Office of Pharmaceutical Quality Progress Update

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Outline

- Reminder of OPQ Mission, Objectives and Organization
- OPQ Quality Initiatives
- Enhancing Communication and Collaboration
- Policy Developments
- Operational Excellence and IT Implementation
- Drug Application Evaluation
- Facility Evaluation
- Closing Remarks

OPQ Mission and Objectives

Office of Pharmaceutical Quality

Mission

OPQ assures that quality medicines are available to the American public

Vision

OPQ will be a global benchmark for regulation of pharmaceutical quality

Slogan

‘One Quality Voice’

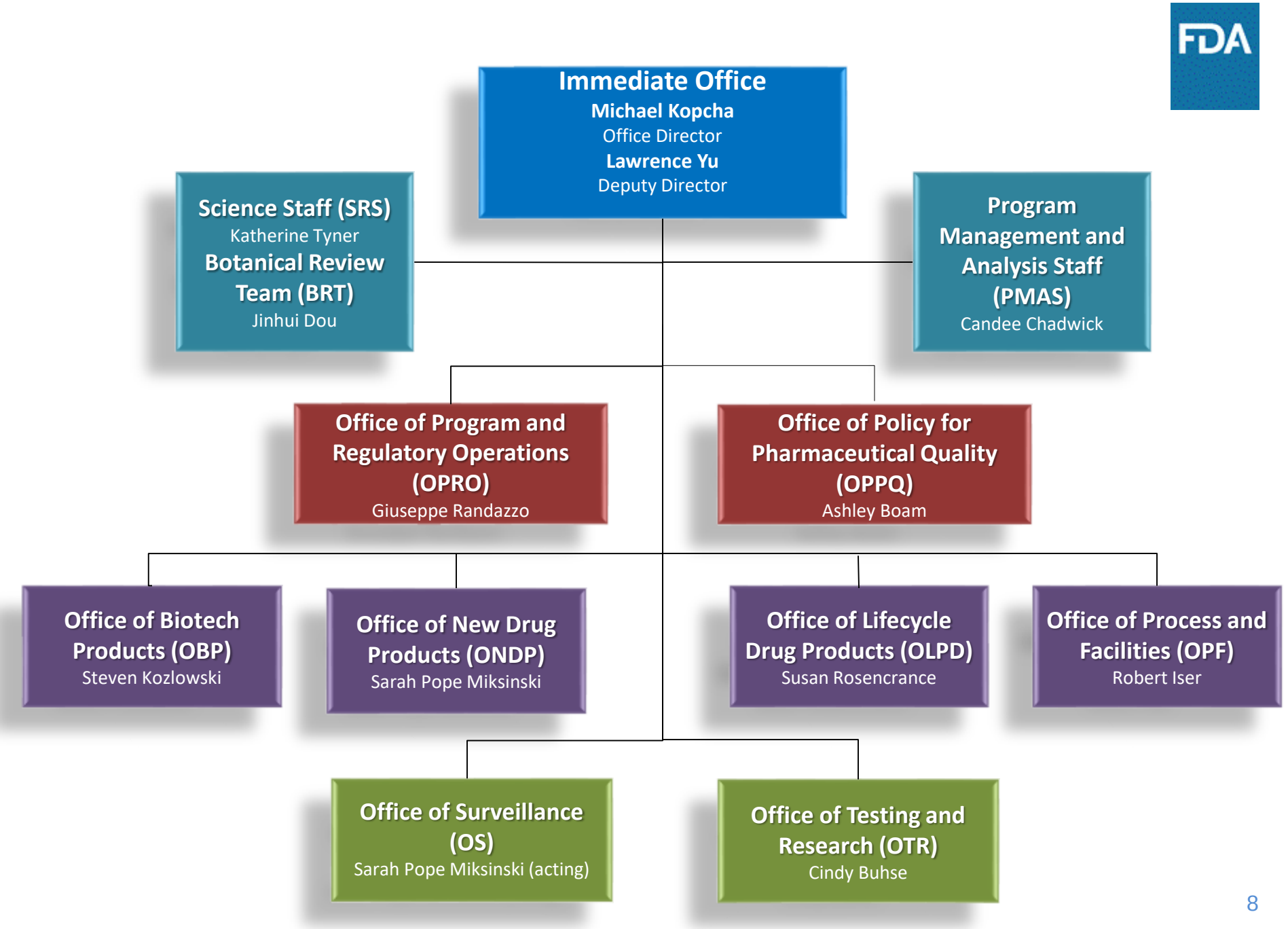
OPQ Objectives

- Provide seamless integration of review, inspection, surveillance, and research across the product lifecycle
- Assure that all human drugs meet scientifically-sound quality standards to safeguard clinical performance
- Enhance science- and risk-based regulatory approaches
- Transform product quality oversight from a qualitative to a quantitative, expertise-based assessment
- Encourage development and adoption of emerging pharmaceutical technology

OPQ Organization

Office of Pharmaceutical Quality

- To keep pace with increasing product complexity, OPQ is organized around discipline and expertise
- The review function matrices across OPQ allow for enhanced interactions, communication, and consistency among sub-offices
- Functional areas align to streamline FDA processes that assess and monitor drug quality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OPQ Quality Initiatives

Emerging Technology Team (ETT)

- Supports industry's development and implementation of innovative approaches in pharmaceutical design and manufacturing
- Identifies and resolves potential scientific and policy issues related to the new approach
- In 2016, OPQ
  - Enabled the approval of the first switch from batch to continuous manufacturing process for an approved drug
  - Accepted 15 projects into the ETT on a variety of innovative technologies

Concept of Operations for Facility Evaluations

- Ensures consistency, efficiency, and transparency in facility evaluations, inspections, and regulatory decision-making for marketing applications
- Improves FDA's operational capacity by eliminating overlap of effort amongst various CDER and ORA offices
- In 2016, in collaboration with ORA and OC, OPQ
  - Designed the processes for pre-approval and surveillance inspections
  - Defined and clarified the roles and responsibilities of CDER and ORA

New Inspection Protocol Project

