Pharmaceutical Quality System
Bringing cGMP into the 21st Century

Granite State
15 March 2012
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ASQ
The Global Voice of Quality™

Agenda

- International Conference on Harmonization
  - ICH Q10 – Pharmaceutical Quality System
- Relationship of Q10 to National cGMP and International Organization for Standardization
  - ISO 9001
  - 21 CFR 210/211 and 21CFR 820
- ICH Q10 Objectives
- Enablers: Knowledge Management and Quality Risk Management (Q9)
- Differences in Operating Management System Controls in Part 820 (QS Regulation) and Part 210/211 (cGMP)

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International Conference on Harmonization

- Launched 20 years ago
- Brings together the drug regulatory authorities of Europe, Japan and United States
- Along…with Pharmaceutical trade associations
- Discuss scientific and technical aspects of product registration

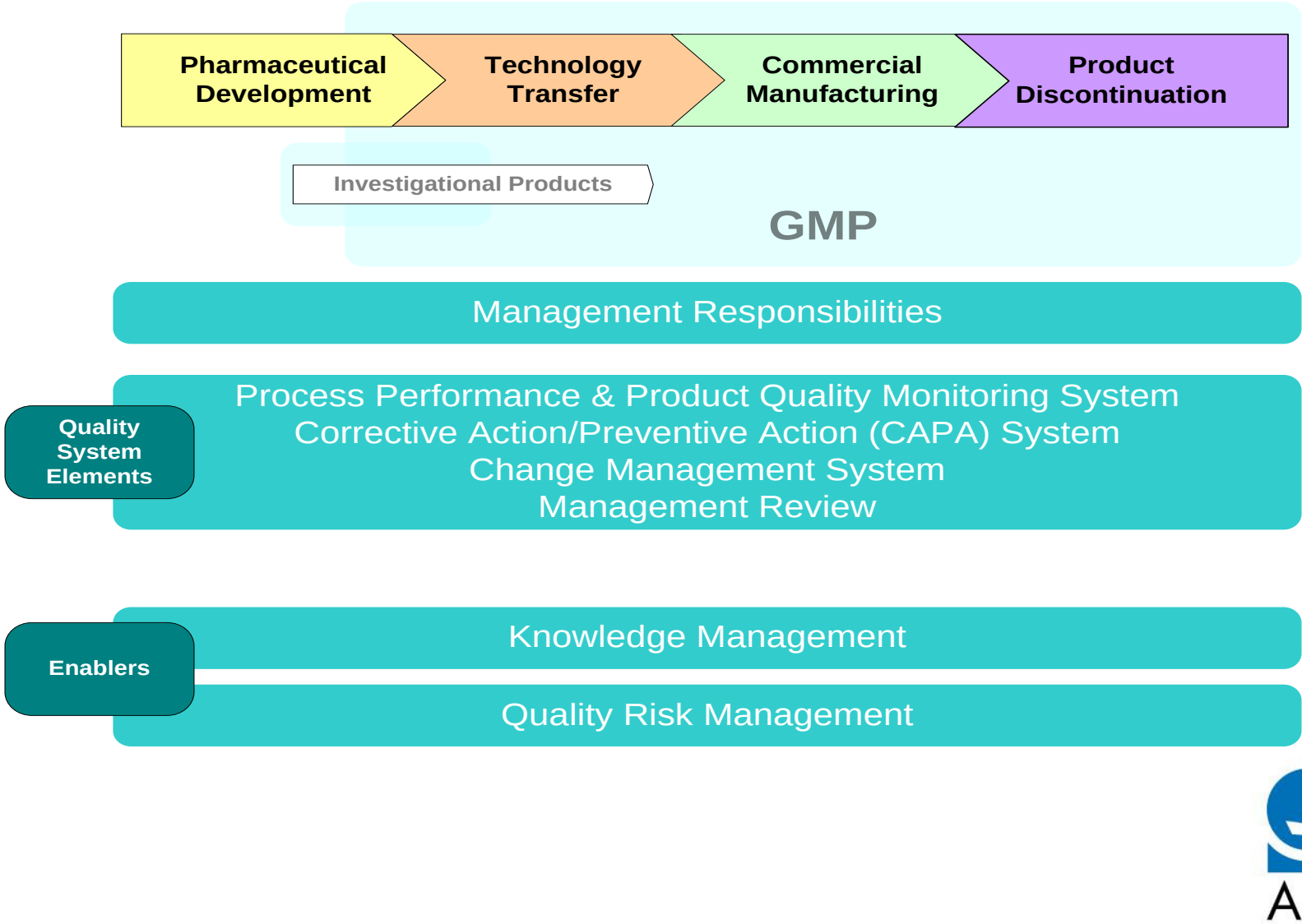
ICH Mission

- Achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration, thereby reducing duplication of testing and reporting carried out during the research and development of new medicines.

ICH Q10 Pharmaceutical Quality System (PQS)

- Recommended for adoption to the regulatory bodies of EU, Japan and US in June 2008.
- Establishes a tripartite guideline
- Describes model for an effective quality management system
- Can be implemented throughout different stages of product lifecycle

Pharmaceutical Quality System (PQS)



History

- Evolution of regional GMPs **1970s**
- Evolution of ISO 9000 approaches **1980s**
- FDA 21st Century initiative **2002**
- ICH Quality Vision / Q8, Q9 **2003**
- Guidance for Industry Quality System Approach to Pharmaceutical cGMP Regulations **2006**
