Connecting People, Science and Regulation

ICH Q7 Chapter 2:
Quality Management

PDA - PIC/S
ICH Q7 Training 01/2014

Disclaimer

- **The slides set is based on the training sessions developed and performed by the members of the ICH Q7 Expert Working Group (EWG) on ICH Q7 2001/2002**
- **The slides have been updated 2012 and represents the views of the PDA / PIC/S committee for the purposes of a general training for regulators and industry.**

◆ ***We focused on elements in ICH Q7 where further explanation and/or clarification is useful.***

Content

- **Principles** *(2.1)*
- **Responsibilities of the Quality Unit** *(2.2)*
- **Responsibility for Production Activities** *(2.3)*
- **Internal Audits (Self Inspection)** *(2.4)*
- **Product Quality Review** *(2.5)*

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2.1 Principles

- **Quality should be the responsibility of ALL** *(2.10)*
  - *Involving senior management*
- **A quality system is needed** *(2.11)*
  - *Consider ISO 9001 and ICH Q10*

2.1 Principles

- **Independence of Quality Unit(s)** *(2.13)*
  - *The Quality Unit should not report to the manufacturing director*
  - *At some (e.g. corporate) level in the organisation quality and production may report into the same person. This should be at a adequately senior level that does not actively influence quality decisions*
- **All activities recorded at the time performed** *(2.15)*
  - *Quality systems should be capable of monitoring occasions where records are not completed at the time activities are performed*

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2.1 Principles

- **Release of Materials**
  - Persons authorized to release intermediates and APIs should be specified *(2.14)*
  - API released to third parties only after release by QU

  - *There might be local / regional requirements on the education / training / experience for persons authorized to release*

2.1 Principles

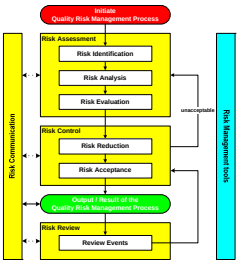
- **Release Under Quarantine**
  - No materials released or used before satisfactory completion of evaluation by Quality Unit (QU) *(2.17)*
    Unless appropriate systems in place to allow for such use
  - May be transferred under quarantine to another unit under company control when authorized by QC with appropriate controls / documentation *(10.20)*
    - *Appropriate controls e.g. technical quality agreements, acceptance by the receiving site having appropriate systems in place*
    - *Local expectation have to be considered (e.g. shipment under quarantine is not allowed to units outside the company)*

2.1 Principles

- **Definition: Critical**
  - Describes a process step, process condition, test requirement, or other relevant parameter or item that must be controlled within predetermined criteria to ensure that the API meets its specification *(Glossary)*
- **Deviations**
  - Deviations documented and explained *(2.16)*
  - Critical deviations investigated and documented *(2.16)*
    - *Modern Quality Systems (e.g. ICH Q10) expect to address critical deviations appropriately (e.g. root cause analysis, CAPA, trending)*
    - *The level of effort should be in line with the significance of the issues*

Quality Risk Management

- *There are regional requirements to include the principles given in ICH Q9 to the Quality Management section of Q7*



- **The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient**
- **The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk**

2.2 & 2.3 Responsibilities

- **Responsibility for Production Activities** *(2.3)*
  - Intentionally did not refer to “Production Unit”
  - Depending on company some of these functions are performed by production, engineering, technical maintenance, etc
  - Did not want to impose organizational structure
- **Responsibilities of the Quality Unit** *(2.2)*
  - Involved in all quality-related activities *(2.20)*
  - Review and approve all quality related documents *(2.21)*
  - Non-delegatable activities *(2.22)*

2.2 & 2.3 Responsibilities

Clarification of terms

- **Release**
  - Final authority
- **Review and approval**
  - Authority but this may be shared authority
  - More than one group or person may be required to review and approve
- **Assuring (making sure) that other group performs functions and quality oversees or checks**

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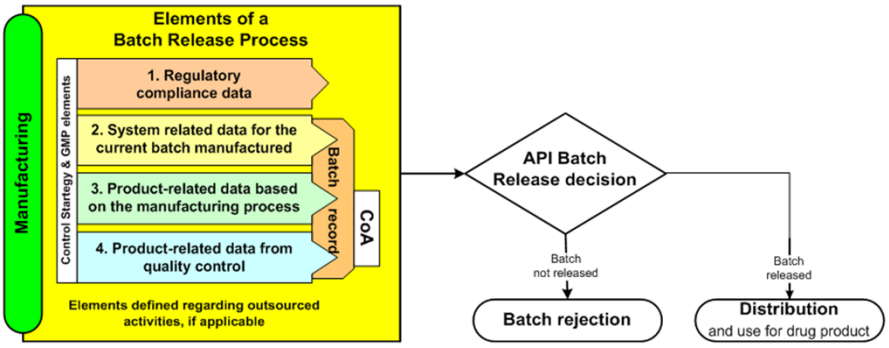
2.2 & 2.3 Responsibilities

