ICH Q10 Pharmaceutical Quality System (PQS)

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICH Q10 PQS Guideline

- Background
- Objectives
- Scope
- Content
- Implementation
- Conclusion

Background

- Vision
  - Move from regulatory guidance to scientific guidance
  - A harmonized pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science
- Companion guidelines
  - high level
  - more visionary
  - less prescriptive
  - flexible regulatory approaches

  - *ICH Q8 Pharmaceutical Development*
  - *ICH Q9 Quality Risk Management*
  - *ICH Q10 Pharmaceutical Quality System*

Background (continued)

- ICH Q8 Finalized November 2005
  - ICH Q8(R1) (Step 2) November 2007
- ICH Q9 Finalized November 2005
- ICH Q10 (Step 2) May 2007
  - Public comments were received from the various Regions and consolidated
  - Comments were considered and incorporated
  - Major issues and revisions discussed
  - Final resolution in in Portland
- ICH Q10 - Finalized June 2008

Objectives of the Guideline

To meet the objectives, ICH Q10 augments Good Manufacturing Practices which are generally not repeated within the Guideline

1. Achieve product realisation
2. Establish and maintain a state of control
3. Facilitate continual improvement

Scope of Guideline

- applies…throughout the product lifecycle (§3.1)
  - Pharmaceutical Development
  - Technology Transfer
  - Commercial Manufacturing
  - Product Discontinuation

Scope of Guideline (continued)

- …applies to the systems supporting the development and manufacture of
  - pharmaceutical drug substances (i.e., API) and
  - drug products, including biotechnology and biological products
- …application is appropriate and proportionate to lifecycle stage
- …includes…new and existing products.

Content

1. Pharmaceutical Quality System
2. Management Responsibility
3. Continual Improvement of
   Process Performance and Product Quality
4. Continual Improvement of the
   Pharmaceutical Quality System
5. Glossary

- Annex 1 - Potential Opportunities to Enhance Science and Risk Based Regulatory Approaches
- Annex 2 - Diagram of the ICH Q10 Pharmaceutical Quality System Model

Content: §1 – PQS

- Introduction / Scope / Objectives
- Relationship of ICH Q10 to
  - Regional GMP Requirements, ISO Standards and ICH Q7
  - Regulatory Approaches
- Enablers
  - Knowledge Management
  - Quality Risk Management
- Design and Content Considerations
- Quality Manual

Content: §2 – Management Responsibility

- Management Commitment
- Quality Policy, Quality Planning
- Resource Management
- Internal Communication
- Management Review
- Management of
  - Outsourced Activities and Purchased Materials
  - Change in Product Ownership

Content: §3 – Continual Improvement of Process Performance & Product Quality

Two major sections:

- §3.1 Lifecycle Stage Goals – 4 stages
- §3.2 PQS Elements – 4 elements

Content: §3.1 Lifecycle Stage Goals

- 1 Pharmaceutical Development
  - design product and process to consistently deliver the intended performance and meet the needs of [parties]
  - exploratory and clinical development studies are inputs
- 2 Technology Transfer
  - transfer product/process knowledge between development and manufacturing, and within or between sites

Content: §3.1 Lifecycle Stage Goals
(continued)

- 3 Commercial Manufacturing
  - achieving product realisation, establishing and maintaining a state of control, and facilitating continual improvement

- 4 Product Discontinuation
  - manage the terminal stage of the product lifecycle effectively

Content: §3.2 PQS Elements

1 Process Performance and Product Quality Monitoring System

- A monitoring system to ensure a state of control is maintained

- The process performance and product quality monitoring system should:
  - Use quality risk management (ICH Q9 for example) to establish the control strategy.
  - Provide the tools for measurement and analysis of parameters and attributes
  - Analyse parameters and attributes
  - Identify sources of variation for potential continual improvement activities
  - Include feedback on product quality from both internal and external sources
  - Provide knowledge to enhance process understanding, enrich the *design space* (where established), and enable innovative approaches to process validation.

