Design and Construction of a Pharmaceutical Facility

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Design and Construction of a Pharmaceutical Facility must consider Good Manufacturing Practices

Good Manufacturing Practices are the basis of the WHO Prequalification Program

Premises

Part One

Premises

Principle

Important aspects to be kept in mind to ensure the suitability of the operations to be carried out for different dosage forms and product range:

- Location
- Design
- Construction
- Adaptation
- Maintenance

Premises

Location

- Geography, climate, noise and economic factors
- Neighbours

  What do they do?
  What impact can they have on the business?
- Pollution/effluent control
- Minimum risk for contamination of products

Premises

Principle

- Premises must be located to minimize risks of cross-contamination, e.g. **not** located next to a malting factory with high airborne levels of yeast

Premises

General

The layout and design should aim to:

- Minimize risks of errors
- Permit effective cleaning
- Permit effective maintenance
- Avoid cross-contamination, build-up of dirt and dust
- Avoid any adverse effect on the quality of products

Premises

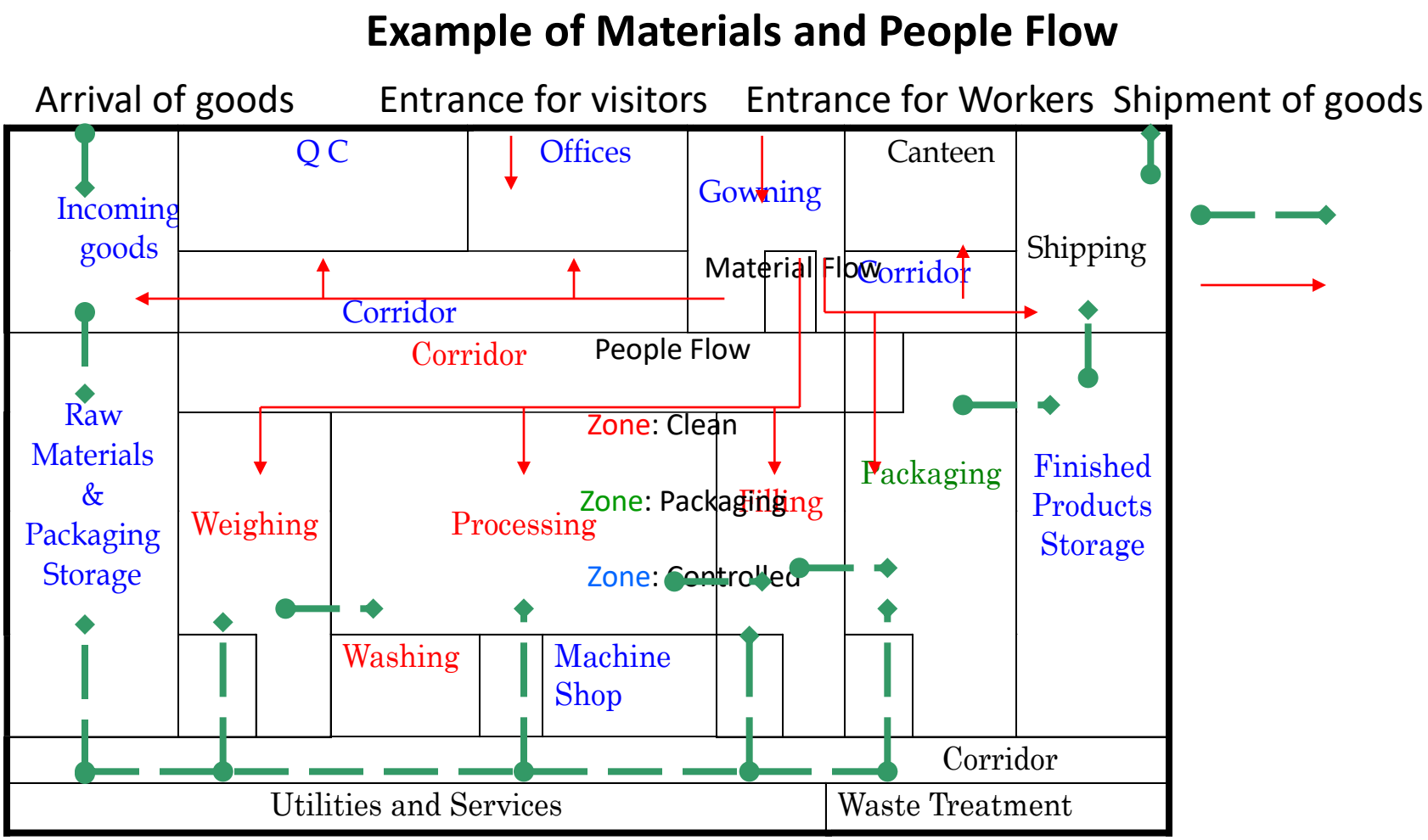
Design Principles

Keep in mind:

