Connecting People, Science and Regulation

# ICH Q7 Chapter 6: Documentation and Records

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 are useful.***

## Content

- **Documentation System and Specifications** *(6.1)*
- **Equipment Cleaning and Use Record** *(6.2)*
- **Records of Raw Materials, Intermediates, API Labeling and Packaging Materials** *(6.3)*
- **Master Production Instructions** *(6.4)*
- **Batch Production Records** *(6.5)*
- **Laboratory Control Records** *(6.6)*
- **Batch Record Review** *(6.7)*



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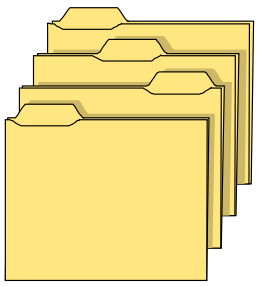
Chapter 6: Documentation and Records

## 6.1 Doc System & Specifications

- **Should have procedures to describe**
  - Issuance, review, approval and distribution of documents *(6.10 / 6.11)*
  - Revision history *(6.12)*
  - Record retention
    - Documents can be in paper or electronic form



# 6.1 Doc System & Specifications

- **Record retention** *(6.13, 6.15)*
  - **What?**
    - Production records, Control records, Distribution records
  - **How long?**
    - At least 1 year after expiry date
    - At least 3 years after complete distribution of the batch for APIs with retest date

◆ *Legal provisions and/or costumer requirements may require a longer retention period to ensure availability of API records along the life of the drug product*



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# 6.1 Doc System & Specifications

- **Record retention** *(6.13-6.16)*
  - Records may be retained as originals or true copies (accurate reproductions)
  - Originals or copies should be available at the establishment where the activity occurred
  - Prompt retrieval from another location by electronic or other means is acceptable
  - If reduction techniques (microfilm) or electronic records are used, suitable retrieval equipment and means to produce hard copy should be readily available

◆ *Maintain the capability to read the records (e.g. IT)*

# 6.1 Doc System & Specifications

- **Entries in records should** *(6.14)*
  - Be indelible
    *(incapable of being removed, erased or washed away)*
  - Made in spaces provided
  - Made directly after performing the activity (2.15)
    - *Back dated data question the reliability of all data*
  - Identify the person making the entry
    - *It is a good practice a second person checking the raw data and the completed record*





# 6.1 Doc System & Specifications

- **Corrections** *(6.14)*
  - Leave the original entry readable
  - Dated
  - Signed
    - *Anything more than obvious corrections there should be an explanation of the why.*

## 6.1 Doc System & Specifications

- **Signature can be** *(6.14)*
  - Full handwritten signature
  - Authenticated and secure electronic signature
  - Initials

- *Initials are preferably unique to individuals*
- *A correlation list is needed to retrieve the full name*

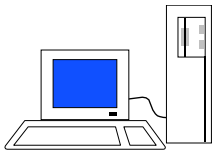




## 6.1 Doc System & Specifications

- **Electronic signatures (if used) should be** *(6.18)*
  - Authenticated
  - Secure

- *An electronic signature should be equivalent security to a pen signature (e.g. unique to the individual)*



## 6.2 Equip Cleaning & Use Record

- **Records of major equipment** *(6.20)*
  - Use
  - Cleaning
  - Sanitization and / or sterilization (if performed)
  - Maintenance

◆ *Unique records per major equipment has shown to be helpful*

◆ *Traceability should also be available to auxiliary equipment*



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## 6.2 Equip Cleaning & Use Record

- **These records should include** *(6.20)*
  - Date
  - Time (if appropriate)
  - Product

◆ *including the manufacturing step*

  - Batch number
  - Person performing cleaning and maintenance

◆ *Note: Making sure that the premises and equipment are maintained and records kept (2.3-7)*

## 6.2 Equip Cleaning & Use Record

- **Dedicated equipment** *(6.21)*
  - Individual equipment records not necessary if batches follow in traceable sequence
  - Records of cleaning, maintenance and use can be part of batch record or maintained separately

◆ *Attention should be given to auxiliary equipment*





## 6.3 Records of Materials

- **For raw materials, intermediates, API packaging and labelling** *(6.30)*
  - Name of manufacturer
  - Identity and quantity of each shipment of each batch
  - Name of supplier
  - Supplier's control number or identity number
  - Number allocated on receipt
  - Date of receipt

## 6.3 Records of Materials

- **For raw materials, intermediates, API packaging and labelling** *(6.30) (cont.)*
  - Results of any test or examination and conclusion
  - Records tracing use
  - *Attention should be given on dispensing activities and with tailings*
  - Final decision regarding rejected materials
  - Master (approved) labels should be maintained for comparison to issued labels *(6.31)*





## Clarification of terms

- **Master Production Instruction**
  - Master recipe or SOP
- **Batch Production Record**
  - Record of actual batch produced
  - *No single preferred or correct system*
    - *Some companies include the blanks to be completed in the Master Instruction so that instructions and results are one document*
    - *Some companies have instruction as one document and then a separate very short document for recording results*
  - *Pay attention in case of updates of individual documents and other affected documents including registration filing*