- ICH Q10 Pharmaceutical Quality System **2008**

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Relationship to ISO and GMP

- Based on ISO 9000 Quality Concepts
  - Customer Focus
  - Integration with Goals and Objectives
- Includes applicable cGMP regulations
- Not intended to create new regulatory expectations

Comparison GMP and ISO/Q10

cGMP	Q10
Manufacturing Operations Focus	Process System Based
Quality Unit QC QA	Quality Management
Commercial Product Investigational Products Phase III	Product Lifecycle
Responsibilities	Senior Management
	Quality Risk Management (QRM)
Corrective Action	Corrective Action Preventive Action
	Continual Improvement

ICH Q10 Objectives

- **Achieve Product Realization**
  - Deliver products with quality attributes to meet the needs of patients and agencies
- **Establish and Maintain a state of control**
  - Effective monitoring systems for process performance and product quality…QRM can be useful
- **Facilitate Continual Improvement**
  - Knowledge Management and QRM

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Enablers

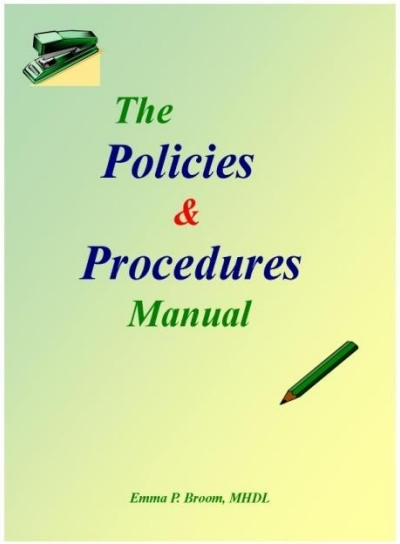
- **Knowledge Management**
  - **Product and Process knowledge from development thru discontinuation**
    - Development studies
    - Technology transfer
    - Process validation studies
    - Manufacturing experience,
    - Innovation
    - Change Management
  - **Systems:**
    - Sharepoint, LIMS, SAP,
    - Trackwise, Document Management Systems

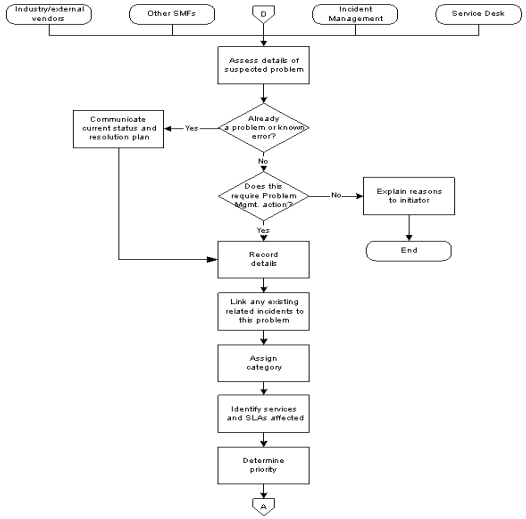
Quality Risk Management

- Proactive approach to”
  - Identifying
  - Scientifically evaluating and
  - Controlling Potential Risks
- Facilitates Continual Improvement
  - Process performance
  - Product Quality

