Equipment

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After completion of this topic, students will be able to learn about

- Equipment selection
- Purchase specifications
- Maintenance

- Equipment is generally one of the major inputs along with people facilities, materials, and systems.

- The quality of the manufactured product much depends on the suitability, and level of the technology of the equipment used since it is major requirement in the manufacture of the pharmaceutical products.

- The regulatory literature on GMP in various countries gives enough importance and provide guide lines on the management of equipment in pharmaceutical plants.

- Equipment may be defined as a physical entity or any piece of plant, machinery, instrument etc which is used to carry out a general or specific activity in the pharmaceutical plant.

- It can be a single piece, for example tablet compression, weighing machine, mixer, granulator, dryer, HPLC etc.

or

- Integrated system that is, group of equipment come together to perform single activity. e.g.: water mineralizing plants, air handling systems

Equipment selection

While selecting equipment, following points should be considered.

- Design
- Size
- Location
- Construction

Design

- Design of equipment shoukd meet the user requirements.
- Therefore, User Requirement Specification should be prepared [URS]

It should answer questions like;

i.What operations are to be performed

ii. Capacity- holding as well as out[put

iii. Which materials are to be used and their interaction with material of construction

iv. Cleaning and validation

Are trained operators available

vi. Starting and stopping time of the equipment

vii. Level of technology used

viii. Obsolescence time

Size

- Size is decided on the volumes of materials which we are going to handle. Batch sizes are also directly related to the size of processing equipment.
- Following things should be considered…

1. Physical dimensions of the equipment [lxbxh], size of the room and path in plant through.
2. Holding and output capacity.
3. Minimum and maximum volume of materials e are going to handle.

Location

- It depends upon logical process movement.
- Danger of contamination and mix-ups should be taken into account.

Other factors

- Utility services
- Material handling and movement
- Movement for processing and cleaning
- Men movement for repair and maintainence
- If the equipment is discharging gases, fumes, powders etc, it should be taken into consideration.

Construction

1. Ease of cleaning equioment and surrounding area
2. Ease of operation
3. Ease of maibtainence
4. Material of construction [MOC]

Documents

Machine/equipment manual

Machine/equipment layout drawing showing the position of equipment in the room

Certificate of MOC of equipment

Equipment validation reports

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Identification of equipment

As per CRR-211.105 of USFDA,

All compounding and storage containers, processing lines and ***major equipments*** used during the production of a batch of a drug product shall be properly identified at all times to indicate their contents and when necessary the phase of processing of the batch.

Label

Name of the equipment

Batch number

Batch size

Processing stage

Date and sign of the production supervisor

Equipment log

Register/log book to be maintained for operation, cleaning and Maintainence.

Fields

- Sr. no.
- Name of equipment along with identification nu,ber/code
- Product/ batch nos. Handled
- Date and time of activity carried out
- Name of operator/supervisor

Cleaning and maintanence of equipment

- For achieving the identity, safety, strength and purity of the products being processed. The equipment and utensils should be cleaned, maintained and sanitised at appropriate intervals of time .
- This also avoids malfunctioning or contamination of the product.
- For this SOP’s should be available.

- Levels of cleaning required may be defined and categorized

- Changeover from one batch to another of the same product
- Changeover from one product to another product

May be further subdivided as;

- Changeover from potent to non potent product
- Changeover from non potent to potent product

Wash water analysis should be carried out to find acceptable level of cleanliness.

Al equipments must be cleaned immediately after use and must be checked for cleanliness before use.

Time frame must be defined for rewashing and unused cleaned equipment.

- ✓ Every equipment must have SOP’s for operation, cleaning and maintenance.
- ✓ There may be system to distinguish equipment in three categories:
- Operational equipment (with green card),
- Equipment under maintenance (yellow card),
- Defective equipment (red card).

- ✓ The operator doing cleaning and maintenance must be so trained that their activities of cleaning and maintenance will not affect or contaminate product.
- ✓ Records of all activities on equipment must be chronologically recorded in the equipment log book

Cleaning and washing may be :

A. Manual

B. Automated

-CIP

-SIP

Cleaning-In-Place (**CIP**) and Sterilization-In-Place (**SIP**) are systems designed for automatic cleaning and disinfecting without major disassembly and assembly work

Cleaning validation

Cleaning validation is the methodology used to assure that a **cleaning** process removes chemical and microbial residues of the active, inactive or detergent ingredients of the product manufactured in a piece of equipment, the **cleaning** aids utilized in the **cleaning** process.

cleaning validation:- why it is important?

- Essential to establish adequate cleaning procedures.
- Cleaning validation should be performed in order to confirm the effectiveness of a cleaning procedure.
- The data should support a conclusion that residues have been reduced to an ‘acceptable’ level.