- Provides inspectional assessments to support tracking and improvement of performance across pharmaceutical manufacturers and products
- Enhances the production, utility, and consistency of the establishment inspection reports
- In 2016, in collaboration with ORA and OC, OPQ
  - Completed pilot inspections for sterile drug process facilities

Drug Quality Assessment Enhancements

- Develop tools to support/perform product, process, facility, and benefit-risk assessments
- Create and implement a consistent, standardized, and structured assessment across the drug lifecycle, that provides a concise decision-focused executive narrative supported by a knowledge management system
- In 2016, OPQ
  - Developed a dashboard for drug product quality for solid oral immediate release dosage forms as a formalized risk mitigation platform
  - Developed a benefit-risk assessment framework that balances clinical context with regard to potential product quality issues

Enhancing Collaboration and Communication

Organizations OPQ Engaged in 2016

- U.S. Pharmacopeial Convention (USP)
- ASTM International (ASTM)
- The Pharmaceutical Research and Manufacturers of America (PhRMA)
- Association for Accessible Medicines (AAM) [formerly Generic Pharmaceutical Association (GPhA)]
- Biotechnology Industry Organization (BIO)
- International Pharmaceutical Excipients Council (IPEC)
- American Association of Pharmaceutical Scientists (AAPS)
- International Society for Pharmaceutical Engineering (ISPE)
- Parenteral Drug Association (PDA)
- Product Quality Research Institute (PQRI)
- US National Institute of Standards and Technology (NIST)
- Bulk Pharmaceutical Task Force (BPTF)
- Drug Information Association (DIA)
- Pharma and Biopharma Outsourcing Association (PBOA)
- International Forum on Process Analytical Chemistry (IFPAC)

International Collaboration Initiative

- Enhances mutual understanding of the quality assessment processes and practices in global regulatory agencies
- Identifies best practices in the foreign regulatory agencies to enhance efficiency of our assessment processes
- Sets a foundation for future collaboration among agencies
- In 2016, technical experts from OPQ
  - Visited the Australian Therapeutic Goods Administration (TGA), Japan's Pharmaceutical and Medical Devices Administration (PMDA), the European Medicines Agency (EMA), and Health Canada
  - Discussed the processes and practices used for quality assessment of drug applications, including for generic and innovator drugs during the pre- and post-approval stages

