FDA Quality Oversight: One Quality Voice

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Early 2000s: FDA Embarks upon Pharmaceutical Quality for 21st Century Initiative

Vision

“A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight.”
“21st Century Initiative”: Succeeded at Many Levels

- ‘Enabling’ of modern technology
  - Process Analytical Technology
  - Continuous Manufacturing
- Multiple ICH documents
  - Pharmaceutical Development and QbD
  - Quality Risk Management
  - Quality Systems
- Formation of Pharmaceutical Inspectorate
We Aren’t There Yet....
Current Challenges

- High occurrences of product recalls and defects
- Alarming shortages of critical drugs
- Increasing post-approval supplements
- Limited information on the current state of pharmaceutical quality and facility
Where are we going?
"One Quality Voice"

One Quality Voice for Drugs:
OPQ will centralize quality drug review — creating one quality voice by integrating quality review, quality evaluation, and inspection across the product lifecycle.

One Quality Voice for Patients:
OPQ will assure that quality medicines are available for the American public.

One Quality Voice for Industry:
OPQ will establish consistent quality standards and clear expectations for industry.

One Quality Voice for Health Care Professionals:
OPQ will anticipate quality problems before they develop and help prevent drug shortages.

One Quality Voice for Health Care Purchasers:
OPQ will emphasize quality metrics.
CDER 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

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
OPQ: One Quality Voice
Value Statements (cont.)

• 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: 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
Assuring that All Human Drugs Meet the Same Quality Standards to Safeguard Clinical Performance

- Same quality standards for new and generic drugs
  - Impurities, dissolution etc.

- Clinically relevant specification
  - Connect quality to safety and efficacy, resulting in “clinical relevance,” in which the quality standard becomes a specification established on the clinical performance of the drug product, based on its variation in quality
Enhancing Science- and Risk-based Regulatory Approaches

- Put patients first by balancing risk and availability
- Implement risk-based approaches
  - Review
    - Plan, Do, Check, and Act
    - Inspection
- Advance regulatory science
  - FDA laboratory and sponsored research
  - Additional regulatory science efforts
Transforming Product Quality Oversight from a Qualitative to a Quantitative and Expertise-based Assessment

- Product quality informatics
  - Lifecycle management
- Quality metrics and FDA lab-based surveillance
- Question-based review
Product Quality Informatics

- Enabling an efficient science-driven assessment requires significant transformation in how OPQ collects, evaluates, and learns from the product quality data
- Core areas of Product Quality Informatics:
  - Structured and standardized data submission and collection
  - Knowledge management and communication
    - Established conditions
    - Risk mitigation
  - Post-market surveillance and quality monitoring
  - Intelligent data analysis
Quality Metrics

What

• Objective measures of product quality, facility, and possibly quality management systems

Why

• Induce the right behavior and responsibility for industry—Enable better FDA surveillance of the firms’ quality state
• Reduce product-related shortages and quality related recalls—Promote improved product and process capability
• Achieve product quality without extensive regulatory oversight
Question-based Review

- FDA Manual of Policies and Procedures (MAPP) 5015.10
  - Chemistry Review of Question-based Review (QbR) Submissions

- This MAPP clarifies how drug substance and drug product reviewers should assess drug applications (NDAs, ANDAs, and drug substance DMFs) that follow a Question-based Review format

Providing Seamless Integration of Review and Inspection

- Team-based integrated quality assessment
- New inspection protocol project
  - Pre-approval inspection, surveillance inspection, and for cause inspection
  - Parity of domestic and international facilities
- Program alignment across FDA
Team-based Integrated Quality Assessment (IQA)

- The Office of Pharmaceutical Quality (OPQ) will use a team-based Integrated Quality Assessment (IQA) approach to maximize each team member’s expertise and provide aligned patient-focused and risk-based drug product quality recommendations, inclusive of drug substance, drug product, manufacturing, and facilities.

- Therefore
  - OPQ teams will be expected to work in a highly collaborative model
  - Teams will be expected to collaborate effectively within timelines
  - Collaborations/discussions should involve key stakeholders
  - Communication/discussion of quality risk and link to the patient are critical
IQA Evolution

  – Objective: Evaluate the feasibility, effectiveness, and efficiency of OPQ’s vision for integrated team-based product and process/facility assessment

  – Objective: International inspection and microbiology assessment

• Pilot Phase III, Sept, 2014 to current/OPQ
  – Objective: Integration of review and inspection
OPQ Integrated Quality Assessment Team
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
Program Alignment across FDA

- Transition to distinct commodity-based and vertically-integrated regulatory programs with:
  - Well-defined leads
  - Coherent compliance policy and enforcement strategy development
  - Well-designed and coordinated implementation
  - Investigators, compliance officers, import reviewers, laboratory personnel, and managers who are more specialized in a particular regulatory program
Encouraging Development and Adoption of Emerging Technology

- Formed emerging pharmaceutical technology team
- Drafted emerging pharmaceutical technology guidance
- Continuous manufacturing
  - Sponsored research
  - Published scientific review
  - Planned FDA Science Board presentation
  - Policy
Quality Information in BLAs/NDAs/ANDAs

Technical Assessment

How does it link to the patient?

After Sarah Pope Miksinski