Gray**. Presentation. "Checking In with OPDP – FDA Updates" at the DIA Advertising and Promotion Regulatory Affairs Conference (February 23, 2023)

- **John Concato**. Opening remarks. "Workshop on Draft Guidance on Real-World Data: Electronic Health Records/Medical Claims Data and Data Standards" at the Duke-Margolis Center for Health Policy Expert Workshop (February 27, 2023)

- **Leonard Sacks**. Presentation. "Digital Health Technologies and Decentralized Clinical Trials" for the Israel Ministry of Health (March 7, 2023)

- **Leonard Sacks**. Presentation. "Ensayos clínicos descentralizados" at the CAEME (March 22, 2023)

- **Jennifer Chen** and Twyla Mosey. Presentation. "FDA's Office of Prescription Drug Promotion" at American Society of Hematology Committee on Government Affairs Meeting (March 27, 2023)

- **John Concato**. Presentation. "Real-World Evidence for Regulatory Purposes" at Respiratory Effectiveness Group (REG) (March 30, 2023)

- **John Concato**. Keynote speech. “Regulatory Perspectives on Real-World Data” at the 2023 Duke Industry Statistics Symposium (DISS) (March 30, 2023)

- **Leonard Sacks**. Presentation. “Decentralized Clinical Trials; Mapping the Road to Patient Convenience and Inclusivity” at the Duke University Statistics Symposium (March 31, 2023)

- **Beth Kunkoski**. Discussion. “Informing the Selection of Therapeutic Areas of Sleep to Drive Forward Pathways for Digital Clinical Measures” Digital Medicine Society Fireside Chat (April 19, 2023)

- **Kim Smith**. Workshop. “Keeping it Real: Publication Planning for Real-World Evidence and Patient Experience” at the Annual Meeting of the International Society for Medical Publication Professionals (ISMPP) (April 24, 2023)

- **Katie Gray**. FDA Keynote Address. “OPDP Compliance Actions, Policy Updates, and Newsy Notes” at the 20th Annual Pharmaceutical Compliance Congress (April 25, 2023)

- **Leonard Sacks**. Presentation. “DHT Overview” for the National Institutes of Health (May 1, 2023)

- **John Concato**. Presentation and panel discussion. “How to Collect Quality and Fit-for-Purpose Data” at the Centers of Excellence in Regulatory Science and Innovation (CERSI) (May 2, 2023)

- **John Concato**. Presentation. “Making Real World Decisions with Real World Evidence: From Frameworks to Practice” at the Professional Society for Health Economics and Outcomes Research (ISPOR) (May 7, 2023)

- **John Concato**. Presentation. “Real-World Evidence (RWE): Key Legal and Regulatory Considerations and Trends” at the Food and Drug Law Institute (FDLI) (May 18, 2023)

- **Beth Kunkoski**. Presentation. “Decentralized Clinical Trials” at the Medable/CVS/Harvard Principal Investigator Meeting (May 22, 2023)

- **John Concato**. Presentation. “Real-World Evidence in Regulatory Decision-Making: Enabling its Use Through International Collaboration” at the Biotechnology Industry Organization (BIO) (June 5, 2023)

- **Marsha Samson**. Presentation. “Artificial Intelligence and Machine Learning in Drug Development” at the West Coast Drug Discovery Innovation Program (June 5, 2023)

- **Tala Fakhouri.** Presentation. “Artificial Intelligence in Regulatory Decision-Making for Drug and Biological Products” at the 2023 Annual Symposium on Risks and Opportunities of AI in Pharmaceutical Medicine (June 5, 2023)

- **Beth Kunkoski.** Presentation. “The Modernization of Clinical Trials through Digital Health Technologies (DHTs), Decentralized Clinical Trials (DCTs), and Point of Care Trials” at the REdI Conference (June 6, 2023)

- **John Concato**. Presentation. “CDER/CBER Real-World Evidence Program” at the FDA Science Forum (June 13, 2023)

- **Beth Kunkoski**. Presentation. “An Overview of the Regulatory Landscape: What has Been Done, What is Happening Now and Where Will it Go?” at DtX West (June 21, 2023)

