FDA’s Office of Pharmaceutical Quality (OPQ)
An Overview and Update

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Outline

• Overview/Design of OPQ
• OPQ Accomplishments in 2015
• OPQ 2016 Priorities
• The Partnership of FDA and Industry
Overview/Design of OPQ
Office of Pharmaceutical Quality (OPQ)

Mission
The Office of Pharmaceutical Quality assures that quality medicines are available to the American public

Vision
The Office of Pharmaceutical Quality will be a global benchmark for regulation of pharmaceutical quality

Slogan
‘One Quality Voice’
‘One Quality Voice’ Value Statements

• **Put patients first** by balancing risk and availability

• Have one quality voice by **integrating review and inspection** across product lifecycle

• Safeguard clinical performance by establishing **scientifically sound quality standards**
‘One Quality Voice’ Value Statements

- Maximize focus and efficiency by applying risk-based approaches
- Strengthen the effectiveness of lifecycle quality evaluations by using team-based processes
- Enhance quality regulation by developing and utilizing staff expertise
‘One Quality Voice’ Value Statements

• Encourage innovation by advancing **new technology and manufacturing science**

• Provide effective leadership by emphasizing cross-disciplinary interaction, shared accountability, and joint problem solving

• Build **collaborative relationships** by communicating openly, honestly, and directly
Objectives of OPQ

- A single unit in CDER dedicated to drug product quality that fosters close integration of major functional areas
Objectives of OPQ

• Implement a lifecycle approach to quality that spans pre- and post-approval for both brand and generic drugs
Objectives of OPQ

- Balance potential quality risks with the risk of a patient not getting a drug
- Anticipate quality problems before they develop to help prevent drug shortages
Objectives of OPQ

- Establish consistent, clinically relevant quality standards and clear expectations for industry
- Emphasize quality metrics and surveillance techniques to help monitor quality across facilities
- Encourage use of modern, more efficient manufacturing technologies
OPQ

• To keep pace with increasing product complexity, OPQ is organized based on discipline and expertise

• The review function matrices across OPQ for enhanced interactions, communication, and consistency among sub-offices

• Functional areas align for the purpose of streamlining FDA processes that monitor drug quality
Office of Program and Regulatory Operations (OPRO)

- Manages the business processes associated with drug product quality assessment and facility inspections
- Facilitates a quality management system
- Handles learning and professional development programs
Office of Policy for Pharmaceutical Quality (OPPQ)

- Develops, implements, and updates science- and risk-based policies, standards, and guidance documents related to drug product quality and assessment
- Ensures consistent interpretation and application of drug product quality policies and programs
Office of Biotechnology Products (OBP), Office of New Drug Products (ONDP), and Office of Lifecycle Drug Products (OLDP)

- Perform quality assessment of the drug substance, drug product, and biopharmaceutics portions of applications (NDAs, ANDAs, BLAs, and supplements)
  - Formulation/product design
  - Risk assessment
  - Quality standards and clinically relevant specifications
  - Control strategy related to product attributes
  - Stability
Office of Process and Facilities (OPF)

- Performs quality assessment of the manufacturing process for applications (NDAs, ANDAs, BLAs, and complex supplements)
  - Ensures successful implementation of manufacture at commercial scale
  - Advises on applied microbiological issues related to product quality and manufacture
  - Advises on inspectional and facility issues related to applications
Office of Surveillance (OS)

- Monitors quality and manages information about the entire inventory of CDER-regulated sites and products
  - Generates and manages knowledge related to the ‘state of quality’ for both facility and product using a set of quality metrics
  - Intelligence generated strengthens ability to make risk-based decisions that govern inspection frequency and coverage
  - Allows for rapid response to process trends before serious quality problems occur

Office of Surveillance
Acting Director: Russell Wesdyk
– Office of Testing and Research (OTR)

• Performs research on the manufacture, formulation, and characterization of drug products that supports the development of scientific standards and policies

  – Collaborates with the review and policy offices to help advance science and establish standards related to quality, especially for complex products

• Directs drug product quality surveillance testing and laboratory-based investigational activities.
OPQ’s Key Stakeholders