Sampling methods:

- Swab sampling,
- Rinse fluid,
- Placebo flush

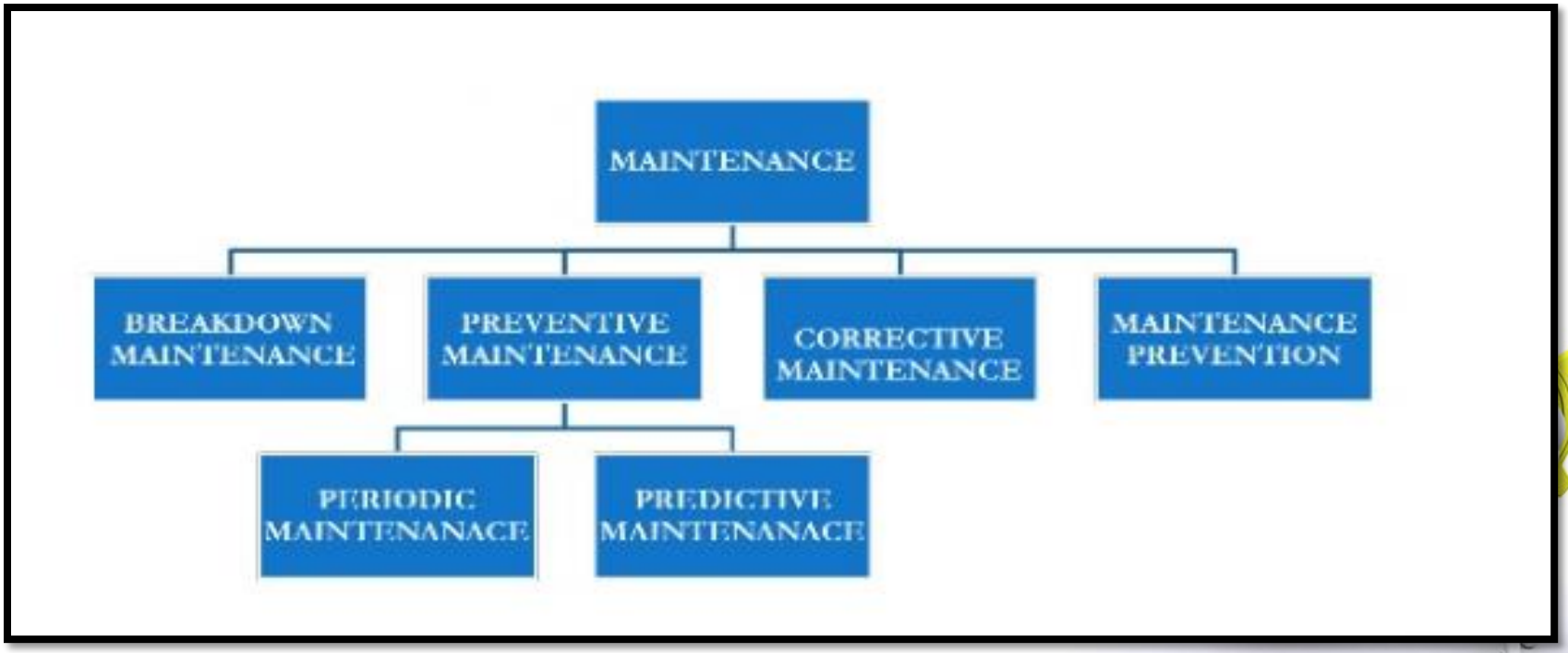
it involves manufacturing a **placebo** product on the cleaned equipment, and then measuring the residues left over from the **cleaning** process in that manufactured **placebo**.

- Visual Examination.
- Analytical method: HPLC, GC, HPTLC, pH , Conductivity, UV, ELISA

Equipment maintenence

Equipment Maintenance: defined as facilities maintain to some desired level of efficiency to keep assets in a satisfactory condition.

Types of maintenence



Planned preventive maintenance programme [PPMP]

- It is a time table of carrying out the preventive maintainence of major equipment in pharmaceutical plant.
- It helps in maintaining the equipment in good state of repair and maintenance all the time.
- It is prepared before the year stars and communicated to all concerned people.
- Prepared by maintenance dept. in consultation with Q.C. dept.

A list of all major equipment is made by the maintenance department based on manufacturers manual.

A list of preventive maintenance jobs to be done is decided, necessary spares and other things are collected before hand and then the preventive maintenence work is carried out on schedule.

