FDA’s Pharmaceuticals for the 21st Century: A Risk-Based Approach

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Session Overview

- FDA’s Pharmaceutical Current Good Manufacturing Practices for the 21st Century initiative -- purpose and scope
- Key components and outcomes
- FDA’s ongoing implementation
- March 2005 risk management guidances
- Integrating risk-based approaches and other aspects of the initiative into drug development and manufacturing
Pharmaceutical cGMPs Initiative: Purpose

- Two-year initiative to assess ways to modernize and enhance regulation of pharmaceutical manufacturing and quality

- Goals of new framework
  - Help facilitate continuous improvement by manufacturers
  - Improve the availability of pharmaceuticals
  - Increase product quality & process efficiency
Pharmaceutical cGMPs Initiative: Scope

Risk-Based Approaches

Review
Compliance
Inspectional
Why Risk-Based Approaches?

- Better utilization of scarce agency resources by focusing on elements of risk
- Maximize public health impacts of agency inspections and compliance activities
- Enhance internal FDA coordination, predictability and consistency
- Encourage best practices in manufacturing
- Reduce regulatory burdens for changes that do not affect safety or effectiveness
Agency Players: Who’s Who (& Where)

Secretary of Health & Human Services

Commissioner of Food & Drugs

Center for Drug Evaluation & Research
CDER

Center for Biologics Evaluation & Research
CBER

Center for Veterinary Medicine
CVM

Office of Regulatory Affairs
ORA

Center for Devices & Radiological Health
CDRH

Center for Food Safety & Applied Nutrition
CFSAN

Office of the Commissioner
OC
Key Elements & Programs

• Risk-Based Approaches
  – Risk-based method for prioritizing cGMP inspections of domestic manufacturing sites
  – Office of New Drug Chemistry (ONDC)
    • Changes to review processes for chemistry, manufacturing and controls (CMC) issues
      – Procedures for changes to approved drugs
      – Guidance on electronic records and signatures (21 CFR Part 11)
      – Draft guidance on computerized systems used in clinical trials
Key Elements & Programs

• Quality Systems Approach
  – Quality systems model adopted agency-wide
  – Preapproval inspection program
  – Draft guidance on quality systems approach to CGMPS
  – Formal dispute resolution for scientific and technical issues related to cGMP disputes
  – Changed procedures for drug cGMP warning letters
  – More timely guidance on cGMP questions
Key Elements & Programs

• Quality Systems Approach: Science-based policies and standards to facilitate innovation
  – Guidance on process analytical technology (PAT)
  – Sterile drug products produced by aseptic processing -- cGMP guidance
  – Comparability protocols

• FDA goal: provide greater regulatory flexibility based on better agency understanding of manufacturer processes
Key Elements & Programs

• Enhanced Internal Regulatory Coordination
  – Pharmaceutical Inspectorate (PI)
  – Joint internal training
  – Product specialists on inspections
  – Improved integration of preapproval and cGMP inspections
Key Elements & Programs

- International Collaboration and Harmonization
- Analysis of cGMP Requirements for Harmonization
  - Draft guidance on cGMPs for combination products
- Council on Pharmaceutical Quality
March 2005 Guidances on Risk Minimization

- Premarketing Risk Assessment
- Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment
- Development and Use of Risk Minimization Action Plans (RiskMAPs)
  - “FDA recommends that RiskMAPs be used judiciously to minimize risks without encumbering drug availability or otherwise interfering with the delivery of product benefits to patients.”
FDA Implementation

- System-wide agency culture change
- Risk-based site selection model for cGMP inspections
- Improving internal policies and programs for regulating drug quality
- Improving training of FDA staff
- Improving cross-agency coordination
- Enhancing international regulatory collaboration
- Incremental changes to cGMPs
Challenges for Agency Implementation

- Cultural issues within FDA
- What is a “risk” is subject to change
  - Knowledge is continuously evolving
  - New information can affect risk assessments and priorities
- Is “risk” to be defined by adverse events, or by risk to the integrity of the Federal Food, Drug and Cosmetic Act and its implementing regulations
- Industry concerns about information-sharing
Industry Integration

- Opportunities yet uncertainties for drug development and manufacturing
- Challenges of evolving agency thinking
- Agency transparency has limits
Risk Management

• Identify Risk
• Analyze Risk
• Eliminate Risk (where possible)
• Mitigate Risk
• Monitor Product Performance
• Continuous process
  – As new information becomes available
  – As product and circumstances change
Integrating Risk-Based Approaches

Scientific/Technical Experts

Company Management

FDA Specialists

Reimbursement Advisors

Products Liability Advisors

Other Specialists

Risk Management
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