Challenges in Implementing Knowledge Management within ICH Q10

SYMPOSIUM - New Frontiers in Manufacturing Technology, Regulatory - Brasilia

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An ICH Vision for Pharmaceutical Quality

The Regulatory System

Quality System

Quality Risk Management

Pharmaceutical Development

Existing GMP

Pharmaceutical Quality System / PQS (Q10)

Pharmaceutical Development (Q8 & Q8R)

Quality Risk Management (Q9)

Drug Substance Guidance (Q11)
Q9 Goal is to reduce patient risk

Opportunities to impact risk using quality risk management

Q8

- Design
- Process
- Materials
- Facilities

Q9

Q10

- Manufacturing
- Distribution
- Patient
Q10 Pharmaceutical Quality System PQS

Pharmaceutical Development → Technology Transfer → Commercial Manufacturing → Product Discontinuation

Investigational products

GMP

Management Responsibilities

Process Performance & Product Quality Monitoring System
Corrective Action / Preventive Action (CA/PA) System
Change Management System
Management Review

PQS elements

Knowledge Management

Enablers

Quality Risk Management

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Q10 PQS

• Q10 encompasses the entire product lifecycle and can be applied whether or not QbD is employed.
  
  – Documentation
  – Training and education
  – Outsourced activities / purchased materials
  – Control Strategy
    • Use quality risk management to establish using parameters and attributes and related facility and equipment operating conditions
  – Monitoring / Handling Quality Defects (CAPA)
    • The level of effort of the investigation should be commensurate with the level of risk.
    • Result should be product and process improvements
Q10 PQS

– Auditing / Inspection
  • For regulators
  • For companies

– Periodic review

– Change management / change control
  • Driven by innovation, continual improvement, the outputs of process performance and product quality monitoring, and CAPA
  • Level and formality commensurate with risk

– Continual improvement – an opportunity to optimize science- and risk-based post-approval change process
Recent ICH Activities

• ICH Quality Guidelines (see ICH web site for latest versions)
  – Q8, Pharmaceutical Development
  – Q9, Quality Risk Management (QRM)
  – Q10, Pharmaceutical Quality System
  – Q11, Development and Manufacture of Drug Substances

and

Quality Implementation Working Group on Q8, Q9 and Q10
  – Questions & Answers
  – Points to Consider

On-going
  – Q7 Quality Implementation Working Group
  – Q3B Expert Working Group
All ICH Quality Topics Relevant

- Q1 Stability series
- Q2 Analytical Validation
- Q3 A, B, C and D Impurities
- Q4 Pharmacopeial Harmonisation
- Q5 A to E on Biotechnology
- Q6 A and B, Specifications
- Q7 GMP for API
- M7: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk
ICH Summary

- Q8, 9 and 10 (Implementation Work Group) IWG introduced
  - Questions and Answers
  - Points to Consider
- Opportunities for industry
- Harmonisation across ICH regions
- Opportunity to move globally
  However
- Challenges for industry with implementation
“Knowledge Management”
Definition, per ICH Q10 §1.6.1

- 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
  - pharmaceutical development studies
  - technology transfer activities
  - process validation studies
  - over the product lifecycle
  - manufacturing experience
  - innovation
  - continual improvement
  - change management activities
What Q10 Calls For?

Less process/product knowledge, more flexible Quality requirements

More process/product knowledge, more stringent Quality requirements, more formalized Quality systems and procedures

Pharmaceutical Development
Technology Transfer
Commercial Manufacturing
Product Discontinuation

Integrated Quality System
Continuous Quality Oversight
Quality Inputs During Technology Transfer and Commercial Manufacturing

- Transfer Master Validation Plan
- Process Validation
- Analytics Transfer protocol/report
- Quality Agreement
- Comparability Protocols/Reports
- Change Management
- Deviations, CAPAs

- QC testing
- Lot release
- Stability Monitoring
- Annual and Periodic Product Reviews
- Product Complaints
- Field Actions
- Change Management
- Deviations, CAPA

Technology Transfer

Commercial Manufacturing
The Concept of “Quality Steward”

