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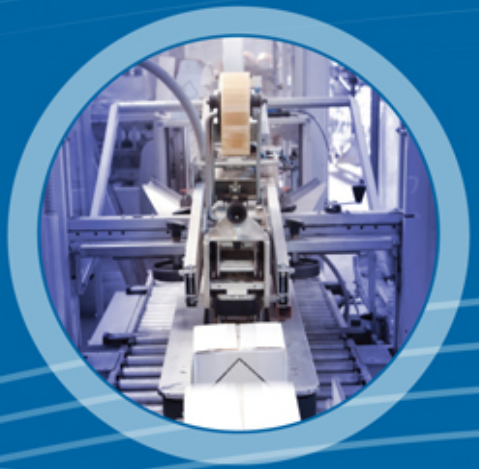
ICH Q7 Chapter 4:
Buildings and Facilities



PDA - PIC/S ICH Q7 Training

Content

- **Design and Construction** *(4.1)*
- **Utilities** *(4.2)*
- **Water** *(4.3)*
- **Containment** *(4.4)*
- **Lighting** *(4.5)*
- **Sewage and Refuse** *(4.6)*
- **Sanitation and Maintenance** *(4.7)*

4.1 Design & Construction

- **Designed to accommodate different processes and to protect operators**
  - *There are also other drivers to design equipment to accommodate different controls (e.g. environment)*

4.1 Design & Construction

- **Where equipment itself provides adequate protection to material, it may be located outdoors** *(4.12)*
  - *Careful consideration on the environmental and weather impact on equipment located outdoors*

4.1 Design & Construction

- **Buildings & facilities should be designed and constructed** *(4.10)*
  - To facilitate cleaning and maintenance
  - To minimize potential contamination
  - With adequate space and flow of materials and Personnel to prevent mix-ups and contamination
  - Where microbiological specifications are established: limit exposure to objectionable microbiological contaminants

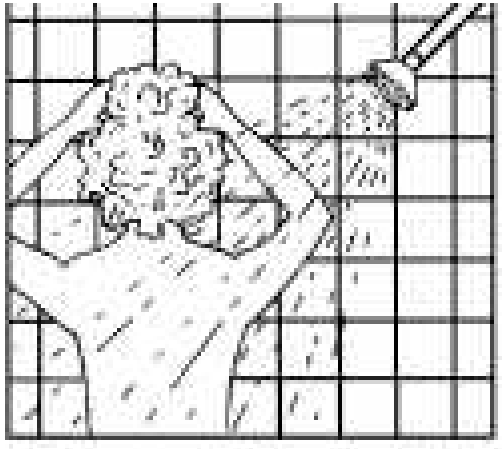
- *When transferring products consider the needs on equipment at the receiving site. It might be necessary to review the design of the existing facility*

4.1 Design & Construction

- **Defined areas or other control systems for** *(4.14)*
  - Receipt, ID, sampling, quarantine of incoming materials
  - Quarantine before release or rejection of intermediates and APIs
  - Sampling of intermediates and APIs
  - Holding rejected materials
  - Storage of released materials
  - Production operations
  - Packaging and labeling operations
  - Laboratory operations - normally separated from production areas: o.k.; in production area if lab measurements not adversely affected and lab does not adversely affect production

4.1 Design & Construction

- **Washing and toilet facilities for personnel separate from manufacturing areas should be easily accessible and include** *(4.15)*
  - Hot and cold water, as appropriate
  - Soap or detergent
  - Air dryer or single-service towels



- *Washing and toilet facility should be located (and used) where they will not affect product quality*

4.2 Utilities

- **Utilities that could impact quality** *(4.20)*
  - **Product contact: Steam, gases, compressed air, HVAC**
    - Qualified and appropriately monitored
    - Action taken when limits exceeded
- **Utility systems drawings available** *(4.20)*

The potential impact on the product quality needs to be understood

Typically the API should be isolated in an environment similar to that in which it would be handled in a dosage form facility

4.2 Utilities

- **Adequate ventilation, air filtration, exhaust systems (where appropriate)** *(4.21)*
  - To minimise risk of contamination & cross-contamination
  - To include equipment for control of air pressure, microorganisms (if appropriate), dust, humidity, & temperature appropriate to stage of manufacture

- *Separate exhausting streams from intake streams*
- *Consider monitoring 'at rest' and in operation and restart of the ventilation system*

4.2 Utilities

- **Appropriate measures to control risk of contamination & cross-contamination from recirculated air** *(4.22)*
- **Particular attention to areas where API exposed** *(4.21)*

ICH Q7 does not define the GMP standards that utilities should meet. Best practice documents from industry associations (base line guidance, technical reports or technical standards etc.) are available describing appropriate measures such as: selection of suitable filters, ratio of returned/fresh air, clean up time, air pressure differences etc.

