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|  | Quality Control And GMP Compliance In  Pharmaceutical Industry  Dr.Sajid Bashir  Dr.Rai.M.Sarfraz |

# GMP & cGMPs

**GMP**

GMP refers to the Good Manufacturing Practice Regulations made by the US Food and Drug Administration under the authority of the Federal Food, Drug, and Cosmetic Act. These regulations, which have the force of law, require that manufacturers, processors, and packagers of drugs, medical devices, some food, and blood take proactive steps to ensure that their products are safe, pure, and effective.

## GMP; (According to Act 1976)

GMPs for pharmaceutical products mean part of QA which:

* Ensure that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization, or product specifications.
* Diminish the risks, inherent in any pharmaceutical production, including contamination, cross contamination and mix ups that cannot be detected completely through the testing of final product.

## cGMP (Current Good Manufacturing Practices)

GMP is also referred to as cGMP, the letter c stands for Current, reminding manufacturers that they must employ technologies and systems that are up-to-date in order to comply with regulations.

## Difference between GMP and cGMP

|  |  |
| --- | --- |
| **GMP** | **cGMP** |
| Good Manufacturing practice without Validation terminology is called GMP. | Good Manufacturing Practice with Validation terminology is called cGMP. |
| GMP refer to Good Manufacturing  Practice that are guideline followed by | cGMP is Current Good Manufacturing  practices that need to be adhered to by |

|  |  |
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| over 100 countries. | participating countries. |
| GMP applies to Pharmaceutical and Healthcare products and help to maintain high standards in these  products. | cGMP is to remind accepting that all guideline must be followed with latest and current production processes. |

**History**

GMP are regulations issued by Food, Drug and Cosmetic Act. This act was passed in 1938.In 1962 law was passed which have impact on GMP. In 1963 first GMP for Finished Pharmaceuticals were made final.

* CGMP Quality Principles for Biologics and Medical Devices are required to maintain product compliance.
* EU-GMP guidelines (European union-GMP guidelines).
* WHO-GMP guidelines (World health organization-GMP guidelines).
* GMP for active pharmaceutical products.
* GMP for biopharmaceuticals.
* cGMP quality principles for biologics and biotechnological products.
* Licensing in pharmaceutical production & GMP documentation.

## Compliance

Compliance is determination through inspection of the extent to which a manufacture is acting in accordance with prescribes regulations, standards and particles.

## Accuracy

Accuracy refers to the deviation of a measurement from a standard or true value of the quantity being measured. We can talk about the accuracy of a single measurement.

# Validation

Validation is the process of establishing documentary evidence demonstrating that a procedure, process, or activity carried out in testing and then production maintains the desired level of compliance at all stages.

## Process Validation

Process validation is defined as the collection and evaluation of data, from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products.

Process validation is a requirement of current Good Manufacturing Practices (GMPs) for finished pharmaceuticals and of the GMP regulations for medical devices and therefore applies to the manufacture of both drug products and medical devices.

## Stages of Validation

The Process validation activities can be described in three stages:

**Stage 1 - Process Design:** The commercial process is defined during this stage based on knowledge gained through development and scale-up activities.

**Stage 2 - Process Qualification:** During this stage, the process design is confirmed as being capable of reproducible commercial manufacturing.

**Stage 3 - Continued Process Verification:** Ongoing assurance is gained during routine production that the process remains in a state of control.

## Types of validation

* Prospective Validation
* Concurrent Validation
* Retrospective Validation
* Revalidation (Periodic and After Change)

## Prospective Validation:

Prospective validation is carried out during the development stage.

## Concurrent validation:

Concurrent validation is carried out during normal production. It requires a full understanding of the process based on prospective work.

## Retrospective Validation:

Retrospective validation is the analysis of accumulated results from past production batches manufactured under identical conditions to assess the consistency of a process.

It involves very close and intensified monitoring of all the manufacturing steps and critical points in at least the first three production-scale batches

## Revalidation:

Periodic revalidation offers the opportunity to check that the systems are still operating as originally validated and that no unintended changes have affected the process, system or piece of equipment and the end result.