OPQ Policy Developments

Clinical Relevance

- OPQ's focus includes:
  - Conducting risk-based evaluations on clinically-relevant product attributes
  - Being patient-centric and linking quality to patient outcomes
    - Being patient-centric is more than just clinically relevant specifications. Specifications are a sub-set of clinical relevance
    - Involves multi-discipline team approach to assessing the totality of the evidence in a benefit/risk profile of the product

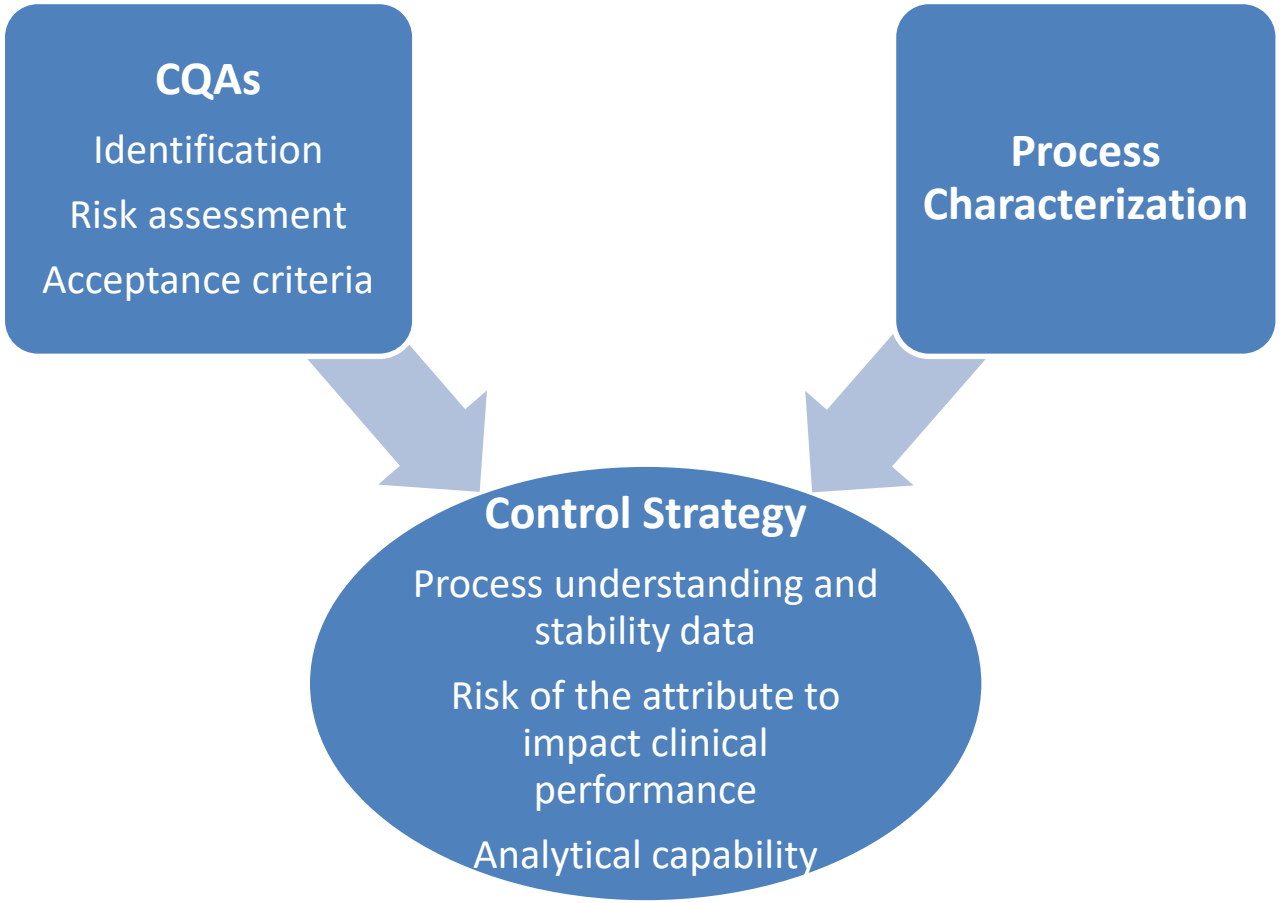


Clinical Relevance and Specifications

1. No one size fits all approach (e.g. need to consider context of use, regulatory framework, extent of the product and process knowledge, etc.)
2. Emphasis on specifications that focus on clinical relevance rather than process capability
3. Linking quality to clinical performance helps to assure that drug product will perform as indicated in the label (benefits and risks)

