CHAPTER 3 -
PREMISES AND EQUIPMENT

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   • General
   • Production Areas
   • Storage Areas
   • Quality Control Areas
   • Ancillary Areas
3. Equipment

- Design and Construction
- Location and Installation
- Pipes and pipelines
- Maintenance and Calibration
- Cleaning
- Designated for intended use
- Verification (see Appendix 2)
PRINCIPLE

• Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out.

• Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build up of dust or dirt and, in general, any adverse effect on the quality of products.
To facilitate proper operation, cleaning and maintenance, premises for manufacturing shall be of:

- Suitable size
- Design
- Construction
- Location
GENERAL

• Premises shall be carefully maintained, ensuring that repair and maintenance operations do not present any hazard to the quality of products.
• They shall be cleaned and, where applicable, disinfected according to detailed written procedures.
• Steps shall be taken in order to prevent the entry of unauthorized people.
• Production, storage and quality control areas shall not be used as a right of way by personnel who do not work in them.
GENERAL

Example of lighting and ventilation used in production area
LIGHTING FACILITIES

- LED lighting: ideal for warehouses, processing areas
- Fluorescent lighting: cost-effective, best for employee areas and packaging

Protection against contamination in case of glass breakage

i.e. Plastic coated shatterproof bulbs
GENERAL

VENTILATION

• **Good air quality** can be achieved by **controlling** the direction of airflow, level of particulates, dust, vapour, microbial load, temperature and humidity.

• **Air Handling Unit (AHU):** An equipment used to circulate air

• **Heating, Ventilation and Air Conditioning (HVAC):** a term for the collective mechanical equipment used to control air quality in a manufacturing facility;
  – central unit to which AHU is connected
GENERAL

Horizontal unidirectional flow, vertical unidirectional flow and turbulent flow

Air-handling unit

EXAMPLE

UDAF, unidirectional airflow; HEPA, high-efficiency particulate air.
GENERAL

Examples of ventilation system:

- HVAC system
- Centralized air condition
- Wall type air condition
GENERAL

Examples of supporting equipment for ventilation system

Dehumidifier
Exhaust fans
• Direction of air flow within the production area shall never be from a dirty area to a clean area.

• Dry or powdered product should have a dust collection system installed.

• For the rest of the areas where there is product exposure, suitable ventilation is required.
GENERAL

• WINDOW
  – Windows & other openings shall be so constructed as to avoid accumulation of dirt

• DOOR
  – Where appropriate, be self-closing & self fitting

Both windows and doors should be smooth, non-absorbent surfaces
GENERAL

Ensure that bottom and top of doors and windows are sealed

- Rubber protect
- Sealed
- Drop down seal
- Gaps
Self-closing doors are recommended
Premises shall be located at a suitable site approved by the relevant authorities.

– Appropriately located (i.e. away from dusty roads, garbage dump, pollution sources and other potential sources of contamination such as foundries and chemical processing plant)

– With convenient access to roads for the easy transport of starting materials and finished products.
GENERAL

• Premises shall be situated in an environment which, when considered together with measures to protect the manufacture, presents minimal risk of causing contamination of materials or products.
• **TM and HS may share** the same manufacturing facilities provided **cross-contamination is adequately addressed** (examples include but not limited to: by performing cleaning verification or the use of separate equipment, etc.).

• **Dedicated and self-contained facilities** must be available for the production of particular products, such as highly sensitising materials (e.g. penicillins) or biological preparations medicinal products (e.g. from live micro-organisms i.e. these products shall not be produced in the same facilities used to produce TM and HS.)
GENERAL

• Premises shall be designed, constructed and maintained to protect against access and harboring of vermin, rodents, birds, insects or other animals.

• Protection can be done by implementing a pest control program
GENERAL

Ensure that all main openings are **effectively protected** against entry of flies, mosquitoes and rodents (e.g. air curtains provided/ mosquito electrolucutor provided)

mosquito electrolucutor

air curtains
GENERAL

• Premises should be designed with logical flow of materials in mind (from receiving of materials → production (including packing) → storage of finished products), so as to prevent mix up and cross-contamination.

