FDA’s Evolving Approach to Pharmaceutical Quality

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IQ at Year 5: Past, Present, and Future
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**Objectives:**

- Encourage the early adoption of new technological advances
- Facilitate industry application of modern quality management
- Encourage implementation of risk-based approaches
- Ensure that regulatory review, compliance, and inspection policies are based on state-of-the-art pharmaceutical science
- Enhance the consistency and coordination of FDA's drug quality regulatory programs
Quality Related Guidance and Initiatives
Drug Shortages – State of Quality?
Delivering on the 21st Century Quality Goals

CDER’s Office of Pharmaceutical Quality (OPQ)

January 11, 2015

Advances FDA’s Quality Initiative to the next level
FDA OPQ Organization

Immediate Office
Acting Director: Janet Woodcock
Deputy Director: Lawrence Yu

Office of Program and Regulatory Operations
Acting Director: Giuseppe Randazzo

Office of Policy for Pharmaceutical Quality
Acting Director: Ashley Boam

Office of Biotechnology Products
Director: Steven Kozlowski

Office of New Drug Products
Acting Director: Sarah Pope Miksinski

Office of Lifecycle Drug Products
Acting Director: Susan Rosencrance

Office of Testing and Research
Director: Lucinda Buhse

Office of Surveillance
Acting Director: Russell Wesdyk

Office of Process and Facilities
Acting Director: Robert Iser
FDA OPQ Mission, Vision, and Slogan

**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: 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
- 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
• 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
OPQ: Patient-Centric

• Quality is the underpinning of safety and efficacy. Quality standard shall be based on clinical performance
• Quality assurance in pharmaceutical manufacturing ensures consumers have access to medicines that are safe and effective
• A high quality drug product is a product that reproducibly delivers the therapeutic benefit to the consumer as stated in the label, is free of defects, and presents no undeclared risk (e.g., isn’t contaminated)
OPQ: A Matrix Approach

- **Functions:** Operation (project management), policy, review, **inspection programs** (in collaboration with ORA), surveillance, and research
  - OPQ: Pre-approval, routine surveillance, and directed inspections
  - OC/OMQ: Enforcement actions and related for-cause inspections
- **Expertise:** Biopharmaceutics, drug substance, drug product, process, facility, microbiology, inspection (in collaboration with ORA), analysis, policy, and project management
- Team-based integrated quality assessment
  - ANDAs, BLAs, and NDAs
  - Status of Product Quality and Facilities
OPQ: Performance Excellence

- Adopt principles of quality systems into OPQ operation to make OPQ a learning organization
  - Process Performance & Product Quality Monitoring System
  - Preventive Action and Corrective Action Systems
  - Change Management System
  - Management Review
- Enablers
  - Knowledge & lifecycle management
  - Quality risk management
OPQ: Objectives

- Assuring that all human drugs meet the same quality standards to safeguard clinical performance
- Enhancing science- and risk-based regulatory approaches
- Transforming product quality oversight from a qualitative to a quantitative and expertise-based assessment
- Providing seamless integration of review, inspection, surveillance, and research across the product lifecycle
- Encouraging development and adoption of emerging pharmaceutical technology
OPQ: Major Achievements for the Past Ten Months

- Published unprecedented number of guidances
  - Quality Metrics
  - Established Conditions
  - BCS Biowaiver
  - Dissolution for BCS Class 1 and 3 Immediate Release Dosage Forms
  - Analytical Procedures and Methods
  - Size, Shape, and other Attributes
  - Near IR Analytical Procedures
  - Environmental Assessment
  - Allowable Excess Volume and Vial Fill Size
  - Botanicals
OPQ: Major Achievements for the Past Ten Months (cont.)

• Conducted team-based, patient-focused Integrated Quality Assessment for all NDAs, BLAs, and ANDAs submitted after October 1, 2014
  – Process, coordination, and communication with internal and external customers
• Significantly reduced the generic backlog
• Initiated the pilot for New Inspection Protocol Project
• Enhanced collaboration within OPQ and among OPQ, OC, and ORA
Team-based Integrated Quality Assessment (IQA)

A team of experts performing a quality assessment of an application (NDA, BLA, ANDA) based on risk and knowledge management.
**Previous Review Process**

- No formal risk assessment process to define scope and extent
- Discipline reviewers worked in isolation
- Independent reviews (or assessments)
- Separate review templates
- Rare communications between review functions and facility inspections

**Team-based Integrated Quality Assessment**

- Formal risk assessment process to enhance efficiency and effectiveness of review and inspection
- Team of discipline reviewers with constant communication
- A single collaborative review (or assessment)
- Consolidated review template
- Integration of review with inspection for more informed decisions on facility acceptability and application approvability
The Review Team

**Discipline Reviewers**

- Drug Substance Experts
- Product Experts
- Process Experts
- Facility Experts
- ‘One Quality Voice’

**Technical Advisors**
- OPQ Laboratories
- Policy Surveillance
- Others as needed

- Application Technical Lead (ATL) – oversees the scientific content of the assessment
- Business Process Manager (BPM) – manages the process, adhering to the established timelines
New Inspection Protocol Project

- Goal: To develop a new paradigm for inspections and reports that will advance pharmaceutical quality
  - Standardized approach to inspection
  - Data gathering to inform “quality intelligence” of sites and products
  - Risk-based and rule-based process, using expert questions
  - Semi-quantitative scoring to allow for comparisons within and between sites
  - More common inspection report structure
  - Recognize and reward positive behaviors in cases where facilities exceed basic compliance
Project Organization

New Inspection Protocols Project (NIPP) Steering Committee
CDER ORA

Pre-Approval Inspection Subgroup
- Observations to inform premarket review decisions

Surveillance Inspection Subgroup
- Observations on state of quality in a facility to assess quality risk

For Cause Inspection Subgroup
- Evidence of cGMP violations to support enforcement

Escalation/transition to “For Cause” when conditions indicate
OPQ: Major Achievements for the Past Ten Months (cont.)

- Improved the IT system (Panorama)
- Improved the coordination and integration of OPQ research into policy development and regulatory review
- Made major progress in promoting/facilitating emerging pharmaceutical technology
  - OPQ-ORA emerging technology team
  - Brookings institute meeting on continuous manufacturing
  - Biomedical Advanced Research and Development Authority (BARDA)-FDA continuous manufacturing innovation initiative
  - External research collaboration
OPQ: Opportunities

- Quality Metrics
- Clinically Relevant Specification
- Process Capability
- Quality for Breakthrough Therapy
  - Statistical approach to Quality
- Biosimilars
Growing 6σ Capability

Since 2007, The Actual Number of Parameters Achieving 6 Sigma has Doubled

At the end of 2014,
- 82% of the parameters were performing at a 6σ level
- 14% of the parameters were performing between 3σ and 6σ levels
- 4% of the parameters had CAPA’s open to improve performance
OPQ: Moving Forward

• The launch of FDA OPQ is a milestone in FDA’s efforts to assure that quality medicines are available to the American public

• With a motto of “One Quality Voice,” OPQ embodies the closer integration of policy, review, inspection, surveillance, and research for the purpose of strengthening pharmaceutical quality