U.S. FOOD & DRUG ADMINISTRATION

CDER | Office of Pharmaceutical Quality

2022 Annual Report

Strategic Priorities

OPQ uses four strategic priorities to assure that quality drugs are available to the American public.This report shares accomplishments related to each of these priorities in 2022.

Collaboration
Strengthen OPQ's collaborative culture

Engagement
Strengthen partnerships and engage stakeholders

Innovation
Promote the availability of better medicines

Communication
Elevate awareness and commitment to the importance of pharmaceutical quality

Collaboration

The Office of Pharmaceutical Quality (OPQ) in FDA's Center for Drug Evaluation and Research (CDER) uses assessment, inspection, research, surveillance, and policy to assure that quality drugs are available to the American public. OPQ functions cover every type of human drug including new drugs, generics, over-the-counter drugs, and biologics including biosimilars. In 2022, Congress reauthorized the Prescription Drug User Fee Act, Generic Drug User Fee Amendments, and Biosimilar User Fee Act which allow FDA to collect fees from companies submitting drug applications in exchange for regulatory performance goals. OPQ helped FDA negotiate user fee agreements, prepare for new user fee programs, and enable on-time action on >90% of submissions with user fee goal dates. These actions include approving:

- **7 biosimilars**, and making 2 determinations of interchangeability, which improve patient access to biologic medicines
- **914 generic drugs**, including 86 complex generics, which increase competition in the market
- **99 new drug applications**, including 20 new drugs for rare or orphan diseases, which provide new treatment options for patients

OPQ's quality assessment of a drug application employs a team of experts in drug substance, drug product, manufacturing, and biopharmaceutics (the relationship between the properties of a drug and its action in the body). Throughout the public health emergency, OPQ continued to use a collaborative quality assessment approach to enable the approval of 608 submissions related to drugs used to treat patients with COVID-19, as well the emergency use authorization of 2 products to be used during the public health emergency. To avoid or mitigate potential drug shortages, OPQ prioritized and expedited the quality assessment of 303 submissions in 2022.

303 expedited application assessments to avoid or mitigate drug shortage

608 approvals related to drugs used to treat patients with COVID-19

In addition to application assessment, OPQ collaborates to sample, test, and surveil the quality of marketed drugs. With more than 140,000 drug products in CDER's product catalog, the program applies a risk-based approach to test potentially harmful products. Many years of sampling and testing have shown that the vast majority of drugs meet or exceed quality standards. Since 2018, CDER has been using data analytics to sample products with potential quality risks for testing. In July 2022, OPQ updated the drug sampling and testing results with data from 2018-2021, which showed that this data-driven, risk-based approach has effectively targeted products that fail quality tests. The sampling and testing program enabled FDA to protect patients and consumers from poor quality products, such as hand sanitizers contaminated with benzene or methanol.

Innovation

The COVID-19 public health emergency placed global restrictions on travel and in-person interactions, which has limited FDA's ability to conduct facility inspections. In light of these restrictions, OPQ has relied on the alternative tools described in the July 2022 draft guidance on remote regulatory assessments, such as requesting information from a facility in lieu of an inspection. In 2022, OPQ staff conducted 65 pre-license facility inspections in 18 countries and 10 states and used remote regulatory assessments to act on 85 regulatory submissions. While inspection remains the gold standard, FDA will continue to use remote regulatory assessments to augment inspection activities.

65 pre-license facility inspections conducted

85 applications acted on using remote regulatory assessments

Facility assessments are a part of OPQ's overall quality assessment process which has benefitted from the Knowledge-aided Assessment and Structured Application (KASA) system, a novel IT system which improves knowledge management to enhance the efficiency, effectiveness, and consistency of quality assessments. In 2022, OPQ introduced 16 new analytic features for application data and used KASA to assess over 500 generic drug applications. KASA was acknowledged

3 approvals of applications using emerging technologies

with a second consecutive FedHealth IT Award, which celebrates federal programs for driving innovation and results, as part of CDER's Structured Review/Workflow Management Program. In November 2022, an FDA Advisory Committee voted unanimously to further expand KASA for the assessment of new drugs and biologics.

Recent scientific innovations have resulted in advanced manufacturing technologies that are able to produce drugs in more expedient and flexible ways. Advanced manufacturing is part of the overall U.S. strategy to strengthen and secure pharmaceutical supply chains. OPQ leads CDER's Emerging Technology Program, which provides a venue for stakeholders to discuss and resolve potential technical and regulatory issues related to new technologies prior to filing regulatory submissions. In 2022, the Emerging Technology Program held 12 meetings with stakeholders who are adopting emerging technologies and supported the approval of 3 applications using emerging technologies such as continuous manufacturing.

Several Emerging Technology Program meetings addressed smaller, mobile drug manufacturing processes that might be deployed to multiple locations, including at the point of care. As these novel distributed manufacturing technologies have the potential to improve the robustness of the drug supply chain, OPQ leads CDER's Framework for Regulatory Advanced Manufacturing Evaluation (FRAME) initiative to proactively examine the existing regulatory framework and prepare for policy development. FDA published a discussion paper on distributed manufacturing for human drugs in October 2022 to solicit public feedback on areas of policy consideration for this technology. OPQ then led a three-day workshop on distributed manufacturing with the Product Quality Research Institute in November. Feedback from stakeholders is helping to inform FDA's evaluation of the existing regulatory framework and prepare FDA for new manufacturing technologies.