- An End to End view of product quality throughout the product lifecycle
- A broad understanding of Quality systems and procedures and linkages therein
- Scientific and technical knowledge to understand and assess process performance and product quality issues – strong partnership with technical SMEs
- Partnership with product supply and regulatory affairs
- Single point of contact (SPOC) for Quality functions, coordinating different Quality inputs on matrix project teams.
- Drive product specific Quality decision making
- Streamline knowledge management

Established by pharma/biotech industry leaders
Key Business Roles

- Member of the CMC team, member of the product supply team, representing “Quality”

- Liaise and coordinate amongst different Quality functions

- Lead multi-disciplinary investigations with potential product Quality impact

- Lead product specific risk assessments

- Change management agent

- Quick escalation to Quality Sr. management – Q10
Quality Steward for Development

- Requires significant level of technical and scientific knowledge
- Understands phase-appropriate GMP concepts
- Actively participates in CQA and control strategy discussions
- Proposes sampling plan and product specifications
- Manages GMP stability programs
- Leads investigations with potential product quality impact
- Quality SME for partner/CMO audits
- Responsible for relevant regulatory submissions/interactions
Quality Steward for Commercial

- Requires higher level of regulatory and compliance knowledge/experience
- Member of Product Supply Chain Team (PSCT)
- Provide assessment of overall “Product Health”
- Recommend improvement actions based on review of trends and issues

Ad Hoc Quality Sub Team Members
- Change Control Board
- Analytical Method Management
- Inspection Management
- Compliance
- Process Validation

PSCT

- PROP Finance
- PMTL Planning
- Quality Steward
- CMC RegA
- Manufacturing Science
- Operations
- PTTL DS
- PTTL DP

Product Quality Sub-team
- External Quality
- Product Complaints
- Investigations CAPA
- Stability
- QC IP/FP
- Lot Disposition
Summary Quality Steward Role

Quality Steward Role Adds Value:

- Enables coherent quality oversight
- Allows easier project hand-over from development to commercial
- Provides easier communication
- Facilitates consistent quality procedures and decision making cross products, cross sites
- Improve efficiency by separating accountability between product related decisions vs. operation related decisions

Keeping Pulse on the overall Product Health
Guide Series
Product Quality Lifecycle Implementation, from Concept to Continual Improvement
Available from www.ISPE.org

• Part 1, Product Realization using QbD, Concepts and Principles
  – Overview
  – Criticality
  – Design Space
  – Control Strategy
• Part 2, Product Realization using QbD, Illustrative Example
  – Drug product and API
• Part 3, Change Management System as a Key Element of a Pharmaceutical Quality System
• Part 4, Process Performance and Product Quality Monitoring System
Process Validation Discussion Papers

- Topic 1 – Stage 2 Process Validation: Determining and Justifying the Number of Process Performance Qualification Batches
  Comments to pvstage2@ispe.org

- Topic 2 – Stage 3 Process Validation: Applying Continued Process Verification Expectations to New and Existing Products
  Comments to pvstage3@ispe.org
• Q: Does Q10 suggest an ideal way to manage knowledge?

A: No

• Q: Is a specific computerized information management system required for implementation of KM?

A: No, but such systems can be invaluable in capturing, managing & assessing complex data and information
ICH IWG – Q10 Q&A
Excerpts on KM

• Q: Will regulatory agencies expect to see a formal* KM approach during inspections?

  A: No. However it is expected that knowledge from processes and systems is appropriately utilized

*Formal refers to a structured approach using recognized methodology or tools, executing and documenting something in a transparent and detailed manner

Find the complete Q&A at ICH Quality Guidelines
Q: Software Solutions – Is it necessary to purchase “ICH compliant” software solutions in order to successfully implement these ICH guidelines?

A: No. ICH has not, nor does it intend to, endorse any commercial products.
Closing Thoughts

• Knowledge Management is a key enabler of ICH Q10 and can help your organization realize the objectives of an effective PQS

• Effective knowledge management supports the iteration and advancement of product and process understanding as knowledge flows, grows and evolves across the lifecycle

• Your knowledge is an asset to your organization, and approaches exist to help manage as such
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