Content: §3.2 PQS Elements (continued)

2 Corrective Action and Preventive Action (CAPA) System

- A system for implementing
  - *corrective actions* resulting from the investigation of complaints, product rejections, non-conformances, recalls, deviations, audits, regulatory inspections and findings
  - *preventive actions* resulting from trends from process performance and product quality monitoring
- CAPA methodology should result in product and process improvements and enhanced product and process understanding

Content: §3.2 PQS Elements (continued)

3 Change Management System

- A change management system ensures continual improvement is undertaken in a timely and effective manner.
  - It should provide a high degree of assurance there are no unintended consequences of the change

- Change Management should, as appropriate for the lifecycle stage:
  - Use Quality risk management (Q9) to evaluate proposed changes
  - Evaluate proposed changes relative to the marketing authorisation and need for a change to the regulatory filing
  - Evaluate proposed changes using expert teams
  - Evaluate the change after implementation to confirm the change objectives were achieved and that there was no deleterious impact on product quality.

Content: §3.2 PQS Elements (continued)

4 Management Review of Process Performance and Product Quality

- Management reviews provide assurance that process performance and product quality are managed over the lifecycle
- Includes data from a wide range of external and internal sources
- Results in appropriate actions, such as:
  - Improvements to manufacturing processes and products
  - Training and/or realignment of resources
  - Capture and dissemination of knowledge

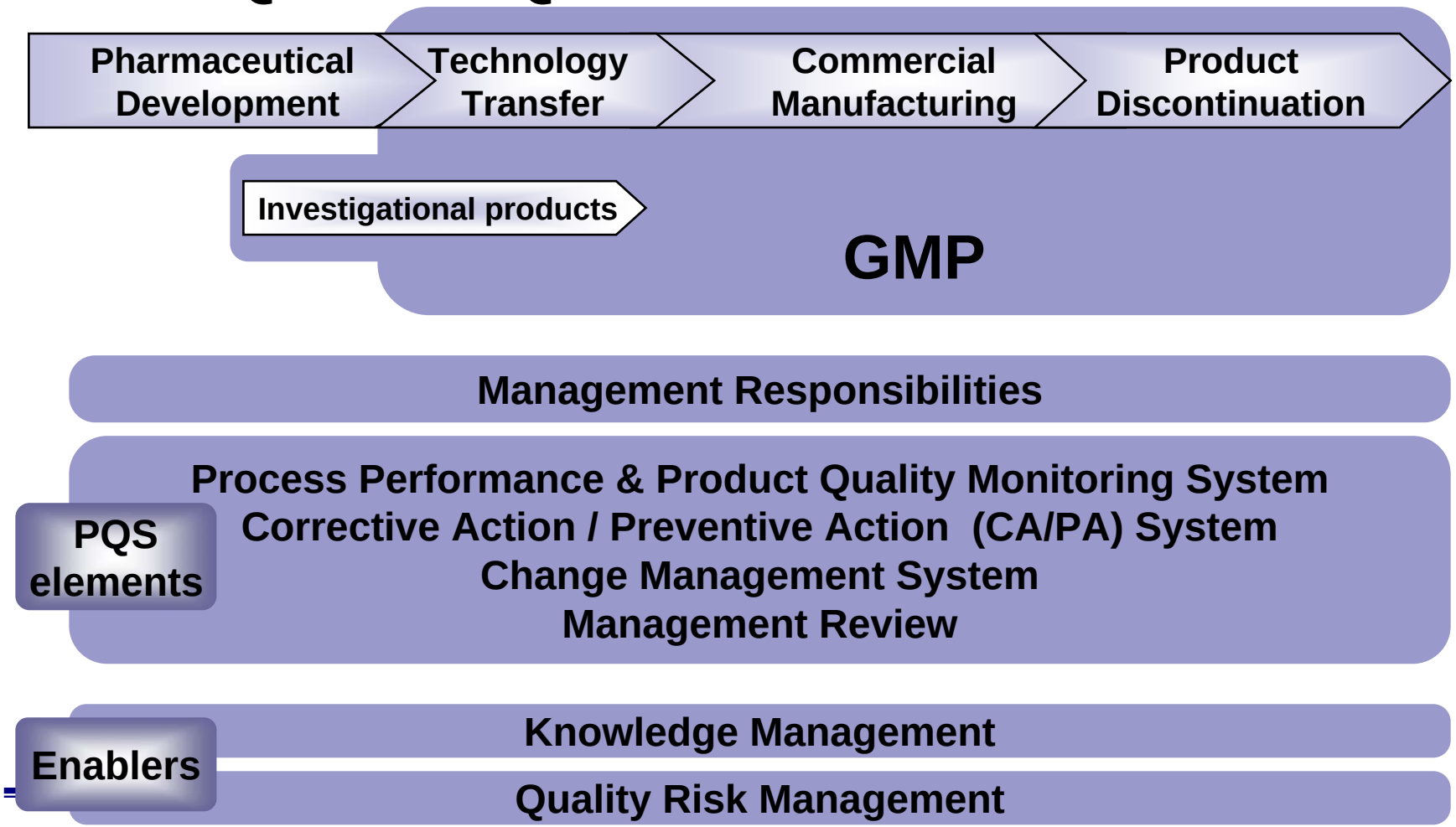
Content: §4 – Continual Improvement of the PQS

