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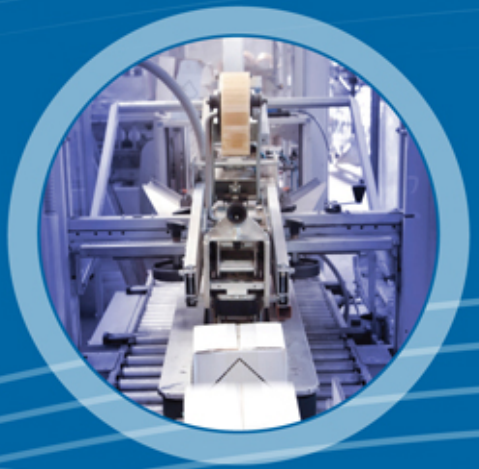
ICH Q7 Chapter 19: APIs for Use in Clinical Trials



PDA - PIC/S ICH Q7 Training

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APIs For Use In Clinical Trials

- This is nearly a stand-alone chapter

ICH Q7 Chapter 19

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	Expectation
Appropriate GMP concepts should be applied with suitable mechanism of batch approval *(19.20)*	*Controls expected for commercial batches may be inappropriate*
Quality unit independent from production for approval / rejection of batches *(19.21)*	*Other quality functions may be performed by production (Section 2.2)*
Some testing functions can be performed outside of quality unit *(19.22)*	*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

ICH Q7 QaA *Clarification of Uncertainties*

1. Is it permitted to use the same equipment to manufacture materials to be used in pre-clinical and clinical trials?

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