Implementation of ICH Q8, Q9, Q10

Pharmaceutical Quality System (PQS)

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

Structure of this session

- Introductory Presentation for PQS Break out Session (10 mins)
  - Learning Objectives
  - Key Messages
- Break-out into sub groups (70 mins)
  - Training/Discussion
  - Feedback on barriers to implementation
  - Feedback on issues where further clarification is required
- Feedback from each sub-group (40 mins)

Learning Objectives

- To review the key aspects of ICH Q10
- To understand the role and responsibilities of senior management
- To determine the practical application of ICH Q10 throughout the product lifecycle
  - New products
  - Legacy products
- To demonstrate how Continual Improvement can be used to improve both product quality and the PQS itself

Key Message: What is ICH Q10?

- **ICH Q10 is a guideline on the essential elements of a PQS throughout the product life cycle**
- **ICH Q10 complements Q8 and Q9**
  - ICH Q8 - strengthens the link between development and manufacturing
  - ICH Q9 - as an enabler of the PQS
- **Implementation of PQS should provide enhanced assurance of product quality**
- **GMP is applicable to the Manufacturing part of the life cycle**
  - Manufacturing of Investigational (medicinal) Product
  - Manufacturing of commercial products

Key Message: What is ICH Q10?

- A ICH Q10 type PQS reinforces/introduces some elements e.g.
  - Link manufacturing and development (incl. feedback)
  - Continual improvement
    - Products
    - Processes
    - PQS itself
  - Role and Responsibilities of Senior Management
  - Quality Risk Management and Knowledge Management
  - Product Lifecycle
    - Development through to Discontinuation
  - Management of outsourcing and purchasing material

Key messages

- Building quality into the product during development is fundamental
- ICH Q10 is a harmonised model of a PQS based on ISO Quality Management Systems (ISO 9000 series) which reinforces GMP and introduces some elements beyond GMP
- No intent to create new regulatory expectations
- Applies to e.g.
  - Drug Substance (small molecule & biotech)
  - Drug Product
  - Enhanced and Traditionally Developed Products

Key Messages: Knowledge Management and PQS

- The company should capture and use knowledge gained during development and manufacturing using a systematic approach
  - For continual improvement of the current products as well as future products
  - Each company should consider how this is achieved
- Examples
  - QTPP may evolve during lifecycle – during development and commercial manufacture - as new knowledge is gained
  - The Control Strategy is refined during product transfer and commercial manufacturing
  - Use of prior knowledge of similar products at the manufacturing site

