ONDQA Perspective on Post Approval Changes

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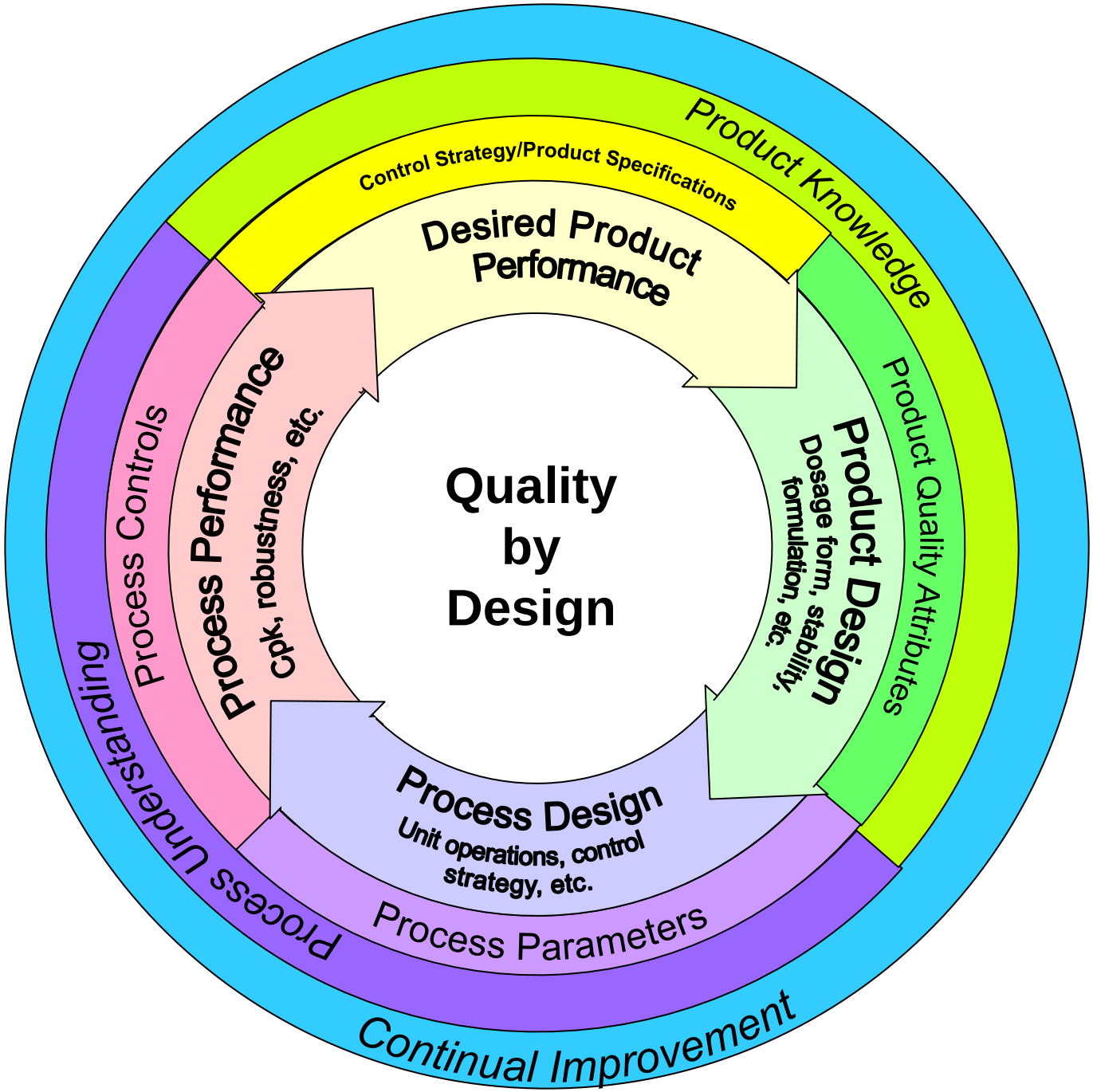
Overview

- What is quality by design (QbD)?
- QbD approach to post-approval CMC changes
- ONDQA Pharmaceutical Quality Assessment System (PQAS)
- ONDQA reorganization
- Division of Post-Marketing Evaluation (DPME) – mission and risk-based quality assessment
- Type of NDA supplements
- Summary