## Equipment Validation

Qualification of utilities and equipment generally includes the following activities: Selecting utilities and equipment construction materials, operating principles, and performance characteristics based on whether they are appropriate for their specific uses.

Verifying that utility systems and equipment are built and installed in compliance with the design specifications (e.g., built as designed with proper materials, capacity, and functions, and properly connected and calibrated).

Verifying that utility systems and equipment operate in accordance with the process requirements in all anticipated operating ranges.

# Standard Operating Procedure

Standard operating procedure is a step by step procedure or directions as established by quality assurance industry involved in facility producing a product, testing or research. A standard procedure does not need explanation or publication because it is standard.

## Purpose of SOP

* + To perform a job perfectly.
  + To ensure that production operations are performed consistently.
  + To ensure that process continue uninterrupted.
  + To ensure that failure occur in manufacturing.
  + To serve as checklist for auditor.
  + To serve as historical record for the change over.
  + To serve as training document for teaching user about the process.

## Structure of SOP

The content of standard operating procedure should include the following minimum:

* + Title page
  + Header with title of SOP
  + Department name
  + Effective date
  + Revision date and Review date
  + Page no
  + Purpose and Scope
  + Responsibilities and accountabilities
  + Procedure
  + Stamp

# ISO

Popular name for international organization for standardization (IOS), a voluntary, non treaty federation of standard setting bodies of some 130 countries, founded in

1947 in Geneva as a UN agency, it promote development of standardization related activities to facilitate international trade in goods and services, and cooperation on economic, intellectual, scientific, and technological aspects.

## ISO 9000

ISO 9000 is a series, or family, of standards. ISO 9001 is a standard within the family. The ISO 9000 family of standards also contains an individual standard named ISO 9000.

## ISO 9000 Series standards

The ISO 9000 family contains these standards:

* + ISO 9001:2015: Quality management systems - Requirements.
  + ISO 9000:2015: Quality management systems - Fundamentals and vocabulary

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* + ISO 9004:2009: Quality management systems – Managing for the sustained success of an organization.
  + ISO 19011:2011: Guidelines for auditing management systems.

# CAPA

Corrective and preventive action are improvements to an organization's processes taken to eliminate causes of non-conformities or other undesirable situations. Failure to abide to proper CAPA handling is considered as violation of federal regulations on good manufacturing practices. CAPA is a concept within good manufacturing practice (GMP).

## Examples of Corrective actions:

* + Visible or Audible Alarms
  + Process Redesign
  + Product Redesign
  + Improvements to maintenance schedules
  + Improvements to material handling or storage

# Incineration

Incineration is a waste treatment process that involves the combustion of organic substance contained in waste materials described as “thermal treatment”.Incineration of waste material convert the waste into ash, flue gas and heat.

## Incinerators:

Incinerator can be understood more precisely as a furnace where waste is burnt. . Following are the types of plants for burning waste:

* + Fixed grate
  + Moving grate
  + Rotary kiln

# CURRENT GOOD MANUFACTURING PRACTICE REGULATIONS

## ORGANIZATION AND PERSONNEL:

It further includes

* + **Responsibilities of QC unit:** They have total responsibility to ensure that adequate systems and procedures exist and are followed to ensure product quality.
  + **Personnel qualifications:** Each person engaged in the supervising, manufacture, processing, packing, or holding of a drug product shall have education, training, and experience.
  + **Personnel responsibilities:** Personnel engaged in the manufacture, processing, packing, or holding of a drug product shall wear clean clothing appropriate for the duties they perform.
    - Protective apparel, such as head, face, hand, and arm coverings, shall be worn as necessary to protect drug products from contamination.
    - Personnel shall practice good sanitation and health habits.
    - Only personnel authorized by supervisory personnel shall enter those areas of the buildings and facilities designated as limited access areas.
    - Any person shown at any time (either by medical examination or supervisory observation) to have an apparent illness or open lesions shall be excluded from direct contact to components.
  + **Consultants:** Any consultants advising on scientific and technical matters should possess requisite qualifications for the tasks.