Key Message: The PQS should be fit for purpose

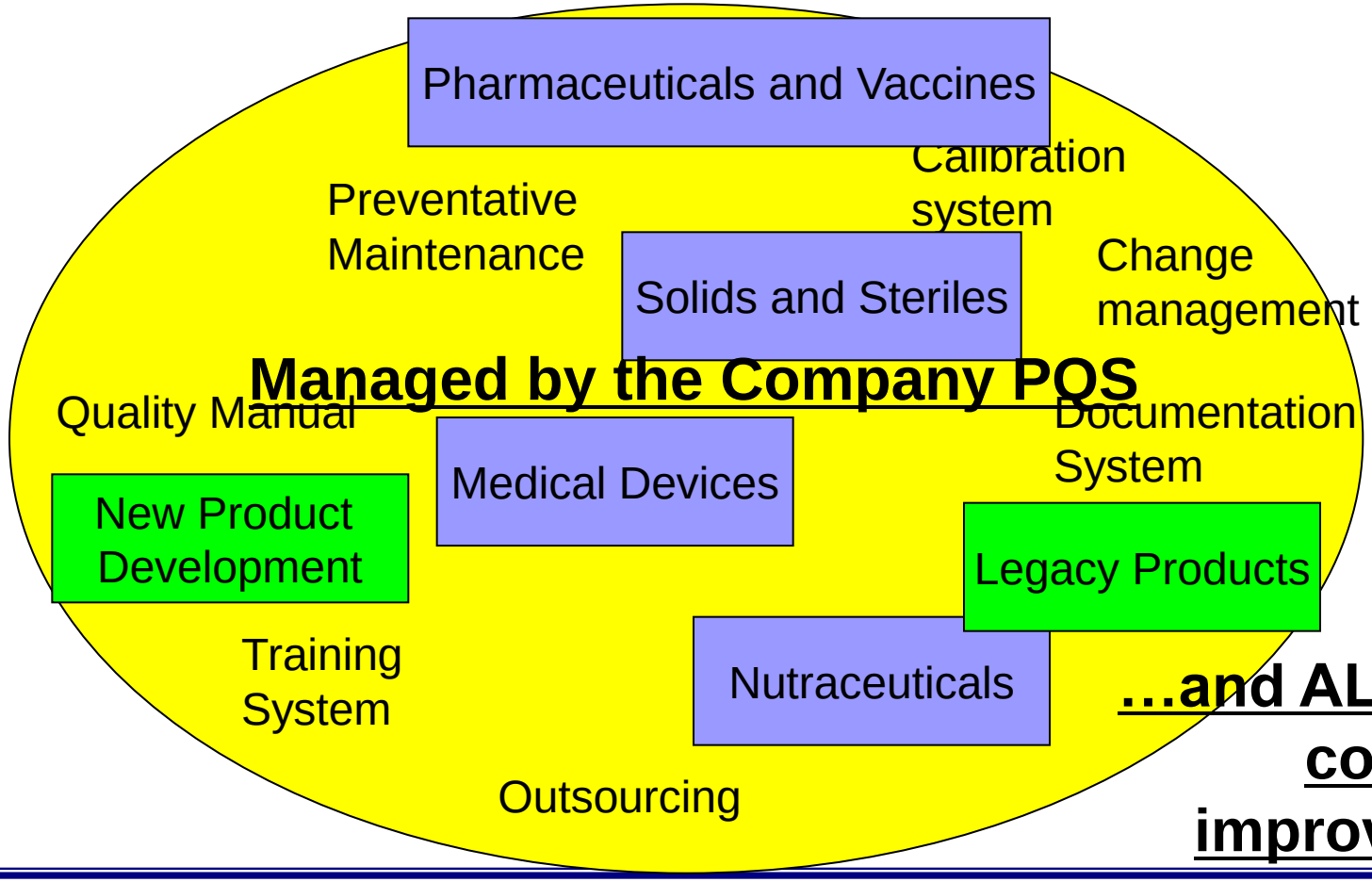
- Applied in a structured and consistent manner that is appropriate and proportionate to each of the product lifecycle stages
- Implementation of PQS/Q10 type take into account the size and complexity of the company's activities (incl. products)
- The vision, objectives, design and the implementation should be pragmatic, clear and therefore understood
  - The PQS must be linked to real practices and integrated into daily work

Breakout C: Pharmaceutical Quality System

Different Types of Products

At Different Stages of Product Lifecycle

All need 'relevant' supporting processes



…and ALL need continual improvement

Implementation of ICH Q8, Q9, Q10

PQS Breakout Sub-Group Work

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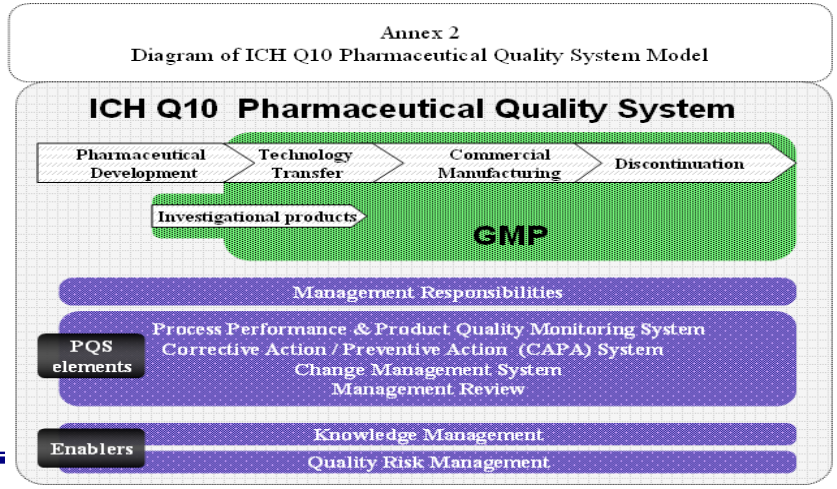
Role and Responsibilities of Senior Management

- The decision to have enhanced development approaches (QbD) reinforces the need for a strong link between quality systems in development and manufacturing
- Senior management demonstrates commitment to the PQS by :
  - Granting adequate resources to implement, support and manage the PQS
  - Communicating the importance of the PQS
  - Ensuring strong interfaces between all relevant functions e.g. Development, manufacturing, Quality Unit (QA, QC, QP), engineering, supply chain and management of outsourced activities
  - Participation in the system through the conduct of management review (including process performance), product quality reviews and the PQS itself

