UNIT-IV

QUALITY CONTROL & STANDARDIZATION OF HERBAL MEDICINE

Points to be covered in this topic

- ❑ Stability testing of herbal medicines
- ❑ Application of the various chromatographic techniques in standardization of the herbal product
- ❑ Preparation of documents for new drug application and export registration
- ❑ GMP requirements & drugs and cosmetics act provisions

❑ STABILITY TESTING OF HERBAL MEDICINES

❖ INTRODUCTION

- A stability study is a routine procedure that ensures the maintenance of herbal medicines, its **safety, quality and efficacy** throughout the **shelf life.**
- The stability testing is used in **investigating the quality of herbal products** which varies with the time under the influence of environmental factors such as; **temperature, humidity, light, oxygen, moisture,** other ingredient or excipient in the dosage form, the particle size of the drug, **microbial contamination, trace metal contamination, leaching from the container, etc.** and also provide statistics for the determination of shelf lives.
- Stability studies should be performed on at least **three production** batches of the herbal products for the proposed shelf life, which is normally denoted as **long term stability** and is performed under natural atmospheric conditions.

❖ FACTORS AFFECTING STABILITY OF HERBAL MEDICINES

1. **Physical instability:**

- Herbal medicines are usually susceptible to **physical instability** due to the presence of **impurities and reaction with the container.**
- **Microbial contamination and insect feeding** affect the **secondary metabolites** and chemical composition of the plants.

2. **Chemical instability:**

- Herbal drugs are subjected to degradation during storage by **hydrolysis, oxidation, crystallization, emulsion breakdown, enzymatic deterioration and chemical reaction** with the additives and excipients.
- **Temperature** - The rate of degradation of most chemical increase with an increase in temperature.
- Moisture absorbed on to the **surface of solid drug** will increase the rate of decomposition.

- **Presence of enzyme** in product also **increases rate of chemical degradation.** Light Many chemical reactions induced by exposure to light of high energy.

3. **Environmental conditions:**

Environmental conditions such as; **altitude, temperature, rainfall, soil, storage conditions** as well as different harvesting procedures, time and method of collection, manufacturing processes (selecting, drying, extracting, purifying and genetic variability) can create variability in the **product quality, stability** and in the concentration of active constituents.

4. **Variability in the complex mixture:** - Herbal formulations are the complex mixtures of different components obtained during the **extraction process**. Each component has variable **shelf life, activity, concentration & consistency.**

5. **Drug interaction, deterioration, decomposition during storage:**

Moisture content above the **critical value and growth of micro-organisms** in natural products can cause the interaction of active components with the **packaging material.**

❖ ROLE OF MARKERS IN DETERMINING THE STABILITY OF HERBAL DRUGS:

- **Markers are chemically known compounds,** which may or may not have a **therapeutic effect**, they are used to calculate the **quantity of herbal medicinal ingredients** in herbal medicinal products.
- It is important to isolate and structurally elucidate chemically defined substances in plants, drugs or drug preparation so that, they can be used as markers that not only help to understand the active principle of herbal drugs but also can **enhance analytical quality control.**

❖ ANALYTICAL METHODS TO DETERMINE THE STABILITY OF HERBAL PRODUCTS:

The analysis of herbal preparation is mostly done by modern chromatographic or spectroscopic methods like; **HPLC, gas chromatography (GC), TLC, quantitative determination by UV visible spectroscopy**/combination of these.

- HPLC and GC methods can be used for **identification and purity testing** as well as the detection of single compound for the assay.

❖ SHELF LIFE OR EXPIRATION DATE:

- An expiration date is defined as the time up to which, the **herbal product** will remain stable when stored under recommended **storage conditions**. Thus, an expiration date is a date beyond which it is predicted that the herbal product may no longer retain fitness for use.
- **Shelf life** is the time during which the product, if stored appropriately as per the manufacturer's instructions, will retain **fitness for use** (>90% of label claim of potency).

❖ PROTOCOL FOR STABILITY TESTING:

A well-designed stability protocol should contain the following information:

(a) Batches: Stability studies at **developmental stages** are generally carried out on a **single batch** while studies intended for **registration of new product** or unstable established product are done on first three production batches, while for stable and well-established batches, even two are allowed.

(b) Containers and closures: The testing is done on the product in immediate containers and closures proposed for marketing. The packaging materials include; **aluminum strip packs, blister packs, HDPE bottles, etc.**

(c) The orientation of storage of containers:. This orientation helps to determine, whether the contact between the **drug product or solvent and the closure** results in the extraction of chemical substances from the closure components or adsorption of product components into the container closure.