## Buildings and facilites:

* + Building and facilities are only acceptable only if they are suitable for intended purpose and can be maintained.
  + The regulations in this section include
    - Design
    - Structural features
    - Functional aspects of building
    - Facilities
  + Each building’s structure, space, design and placement of equipment must be such to enable thorough cleaning, inspection, and safe and effective use for the designated operations.
  + Floors, walls and ceilings are constructed of smooth, easily cleanable surfaces and are kept clean and in good repair

## Equipment:

* + Equipment used shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.
  + The equipment’s surfaces and parts must not interact with the processes or product’s components so as to alter the purity, strength or quality.
  + Standard operating procedures must be written and followed for the proper use.
  + Automated equipment and computers used in the processes must be routinely calibrated, maintained, and validated for accuracy.
  + Utensils, transfer piping and drugs contact surfaces of equipment are well- maintained and clean and are sanitized at appropriate intervals.

## Control of components, containers, and closures:

**General requirements**: Written procedures must be available that describe the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components (raw materials) and drug products.

* + Receipt and storage of untested components, drug product containers, and closures.
  + Testing and approval or rejection of components, drug product containers, and closures
  + **Use of approved components, drug product containers, and closures** These shall be rotated so that the oldest approved stock is used first.
  + **Retesting of approved components, drug product containers, and closures:** Materials that are subject to deterioration during storage should be retested at an appropriate time based on stability profiles.
  + **Rejected components, drug product containers, and closures:** These shall be identified and controlled to prevent their use in manufacturing.
  + **Drug product containers and closures:** Containers and closures (product contact materials) must protect the product and must be non-reactive with or additive to the product, suitable for their intended use, and controlled using written procedures.

## Production and procedure control:

* + **Written procedures and deviation:** Written standard operating procedures (SOPS) for each production process and control procedure are necessary. Any deviation from an SOP must be investigated, recorded, and approved prior to final product acceptance
  + **Charge-in of components:** The procedures used to formulate a batch shall be written and followed.
  + **Calculation of yield:** Actual yields and theoretical yields shall be determined. All products are to be formulated to provide not less than 100% of the required amount of active ingredient. Records are to be maintained of each component and the quantity, which is incorporated into a batch.
  + **Equipment identification:** Equipment shall be properly identified.
  + **Sampling and testing of in-process materials and drug products:** Significant in-process steps are to be identified and appropriate sampling, testing, and approvals obtained before proceeding further in the production cycle. Rejected material must be controlled.
  + **Time limitations on production:** If required, time limitations will be placed on in-process steps
  + **Control of microbiological contamination:** Appropriate procedures are to be prepared for the control and prevention of microbiological contamination. The sterilization process must be validated.
  + **Reprocessing:** Reprocessing of product is allowed providing there are written procedures covering the methods and QC unit review to be used.

## Packaging and labeling control:

* + **Materials examination and usage criteria:** Labeling and packaging materials which are to be received, identified, stored, sampled, and tested following detailed written procedures.
  + **Labeling issuance:** Strict control shall be exercised over labeling for use in drug product labeling operations.
  + **Packaging and labeling operations:** There shall be written procedures designed to ensure that correct labels, labeling, and packaging materials are

used for drug products. Special controls must be exercised over labeling to ensure that only the correct labels are issued to packaging for a specific product and that the quantities used are reconciled with the quantity issued.

* + **Drug product inspection:** Packaged and labeled products shall be inspected for correct labels.
  + **Expiration dating:** Following appropriate stability studies at prescribed temperature conditions, products on the market shall bear an expiration date to ensure that they are used within their expected shelf life.

### HOLDING AND DISTRIBUTION

* + Written procedures must be established and followed for the holding and distribution of product. Finished pharmaceuticals must be quarantined in storage until released by the quality control unit. Products must be stored and shipped under conditions that do not affect product quality.
  + Ordinarily, the oldest approved stock is distributed first.
  + Describes the requirements for warehousing holding product under appropriate conditions of light, temperature, and humidity.