• Personal flow should be different from material flow
GENERAL

A.) STRAIGHT LINE FLOW

B.) L – SHAPED FLOW

C.) U – SHAPED FLOW
Example of Materials and Personnel Flow

Arrival of goods  Entrance for visitors  Entrance for Workers  Shipment of goods

Incoming goods  QC  Offices  Gowning  Canteen  Shipping

Corridor  Corridor

Starting Materials & Packaging Storage

Weighing  Processing  Filling  Packaging  Finished Products Storage

Washing  Machine Shop

Corridor

Utilities and Services  Waste Treatment

Source: WHO Module 'on Premises'

Material Flow

Personnel Flow

Zone: Processing

Zone: Packaging

Zone: Controlled environment

Source: WHO Module 'on Premises'
• Defined areas for the following operations are required:
  - Receiving and quarantine of incoming materials
  - Sampling
  - Storage of starting and packaging materials
  - Weighing /Dispensing
  - Processing
  - Storage of bulk/intermediate products
  - Packaging
  - Equipment washing
  - Storage of quarantine finished products
  - Storage of approved finished products
  - Designated area for quality control
Equipment washing areas

**GENERAL**

Hoses shall be stored to allow them to dry so as to prevent retention of liquid.
Storage of Quarantine Materials

• Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked and their access restricted to authorized personnel.

• Any system replacing the physical quarantine shall give equivalent security.
Weighing / Dispensing

The weighing of starting materials should be carried out in a separate weighing area designed for that use, complete with provisions for dust control.
PRODUCTION AREAS

- Interior surfaces (walls, floors, and ceilings) shall be smooth, free from cracks and open joints, and shall not shed particulate matter and shall permit easy and effective cleaning and, if necessary, disinfection.

- Coving of junctions between walls and floors in the production areas is encouraged to facilitate cleaning.
PRODUCTION AREAS

Rounded corner coves facilitate easy cleaning & sanitizing

Coving strip support floor covering for mop-able cleaning & sanitizing
PRODUCTION AREAS

Covings at walls, ceiling and floor Joints are encouraged
Where appropriate:

- Water-proof
- Non-absorbent
- Washable
- Non-slip material
- Without crevices
- Easy to clean & disinfect
PRODUCTION AREAS

Ensure that the floorings are smooth, impervious and continuous and does not allow collection of dust (preferably epoxy coated)
PRODUCTION AREAS

Solid concrete with epoxy or polyurethane resin finish is suitable for processing areas as it has a non-porous topping with non-skid surface & retards bacterial growth.

Solid concrete for warehouse
PRODUCTION AREAS

WALLS AND CEILINGS

Where appropriate:

- Smooth
- Water-proof
- Non-absorbent
- Washable
- Easy to clean & disinfect
PRODUCTION AREAS

• Ensure that walls are smooth and not prone to catch dust
• Ensure that the walls and floors are washable
Any open channels shall be avoided, but if required they shall be shallow enough to facilitate cleaning and disinfecting.

All drainages shall have trapped gullies.

The water trap prevents foul air passing through the drain from stagnant or dirty water within the connection pipe work.
PRODUCTION AREAS

Ensure that the premise is neat and clean and is free of pooled water. Floorings are sloped to self drain the spilled water or washings.
PRODUCTION AREAS

• Production areas shall be well lit, particularly where visual on-line controls are carried out.

• Pipework, light fittings, ventilation points and other services shall be designed and sited to avoid the creation of recesses which are difficult to clean. As far as possible, for maintenance purposes, they shall be accessible from outside the manufacturing areas.