- Material flow
- People flow
- Process flow

Ensure logical flow

Premises


Example of Materials and People Flow
Arrival of goods
Entrance for visitors
Entrance for Workers
Shipment of goods
Q C
Offices
Gowning
Canteen
Incoming goods
Material Flow
Corridor
Shipping
Corridor
Corridor
People Flow
Raw Materials & Packaging Storage
Zone: Clean
Zone: Packaging
Zone: Controlled
Weighing
Processing
Filling
Packaging
Finished Products Storage
Washing
Machine Shop
Corridor
Utilities and Services
Waste Treatment

Premises

Design

- Suitable design and construction to facilitate good sanitation
- Cleaning and disinfecting according to detailed written procedures – records maintained
- Maximum protection against entry of insects, birds and animals
- Procedure for rodent and pest control

Premises

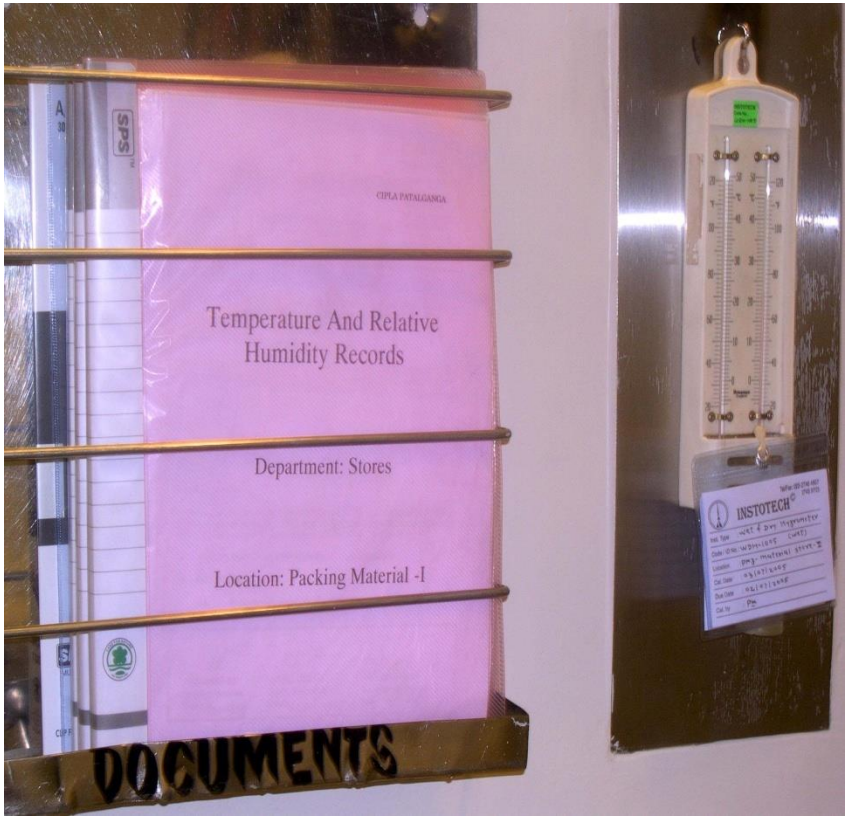
Construction

- Suitable materials
- Electrical supply
- Suitable lighting (especially for visual on-line checks)
- Temperature and relative humidity control
- Appropriate and effective ventilation

These may affect products during manufacture or storage as well as functioning of equipment

Basic Principles of GMP

- The temperature and relative humidity should be controlled, monitored in accordance with an SOP, and the results recorded. The limits should be appropriate according to the materials stored and product processed



Premises

Construction

- Dust generating operations
  - *e.g. during sampling, weighing, mixing, packing of powders, etc.)*
- Measures should be taken to prevent cross-contamination
- Measures to facilitate cleaning