## Laboratory controls:

* + **Testing and release for distribution:** Written procedures in the form of specifications, standards, sampling plans, and test procedures that are used in a laboratory for controlling components and finished drug products. Acceptance criteria for sampling and approval shall be adequate to support release of product for distribution.
  + **Stability testing:** There shall be a written testing program designed to assess the stability characteristics of drug products. The results of this testing shall be used in assigning appropriate storage conditions and expiration dates.
  + **Special testing requirements:** Special testing requirements are given for sterile and/or pyrogen-free ophthalmic ointment and controlled-release dosage form products.
  + **Reserve samples:** Reserve sample quantity and retention times are described

## Records and reports:

* + **General requirements:** Describes record retention time and availability for inspection.
  + **Equipment cleaning and use log:** A written record of ling major equipment cleaning, maintenance, and use shall be included in major equipment logs.
  + **Component, drug product container, closure, and labeling records:** Deals with the issues of the receipt, testing, and storage of components, drug product containers, and closures. Details the various records and documents that should be generated during the manufacture of drug products and that are to be available for review.
  + **Master production and control records:** A master production record must be prepared for each drug product, describing all aspects of its manufacture, packaging, and control. Individual batch records are derived from this approved master.
  + **Batch production and control records:** Calls for batch production and control records with information about the production and control of each batch
  + **Production record review**: All drug product batch records shall be reviewed and approved by the QC unit (QA/QC) before the batch is released.
  + **Laboratory records:** Complete records of any laboratory testing shall be maintained to include raw data, test procedures and results, equipment calibration, and stability testing.
  + **Distribution records:** Distribution records include warehouse shipping logs, invoices, bills of lading, and all documents associated with distribution. These records should provide all the information necessary to trace lot distribution to facilitate product retrieval if' necessary.
  + **Complaint files:** Records of complaints received from consumers and professionals are to be maintained along with the report of their investigation and response.

## Returned and salvaged drug products:

* + **Returned drug products:** Records are to be maintained of drug products returned from distribution channels and the reason for their return. These

data can be used as part of the total lot accountability, should the need arise, to trace its distribution and/or for its recall,

* + **Drug product salvaging:** Drug products that have been stored improperly are not to be salvaged.

## ADDITIONAL cGMP REGULATORY REQUIREMENTS

1. **Active pharmaceutical ingredients and excipients:**

The application of the regulation is focused on all of the defining elements of chemical purity and quality, including following:

* + Specifications and analytical methods for all the reactive and nonreactive components used in the synthesis.
  + Critical chemical reaction steps
  + Handling of chemical intermediates

## Medical devices:

* + The regulations for “good manufacturing practice for medical devices” are similar in organizational structure to those for finished pharmaceuticals.
  + Each device has a specific design with individual performance features and utility. For many devices, specific standards are stated in the regulations.
  + Devices covered by cGMP regulations include
    - intraocular lenses,
    - hearing aids,
    - intrauterine devices,
    - cardiac pacemakers,
    - clinical,
    - catheters,
    - cardiopulmonary bypass heart-lung machine console,
    - dental X-ray equipment,
    - surgical gloves,
    - condoms,
    - prosthetic hip joints,
    - traction equipment,
    - computed tomography equipment,
    - powered wheelchairs

## Biologics

* + Nature of blood, bacterial, and viral products requires specific additional mandates i.e. blood collection procedures, contamination, cell propagation and fermentation, inactivation of infectious agents.
  + While the basic regulations for finished pharmaceuticals apply to biologic products.

## Noncompliance With cGMP Regulations:

* + Noncompliance with cGMP regulations can lead to a number of regulatory actions by the FDA. Noncompliance with cGMP regulations during a regularly scheduled FDA inspection can lead to various actions, depending on the severity of the offenses.
  + In most instances, time for corrective action is given with the firm required to institute and document corrective measures and undergo another inspection.
  + In a worst-case scenario, the FDA is empowered to remove violate products from the market, withdraw product approvals, and restrict further applications.
  + All FDA actions are subject to appeal.

# Quality

it is a combination of all the characteristics of a product that determine the degree of acceptability of the product.

# Quality control

Quality control is “systematic control of these variables encountered in manufacturing process which affect the excellence of the end product.”

The 4 Main responsibilities of quality control in pharmaceutical industry include:

* Efficacy
* Safety
* Quality
* Compliance

## Objectives of quality control

### Establishment of quality standard:

Main motive of QC is the economical production of a high quality product at the quality level the customer wants.