Clinical Relevance and Specifications

4. Sponsors should pursue development of a patient-focused, risk-based, overall control strategy



Quality Policy

- In 2016, OPQ
  - Issued 12 Guidance documents reflecting Agency's current thinking on various regulatory topics, including high-profile issues
  - Published 5 MAPP documents, 4 final and 1 interim
  - Responded to 568 external inquiries

Guidance Published in 2016

- Immunogenicity-Related Considerations for Low Molecular Weight Heparin Guidance for Industry (2/18/16)
- Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity (3/4/16)
- Comparability Protocols for Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Information Guidance for Industry – Draft (4/19/16)
- Data Integrity and Compliance With Current Good Manufacturing Practice Guidance for Industry – Draft (4/14/16)
- Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products – Draft (4/22/16)
- Quality Attribute Considerations for Chewable Tablets Guidance for Industry – Draft (6/16/16)
- Elemental Impurities in Drug Products – Draft (6/30/16)
- Regulatory Classification of Pharmaceutical Co-Crystals – Draft (8/16/16)
- Contract Manufacturing Arrangements for Drugs: Quality Agreements – Final (11/22/16)
- Botanical Drug Development – Final (12/28/2016)

OPQ Operational Excellence and IT Implementation

Key Performance Indicators (KPI)

- Monthly collection of data in five functional areas: review, inspection, research, program innovation, and human capital
- Assist in understanding the workload and workflow in OPQ
- Provide a more comprehensive view of the performance portfolio across the office
- Serve as a complement to measures used in the reporting of User Fee Act performance
- Used to prepare OPQ monthly and annual reports
- Undergo continuous improvement of collection and presentation methods
  - Refine the list of KPIs to increase alignment between the collected data and organizational goals for performance

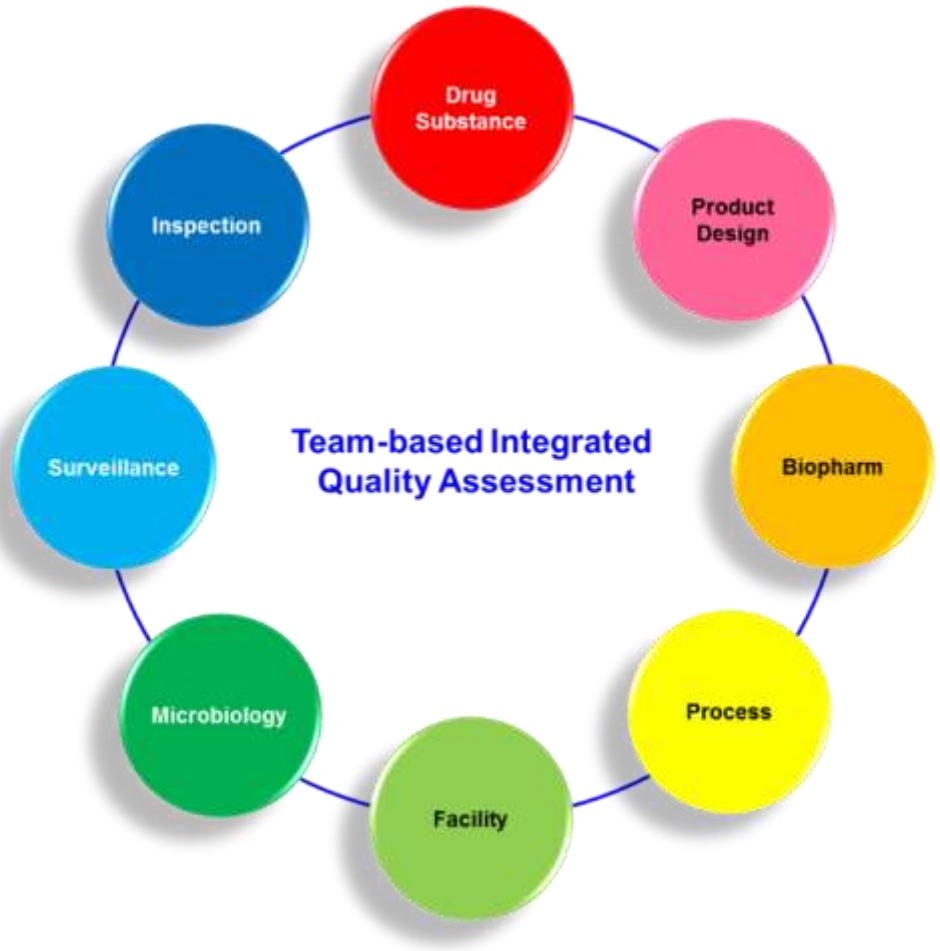
Drug Master File (DMF) IT Implementation