AUTOMATIC, MECHANICALAND ELECTRONIC EQUIPMENT

These types of equipment includes computers or related systems that will perform a function satisfactorily, may be used in the manufacture, processing, packing, and holding of a drug product.

It should be routinely calibrated, inspected or checked according to a written program designed to assure proper performance.

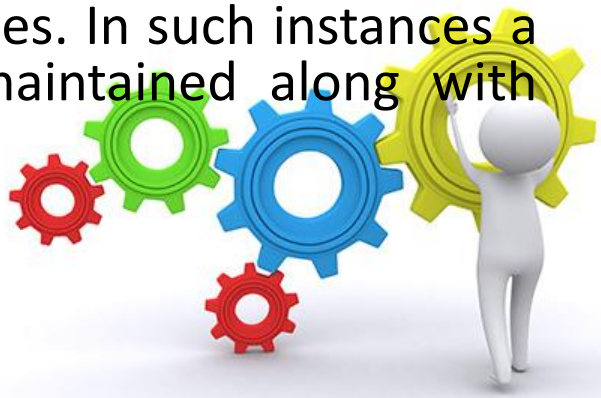
Written records of those calibration checks and inspections shall be maintained

Appropriate controls shall be exercised over computer or related system to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Input and output from the computer or related system of formulas or other records or data shall be checked for accuracy.

The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system.

A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data.



Purchase specification

- Detailed description of the measurable characteristics desired in an equipment to be purchased such as quality, size, weight , performance parameters, safety requirements etc.
- The documents used for the procurement of equipment should consist:

1. User Requirement Specification
2. Relevant Standard Demand Specifications
3. Purchase Agreement.

Purchase specification of water bath

- 10 L to 15 L water tank volume
- Water circulation to maintain uniform temperature
- Working temperature : ambient +5˚C to 100˚C
- Stability : ±0.1˚C or less
- Increment : ±1˚C or less
- Microprocessor control for precise temperature
- Over-temperature cut-off
- Audible and visible alarms
- LED display with 0.1˚C resolution for temperature
- Operable at 220 volts
- 5 year equipment maintenance

Purchase specification of UV-VIS Spectrophotometer, double beam

- Wavelength : 190-900 nm or more
- Optical System : Double beam with double monochromator
- Light Source : D2 and Tungsten
- Wavelength accuracy : +/- 0.1 nm
- Spectral Bandwidth : at least, 0.5, 1, 2, 5 (variable)
- Photometric Range : at least -0.3~3 Abs
- Photometric Modes : Abs,%T
- Stray Light minimum
- Wavelength Scan Speed : 800-10 nm/min
- Baseline Stability : +/-0.0008Abs/Hour or less
- Detector : Photomultiplier R928
- Control : By Computer
- Quartz Cuvette
- Branded Computer monitor with latest specification
- Laser Printer
- D2 Lamp, tungsten Lamp
- 5 years maintenance of the system

Equipment qualification is the action of proving that any equipment works correctly and actually leads to accurate and reliable results.

Qualification is an act or process to assure something complies with some condition, standard, or specific requirements.

It is final series of inspections and tests to ensure that criticxal requirements necessary for product quality are staisfied and that documents and procedures necessary to properly operate and maintain the equipment are in place

DQ

- Design Qualification: proof the suitability for the intended process.

IQ

- Installation Qualification: verify that system has been built up according specifications.

OQ

- Operational Qualification: verify that the equipment operates as specified and meets the predetermined requirements

PQ

- Performance Qualification: verify that the system functions within the required range of operation

The first stage of the qualification process is called Design Qualification. The design qualification ensures the design's suitability for the intended process. The evaluation can comprise the following aspects:

- Ambient temperature
- Insulation
- Temperature control units
- Airflow in the storage compartment
- Minimum and maximum load
- Monitoring devices and system
- Alarm settings

Installation Qualification- verify that the system in question has been built up according to the specifications previously agreed upon. It leads to operational conformance.

This verification can include the following four aspects:

- Document Verification – collecting relevant documentation of the system as provided by operating and maintenance manuals, spare parts lists, drawings and certifications
- Equipment Installation Verification – visual and physical inspection of the system: has the system been built up suitably?

Checkpoints include: manufacturer, serial numbers, insulation, dimensions, construction quality of mounted components, general impression especially regarding hygiene and robustness

- Preventative Maintenance – design of a maintenance program based on historical data about failure and breakdown rate of critical components, parts lists with suppliers and delivery time (essential in the event of failure)
- Calibration Verification – critical devices ask for a calibration

Operational Qualification verifies that “the process or equipment operates as specified and meets the predetermined requirements for control of the design operating parameters

Performance Qualification, establishes confidence that the system performs as predetermined under real conditions