• Separate areas shall be used for the production of finished products intended for external use or application and finished products intended for internal consumption solely.
In cases where dust is generated (e.g. during sampling, weighing, mixing and processing operations, packaging of dry products), specific provisions shall be taken to avoid cross-contamination and facilitate cleaning.
Premises for the packaging of products shall be specifically designed and laid out so as to avoid mix-ups or cross-contamination.
• Premises shall preferably be laid out in such a way as to allow the production to **take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels**.

• **Adequacy of working space**, which shall allow orderly and logical placement of equipment and materials and to suit the operation, **efficient flow of work**, effective communication and supervision as well as to avoid crowding and disorders.
CHANGING ROOM

- Changing rooms shall be directly connected to but separated from processing areas.

- Changing rooms into the production areas shall have adequate hand washing and/or sanitizing facilities.

- Paper towels or hand drier should be provided whichever is suitable.
- Fabric Towels are not recommended.
PRODUCTION AREA

CHANGING ROOM

➢ Store working shoes separately

➢ Separate areas shall be available for the storage of clean protective garments away from the dirty and soiled ones.
STORAGE AREAS

Storage areas shall be of sufficient capacity to allow orderly storage of various categories of materials and products with proper segregation.
Storage areas should be maintained in a clean, dry & orderly condition. Goods should be stored off the floor and away from walls that will permit easy cleaning and the use of pest control agents without risk of contamination.
STORAGE AREAS

• Segregated and secured areas (e.g. under lock and key) shall be provided for the storage of rejected, recalled or returned materials or products.

• Highly active materials or products (e.g. flammable, explosive or toxic substances) shall be stored in separate, safe and secure areas.
STORAGE AREAS

- Receiving and dispatch bays shall protect materials and products from the weather.

- Reception areas shall be designed and equipped to allow containers of incoming materials to be cleaned, where necessary, before storage.
STORAGE AREAS

- There shall normally be a separate sampling area for starting materials.

- If sampling is performed in the storage area, it shall be conducted in such a way as to prevent contamination or cross-contamination (e.g. by using sampling booth).
Printed packaging materials are considered critical to the conformity of the products, and special attention shall be paid to the safe and secure storage of these materials.
STORAGE AREAS

• Crude (i.e. unprocessed) natural materials shall be stored in separate areas.

• The store area shall be well ventilated and equipped in such a way as to give protection against insects, or other animals, especially rodents.
STORAGE AREAS

• Effective measures shall be taken to prevent the spread of any such animals and microorganisms brought in with the crude natural materials to prevent fermentation, mould growth and cross-contamination.

• Containers shall be located in such a way as to allow free air circulation.
STORAGE AREAS

• Special attention shall be paid to the cleanliness and good maintenance of the storage areas particularly when dust is generated.

• Storage of plant materials, animal materials including parts, microorganisms, extracts, tinctures and other preparations that require special conditions of temperature, humidity or light protection; these conditions shall be provided and monitored.
If testing is done within the premises, quality control laboratories should be separated from production areas. This is particularly important for laboratories for the handling of microorganisms.
QUALITY CONTROL AREAS

Control laboratories shall be designed to suit the operations to be carried out in them. **Sufficient space shall be given to avoid mix-ups and cross-contamination.**
QUALITY CONTROL AREAS

There shall be adequate suitable storage space for samples (including retained and reference samples) and records.
Separate rooms may be necessary to protect sensitive instruments from vibrations, electrical interference, humidity, etc.

Special requirements are needed in laboratories handling particular substances such as microorganisms.
ANCILLARY AREAS

• Rest and refreshment rooms and toilets shall be separated from other areas and shall not have direct access to controlled areas (e.g. production and storage areas).

• Facilities for changing clothes, and for washing and toilet purposes shall be easily accessible and appropriate for the number of users.
ANCILLARY AREAS

- Maintenance workshops shall be separated from production areas. Whenever parts and tools are stored in the production area, they shall be kept in rooms or lockers reserved for that use.