- In 2016, the DMF WG in OPQ
  - Streamlined the review of DMFs
  - Coordinated OPQ input to the Office of Business Informatics to formalize DMF review and communication procedures for reviewers and project managers
  - Successfully incorporated DMF review tools into CDER Informatics Platform

Drug Application Evaluation in OPQ

Integrated Quality Assessment (IQA)

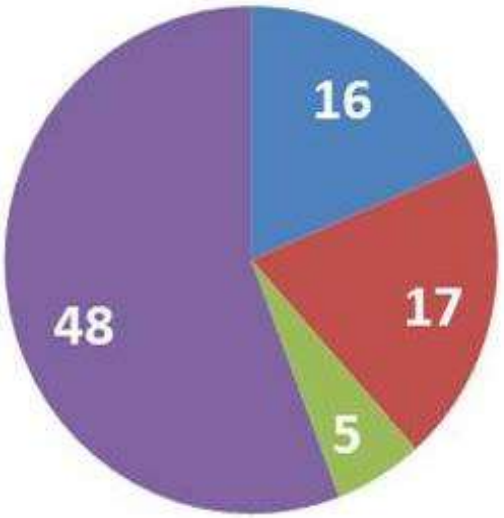
- IQA team provides aligned, patient-focused, and risk-based drug product quality recommendations for BLAs, NDAs, and ANDAs, inclusive of drug substance, drug product, manufacturing, and facilities.
- OPQ IQA Teams consist of:
  - Application Technical Lead (ATL)
  - Regulatory Business Process Manager (RBPM)
  - Discipline Reviewers (includes ORA)
  - Other as needed – Lab (OTR), Policy (OPPQ), Surveillance (OS)
- IQA integrates review and inspection functions



OPQ's Review – UFAs Numbers

UFAs	FY 2016 % of Application Review Meeting UFA Deadlines
PDUFA	
Originals	~96%
Manufacturing Supplements	97%
BSUFA	
Originals	100%
Manufacturing Supplements	100%
GDUFA	
Originals	98%
Manufacturing Supplements	100%