- **Karen Hicks**. Presentation and panel discussion. “DEI DIAmond Session: Navigating the Constellation of Efforts to Increase Representation in Clinical Research – FDA Views & Priorities” at the DIA 2023 Global Annual Meeting in Boston (June 26, 2023)

- **Amie O’Donoghue**. Presentation. “A Content Analysis of Dosage Form Presentations in Prescription Drug TV Ads” at the National Conference on Health Communication, Marketing, and Media (July 19, 2023)

- **Leonard Sacks**. Presentation. “Decentralized Clinical Trials” at SACHRP (July 19, 2023)

- **John Concato**. Discussion. “FDA’s Real-World Evidence Program” at the International Regulator’s Meeting at the International Conference on Pharmacoepidemiology (ICPE) (August 25, 2023)

- **Leonard Sacks**. Presentation. “DCTs – A Work in Progress” at Fierce (September 8, 2023)

- **Tala Fakhouri**. Presentation. “Considerations for the Use of Artificial Intelligence and Machine Learning to Support Regulatory Decision-Making for Drug and Biological Products: A Risk-Based Approach” at the ACRO Meeting in Washington, DC (September 13, 2023)

- **John Concato** and **Motiur Rahman**. Presentation. “Real-World Evidence Cluster” at a workshop on EMA and FDA Collaborations (September 14, 2023)

- **Atasi Podda**r. Presentation. “Patient Engagement Collaboration: Enhancing the Diversity of Clinical Trial Populations” at the FDA and CTTI Patient Engagement Collaborative Meeting (September 14, 2023)

- **Katie Gray**. Opening comments. “The Future of Prescription Drug Promotion and Digital Marketing” at the Virtual Public Workshop hosted in collaboration with Duke Margolis (September 14, 2023)

- **Tala Fakhouri**. Presentation. “Building New Technical Collaborations – Artificial Intelligence in Pharmacovigilance” at the EMA-FDA Workshop (September 15, 2023)

- **Marie Bradley**. Presentation. “Overview of FDA’s Real-World Evidence Program, Guidances, and Research Projects” at the Pharmaceutical Users Software Exchange (PHUSE) Computational Science Symposium (CSS) (September 20, 2023)

- **Marsha Samson**. Presentation. “AI: Current Realities and Future Opportunities to Advance Clinical Development” at the 2023 DPHARM Disruptive Innovations to Modernize Clinical Research Meeting in Boston (September 20, 2023)

- **Tala Fakhouri**. Presentation. “AI and Drug Development: What Does Pressing Forward Mean?” at the Research!America Meeting (September 20, 2023)

- **Kim Smith**. Presentation and panel discussion. “Leveraging All Available Data” at the CTTI Meeting (September 21, 2023)

- **Tala Fakhouri**. Presentation. “Maximally Leveraging All Available Data” at the CTTI Fall Member Meeting (September 21, 2023)

- **Atasi Poddar**. Moderator. “Race and Research – A Road Map” discussion at the Citizens’ Advisory Committee for Special Education (CACSE) (September 27, 2023)

- **Khair ElZarrad**. Presentation. “FDA’s Real-World Evidence Program” at the Duke-Margolis Center for Health Policy: State of Real-World Evidence Policy (September 28, 2023)

- **Beth Kunkoski**. Presentation. “FDA Expectations for Digital Health Technologies in Decentralized Clinical Trials” at Regulatory Affairs Professionals Society Converge (October 4, 2023)

- **Jean-Ah Kang**. Presentation. “Office of Prescription Drug Promotion (OPDP)” at the Georgetown University Medical Center, Clinical Research Unit (October 4, 2023)

- **Jamie Gamerman**. Presentation. “Actionable Steps to Meeting Regulatory and Ethical Considerations in Clinical Trial Diversity” at the Regulatory Affairs Professionals Society (October 5, 2023)

- **Mathilda Fienkeng**. Presentation. “Diversity In Clinical Trials for The Clinical Trial Investigator: A Regulatory Perspective” at the Achieving Data Quality & Integrity in Clinical Trials Involving High Consequence Pathogens Clinical Course (October 6, 2023)

- **Leonard Sacks**. Presentation. “DCTs - A Work in Progress” at SCDM (October 10, 2023)