Concept of Product Lifecycle Covered by PQS

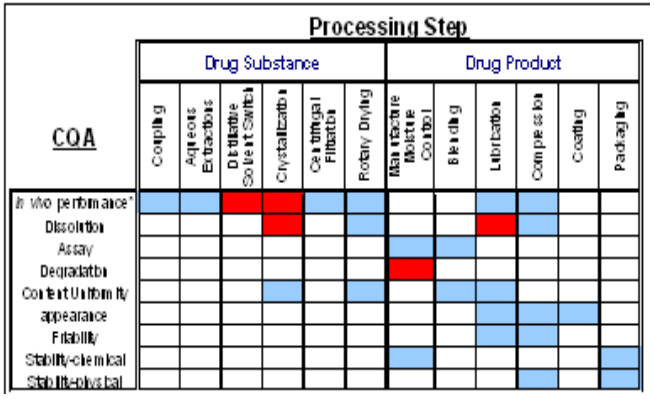
- The development of a product is done under the framework of a PQS that is appropriate and proportionate e.g.
  - This PQS should be a general system (encompassing all products) such as organisation, quality policy, general documentation e.g. procedures, records, decisions, archiving
  - At a product specific level facilitates a comprehensive understanding of development that feeds into manufacturing



PQS and Product Lifecycle
Example from case study

- Using QRM as an enabler the PQS ensured
  - The Quality Risk Management processes were performed at key stages by involvement of the right technical disciplines
  - Selection of appropriate tools respecting the different aspects of the QRM process and appropriate training
  - Defined and documented processes as required in the PQS
  - Appropriate management review

- The knowledge gained during the development process was captured and shared with manufacturing



Breakout C: Pharmaceutical Quality System

Continual Improvement of the Product

Inputs

- Manufacturing Experience
- Deviations / CAPA
- Performance Monitoring
- Customer Complaints
- Management Reviews
- Material Variance

Continual Improvement

Product Lifecycle Adjustment

- Readily achieved as part of routine feedback
- Require permanent & substantial process/facility design to improve original concept

Expanded Body of Knowledge

Feed Forward

Feedback

Product Lifecycle Management

Breakout C: Pharmaceutical Quality System

Continual Improvement of the PQS

Inputs

- PQS Processes: (e.g. Complaint, deviation, change management)
- Outsourced activities
- Self-assessment processes (audits, risk assessments, trending)
- External assessments (e.g. inspections)
- Emerging regulations
- Changes in business environment
- Product ownership

Continual Improvement

PQS Adjustment

- Improvements to PQS and related processes
  - Allocation of resources
  - Personnel training
  - Revisions to quality policy and objectives
  - Documentation
  - Communication

Expanded Body of Knowledge

Feed Forward

Feedback

PQS Management

Continual Improvement of Legacy Products

- ICH Q9 and Q10 can on their own bring advantages to legacy products
  - Traditionally developed, and extensive QC laboratory testing
- Most companies/sites manufacture legacy products and there are significant advantages to continually improve
  - Principles of ICH Q8, Q9, Q10 can be equally applied to these
    - To improve products and process understanding
    - To improve product quality and reduce waste (e.g. rejects)
    - To reduce process variability
    - To include RTRT to reduce lead times and QC testing
- There are challenges of introducing and new technologies (e.g. RTRT) to older products
  - More data = possible risk of uncovering problems/issues

Continual Improvement of Legacy Products

- However, industry must be encouraged to improve legacy products and processes
  - No sense to stay working with old technology and ways of working
  - PQS has to be able to deal with the knowledge gained from Continual Improvement of legacy products

- Industry can work with regulators to consider and corntol the risks
  - The regulators will encourage and support companies who want to improve legacy products and processes
  - Dialogue will be welcomed

Topics to discuss (1)

- Is a PQS mandatory? Is ICH Q10 mandatory?
- What is the added value for a company in implementing an ICH Q10 type PQS across the life cycle?
- What modifications to a company's existing PQS is envisaged to meet ICH Q10 intentions?
- How can Q10 type PQS facilitate in handling an enhanced development approach?
- How might a PQS support continual improvement?
- What do you see as the top 3 'high risk' elements that are managed by a PQS?
- Are there any barriers to practical implementation of an ICH Q10 type PQS?

Topics to discuss (2)

- Which PQS elements do you think are most useful in a development site?
- Is it necessary to describe PQS elements in regulatory submission (Q-CTD)?
- What is important in a PQS at the global/corporate level and at the local/site level?
- What are the key elements to settle before designing a PQS ?