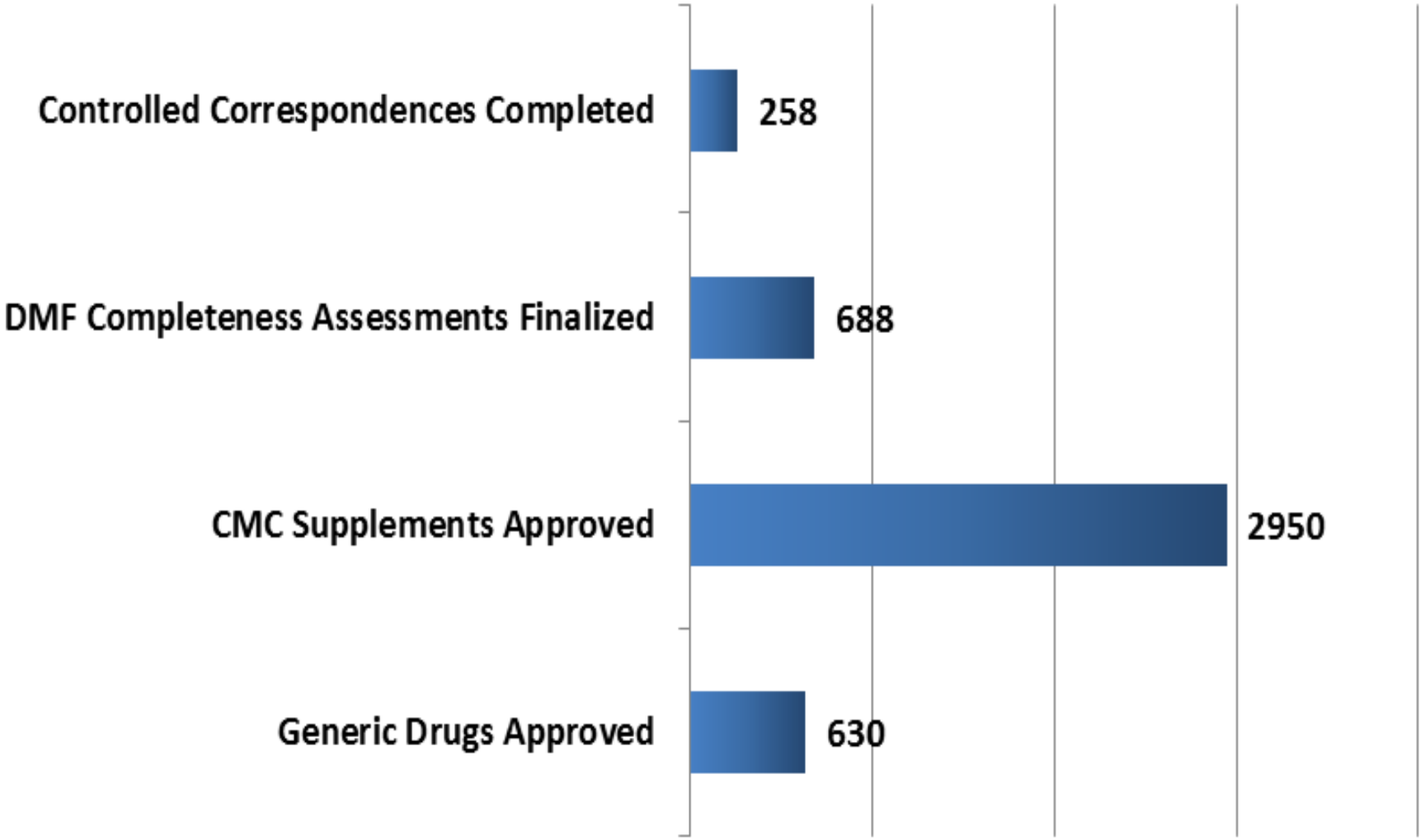
NDA and BLA Original Approvals in 2016



- Breakthrough Therapies (BTT)
- New Molecular Entities (NME)
- BTT and NME
- 505(b)(2)

- Breakthrough Therapies (BTT)
- New Molecular Entities (NME)
- BTT and NME
- Biosimilars
- New Dosage Forms

GDUFA


Controlled Correspondences Completed
258
DMF Completeness Assessments Finalized
688
CMC Supplements Approved
2950
Generic Drugs Approved
630

