






# ICH Q7 Chapter 19: APIs for Use in Clinical Trials



PDA - PIC/S  
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ICH Q7 Training  
Chapter 19: APIs for Use in Clinical Trials





## 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.*

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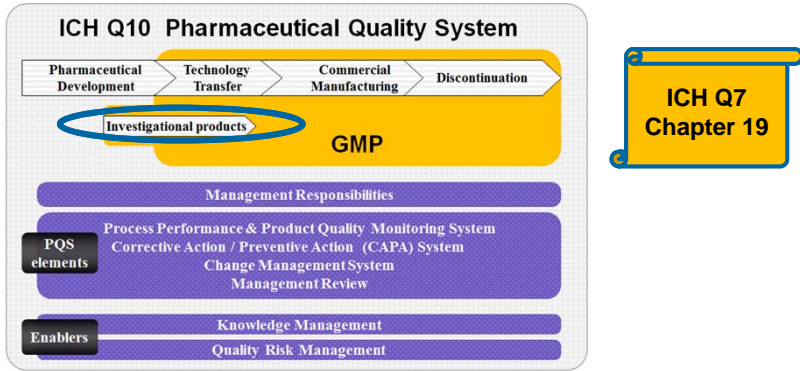
- **General (19.1)**
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## APIs For Use In Clinical Trials

- **This is nearly a stand-alone chapter**



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## APIs For Use In Clinical Trials

- **Why is there a special section on APIs for clinical use?**
  - Processes and controls change during development
  - Few batches may be produced identically
  - Batches are frequently produced in small non-commercial scale equipment
- **Addresses unique circumstances related to production of APIs for clinical use**



## 19.1 General

- **Controls should be consistent with stage of development of drug product incorporating the API** (19.11)
- **Process & test procedures should be flexible to provide for changes during development** (19.11)
- **Clinical use material should be manufactured in suitable facilities using appropriate procedures to ensure API quality** (19.11)
  - ◆ *Control and use should be proportionate to the risk of patient safety*



## 19.2 Quality

### Standard

Appropriate GMP concepts should be applied with suitable mechanism of batch approval (19.20)

Quality unit independent from production for approval / rejection of batches (19.21)

Some testing functions can be performed outside of quality unit (19.22)

### Expectation

*Controls expected for commercial batches may be inappropriate*

*Other quality functions may be performed by production (Section 2.2)*

*R & D frequently performs testing*



## 19.3 Equipment and Facilities

- **During all phases of clinical development, procedures should be in place to ensure (19.30)**
  - Equipment is calibrated, clean and suitable for its intended use
  - Materials are handled in a manner that minimizes the risk of contamination and cross-contamination





## 19.4 Control of Raw Materials

- **Raw materials should be evaluated (19.40)**
  - By testing or
  - Received with a suppliers Certificate of Analysis (CoA) and subjected to identity testing (*see also 7.30*)
- **CoA should suffice for hazardous materials (19.40)**
- **In some instances, suitability can be based on acceptability in small-scale reaction (use testing) (19.41)**



## 19.5 Production

- **Documented in lab notebooks, batch records or other appropriate means (19.50)**
- **Documents should include information related to materials, equipment used, processing and scientific observations (19.50)**
- **Expected yields can be more variable and less defined than commercial process yields (19.51)**

◆ *Investigations into yield variations are not expected*



## 19.6 Validation

- **Process validation normally inappropriate because of (19.60)**
  - Process changes during API development
  - Production of a single or limited number of API batches
- **Combination of controls, calibration, and where appropriate, equipment qualification, ensures API quality during the development phase (19.60)**



## 19.6 Validation

- **Process validation should be conducted in accordance with Section 12 on process validation when batches are produced *for commercial use, even when such batches are produced on a pilot or small scale* (19.61)**





## 19.7 Changes

- **Changes expected during development as knowledge is gained and production is scaled up (19.70)**
- **Changes in production, specifications, test procedures *should be adequately recorded* (19.70)**

◆ *The level of effort and formality of change controls are not equivalent to those expected for commercial material (Section 13)*



## 19.8 Laboratory Controls

- **Analytical methods should be scientifically sound, but need not be validated (19.80)**
- **Sufficient quantity of reserve samples for each batch should be retained for appropriate time period after (19.81)**
  - Approval
  - Termination
  - Discontinuation of an application



## 19.8 Laboratory Controls

- **Expiry and retest dating not expected in early stages of clinical development but is expected for existing APIs used in clinical trials (19.82)**
  - ◆ *Stability studies not normally performed for development batches*
  - ◆ *Stability studies for registration often conducted simultaneously with development*
  - ◆ *It may be necessary to consider testing prior use for formulation if there is no retest / expiry date specified*



## 19.9 Documentation

- **Systems should be in place to (19.90)**
  - Ensure information obtained during development and manufacturing is documented and available
  - Retain production and control records for an appropriate period after approval, termination, or discontinuation of an application
  - ◆ *Records should be available at the place of manufacturing e.g. for inspections (i.e. retrievable to that location)*
  - ◆ *Regional requirement for record keeping have to be considered and might be as longer than for commercial*





## 19.9 Documentation

- **Development and implementation of analytical methods for release of API batches for use in clinical trials should be appropriately documented (19.91)**



## Key Messages

- **GMPs for APIs on investigational medicinal products need to be risk based**
- **Unique circumstances are**
  - Processes and controls change during development
  - Few batches may be produced identically
  - Batches are frequently produced in small non-commercial scale equipment



## Acknowledgement

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