Basic Principles of GMP

Design of areas for weighing of materials

- Proper air supply
- Dust control measures (including extraction of dust and air)
- Easily cleanable surfaces
- No areas for dust accumulation
- Protection of material, product and operator

Premises

Maintenance

- Careful maintenance done
- Repairs and maintenance should not present any hazard to the quality of the products

Basic Principles of GMP

Basic Principles of GMP

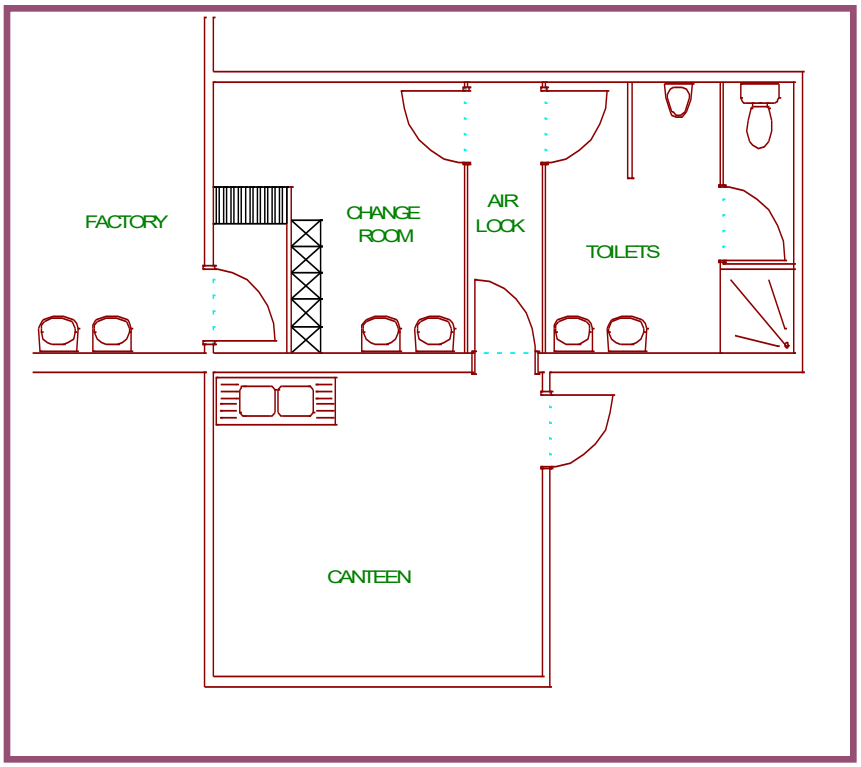
Premises Part two

Premises

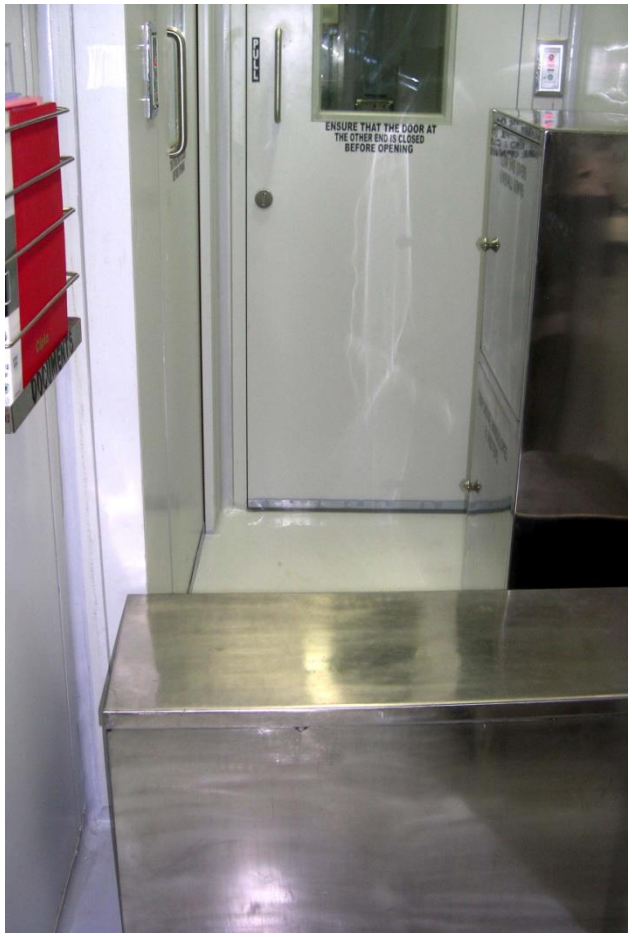
Ancillary Areas

- Rest and refreshment rooms separate from manufacturing and quality control areas
- Changing, washing and toilet areas accessible and appropriate numbers
- Maintenance workshops separated from production - if not possible – tools in reserved areas
- Animal houses well isolated – separate air handling and entrance