# 6.4 Master Production Instructions

- **A Master Production Instruction should include** *(6.41)*
  - Name of intermediate or API being manufactured
  - Identifying document reference code
  - Complete list of raw materials and intermediates
  - Accurate statement of the quantity or ratio of each material to be used (including unit of measure)
  - Major production equipment to be used
  - Special notations or precautions ◆ *(e.g. safety instructions)*
  - Instructions for storage of intermediate or API where appropriate



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# 6.4 Master Production Instructions

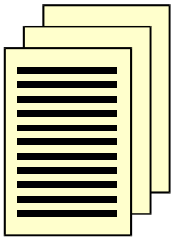
- **A Master Production Instruction should include**
  - Detailed production instructions
    - Sequences to be followed
    - Ranges of process parameters
    - Sampling instructions
    - In-process controls with acceptance criteria
    - Time limits
    - Expected Yield

      ◆ *The quantity of material or the percentage of theoretical yield anticipated at any appropriate phase of production based on previous laboratory, pilot scale, or manufacturing*

    ◆ *Separate Master Production Instructions (Master Batch Record) are needed for rework / reprocessing*

## 6.5 Batch Production Records

- **Should be prepared for each intermediate and API** *(6.50)*
- **Should include complete information relating to production and control of the batch** *(6.50)*







## 6.5 Batch Production Records

- **Prior to issuing for use** *(6.51)*
  - Checked that it is the correct version and a legible accurate reproduction of the master
  - Numbered with a unique batch or identification number, dated and signed

◆ *In case of an update of the Master Production Instructions ensure the unused copies of the older version are destroyed*

# 6.5 Batch Production Records

- **Documentation of completion of each significant step should include** *(6.52)*
  - Dates
  - Times, when appropriate
  - Identity of major equipment
  - Specific information for each material used
    - Weights or amount
    - Batch or identification number

◆ *In continuous production, the product code, date and time can serve as the unique identifier until final number is allocated*



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# 6.5 Batch Production Records

- **Documentation of completion of each significant step should include** *(6.52)*
  - Actual results for critical process parameters
    - ◆ *Highlight critical parameters in the batch record in an appropriate manner*
  - Sampling
  - Signatures of persons
    - Performing each critical step in the operation
    - Directly supervising or checking critical step
  - In-process or lab test results
  - Actual yield

## 6.5 Batch Production Records

- **Documentation of completion of each significant step should include** *(6.52)*
  - Description of packaging and label
  - Representative label
  - Results of release testing
  - Any deviation noted
  - Investigation (if appropriate)
    - *Critical deviations should be investigated*
    - *Initiate investigations in a timely manner*
    - *Investigation should extend to other batches that may be associated*





## 6.6 Laboratory Control Records

- **Complete data from all tests conducted** ***(6.60)***
- **Description of sample** ***(6.60)***
  - Material name or source
  - Batch number or other distinctive code
  - Date taken
  - Quantity and date received for testing (where appropriate)
- **Reference to test method used** *(6.60)*
- **Weight or measure of sample used** *(6.60)*

## 6.6 Laboratory Control Records

- **Data on preparation and testing of** *(6.60)*
  - Reference standards, Reagents, Standard solutions
- **Complete record of raw data generated in addition to graphs, charts, and spectra** *(6.60)*
  - *Manage the transcription of data into an electronic system (e.g. LIMS) by appropriate controls*
  - *Traceability to the reference standard / spectrum used*
  - *There must be a clear and permanently recorded audit trail of any ammentments to raw electronic data*
- **Record of calculations including** *(6.60)*
  - Units of measure, Conversion factors, Equivalency factors





## 6.6 Laboratory Control Records

- **Statement of test results and comparison with acceptance criteria** *(6.60)*
- **Signature of person who performed each test** *(6.60)*
- **Date the test was performed** *(6.60)*
- **Date and signature of person reviewing for** *(6.60)*
  - Accuracy
  - Completeness
  - Compliance with established standards

## 6.6 Laboratory Control Records

- **Any modification to an analytical method** *(6.61)*
  - *Handle under change control*
- **Calibration of lab instruments** *(6.61)*
  - *Consider difference on 'calibration' versus 'verification' in a daily operations*
  - *Contractors should follow the companies procedures*
- **Stability testing on APIs** *(6.61)*
- **Out of specification (OoS) investigations** *(6.61)*





## 6.7 Batch Records Review

- **Review of batch production record and lab control records before batch is released or distributed** *(6.70)*
  - According to written procedure
  - Any deviations, investigations or OoS should be included in this review
    - *... and conclude before release*
- **Review by quality unit for critical process steps** *(6.71)*
- **Non-critical process steps may be** *(6.71)*
  - Reviewed by qualified production personnel
  - Following procedures approved by quality unit
    - *Independency of the review must be given*

## 6.7 Batch Records Review

- **Quality unit is responsible for releasing or rejecting all APIs** *(Section 2.22-1)*
- **Quality unit can delegate to production the authority for release of intermediates** *(6.73)*
  - Except intermediates that are sold ("*shipped outside the control of the manufacturing company*")





## Key Messages

- **Documents need to be managed: issued, distributed, when and where used, reviewed, archived etc.**
- **Documentation system needs to be described and maintained appropriately**
  - Equipment, Cleaning & Use Record
  - Records of Materials
  - Master production instructions, batch record and batch record review
  - Laboratory Control Records

# Acknowledgement


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