- **Helen Sullivan**. Presentation. “Character-Space-Limited Online Prescription Drug Communications: Four Experimental Studies” at the FDA Social Media Research Community of Practice Meeting (October 12, 2023)

- **John Concato**. Discussion. “A Roadmap for Evidence Generation in Therapeutics” at the Harvard Club of Boston: Advancing Medication Practice through Better Data, Analytics, and AI (October 13, 2023)

- **John Concato**. Session chair. “Methodological Insights on External Controls and Sensitivity Analyses” at the DIA Real-World Evidence Conference (October 16, 2023)

- **Motiur Rahman**. Presentation. “Overview of FDA’s Real-World Evidence Demonstration Projects” at the DIA Real-World Evidence Conference (October 16, 2023)

- **Kim Smith**. Presentation. “CDER Real-World Evidence Program: Update and Examples” at DIA Real- World Evidence Conference (October 16, 2023)

- **Jason Cober**. Moderator. DIA roundtable webinar presenting best practices and recommendations when marketing prescription drug products through Responsive Search Ads (RSA) (October 18, 2023)

- **John Concato**. Presentation. “FDA, Real-World Data, & Clinical Trials” at AIFA Days UNIMORE (October 19, 2023)

- **Khair ElZarrad**. Closing remarks. FDORA Public Meeting on Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies (October 19, 2023)

- **Mathilda Fienkeng**. Presentation. “FDA Basics: An Overview of FDA Communication of Drug Information” at the CAMPhA USA Annual Convention (October 22, 2023)

- **John Concato**. Session participant. “U.S. FDA and Real-World Evidence” at Guglielmo Marconi University (October 23, 2023)

- **Kim Smith**. Presentation. “U.S. FDA and Real-World Evidence” at TOPRA Symposium 2023 (October 24, 2023)

- **John Concato**. Presentation. “Real-World Evidence: Another Tool in the Toolbox” at EBHC Conference (October 26, 2023)

- **Katie Gray**. Presentation. Regulatory updates at the 24th Annual Pharmaceutical Compliance Forum (PCF) Pharmaceutical and Medical Device Ethics and Compliance Congress (October 26, 2023)

- **John Concato**. Presentation. “Considerations for Clinical Trial Design Optimization Panel: Regulatory Aspects of Externally Controlled Clinical Trials” at the Critical Path Institute (October 27, 2023)

- **Cecilia Almeida**. Presentation. “Hospital/Healthcare Systems Point of Care Surveillance and Monitoring of Drug Shortages: COVID-19 Critical Care Drug Monitoring Survey Portal” at the Duke-Margolis Center for Health Policy FDA Convening Virtual Expert Workshop: Understanding How Health Systems Track Drug Shortages: Current Approaches and Future Needs (October 30, 2023)

- **Katie Gray**. Presentation. “Update on OPDP Policy and Compliance Activities” at the FDLI Advertising & Promotion for Medical Products Conference (November 2, 2023)

- **Amy Muhlberg** and **Helen Sullivan**. Presentation. “Final guidance - Presenting Quantitative Efficacy and Risk Information in Direct-to-Consumer (DTC) Promotional Labeling and Advertisements” at the FDLI Advertising and Promotion for Medical Products Conference (November 3, 2023)

- **Leonard Sacks**, **Ryan Robinson**, and **Mili Duggal**. Science Spotlight Presentation. “Bringing Clinical Trials to Patients” at Office of Women’s Health Public Webinar (November 8, 2023)

- **Beth Kunkoski**. Discussion. DiMe Extending the V3 Framework: A Workshop – Fireside Chat (November 9, 2023)

- **Karen Hicks**. Presentation. “Diversity in Clinical Trials: Principles Relevant for Clinical Trials with Artificial Intelligence” at the meeting of DIA Innovating Clinical Trials in Europe. Session 5/Leveraging Artificial Intelligence in Clinical Trials—Opportunities and Ethical Considerations (November 16, 2023)

- **Karen Hicks**. Opening and closing remarks. FDORA Public Workshop to Enhance Clinical Study Diversity (November 29 and 30, 2023)

- **Mathilda Fienkeng**. Opening remarks 2nd day. FDORA Public Workshop to Enhance Clinical Study Diversity (November 29, 2023)