Quality by Design
Desired Product Performance
Control Strategy/Product Specifications
Product Knowledge
Product Quality Attributes
Product Design
Dosage form, stability, formulation, etc.
Process Design
Unit operations, control strategy, etc.
Process Parameters
Process Performance
Cpk, robustness, etc.
Process Controls
Process Understanding
Continual Improvement

What is Quality by Design (QbD)

- **In a Quality by Design system:**
  - The product is designed to meet patient needs and performance requirements
  - The process is designed to consistently meet product critical quality attributes
  - The impact of starting raw materials and process parameters on product quality is understood
  - The process is continually monitored, evaluated and updated to allow for consistent quality over time
  - Critical sources of variability are identified and controlled
    - Appropriate control strategies are developed

QbD Approach to Post-Approval CMC Changes

- Proactive approach to continual improvement and innovation instead of reactive compliance approaches
- Manufacturing experience and knowledge provides opportunity to evaluate and improve processes
- Manufacturing experience and product knowledge can be used to establish a “design space”
- Introduction of innovative processes and controls is encouraged and will be facilitated
- Robust Pharmaceutical Quality System (PQS) is essential to implement scientific risk based change control

ONDQA Pharmaceutical Quality Assessment System (PQAS)

- PQAS promotes the science and risk-based approach to regulation as described in the Pharmaceutical Quality Initiative for the 21st Century
- PQAS was established to encourage the pharmaceutical industry to apply QbD principles to drug development
- Submission of knowledge-rich, scientific information that demonstrates product and process understanding
- Innovation and continual improvement facilitated throughout product life cycle
- Regulatory flexibility based on enhanced product knowledge and process understanding

ONDQA Reorganization

- ONDC was reorganized to Office of New Drug Quality Assessment (ONDQA) in November 2005
- Objective: To implement PQAS
- Separation of pre-marketing (INDs/NDAs) from post-marketing (supplements/annual reports) review activities to better utilize limited resources
- Establishment of Manufacturing Science Branch and recruitment of pharmaceutical scientists, chemical engineers, and industrial pharmacists to complement current review staff

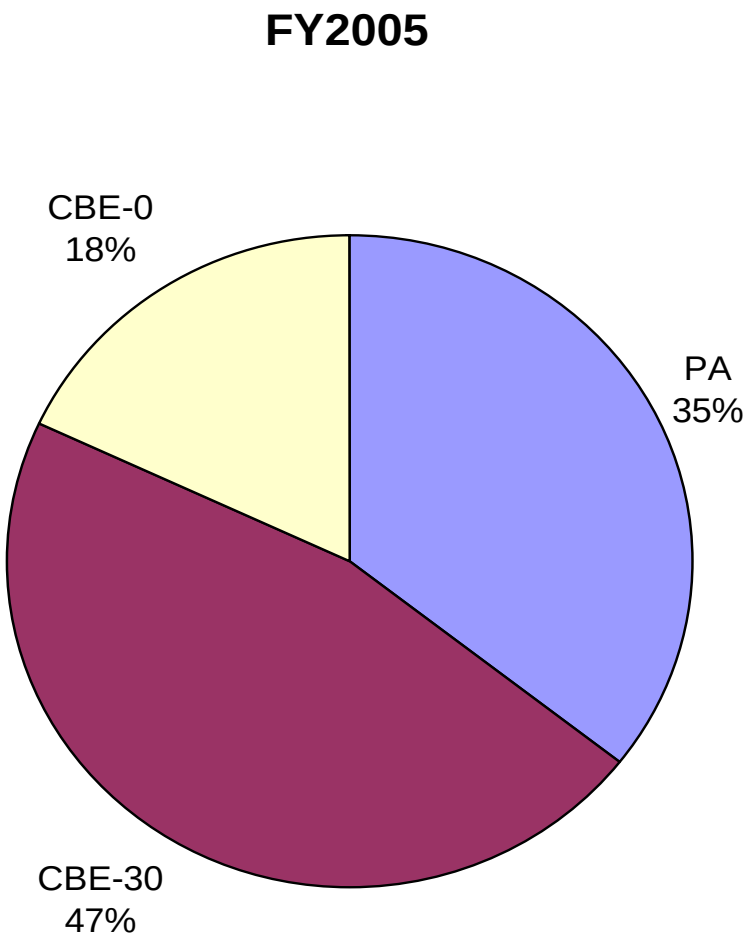
Division of Post-Marketing Evaluation (DPME) - Mission