Facility Evaluation in OPQ

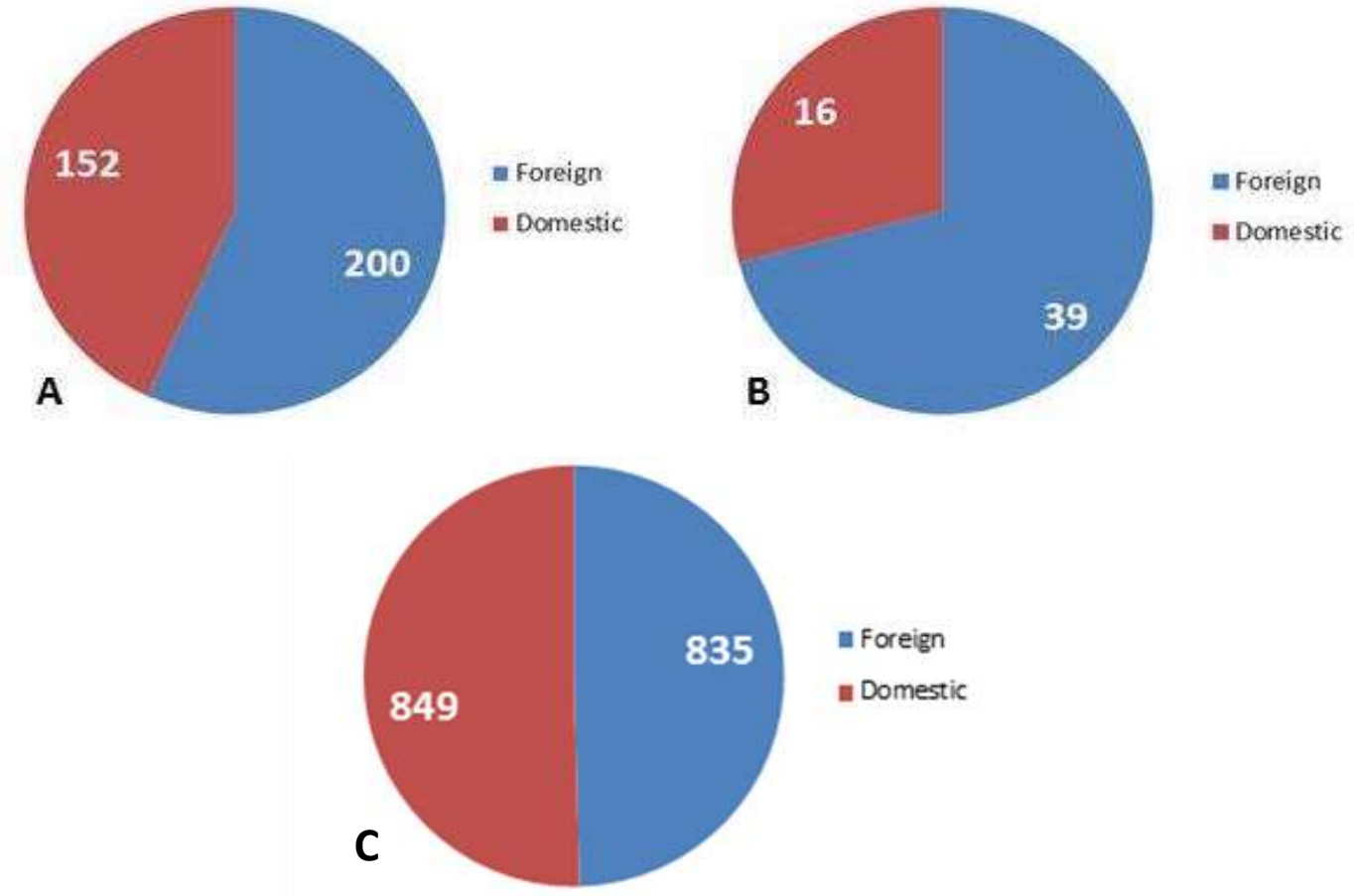
Facility Evaluation in OPQ

- OPQ works closely with CDER's OC and FDA's ORA to provide "One Quality Voice" regarding facility evaluation and inspection
- These offices collectively participate in Pre-Approval, Surveillance, For Cause, and Post-Approval facility inspections
- Each type of inspection includes three potential aspects:
  - planning the strategy for the inspection,
  - conducting the inspection,
  - communicating the findings of the inspection to support decision-making or follow-up actions

Facility Evaluation and Inspection

- Pre-approval
  - Directly supports the review of marketing applications
  - Ensures data accuracy in the application, and high manufacturing quality at the facility
- Surveillance
  - System-based inspection, not necessarily an assessment of a specific product
  - Identifies and mitigates quality problems at facilities before they lead to recalls or enforcement actions
- Post-approval
  - Linked to a specific application, but initiated after approval
  - Ensures commercial-scale processes conform to application commitments, and informs lifecycle risk

Facility Inspections Performed in 2016



A) **Pre-approval inspections** performed in CY2016, B) **Post-approval inspections** performed in CY2016, C) **Site surveillance inspections and non-site surveillance inspections** performed in FY2016.

Working Together to Achieve the Vision

"A maximally **efficient**, **agile**, **flexible** pharmaceutical manufacturing sector that **reliably produces high quality** drugs without extensive regulatory oversight."