Quality Manual

- Quality Manual or Equivalent
  - Quality Policy
  - Scope of PQS
  - Identification of quality system processes
    - Sequence and interaction
    - Management Responsibilities





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Management Responsibilities

- Management Commitment
- Quality Policy
- Quality Planning
- Resource Management
- Internal Communication
- Management Review
- Outsourced Activities
- Change in Product Ownership

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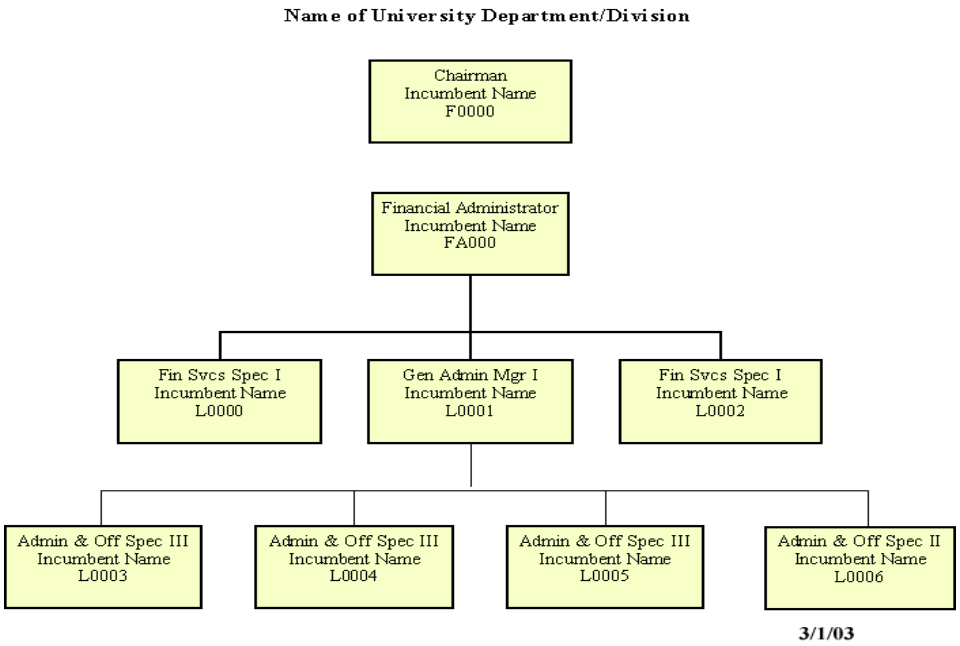
Management Commitment

- Effective PQS is in place to achieve quality objectives
- Roles Responsibilities defined



Management Responsibilities

- Quality Policy
  - Sets the standard and direction
- Quality Planning
  - Established objectives needed to implement quality policy
- Resources
  - Provide adequate resources 6Ms
  - Appropriately applied
    - Projects
    - Processes
    - Site