- **Atasi Poddar**. Presentation. “Recent Updates from FDA Guidances on Informed Consent and IRB Review for Expanded Access Use of Investigational Drugs” at the PRIM&R Annual Conference in Washington, DC (December 6, 2023)

- **Kim Smith**. Presentation. “FDA Structure and Mandate” at the FDA Clinical Investigator Training Course (December 6, 2023)

- **John Concato**. Presentation. “Real-World Evidence” at the FDA Clinical Investigator Training Course (December 6, 2023)

- **John Concato**. Keynote speech. “Comments on Causal Inference” at the Duke-Margolis Center for Health Policy: Leveraging RWE to Determine Causal Inference Meeting (December 12, 2023)

Resources (Links)

Publicly available online resources (see also Appendices A–C):

1) Information about **U.S. Food & Drug Administration** (FDA) available at https://www.fda.gov/

2) Information about FDA **Center for Drug Evaluation and Research** (CDER) available at https://www.fda.gov/about-fda/fda-organization/center-drug-evaluation-and-research-cder

3) Information about FDA/CDER **Office of Medical Policy** (OMP) available at https://www.fda.gov/about-fda/cder-offices-and-divisions/office-medical-policy

4) Information about FDA/CDER/OMP **Office of Medical Policy Initiatives** (OMPI) available at https://www.fda.gov/about-fda/cder-offices-and-divisions/office-medical-policy-initiatives-ompi

5) Information about FDA/CDER/OMP **Office of Prescription Drug Promotion** (OPDP) available at https://www.fda.gov/about-fda/cder-offices-and-divisions/office-prescription-drug-promotion-opdp

6) "Decentralized Clinical Trials for Drugs, Biological Products, and Devices" information available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/decentralized-clinical-trials-drugs-biological-products-and-devices

7) "Digital Health Technologies (DHTs) for Drug Development" information available at https://www.fda.gov/science-research/science-and-research-special-topics/digital-health-technologies-dhts-drug-development

8) "Real-World Evidence" information available at https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

9) E6(R3) Guideline for Good Clinical Practice available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e6r3-good-clinical-practice-gcp

Helpful Acronyms and Abbreviations

Acronym/Abbreviation	What It Means
AI	Artificial Intelligence
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CERSI	Center of Excellence in Regulatory Science and Innovation
CMS	Centers for Medicare & Medicaid Services
CTTI	Clinical Trials Transformation Initiative
DAPR I	Division of Advertising and Promotion Review I
DAPR II	Division of Advertising and Promotion Review II
DCT	Decentralized Clinical Trial
DCTQ	Division of Clinical Trial Quality
DHCoE	Digital Health Center of Excellence
DHT	Digital Health Technology
DMPD	Division of Medical Policy Development
DMPP	Division of Medical Policy Programs
DPPRO	Division of Promotion Policy, Research, and Operations
DTC	Direct-to-Consumer
eCTD	Electronic Common Technical Document
EHR	Electronic Health Record
EUA	Emergency Use Authorization
FDA	United States Food and Drug Administration
FR	Federal Register
FRN	Federal Register Notice
HCP	Health Care Provider
HHS	Health and Human Services
ICH	International Council for Harmonisation
IFU	Instructions for Use
IRB	Institutional Review Board
MG	Medication Guide

Acronym/Abbreviation	What It Means
ML	Machine Learning
MPPRC	Medical Policy and Program Review Council
OCE	Oncology Center of Excellence
OMB	Office of Management and Budget
OMP	Office of Medical Policy
OMPI	Office of Medical Policy Initiatives
OPDP	Office of Prescription Drug Promotion
OSP	Office of Strategic Programs
PDUFA	Prescription Drug User Fee Act
PMI	Patient Medication Information
PPI	Patient Package Insert
PRIM&R	Public Responsibility in Medicine and Research
REMS	Risk Evaluation and Mitigation Strategy
RWD	Real-World Data
RWE	Real-World Evidence
SC	Subcommittee
SLC	Safety Labeling Changes
WHO	World Health Organization

U.S. FOOD & DRUG
ADMINISTRATION

Center for Drug Evaluation and Research

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