### Locating quality deviations:

It is necessary to analyze the trend and extent of quality deviations in a manufacturing process, which should be explained by statistical techniques.

### Evaluating methods and processes of production:

It is a corrective measure to maintain the quality.

### Production of standard quality goods

QC aim at manufacturing standard quality products and avoids producing inferior quality goods.

### Improvement in quality

Aims at creating quality consciousness at all levels in the organization.

## Quality variation

If the product deviate from the define standards of specification then its called quality variation.

## Source of quality variation

### MATERIALS:

* + Variations among suppliers of same substances.
  + Variations among batches from same suppliers.
  + Variations within a batch

### METHODS:

* + Wrong procedure.
  + Inadequate procedure.
  + Negligence in procedure by chance.

### MACHINES

* + Variation of equipment of same process.
  + Difference in adjustments of equipment.
  + Aging of machines and improper care.

### MEN:

* + Improper working conditions.
  + Inadequate training and understanding.
  + Lack of interest and emotional upheavals.
  + Dishonesty, fatigue and carelessness.

## Quality control at different steps

1. **Quality control in warehouse:**

### Raw Material Control

Each raw material is sampled according to standard sampling procedures and is sent to the quality control laboratory for testing according to the written procedures as specified in USP. If acceptable, it is moved to the release storage area, after being properly stickered to indicate:

* + - Name of material
    - Item number
    - Lot number
    - Date of release
    - Re-assay date
    - Signature of quality control inspector

### Any raw material not meeting specifications must be isolated from the acceptable materials, stickered as a rejection, and returned to the supplier or disposed of promptly.

In general, raw materials may be classified into two groups:

* + - Active or Therapeutics
    - Inactive or Inert

### Active or Therapeutic Materials: -

Usually performed either chemically, microbiologically, biologically, or by all three methods.

**Active Materials: -** One of the most important decisions to be made in raw material control is the degree of purity (almost 97%) to be maintained for each material.

Its specifications normally include:

* + Identification
  + Solubility
  + Melting range
  + Loss on drying
  + Residue on ignition
  + Assays

**Antibiotics:** The sample must be taken in a relatively:

* + Dry atmosphere
  + Free from dust
  + Free of both chemical and microbial airborne contamination **Instruments:** Raw materials cannot be adequately evaluated without special instrumentation such as:
  + Spectrophotometry
  + Column, gas, thin layer and HPLC chromatography
  + X-ray diffraction
  + Calorimetry

1. **Inactive or Inert Materials: -** Important specifications of inert materials are:
   * Color, odor and foreign matter
   * Particle size
   * Heavy metal content (arsenic, selenium)
   * Water content
   * Microbial limit
   * Residue on ignition
   * pH

## Quality Control before Start-up:

### Environmental and Microbial Control and Sanitation:

* + - **Personal cleanliness** and proper hair covering and clothing should be required.
    - **Floors, walls and ceilings** should be resistant to external forces, capable of being easily cleaned and in good repair.
    - **Ventilation** in manufacturing departments is usually designed so that dust can be contained and removed.
    - **Water supply** may be potable, distilled or deionized and must be under adequate pressure to keep the water flowing.

### Raw Materials:

* + - Quality Control should check the original containers of **released raw materials.**
    - The containers should be **properly labeled** with a sticker that bears all the information **(name, dosage form, item number, lot number, weight and signature.).**
    - Raw materials intended for use in specific products should be stacked and stored together in an appropriate staging area with proper identification.

### Manufacturing Equipment’s: -

* + - Manufacturing equipment and utensils should be thoroughly **cleaned and maintained in accordance with SOP.**

### Equipment should be disassembled and thoroughly cleaned to remove drug residues from previous operations.

* + - **Adequate records** of such procedures and tests should be monitored by quality control personal.
    - **Weighing and measuring equipment** used in production and quality control processes such as thermometer and balances should be calibrated and checked at suitable intervals.

## Quality Control during Production:

### Raw Material Processing: -

Depending upon the nature of product, quality control personal should check and verify the temperature and humidity in the area required for the product.

At certain points, samples are to be taken to the quality control laboratory for potency assay and any other testing that is necessary to ensure batch uniformity and purity.