- Office of Generic Drugs (OGD)
- Office of Regulatory Affairs (ORA)
- Office of New Drugs (OND)
- Office of Compliance (OC)
OPQ Accomplishments in 2015
OPQ Accomplishments - 2015

• OPQ is responsible for meeting program performance goals under the:
  1. Generic Drug User Fee Amendment (GDUFA)
  2. Prescription Drug User Fee Act (PDUFA); and
  3. Biosimilar User Fee Act (BsUFA)

• In 2015 all performance goals were met or exceeded in each program area
OPQ Accomplishments - 2015

• Reduced the generic backlog (pre FY-2015 ANDAs) by more than 40%  
  – Reduced actions pending OPQ from 2400 to 1471

• Contributed to the approval or tentative approval of 726 ANDAs – the highest number in the history of the generic drug program.
2015 ANDA Approvals

![Bar chart showing 2015 ANDA Approvals]

- Tentative Approvals
- Full Approvals

January: 5 Tentative, 25 Full
February: 13 Tentative, 27 Full
March: 6 Tentative, 19 Full
April: 19 Tentative, 49 Full
May: 13 Tentative, 47 Full
June: 10 Tentative, 57 Full
July: 12 Tentative, 47 Full
August: 6 Tentative, 58 Full
September: 14 Tentative, 61 Full
October: 21 Tentative, 51 Full
November: 6 Tentative, 61 Full
December: 20 Tentative, 79 Full
OPQ Accomplishments - 2015

• Approaching steady state with CMC supplements; backlog under control

• At steady state with chemistry-related Controlled Correspondences (no backlog!)
Status of CMC Supplements - 2015

Pending CMC Supplements (PAS and CBE)
Status of Chemistry-Related Controlled Correspondence - 2015
OPQ Accomplishments - 2015

• Played a critical role in the following high-profile CDER approvals

1. First generic version of Copaxone (glatiramer acetate injection) used to treat patients with relapsing forms of multiple sclerosis (MS)

2. First biosimilar product – Zarxio (filgrastim-sndz) for the treatment of neutropenia associated with chemotherapy
OPQ Accomplishments – 2015

3. First continuous manufacturing process
   - Orkambi, a combination therapy for treatment of cystic fibrosis (CF)
OPQ Accomplishments - 2015

4. First 3D-printed drug product – Spritam
   - A groundbreaking technique that uses three-dimensional printing to produce a porous formulation that rapidly dissolves with a sip of water
I. Facility Assessments/Inspections

**OPQ Priority**: A more rigorous and comprehensive approach to drug quality surveillance and inspection

- **Quality Metrics** to better monitor the current status of product and facility across the inventory of FDA-regulated sites and inform FDA risk-based surveillance inspection planning

- **New Inspection Protocol Project (NIPP)** – Provides a more quality-focused, semi-quantitative approach to inspections with more streamlined and structured reporting
I. Facility Assessments/Inspections

• Common Informatics Platform that integrates the knowledge captured during review, inspection, and surveillance activities

Facility Quality System

- Application Review Findings
- FDA Site Inspections
  • New Inspection Protocol Project (NIPP)
- FDA Surveillance Testing
- Other Quality Information
  • Quality Metric Data
  • Defect Reports
  • Recalls
  • Complaints
- Trusted Partner Information
  • Inspection
  • Testing
  • Other
II. Team-based Integrated Quality Assessment (IQA)

**OPQ Priority**: Quality assessments of ANDAs, NDAs, and BLAs that effectively align patient-focused and risk-based recommendations

- A team of subject-matter experts performing a quality assessment of an application (ANDA, NDA, BLA) based on risk and knowledge management
- This approach is on-going for all original ANDAs*, NDAs, and BLAs

* ANDAs submitted after October 1, 2014
II. Team-based Integrated Quality Assessment (IQA)

Inclusive of drug substance, drug product, manufacturing, and facilities, and maximizes each team member’s expertise

Science- and Risk-Based approach that is patient-focused
II. Team-based Integrated Quality Assessment (IQA)

The IQA Review Team

Drug Substance Experts | Product Experts
---|---
‘One Quality Voice’