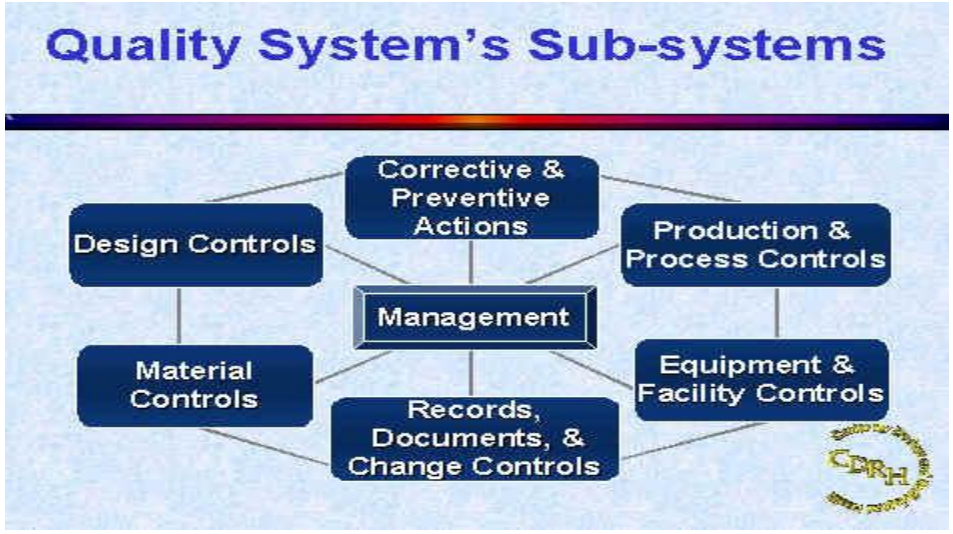
Internal Communication

- Appropriate communications processes
  - All levels of company
  - Sharepoint
  - Huddles
  - GEMBA
  - Bulletin Boards
  - Newsletters
- Escalation of product quality and PQS as needed…
  - Notification to Management

Management Review

- Senior Management Governance PQS
  - Suitable Adequate Effective
- Product Quality and Process Performance
- Quality System Performance

Note: 21 CFR 820



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Outsourced Activities and Purchased Materials

- PQS and Management Responsibilities extend to control and review of any outsourced activities and purchased materials
- Process must be in place:
  - Assess suitability of outsourced operations and material suppliers
  - Ensure use of qualified suppliers and approved supply chains
    - Audits, questionnaires
  - Define responsibilities and communication processes
    - Quality agreements

Outsourced Activities and Purchased Materials

- Review performance of outsourced process
- Review quality of material
- Make needed improvements
- Monitor incoming materials to ensure they are from qualified suppliers and approved supply chains

PQS System Elements

- Elements are required under GMP however intent is to promote lifecycle aproach
  - Different goals of each stage

- Process Performance and Product Quality Monitoring
- Corrective and Preventive Action
- Change Management System
- Management Review of Process Performance and Product Quality

Product Quality and Process Performance

- Plan and execute system for monitoring
  - PQPQM
- Use QRM to establish control strategy
- Facilitate feedback/feedforward
  - C2Q
  - Parameters
  - Attributes
- Reduce and control variation
- Process Analytical Technology
- Enable innovation and continual improvement

Product Quality

- Measured at various stages before, during and after manufacturing process
- Annual Product Reviews (APR)

CAPA System

- Investigation of non conformances
  - Reactive: planned deviations, rejections, complaints, recalls, audits
  - Proactive: feedback from trends
  - Structured investigation process
  - Use QRM ensure degree and formality is commensurate with risk

Change Management System

- Risk Based approach to ensure proposed changes have impact to marketing authorization
- Proactive..driven by data
  - Data Driven Decisions…
  - Outputs from monitoring, trending,
  - innovation, (appears 10 times in Q10)
  - continual improvement
  - Assure no unintended consequences

Management Review

- **Process Performance and Product Quality**
  - Results from inspections
  - Annual Product Reviews
  - Customer Satisfaction, complaints, recalls
  - Conclusions of process performance and product quality monitoring
  - Effectiveness of PPC and CAPA
- **Output …Appropriate Actions**
  - Improvements to Mfg
  - Provision of training or realignment of resources
  - Capture and disseminate knowledge

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Continual Improvement of PQS

- Measurement of achievement of Objectives
  - KPI
    - Performance Indicators to monitor effectiveness
    - Audits, CAPA, complaints, recalls—internal
    - Emerging regulations
    - New technology
    - Change in business strategy
  - Outcomes of Review and Monitoring
    - Impromement to PQS and Processes
    - Revision to Quality Policy and Objectives
    - Allocation and Reallocation of Resources

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PQS Today

- Globalization and complex supply chains
- Increased Outsourcing
- Cost Reduction
- RIFs

Operating Manufacting Control System

210/211 (cGMP)	820 (QS)
211.84 Testing and Approval or rejection of components, drug product containers, and closures	820.30 Design Controls
211.103 Calculation of yield	820.50 Purchasing Controls
211.137 Expiration dating	820.100 Corrective and Preventive Action
211.165 Testing and release for distribution	
211.166 Stability Testing	
211.167 Special Testing Requirements	
211.170 Reserve Samples	