### Compounding: -

The production process begins with the setup of the manufacturing equipment to prepare the finished dosage form within the specified limits for the particular product.

A variable group of tests that are widely used for in-process controls include:

* + - Loss on drying
    - Organoleptic evaluation Granulation / Mixing
    - Assay
    - Thickness
    - Friability
    - Hardness
    - Weight variation Compression / filling
    - Disintegration time
    - Viscosity
    - pH
    - Assay
    - Above mentioned parameters
    - leakage test

Blistering

All testing performed according to the specification defined in official books (USP, BP, EP)

### Finished Product Control

* + - Final testing of finished product is made in quality control laboratories.
    - These tests are designed to determine compliance with specifications.
    - This testing along with in-process testing, assures that each unit contains the amount of drug claimed on the label.

Tests required by the official compendia on the ingredients and the dosage forma apply to all manufacturers of a specific compendia product.

## Quality Control in Packaging and Labeling

Product safety refers to all components and aspects of a medicine that have mentioned below:

* The active ingredient
* All auxiliary components
* Packaging
* Labeling
* Product information

The need to determine authenticity has an impact on several steps of the manufacturing process of medicines, including packaging design, labeling, and packaging information development.

### Packaging design:

Recently, it has been stated that simple changes concerning format and style of design can make medicine packaging safer for patients. These changes which can be summarized as follows:

* + - **Information on packaging:** Certain items of information are vital for the safe use of the medicine and are mandatory per legislation and regulations.
    - **Format of information:** The information must be presented in an intelligible manner that is easily understood by all those involved in the supply and use of the medicine.
    - **Style of packaging:** There is potential for confusion between both similarity in drug names and similarity in medicine packaging. The different user contexts, such as in homes and workplaces,

pharmacies, hospital wards, and care homes, are of particular importance to how the packaging is styled.

### Labeling:

The purpose of a label for a prescribed medicine is:

* + - To **describe** and **identify** the medicine.
    - To contribute to **optimal therapeutic outcome** and to **avoid medication errors.**
    - To achieve **appropriate handling and storage.**
    - **Important information** for the patient relating to the safe and effective use of the medicine should be prominent and in one section of the label.
    - **Patient information leaflets** produced either by the manufacturer or dispensing pharmacist should be provided with all medicines when they are supplied to the patient.
    - When **color** is used it should be designed to improve visual definition by way of contrast not to give priority to corporate design.
    - I**.V. and other injectable products** present more significant problems and require special attention in labeling.

## Requirements

**Industry design and layout**

* It should **not** be located in **residential area.**
* It shall **not** be adjacent to **open sewerage drains, public lavatory.**
* It size must **not be less than 2000 square yards.**
* **Building layout** of adequate size and suitable size get it approved from

### central licensing board.

* Design shall aim at minimizing the risk of errors facilitate good sanitation and permit effective cleaning and maintenance in order to avoid cross contamination.
* Proper services like electrical supply, lightning, for controlled temperature, humidity **HVAC is installed.**
* Premises shall be designed to provide **maximum protection** against the entry of **insects.**
* **Floors, walls, ceilings** should be of such material that permit **easy cleanliness.**
* Signs indicating smoking restriction, location of emergency kits must be pasted.

## Departments:

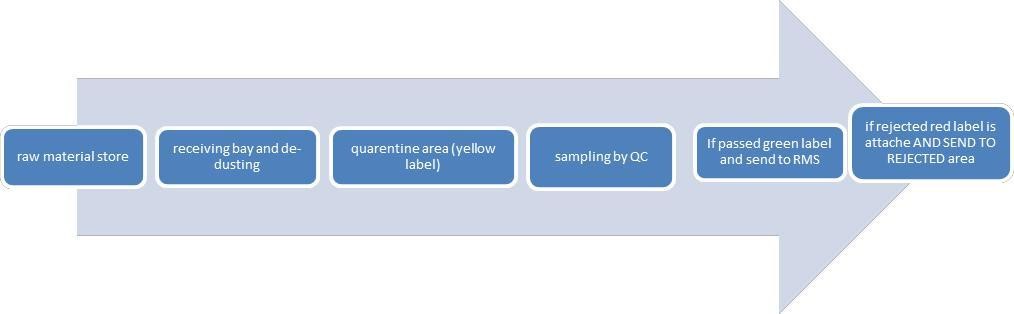
* Storage area (Warehouse)
* Dispensing area
* Production area
* Sterile area ( For injectable, ocular preparations)
* QC
* QA

## Storage area (warehouse):

The storage area must be spacious enough to store large amount of material and subsequent sections can be made like rejected area, recall area, quarantine area.