4.2 Utilities

- **Permanent pipework appropriately identified** *(4.23)*
  - ID, documentation, computer control or other
- **Drains equipped to prevent back-siphonage** *(4.24)*

- *Sanitisation is possible to avoid microbial growth*

4.3 Water

- **Water demonstrated as suitable for intended use** *(4.30)*
- **Process water meets WHO guidelines for potable/drinking water quality** ◆ **at minimum** *(4.31)*

◆ *Full testing is necessary monitored by*
a) the supplier and data available to the manufacturer (e.g. city water) or
b) the company itself (at the point of receiving for city water / own well)

◆ *The frequency of tests should be consistent with seasonal variations*

- **If process water treated to achieve defined quality, process validated and monitored with appropriate action limits** *(4.33)*

◆ *Sampling is usually done at the point of use*

4.3 Water

- **If potable water is insufficient to assure API quality and tighter chemical and/or microbiological specs are needed. Specifications may be established for** *(4.32)*
  - Physical/chemical attributes
  - Total microbial counts
  - Objectionable organisms
  - Endotoxins

- *A rational of using different water quality at different manufacturing steps shall be justified*
- *Typically at the final processing step of the API 'purified water' is used to ensure consistency of quality*

4.4 Containment

- **Dedicated production areas for highly sensitizing material (e.g. penicillin, cephalosporins)** *(4.40)*
  - Includes air handling and/or processing equipment
- **Dedicated areas considered for infectious, high pharmacological activity, high toxicity materials** *(4.41)*
  - Unless validated inactivation and/or cleaning procedures

A dedicated production area may be required where the process can not be contained in safe limits required. This should be determined based on Quality Risk Management principles (ICH Q9) taking into account e.g. the toxicity, potency, sensitizing nature and carry over limits.

4.4 Containment

- **Appropriate measures to prevent cross-contamination from personnel & materials movements across dedicated areas** *(4.42)*
  - *Consider appropriate pressure differences between rooms / corridors*
  - *Consider separation of gowning areas, equipment, flow of material, corresponding ancillary areas such as washing machines for clothes, canteen etc. for different facilities*
- **Activities involving highly toxic non-pharmaceuticals should not be in buildings and/or equipment used for APIs** *(4.43)*

4.5 - 4.7 Lighting, Sewage & Refuse, Sanitation, Maintenance

- **Adequate lighting** *(4.50)*
- **Waste removed in timely manner** *(4.60)*
  - Waste containers clearly identified ◆ and segregated
- **Buildings maintained and kept clean** *(4.70)*
- **Procedures for facility sanitation** *(4.71)*
  - Including cleaning schedules, methods, equipment, materials, ◆ *procedure addressing spillage*
- **Procedures for use of pest control agents and cleaning/sanitizing agents to prevent contamination** *(4.72)*

◆ *Avoid using open pest control devices in clean rooms*

Key messages

- **Difference in design, features, and level of control necessary for API facilities compared to the manufacture of final dosage forms**
  - *Final isolation and filling of APIs are likely to be more similar to those for handling starting materials in drug product facilities*
- **Controls for APIs that could be sensitizing, toxic, or require microbial control will be different**

Key Messages

- **Designed to accommodate different processes and to protect operators**
  - Controls are most critical when API systems are open
- **Focus on utilities that could impact quality**
  - Product contact: Steam, gases, compressed air, HVAC
- **Prevent cross-contamination from personnel & materials**
  - Appropriate containment

ICH Q7 QaA *Clarification of Uncertainties*

1. When are dedicated production areas expected?
2. To what extent can quality risk management be used in establishing appropriate containment measures to prevent cross-contamination?

ICH Q7 Q&A, 2015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