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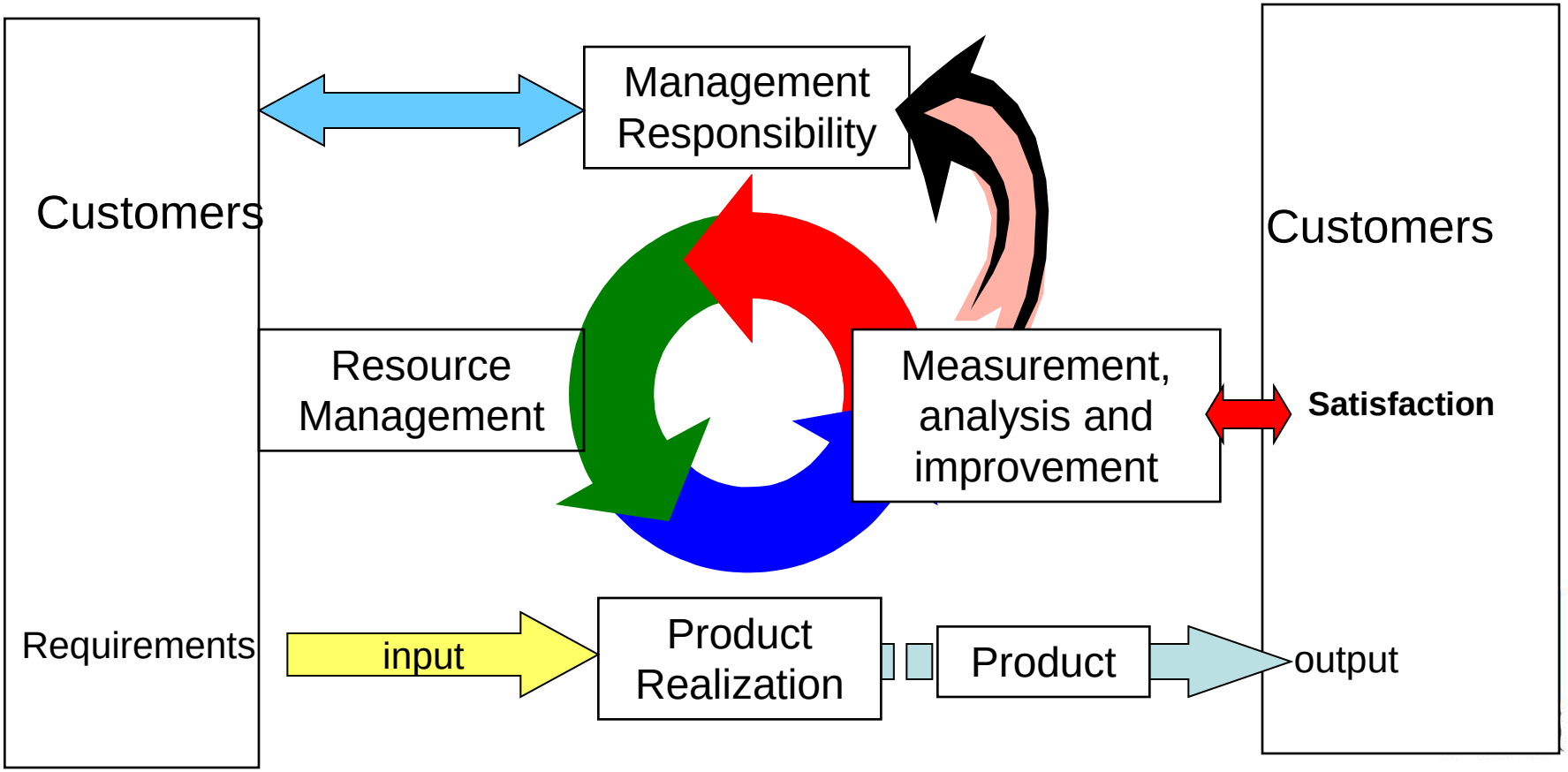
Pharmaceutical Quality System

- Summary



Thank You

- Website ASQBoston.org
- Boscon 24, 25 April 2012

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