**Quarantine** means decision waiting; this area is differentiated by either marking yellow line on floor or by tying yellow ribbon.

**After passing Q.C tests, green label** is attached which means release from store. If material is rejected then **red label** is attached and send to rejected or recall area.



## Dispensing area:

* All the apparatus should be **clean.**
* Balance should be daily **calibrated.**
* Most important is humidity controlled, must be less than 45%. For this humidifier is installed.
* Dispensing should be done in the presence of three persons:
  + Production pharmacist
  + QA pharmacist
  + Dispensing person
* Dispensing should be done according to **dispensing sheet.**
* Weighing is done in **plastic pouch** then tag is attached also called identification tag.
* **Identification tag** contains information of weighed quantity, product name, batch no.
* All steps from start to end should be recorded in batch manufacturing record (BMR).
* The weighed material is **loaded on the trolley** and taken to the production area.

## Production Area

### Syrup section:

* + It has **manufacturing area, washing area, filling area, storage.**
  + It must be provided with **adequate material and apparatus,**

like tanks 500 L, 1000 L, 1500 L etc.

* + Most important is the order of mixing **strictly follows the SOP.**
  + **After manufacturing sampling is done** if QC passes it then taken to the filling section. If not then it is reprocessed.
  + **Perform all the tests for finished product** like color, density, assay, volume checked, sealing should be checked.
  + Then it is **packed in unit carton** these are placed in master carton label should be affixed, and transferred to the finished goods store,
  + The **sample must be retained in retained area for two years** in addition to its shelf life.

### Tablet Section

* + **Low humidity for effervescent tablets** and moisture sensitive drugs
  + **Pressure** with in areas like mixing and tableting area should remain on

**negative** side than control corridor

* + All area should be free from dust and floating particles, if possible air conditioned.
  + It should contain mixing equipment’s (MDM, Fluidized bed dryer) compression machines and blistering machines.
  + In coating section suitable exhaust systems.
  + Temp control, air control should be such that there should be comfortable working environment

### STERILE AREA

**Cleanroom** are areas specially constructed and maintained to reduce the probability of environmental contamination of sterile products during the manufacturing process ,include air flow through high-efficiency particulate-air (HEPA) filters ,use of horizontal flow clean benches, vertical flow clean benches, biological safety cabinets, and barrier isolators.

* + **Ante-area** provides a clean area for personal hygiene and for donning personal protective equipment such as hair covers, gloves, gowns, or full clean room attire.
  + **Buffer area** contains the work surfaces for the staging of supplies and equipment
  + **HEPA** filters purify air up to 99.97%
  + **Positive-pressure air flow** is used to prevent contaminated air from flowing into the clean room.

In order to achieve this, the air pressure inside the clean room must be greater than the pressure outside the room, so that when a door or window to the clean room is opened, the air flow is outward.

## Equipment’s

1. **Laminar Flow Work Benches (LFWB)** is specially designed to create an aseptic environment for the preparation of sterile products.

Types of laminar flow work benches:

* 1. Horizontal laminar flow hoods
  2. Vertical laminar flow hoods

1. **Biological Safety Cabinets (BSCs**) are vertical flow hoods with four major types available. They are differentiated by the amount of air re-circulated in the cabinet. Four types of cabinets are used
2. Type A
3. Type B1
4. Type B2
5. Type B3

## Compounding aseptic isolator (CAI)/barrier isolators:

Compounding aseptic containment isolators protect workers from exposure to hazardous drugs. Isolators use unidirectional or turbulent air flow to remove contaminants from the unit. It uses positive air pressure to keep external airborne particles out of the isolator.

