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# Perspectives on New Paradigms of Risk and Compliance in Pharmaceutical Development: Quality by Design, PAT, and Design Space

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# Acknowledgements

- Helen Winkle, Director of OPS
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  - \*Jon Clark, Associate Director of OPS
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# Presentation Outline

- Overview of Office of Pharmaceutical Science
  - Pharmaceutical cGMPs for the 21<sup>st</sup> Century Initiative
  - Quality Management Systems
    - Internal Efforts
    - Customer Focus – Conformia Cooperative Research and Development Agreement (CRADA)
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# Office of Pharmaceutical Science - Overview

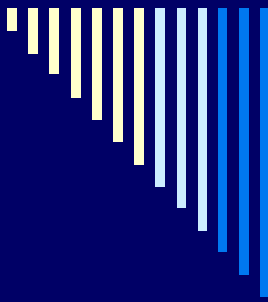
- Created in a 1995 CDER reorganization
  - Employs about 500 of CDER's 1700 employees
  - Includes for subordinate offices:
    - Office of Biotechnology Products (OBP)
    - Office of Generic Drugs (OGD)
    - Office of New Drug Quality Assessment (ONDQA)
    - Office of Testing and Research (OTR)
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# Office of Pharmaceutical Science - Overview

- Umbrella organization over the activities of chemistry, manufacturing, and controls (CMC) review in the Center of Drug Evaluation and Research
  - Activities include:
    - Assessment of product and process design
    - Evaluation of product quality in light of established standards
    - Setting and maintaining new quality standards
  - Regulate a range of products (including synthetic, fermentation, natural source, and biotech new molecular entities, generic drugs and certain over the counter products)
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# Office of Pharmaceutical Science (OPS)

CDER/OPS

New Drug  
CMC

Generic  
CMC

Biotech  
CMC

Microbiology  
CMC

Chemistry, Manufacturing, and Controls (CMC)



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# OPS Mission

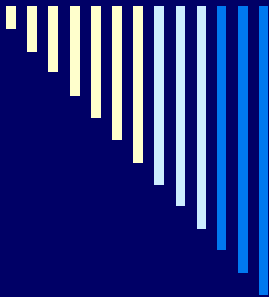
- To ensure timely availability of high quality drug products to U.S. patients:
    - Through effective and efficient scientific assessment of relevant pharmaceutical and biotechnology information in regulatory submission, and;
    - By facilitating those scientific and technological innovations that improve understanding of product performance, quality, and efficiency of development, manufacturing, and quality assurance processes.
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# OPS Objectives

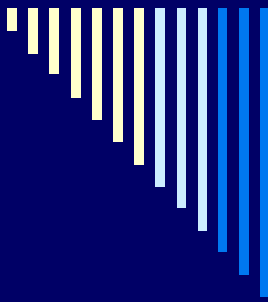
- OPS main objectives are to:
    - Ensure pharmaceutical product is high quality
    - Demonstrate quality in internal systems and activities
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# Pharmaceutical cGMPs for the 21<sup>st</sup> Century – A Risk-Based Approach

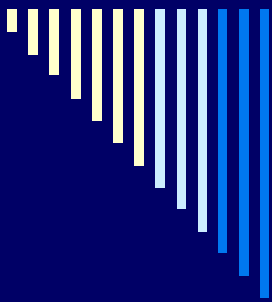
- Announcement 2002
  - Final Report 2004
    - Encourage the early adoption of new technological advances by the pharmaceutical industry
    - Facilitate industry application of modern quality management techniques, including implementation of quality systems approaches
    - Encourage implementation of risk-based approaches that focus both the industry and Agency attention on critical areas
    - Ensure that regulatory review, compliance, and inspection policies are based on state-of-the-art pharmaceutical science
    - Enhance the consistency and coordination of drug quality regulatory programs by further integrating quality systems approaches
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# Pharmaceutical cGMPs for the 21<sup>st</sup> Century – A Risk-Based Approach

- Dr. Janet Woodcock desired state:
    - “A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight.”
      - Science-based decisions
      - Risk-based approach
      - Regulatory flexibility
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# Science, Risk Management, and Regulatory Flexibility - Pharmaceutical Manufacturing

- Quality by Design – Science - Built into the product (product and manufacturing process design)
- PAT –Design, Analysis, and Control
- Design Space – Regulatory flexibility based on science and risk management activities