- Animal houses shall be well isolated from other areas, with separate entrance (animal access) and air handling facilities.
ANCILLARY AREAS

A separate room may be needed for storing clean, idle equipment which should be kept dry at all times.
Equipment shall be

- designed
- placed
- maintained

...to suit their intended use...
LOCATION & INSTALLATION

- Prevent contamination
- Minimize the risk of error
- Tested to ensure that equipment operate appropriately
- Avoid congestion and cross contamination
Pipelines should be constructed using suitable materials (e.g. Stainless Steel) which is stable when in contact with the process materials, during hot sanitation & disinfection.
PIPE & PIPLINES

- Clearly labeled to show:
  - Content (where applicable)
  - Direction of flow
BALANCING & MEASURING EQUIPMENT

- Available in **appropriate range & precision** for production and control operation

- Weighing, measuring, testing and recording equipment should be **serviced and calibrated regularly**.
CALIBRATION

Calibration of equipment / measuring device should have the following:

- Specified Tolerances
- Traceable Standards
- Measurement Calibration
- Competent Personnel
- Approved Procedures
- International Standards
- National Standards
- Reference Standards
- Industry Standards
- Measurement Calibration
Determine the **accuracy of measuring instruments**.

Calibrated and checked according to:

- * Frequency
- * Method

And the **records** are maintained.
Calibration Tag

- Shall have **SOP or program for calibration of measuring, weighing, recording and control equipment** (clause 5.43.2)
CALIBRATION

This information is provided as an example and the frequency will be based on the need, previous performance and critically of the equipment.

<table>
<thead>
<tr>
<th>Type of equipment</th>
<th>Requirement</th>
<th>Suggested frequency</th>
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| Reference thermometers (liquid-in-glass)| Full traceable recalibration  
Single point (e.g. ice-point check) | Every 3 years  
Annually                                    |
| Reference thermocouples                 | Full traceable recalibration  
Check against reference thermometer | Every 3 years  
Annually                                    |
| Working thermometers and working        | Check against reference thermometer  
at ice-point and/or working temperature range | Annually           |
| thermocouples                           |                                                                             |                     |
| Balances                                | Full traceable calibration                                                   | Annually           |
CALIBRATION

Third party/external calibration body

- Supplier selection and evaluation should be done prior to the execution following the SOP of selection and purchasing of services and supplies that has an effect to quality testing

- Contract / working agreement should be prepared which clearly defined scope and responsibilities of each party

- Final responsibility belongs to the equipment owner

- Owner should verify the readiness of the equipment when received from the third party / external calibration body
EQUIPMENT: CLEANING

- Designed for easy and thorough cleaning
- Detailed and written procedures
- Stored in clean and dry condition
DEDICATED EQUIPMENT

Dedicated equipment used to manufacture products intended for internal consumption solely shall be separated from equipment used for the manufacturing of products intended for external use or application.
Defective equipment shall be removed and/or clearly labelled.

Repair and maintenance shall not present hazard to the quality of products.
Surface of equipment must not be:

- Reactive
- Additive
- Absorptive
Pipes, hoses, pumps and valves used for treated water, starting materials and products shall be cleaned and sanitised according to written procedures that details the alert and action limits and measures for microbiological contamination.
Must also have SOPs for:

- Equipment assembly (Clause 5.43.1)
- Maintenance, cleaning and sanitation of equipment (Clause 5.43.3)
• Equipment shall be **periodically verified** to determine if they are still operating in a valid state

• Verification of equipment should be **done prior to** the testing method verification

• Verification of Equipment should be done as described in ASEAN Guidelines on Good Manufacturing Practice for Traditional Medicines and Health Supplements, *Appendix 2 - Verification*
REFERENCE

- ASEAN Guidelines on Good Manufacturing Practices for Traditional Medicines
- ASEAN Guidelines on Good Manufacturing Practices for Health Supplements
THANK YOU!

ONE VISION, ONE IDENTITY, ONE COMMUNITY