ICH-GCG Asean Training Workshop on ICH Guidelines
Q8, Q9 and Q10 (New Paradigm)

Introduction to Q10
Pharmaceutical Quality System

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Kuala Lumpur, Malaysia 26-28 July 2010

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

- The information within this presentation is based on the presenter's expertise and experience, and represents the views of the presenter for the purposes of a training workshop.
ICH Q10 PQS Guideline

- Background
- Objectives
- Scope
- Content
- Implementation
- Conclusion
Creation of the ICH Expert Working Group

“Develop a harmonised pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science.”

Brussels July 2003
ICH : a 3 regions process -> GCG

- **United States of America**
  - Food and Drug Administration - FDA
  - Pharmaceutical Research and Manufacturers of America - PhRMA

- **Europe**
  - European Union / European Commission – EU/EC
  - European Federation of Pharmaceutical Industries and Associations – EFPIA

- **Japan**
  - Ministry of Health, Labour and Welfare – MHLW & PMDA
  - Japan Pharmaceutical Manufacturers Association - JPMA
ICH 10 Step Process

Step 1 – Consensus building
- Expert Working Group (EWG) and rapporteur

Step 2 – Industry driven
- Step 2 sign off Brussels May 9th 07
- Expert Working Group (EWG) adopts concept paper as new topic
- Industry driven

Step 2 – Experts Document ‘Consensus text’

Step 3 – Regulator driven
- Draft CHMP guideline
- Step 3 – Regional regulatory Consultation e.g. Draft CHMP guideline
- Includes consultation with non-ICH regions
- EWG review consultation results

Step 4 – Experts Document ‘Consensus text’
- Step 4 approved June 08
- Steering Committee (3 Reg parties) adopts Consensus text as Step 4 document

Step 5 – Regulatory Implementation
Q10: with Q8, Q9, Q-IWG & Q11

Q11 Development and Manufacture of the Drug Substance
Scope of Guideline

- ...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.
ICH Q10 PQS, Annex 2

Pharmaceutical Quality System

- Pharmaceutical Development
- Technology Transfer
- Commercial Manufacturing
- Product Discontinuation

Investigational products

GMP

Management Responsibilities

- Process Performance & Product Quality Monitoring System
- Corrective Action & Preventive Action (CAPA) System
- Change Management System
- Management Review

PQS elements

Enablers

- Knowledge Management
- Quality Risk Management
ICH Q10 PQS – Content

Chapter 1: Pharmaceutical Quality System
Chapter 2: Management Responsibilities
Chapter 3: Continual Improvement of Process Performance and Product Quality
Chapter 4: Continual Improvement of the Pharmaceutical Quality System
Chapter 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
§1 – PQS

- Introduction / Scope / Objectives
- Relationship of ICH Q10 to
  - Regional GMP Requirements, ISO Standards and ICH Q7a
  - Regulatory Approaches
- Enablers
  - Knowledge Management
  - Quality Risk Management
- Design and Content Considerations
- Quality Manual
ICH Q10 and GMP

- GMPs do not drive a *lifecycle approach* to quality
- GMPs provide guidance on the manufacture and control of pharmaceutical product
- GMPs do not address the system needed to bring a quality product to market
- GMPs address CAPA but not proactive continual improvement
- GMPs only touch on management responsibility
§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
§3 – Continual Improvement of Process Performance & Product Quality

Two major sections:
- §3.1 Lifecycle Stage Goals – 4 stages
- §3.2 PQS Elements – 4 elements
§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
§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
§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.
§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
§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.
§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
§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
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

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Potential Opportunity</th>
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<tbody>
<tr>
<td>1. Comply with GMPs</td>
<td>Compliance – status quo</td>
</tr>
<tr>
<td>2. Demonstrate effective PQS, including effective use of quality risk</td>
<td>Opportunity to increase use of risk based approaches for regulatory inspections</td>
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<tr>
<td>management principle</td>
<td></td>
</tr>
<tr>
<td>3. Demonstrate product and process understanding, including effective</td>
<td>Opportunity to facilitate science based pharmaceutical quality assessment</td>
</tr>
<tr>
<td>use of quality risk management principles</td>
<td>enable innovative approaches to process validation</td>
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<td></td>
<td>establish real-time release mechanisms</td>
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## Annex 1 - Potential Opportunities

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| 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 |
What are the benefits of implementing a Pharmaceutical Quality System (in accordance with ICH Q10)?

The benefits are:

- Facilitated robustness of the manufacturing process...
- Consistency in the global pharmaceutical environment across regions
- Enable transparency of systems, processes, organisational and management responsibility
- Clearer understanding of the application of a Quality System throughout product lifecycle
- Further reducing the risk of product failure and incidence of complaints and recalls thereby providing greater assurance of pharmaceutical product consistency and availability (supply) to the patient
- Better process performance
- Opportunity to increase understanding between industry and regulators and more optimal use of industry and regulators resources. Enhance manufacturer’s and regulators’ confidence in product quality
- Increased compliance with GMPs, which builds confidence in the regulators and may result in shorter inspections
Benefits of implementing a PQS /Q10

And by consequence

- Enable transparency of systems, processes, organisational and management responsibility
- Clearer understanding of the application of a Quality System throughout Product Lifecycle
- Enhance Manufacturer’s and Regulators confidence in product quality
- Consistency in the global pharmaceutical environment across regions
Q-IWG : Q&A Relative to PQS

- **How does a company demonstrate implementation of PQS in accordance with ICH Q10?** Through it’s documentation, processes, training/qualification, management and continued improvement efforts… in an easy and understandable way for management, staff and regulatory inspectors,…

- **Is it necessary to describe the PQS in a regulatory submission?**
  
  *No, however relevant elements of PQS,… May be referenced as part of the control strategy, as supportive information*

- **Will there be certification that the PQS is in accordance with ICHQ10?** *No*
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.
Thank you for your attention