Engagement

A multi-agency Federal task force found that a root cause for many drug shortages is the absence of incentives for manufacturers to develop mature quality management systems. Much research now supports the premise that manufacturers with more mature quality practices better anticipate and resist supply chain disruptions. CDER has proposed the development of a rating system that will help incentivize drug manufacturers to achieve quality management maturity (QMM) at their facilities. A QMM rating system could inform regulators and purchasers about the performance and robustness of drug manufacturing facilities and give consumers increased confidence in the availability of

9-0 FDA Advisory Committee vote in favor of establishing a quality management maturity program

drugs. Operationalizing a voluntary QMM rating program for pharmaceutical manufacturers requires a collaborative and transparent partnership among FDA, industry, and other stakeholders.

February 2022 marked the conclusion of two pilot programs on developing QMM assessment protocols for domestic finished dosage form manufacturers or international active pharmaceutical ingredient manufacturers. OPQ subsequently published a whitepaper in April describing the need and considerations for a QMM program and potential impacts on stakeholders. CDER then hosted a two-day QMM workshop in May to discuss lessons from the QMM pilots and CDER's vision for the QMM program. Finally, in November OPQ presented the QMM program to an FDA Advisory Committee that voted unanimously in favor of establishing a QMM program.

Pharmaceuticals are part of global markets and OPQ engages with other international regulators to coordinate regulatory strategies and develop shared regulatory practices. Efficient global regulatory oversight in the future might include harmonized regulatory expectations for data, assessments, inspections, and a shared virtual repository for submissions. OPQ is part of two pilot programs with international regulatory authorities from the International Coalition of Medicines Regulatory Authorities (ICMRA) on hybrid inspections and collaborative assessments of post-approval changes. These pilots aim to develop a common framework that enables collaborative international facility assessments and inspections and global approaches for the assessment of quality-related post-approval changes.

2 pilot programs with international regulatory authorities to develop common frameworks

OPQ also works closely with the International Council for Harmonisation (ICH) to develop harmonized international standards, which help regulated industry operate more efficiently in global pharmaceutical markets by providing consistent expectations. The release of guidance on lifecycle management (ICH Q12) in 2021 led to the 2022 approvals of 4 submissions with established conditions, which define the parts of an application that must be changed by engaging regulators. A major international policy development in 2022 was the adoption of the OPQ-led guideline on continuous manufacturing of drug substances and drug products (ICH Q13). OPQ continues to lead the development of international guidelines in other important areas such as the quality portions of the common technical document (ICH M4Q(R2)), viral safety (ICH Q5A), quality risk management (ICH Q9(R1)), extractables and leachables (ICH Q3E), and analytical procedure validation and development (ICH Q2/Q14). These engagements help assure that global regulatory concerns will not hinder U.S. patient access to medicine.

Communication

Communication enables OPQ to provide information to stakeholders, receive information from stakeholders, and foster effective engagement. A fundamental way in which OPQ communicated in 2022 was by providing guidance to industry on the current regulatory thinking on important topics such as nanomaterials, risk management plans, and comparability protocols for post-approval changes. Collectively these guidance documents enable stakeholders to prepare for regulatory interactions, better protect patients and consumers from risks, and improve drug availability. OPQ also requested formal comments from stakeholders in 2022 on developing policy topics including quality metrics, distributed manufacturing, and the inactive ingredient database. Stakeholders' comments improved FDA's understanding in these critical policy areas.

OPQ regularly communicates by publishing research papers in peer-reviewed scientific journals. This enables OPQ to provide knowledge to stakeholders that can improve risk management and aid drug development. For example, in 2022 OPQ researchers developed and published a method to measure the distribution of an active pharmaceutical ingredient (difluprednate) in a complex drug formulation. Accurately measuring difluprednate distribution in the formulation is important in demonstrating the pharmaceutical equivalence between new and generic drug products. The journal Molecular Pharmaceutics featured this research on its July front cover and OPQ shared this method with generic drug developers to aid their research and development. Important research of another variety revealed that newer viral clearance technologies can perform comparable to, or more robust than, traditional technologies. The findings of this technology analysis are contributing to internal FDA practices and international harmonization efforts related to viral clearance and patient safety.

In various public engagements in 2022, OPQ communicated a vision for the future of drug quality focused on the development of mature quality management practices, the adoption of advanced technologies, and the incentivization of continual improvement. Historically, pharmaceutical regulation focused heavily on data collection prior to the marketing and reactive and punitive measures if problems occurred. The future of drug quality should include adopting innovations, preparing for emergencies, and reducing supply disruptions. Drug quality regulation can become more pragmatic and proactive by using leading indicators of quality problems that can help avoid problems before impact to patients and consumers. Leading indicators will enable OPQ to focus regulatory resources on the most appropriate areas of CDER's site and product catalog, in an effort to assure that quality medicines will continue to be available to the American public.

8 guidance documents for industry

10 topics related to pharmaceutical quality released for public comment

140 scientific papers in peer-reviewed journals

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