Process Experts | Facility Experts Investigators

Technical Advisors
OPQ Laboratories
Policy
 Surveillance
Others as needed

Application Technical Lead (ATL) – oversees the scientific content of the assessment
Regulatory Business Process Manager (RBPM) – manages the process, adhering to the established timelines
II. Team-based Integrated Quality Assessment (IQA) - Advantages

- Close collaboration and communication among disciplines in a team environment yields better decision making

- Assures the application of uniform quality standards and promotes consistent regulatory practices for both brand and generic drug products
II. Team-based Integrated Quality Assessment (IQA) - Advantages

- Integration of quality review with inspection results in more informed decision making on facility acceptability and application approvability
II. Team-based Integrated Quality Assessment (IQA) - Advantages

- Promotes building an integrated knowledge base that allows for:
  - Clear identification of product risks
  - Quickly addressing quality problems
  - Improving overall efficiency and effectiveness in managing the drug product lifecycle
II. Team-based Integrated Quality Assessment (IQA) - Advantages

- Knowledge about quality issues gained from the review of the brand product can be appropriately applied to the review of the generic product
OPQ’s Partnership with OGD

**OPQ**
- Team-based Integrated Quality Assessment

**OGD**
- Application Filing
- Bioequivalence/Clinical Review
- Labeling Review

The ANDA Review

Supported by OGD/OPQ project management
OPQ’s Partnership with OGD

OPQ’s

Integrated Quality Assessment

A single integrated quality recommendation on application approvability
III. Risk Management and Communication

**OPQ Priority:** Formal risk-based regulatory approaches that effectively define the scope and extent of quality assessments

- Currently OPQ employs a formal risk assessment process to best allocate resources based on product risk and patient impact
  - Maintaining structured risk assessments that focus on product failure modes and specific risks to patients
  - Developing use of the structured risk assessment as a communication tool with investigators and reviewers for more informed decision making, knowledge transfer, and good lifecycle management
III. Risk Management and Communication

• **The Desired Future State** – A unified risk evaluation for brand and generic products that integrates the structured risk assessment with the existing drug product knowledge base
  - Provides a risk profile and ranking of a drug product’s critical quality attributes (CQAs) during the pre-marketing phase
  - May also include information on the manufacturing site and quality system
  - Utilized in the post-marketing phase to assess proposed changes and the associated risks to product quality
  - Provides a comprehensive summary of the current state of quality for all approved NDAs/ANDAs of a particular drug product
  - Unique for each drug product and each manufacturer potentially allowing for individualized regulatory oversight of post-approval changes
III. Risk Management and Communication

Past:
Informal risk assessment

Now:
Formal risk assessment for individual applications

Future:
Drug Product Dashboard

RISK RATING TABLE

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<th>4</th>
<th>3</th>
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<td>Likelihood</td>
<td>M</td>
<td>H</td>
<td>M</td>
<td>L</td>
<td>L</td>
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</tbody>
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H = High Risk
M = Moderate Risk
L = Low Risk

Now: Formal risk assessment for individual applications

Future: Drug Product Dashboard

Past: Informal risk assessment
IV. Emerging Technology

**OPQ Priority**: A collaborative approach with manufacturers that encourages innovation and the adoption of new technologies

- The Emerging Technology Team (ETT) within OPQ:
  - Serves as a centralized location for external inquiries on emerging technology
  - Provides a forum for early dialogue with FDA
  - Ensures consistency, continuity, and predictability in review and inspection of new technologies
  - Participates in the team-based integrated quality assessment when new technologies are evaluated
IV. Emerging Technology

• The Emerging Technology Team (ETT) has been actively working on topics such as continuous manufacturing, 3D-printing drug products, novel aseptic filling technology, and new container/closure systems

• Generic manufacturers are encouraged to consider these advanced technologies – we will work with you!
The Partnership of FDA and Industry
Our Common Goal is Drug Product Quality

• OPQ aligns and integrates all quality functions within CDER marking a new era in FDA’s quality oversight.

• Let us communicate, collaborate, and work together to deliver a high quality product that meets the patient’s needs – a true partnership!
Working in true partnership we will achieve the vision

The Vision

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

-Dr. Janet Woodcock
Thank you!