Basic Principles of GMP



Basic Principles of GMP



Basic Principles of GMP

- Separate receiving and dispatch bays
  - *Materials and products protected from weather*
- Area to clean incoming materials provided

Basic Principles of GMP

Cleaning of incoming containers

- Cleaning with a cloth, or duster
- Cleaning by using a vacuum cleaner
- Use of air curtains and air tunnels

Premises

Storage areas - 1

- Storage areas of sufficient capacity
- Orderly storage of categories of materials and products
- Separate and segregated areas: starting materials, packaging materials, intermediates, bulk, finished products, quarantined, released, rejected, returned and recalled products and materials

Basic Principles of GMP

Basic Principles of GMP

Premises

Storage areas - 2

- Appropriate temperature and relative humidity conditions within defined limits
  - *Provided, controlled, monitored and recorded*
- Good storage conditions: clean, dry and appropriate lights

Premises

Storage areas - 3

- Quarantine area: clearly marked and access restricted
- A separate sampling area is the norm: no risk for contamination or cross-contamination
- Segregated areas for rejected, recalled and returned materials and products
- Safe and secure areas for highly active, radioactive materials, narcotics and other materials (risk of abuse, fire, explosion)

Basic Principles of GMP

Premises

Storage areas – 4

Printed packaging materials

- Critical to ensure compliance with correct labelling of products
- Special attention to sampling
- Special attention to safe and secure storage
- Ensure compliance with specifications, prevent mix-ups

Premises

Weighing areas

- Weighing operations – in separated areas
- Appropriate design (see also training material on HVAC)
- Provision for dust control
- Smooth, impervious, durable, easy-to-clean finishes
- Cleaning procedures and records
- Documentation, e.g. SOPs, logs and records

Basic Principles of GMP

Premises

Production areas - 1

Minimize risk of cross-contamination:

- Dedicated and self-contained facilities for some products such as highly sensitizing materials (e.g. penicillins) or biological preparations (e.g. live microorganisms)
- Separate facilities for other products such as some antibiotics, hormones, cytotoxic substances
- Non-pharmaceuticals normally not in the same facility, e.g. pesticides, herbicides

Premises

Production areas -2

- Layout in accordance with sequence of production
- Appropriate cleanliness level
- Adequate work and in-process storage space
- Orderly and logical positioning of equipment

  minimizes risk of contamination, mix-ups and missing production steps
- Specially designed areas for packaging
- Layout to avoid mix-ups and cross-contamination

Premises

Production areas - 3

- Starting and packaging materials, intermediates and bulk exposed to environment:

  Interior surfaces (walls, floors, ceilings) – smooth, free from cracks and open joints

  No shedding of particles

  Easy and effective cleaning permitted

- Disinfection if needed

Premises

Production areas - 4

- Design of pipework, light fittings, and ventilation points – no recesses that are difficult to clean
- Access for maintenance from outside production areas
- Drains of adequate size, and equipped to prevent back-flow
- Open channels avoided

Basic Principles of GMP

Premises

Production areas - 5

- Effective ventilation with air control facilities
- Including filtration of air to a sufficient level to prevent contamination and cross-contamination – also external environment
- Control of temperature and relative humidity where necessary
- Regular monitoring of conditions during production and non-production periods

Premises

Quality Control areas - 1

- QC laboratories should be separate from production areas
- Separate areas for biological, microbiological and radioisotope methods
- Suitable design with sufficient space to avoid mix-ups and cross-contamination
- Suitable space for storage samples, reference standards, solvents, reagents and records

Basic Principles of GMP

Premises

Quality Control areas - 2

- Suitable construction materials
- Prevention of fumes
- Ventilation
- Separate air supply (production and QC)
- Separate rooms for some instruments to protect them from interference (e.g. electrical, vibration, moisture, etc.)

See supplementary training on QC laboratories