- Foster implementation of continuous improvement, innovation and effective manufacturing changes within a process knowledge framework
- Develop a streamlined review process within a risk-based framework, and capture knowledge from evaluation and review
- Develop strategies to streamline review process and to downgrade or eliminate certain types of supplements based upon risk based analysis

DPME – Risk-Based Quality Assessment

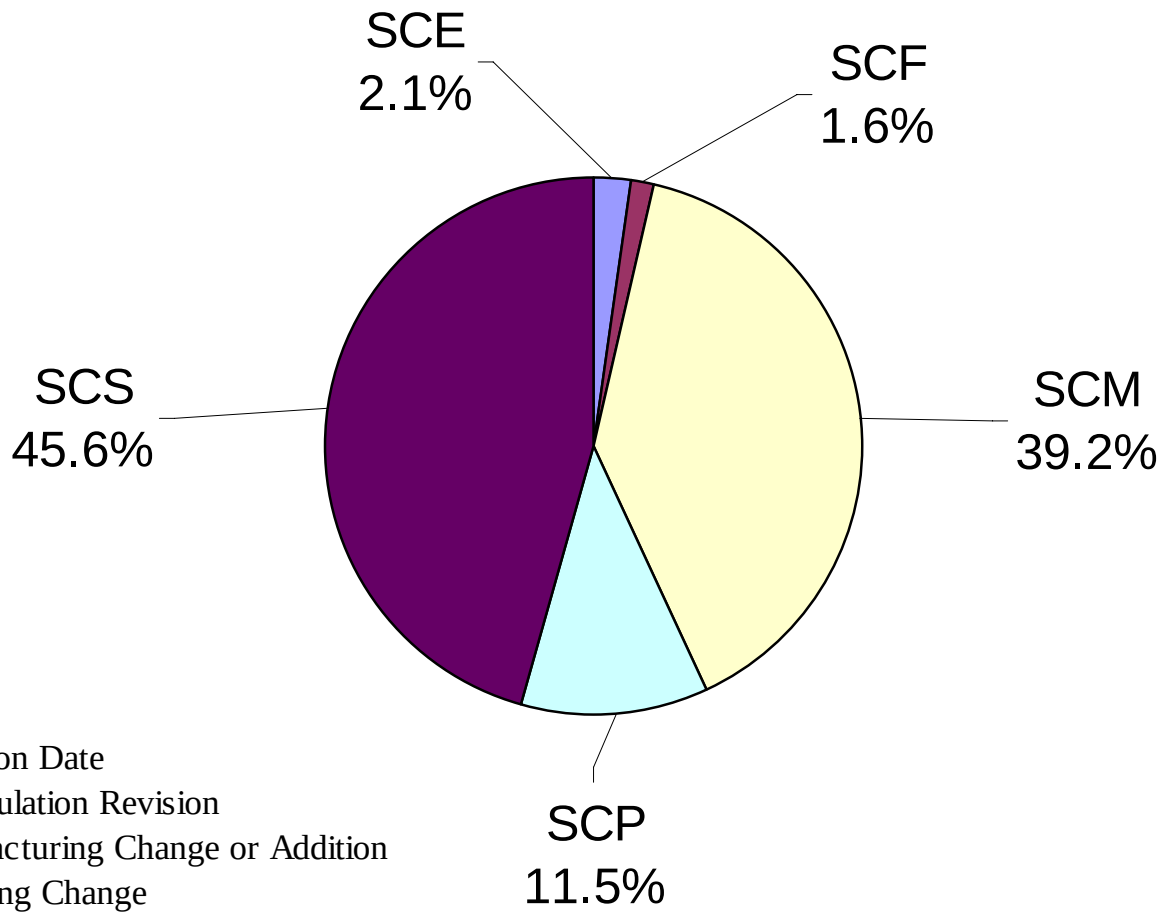
- Approaches to assigning risk categories
  - Impact of proposed change on product performance
  - Degree of understanding of product design, desired product performance and manufacturing process
- Supplement triage based on risk assessment

Types of NDA Supplements Submitted in FY 2005



FY2006 CMC Supplements Received

N = 1809



SCE - Expiration Date
SCF - Forumaulation Revision
SCM - Manufacturing Change or Addition
SCP - Packaging Change
SCS - Control Revision

Summary

- Opportunities
  - FDA QbD initiative, advocating science- and risk-based approaches
  - Pharmaceutical quality system
- Challenges
  - Application of QbD to approved products
  - Transition
  - Dual system