# 21<sup>st</sup> Century Initiative – Internal Implementation Efforts

- New Drug Quality Assessment
    - Implementing risk-based pharmaceutical quality assessment system
    - Focus on critical pharmaceutical quality attributes and their relevance
  - Question-based Review (QbR) - Generics
    - Use the Quality Overall Summary (QOS) in Module 2 ICH CTD to answer standardized questions
    - Example: Which properties or physical chemical characteristics of the drug substance affect drug product development, manufacture, and performance?
  - Quality Management System for CMC Review Process (CDER/CBER)
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# Internal Quality Management System (QMS)

- FDA contracted with Neptune & Company, Inc. to develop a QMS for the CMC review process within CDER and CBER
  - Analyses of CMC review process have identified issues and opportunities for improved efficiency, transparency, consistency in the CMC decision making process
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# Quality Management System (QMS)

- Defined as a structured and documented management system describing the policies, objectives, principles, organization authority, responsibilities, accountability, and implementation plan of an organization for ensuring quality in its work processes, products (items), and services.” (ANSI/ASQ ER-2004 Quality systems for environmental data and technology programs – Requirements with guidance for use)
    - Aligns with 21<sup>st</sup> Century GMP Initiative
    - Opportunity for FDA to do as we say
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# Quality Management System (QMS)

- SMG 2020 provides a Quality System Framework for FDA Internal Activities
    - SMG 2020 is based, in part, on American National Standard ANSI/ISO/ASQ Q9001-2000 Quality Management Systems - Requirements
  - cGMP, EPA, CDC, ANSI, ASQ
  - Current guidance to CMC reviewers and industry
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# Quality Management System (QMS)

- ❑ Start with existing procedures, policies, and guidance
  - ❑ Understand projects underway to modernize FDA review processes (QbD, PAT, Design Space)
  - ❑ Work with individuals at multiple levels in the organization to understand their roles and concerns
  - ❑ Build on what is already being done right
  - ❑ Establish meaningful metrics evaluate components of the CMC review process
  - ❑ Provide a Quality System for facilitating the achievement of goals that is embraced by all levels of the organization
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# Quality Management System (QMS)

## □ OPS QMS Goals

- Optimize performance practices and results
  - Facilitate cross-organization communication and information sharing
  - Share best practices to enhance work products
  - Serve as a mechanism for understanding, managing, and enhancing performance
  - Promote organizational and personal learning
  - Enhance transparency of the FDA review process leading to increased quality of industry submissions
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# Quality Management System

## □ Milestones

- Review background documents to value where the process currently has advanced
  - Develop a Work Plan (proposed approach for working with FDA to develop a QMS)
  - Develop an annotated outline of the Quality Management Plan (document specifying the quality management system for an organization)
  - Assist in eliciting a quality policy (overall intentions and direction of an organization related to quality as formally expressed by top management)
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# Quality Management System

- Milestones (continued)
    - Conduct two sets of interviews with managers/staff/stakeholders at various management levels
      - To understand current practices
      - To establish where and what change would be most beneficial
    - Develop the content of the QMS (this is the heart of the work)
    - Draft the Quality Management Plan
    - Develop a deployment strategy
    - Conduct a lessons learned forum
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# Quality Management System

## □ Status

- Kickoff meeting with FDA contacts mid-February 2006 with ongoing in-person and phone dialogue
  - Work Plan completed April 2006
  - Review of background documents for current process activities is ongoing
  - Draft of annotated outline submitted in mid-April 2006
  - Completed first set of interviews
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# Quality Management System

## □ Next Steps

- Refine the annotated outline
  - Continue background research
  - Prepare for second set of interviews
  - Elicit and document a quality policy statement
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# Quality Management System

## □ Customer Focus

- Conformia Cooperative Research and Development Agreement (CRADA)
    - To get a better understanding of the factors that influence pharmaceutical development
    - Research study entitled “A Survey of Pharmaceutical Needs” designed to uncover the challenges and bottlenecks faced by pharmaceutical and biotechnology companies in bringing new drugs to market.
    - Survey – Useful in identifying key themes related to research issues.
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# Quality Management System

- The factors of focus include:
    - Commercialization Processes
    - Quality by Design, PAT, Design Space
    - ICH Q8, Q9, and Q10
    - Collaboration
    - Communication/Decision Making
    - Information Bottlenecks
    - FDA Perception
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# CDER Conference on CMC

- FDA is cosponsoring event on October 17-18 in Reston, VA
    - These topics and others will be described in detail by the Office Directors and Management staff involved
    - Go to [www.pharmaconference.com](http://www.pharmaconference.com)
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# Thank You

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