Advanced approaches to assure pharmaceutical product quality - Lifecycle management

Japan Pharmaceutical Manufacturers Association (JPMA)
Quality & Technology Committee
Chairman of ICH Quality Group

Kazuhiro Okochi
Agenda

• Japan Pharmaceutical Manufacturers Association (JPMA)

• Pharmaceutical Quality System

• Change Management and Continual Improvement
Structure of JPMA

As of October 2017
Quality & Technology Committee

Chairperson: K. Kamiya (Eisai)
Q&TC (72 companies)

Executive Council
Shionogi, Daiich-Sankyo, Takeda, Astellas, Eisai,

Chairperson: Y. Ikematsu (Eisai)
GMP Expert Committee (34 companies)

Chairperson: H. Suzuki (Bayer)
Pharmaceutical Expert Committee (24 companies)

Group Leader: K. Okochi (Takeda)
ICH Q Group
<Key Activities>

- Implement surveys and studies on good manufacturing practice (GMP).
- Implement pharmaceutical manufacturing technology with subjects related to their physical properties.
- Establish and promote measures to improve reliability and quality of pharmaceutical products.
- Develop guideline(s) on quality topic(s) within the framework of International harmonization in collaboration with ICH Project.
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- Change Management and Continual Improvement
Pharmaceutical Quality System ICH Q10

ICH Q10 Pharmaceutical Quality System

Pharmaceutical Development → Technology Transfer → Commercial Manufacturing → 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

Knowledge Management
Quality Risk Management

Enablers
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Typical Change Management Process Map

Change Identification & Characterisation

Change Impact assessment

No change to perform

Review of effectiveness

Implementation of Change

Action Plan

Change Approval (Internal and/or regulatory approval)

Execution of technical steps

Described in the companies PQS
Different Change Management approaches over the Life Cycle

- **Pre-Clinical Phase**
  - Change Management local Technical R&D function

- **Clinical Phase**
  - Change Management in Development
  - Clinical Trial Application
  - Registration batches

- **Market Phase**
  - Local and corporate Change Management process
  - First regulatory Submission

Consider notification or approval according to regional regulations.
Change Management Process

• Verification by Quality Assurance
  - Consider Process understanding
  - Consider Technical Regulatory Filing
  - Link to Knowledge Management
    - Knowledge management is a systematic approach to acquiring, analysing, storing and disseminating information related to products, manufacturing processes and components.
    - Sources of knowledge include, but are not limited to prior knowledge (public domain or internally documented); pharmaceutical development studies; technology transfer activities; process validation studies over the product lifecycle; manufacturing experience; deviations, customer complaint, returns, CAPA and OOS’s assessments; continual improvement; and change management activities.
Change Management and Continuous Improvement

• Change *WILL* happen throughout the product lifecycle
  - **Proactively** due to business or technical reasons
    - Part of continuous improvement initiatives
      > e.g. new supplier, batch size change, new equipment
  - **Reactively** driven as part of CAPA
    - Due to deviations, OOS, batch rejections

• The PQS must include a *robust* change management system
  - Use of knowledge and Quality Risk Management

• Continual Improvement must be part of our daily working lives
  - Helped by data (e.g. trend data, Statistical Process Control)
  - Driven by people - as part of the culture!
Quality Assurance will:
- Verify if proposed change to operating range is within design space
- Utilise Knowledge and Process Understanding
- Ensure Manufacturing can perform the change without prior notification of health authorities
• Confirmation of successful change: e.g.

• Process Validation
  - Can be operated as a lifecycle monitoring i.e. ‘Continuous Process Verification’

• Annual Product Review (APR)
  - The effectiveness of the change is demonstrated
Continual Improvement

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

**Expanded Body of Knowledge**

**Feed Forward**

**Feedback**

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

**Continual Improvement**
Change Management and Continual Improvement

Raw Materials: Typical Historical Experience with Physicochemical Properties

- USP Limits
- R&D Development Experience
- Initial Launch Experience
- Long-Term Commercial Experience

Raw Materials
- Can be one major source of process variation – even if within the agreed specification limits
- Commercial manufacturing experience will increase our understanding of such raw material batch to batch variation over time
Continual Monitoring

Process Tracking and Trending
– Statistical Process Control
– Address trends before they become problems

Product Quality Monitoring
– Analyze parameters & attributes in the control strategy
– Reduce sources of variation

Control Limits: Derived from Historical Release

Updated Control Chart of Assay; 3 new batches

Trend Limits: Derived from Historical Stability Data

Specs

Trend Limits
Thank you!