Process for a batch release decision



CoA: Certificate of Analysis or batch by batch production; CoC: Certificate of Conformity to a specification
e.g. continuous process, PAT application 'complies, if tested and meets specification'

Based on ICH Q-IWG Points to Consider, 2011

2.2 Responsibilities of the QU

- **Responsibilities that should NOT be delegated** *(2.22)*
  - Releasing or rejecting all APIs
  - Releasing or rejecting intermediates for use outside the control of the manufacturing company
    - *'Manufacturing Company' = part of one organisation. There must be adequate systems in place to control the shipment of the materials*

2.2 Responsibilities of the QU

- **Responsibilities that should NOT be delegated** *(2.22)*
  - Reviewing completed batch production and lab control records of critical process steps before release of the API
    - *Consider situations such as non isolated intermediates allowing delegation with appropriated controls*
    - *Companies should have scientific justification on steps that are non-critical to the final API quality*
  - Performing product quality reviews
    - *Technical details (e.g. collection of data) may be responsibility of others*

2.2 Responsibilities of the QU

- **Responsibilities that should NOT be delegated** *(2.22)*
  Making sure that
  - Critical deviations are investigated and resolved
  - Internal audits are performed
    - *The corrective actions should be implemented*
  - Effective systems are used for maintaining and calibrating critical equipment
  - Materials are appropriately tested and the results reported
  - There is stability data to support retest or expiry dates and storage conditions

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2.2 Responsibilities of the QU

- **Responsibilities that should NOT be delegated** *(2.22)*
  Approving
  - All specifications and master production instructions
  - All procedures impacting the quality of APIs or intermediates
  - Contract manufacturers
  - Changes that potentially impact the quality of APIs or intermediates
  - Validation protocols and reports

2.4 Internal Audits

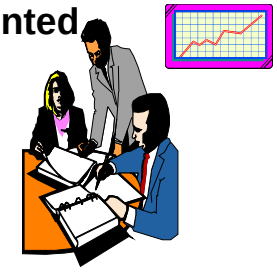
- **To verify compliance with the principles of GMP for APIs** *(2.40)*
  - *Besides compliance with GMP consider to verify compliance with the registration file*
- **Performed regularly in accordance with an approved schedule** *(2.40)*
  - *The auditors have to be independent of the area being audited.*
  - *It is important to audit the design of the systems and compliance with this systems*
  - *The regularity should be defined on risk-based principles and established in written procedures including a justification*
    e.g. 1-2 years, however should not go beyond 3 years (unless defined in regulations)

2.4 Internal Audits

- **Audit findings and corrective action** *(2.41)*
  - Documented
  - Brought to attention of responsible management
  - Corrective actions completed in timely and effective manner *(2.41)*
    - *A system to manage and track actions is necessary (consider formality)*

2.5 Product Quality Review

- **Regular quality review to verify the consistency of the process** *(2.50)*
  - PQR should address the performance on the site level. An End-to-End overview might be helpful for the overall quality performance
- **Normally conducted and documented annually** *(2.50)*
- **Results should be evaluated and an assessment made of need for corrective action or revalidation** *(2.51)*



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2.5 Product Quality Review

- **Review should include *at least*** *(2.50)*
  - Critical in-process controls and critical API test results
  - Batches failing specifications
  - Critical deviations or non-conformances
  - Changes to process, *equipment* or analytical methods
  - Results of stability monitoring program
  - Quality related returns, complaints, recalls
  - Adequacy of corrective actions
- *Typically there should be some element of trending of data, if applicable*

Key Messages

- **Quality and Production Complementary Responsibilities**
  - Some similarities, but intentional differences

Quality Unit	Production
Approving all specifications and master production instructions	Preparing, reviewing, approving instructions for the production of APIs and intermediates

Key Messages

- **Quality and Production Complementary Responsibilities**

Quality Unit	Production
Reviewing completed manufacturing records for critical process steps before release of API for distribution	Reviewing all production records and ensuring these are completed and signed
Making sure that effective systems are used for maintaining and calibrating critical equipment	Making sure that the necessary calibrations, qualification, validations are performed and records are kept

Key Messages

- **Quality need to be independent of production**
- **Quality units**
  - Some tasks can be delegated
  - Some responsibilities should NOT be delegated
- **Internal Audits**
  - Performed regularly, document Audit findings and implement corrective action
- **Product Quality Review**
  - An opportunity to confirm that the overall product performance is under control and to review risks

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Acknowledgement

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PDA
Parenteral Drug Association
PIC/S