- Management Review of the Pharmaceutical Quality System
- Monitoring of Internal and External Factors Impacting the Pharmaceutical Quality System
- Outcomes of Management Review and Monitoring

Content: ..in addition

- §5 – Glossary
- Annex 1 – Potential Opportunities to Enhance Science and Risk Based Regulatory Approaches
- Annex 2 – Diagram of the ICH Q10 Pharmaceutical Quality System Model

ICH Q10 PQS


Pharmaceutical Development
Technology Transfer
Commercial Manufacturing
Product Discontinuation
Investigational products
GMP
Management Responsibilities
PQS elements
Process Performance & Product Quality Monitoring System
Corrective Action / Preventive Action (CA/PA) System
Change Management System
Management Review
Enablers
Knowledge Management
Quality Risk Management

Integration of Q8, Q9, & Q10

- An integrated set of guidelines:
  - Q8 Pharmaceutical Development
  - Q9 Quality Risk Management
  - Q10 Pharmaceutical Quality Systems

- Q8, 9, & 10:
  - Quality by Design, Risk Management, and PQS provide greater product assurance of quality

Integration of Q8, Q9, & Q10 (continued)

- Q8 & 10:
  - Processes for pharmaceutical development are key linkages to product realization within the PQS.
  - Q8 provides for robust development and understanding that serves as the basis for continual improvement.
  - Manufacturers with a robust PQS and appropriate process knowledge can implement many types of improvements.
- Q9 & 10:
  - The PQS should encourage and facilitate the use of Quality Risk Management approaches throughout the system.
  - The design and application of processes within the PQS should be based on appropriate risk management principles and methods

Implementation of Q10

- Annex 1 - Potential Opportunities to Enhance Science and Risk Based Regulatory Approaches
  - Annex reflects potential opportunities to enhance regulatory approaches.
  - The actual regulatory process will be determined by region.

Annex 1 - Potential Opportunities

Scenario	Potential Opportunity
1. Comply with GMPs	Compliance – status quo
2. Demonstrate effective PQS, including effective use of quality risk management principle	Opportunity to increase use of risk based approaches for regulatory inspections
3. Demonstrate product and process understanding, including effective use of quality risk management principles	Opportunity to ■facilitate science based pharmaceutical quality assessment ■enable innovative approaches to process validation ■establish real-time release mechanisms

Annex 1 - Potential Opportunities

Scenario	Potential Opportunity
4. Demonstrate effective pharmaceutical quality system and product and process understanding, including the use of quality risk management principles	Opportunity to: ■ increase use of risk based approaches for regulatory inspections ■ facilitate science based pharmaceutical quality assessment ■ optimise science and risk based post-approval change processes to maximise benefits from innovation and continual improvement ■ enable innovative approaches to process validation ■ establish real-time release mechanisms

Conclusion

- ICH Q10 is not intended to create any new expectations beyond current regulatory requirements. Consequently, the content of ICH Q10 that is additional to current regional GMP requirements is optional.

- The elements of ICH Q10 should be applied in a manner that is appropriate and proportionate to each of the product lifecycle stages, recognising the differences among, and the different goals of each stage