(d) Frequency of testing: The frequency of testing should be such that it is sufficient to **establish the stability** profile of the new drug substance. For products with a proposed shelf life of at least 12 months, the testing frequency at the long-term storage condition should be every 3 months over the first year, every 6 months over the second year and annually thereafter throughout the proposed shelf life expiration date.

(e) Sampling Plan: The sampling plan for stability testing involves planning for the number of samples to be charged to the **stability chambers** and sampling out of the charged batch so as to cover the entire study.

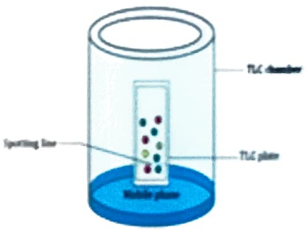
(f) Test parameters: The stability test protocol should define the test parameters that would be used for **evaluation of the stability samples.** The tests that monitor the **quality, purity, potency** and identity which could be expected to change upon storage are chosen as stability tests. Therefore, appearance, assay, degradation products, microbiological testing, dissolution & moisture are standard tests performed on stability test samples.

❑ APPLICATION OF VARIOUS CHROMATOGRAPHIC TECHNIQUES IN STANDARDIZATION OF HERBAL PRODUCT

Chromatography represents the most versatile separation technique and readily available. Chromatography is defined as a **technique of isolation and identification of components** or compounds or mixture into individual components by using the **stationary phase and mobile phase.** Plant materials are separated and purified by using various chromatographic techniques.

❖ Thin Layer Chromatography (TLC):

Thin layer chromatography (TLC) is one of the **most popular and simple chromatographic technique** used for the **separation of compounds**. TLC is being employed extensively in the standardization of herbal products.

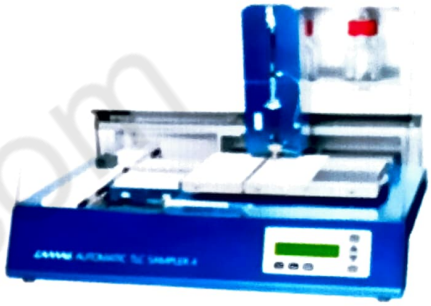


➢ APPLICATION:

- It enables rapid **analysis of herbal extracts** with minimum sample cleanup requirement.
- It enables the **quantification of chemical constituents.**
- TLC can be used to identify natural products like; **essential oils or volatile oil, fixed oil, glycosides, waxes, alkaloids, etc.**
- It is widely used in separating multicomponent pharmaceutical formulations.

- It is used to **purify herbal drug sample** and direct comparison is done between the test sample and the standard sample.
- It is used in **detection of pesticides or insecticides in food and water.**
- It is used in the food industry, to separate and **identify colours, sweetening agent and preservatives.**
- It is used in the herbal **cosmetic industry.**
- TLC is used to separate **non-volatile mixtures.**
- It is used in separation of Vitamins (vitamin E, vitamin D3 and vitamin A).

❖ HIGH-PERFORMANCE THIN LHIN CHROMATOGRAPHY (HPTLC):



- HPTLC technique is widely employed in pharmaceutical industry in process development, **identification and detection of adulterants in herbal products** and helps in standardization of herbal drugs.
- HPTLC is an advanced **sophisticated form of TLC.** It is more efficient than TLC due to the smaller particle size of adsorbent (mean particle size 5 - 6 µm) and narrow range of particle size distribution (4-8 µm).
- It has also been reported that **mobile phases of pH 8** and above can be used for HPTLC.

➢ APPLICATIONS:

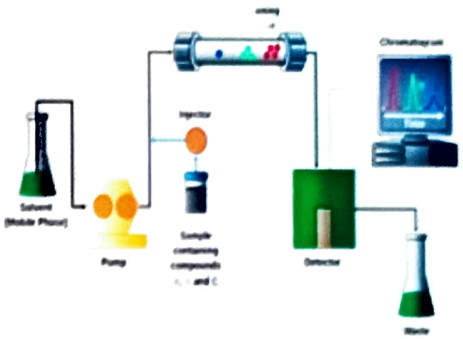
- HPTLC is suitable for both the qualitative and quantitative analysis of herbal extracts and formulations.
- Due to integrated software, all the **analysis parameters and results can be stored digitally.**
- It enables rapid analysis of herbal extracts with minimum **mobile phase.**
- In HPTLC, application of sample, **scanning and data analysis** can be performed individually.
- HPTLC do not require extensive sample clean-up procedure.

❖ HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC):

- HPLC is another form of separation technique used in **analytical chemistry and in herbal drug** research for the separation, identification

and quantification of components of a mixture.

In HPLC, high pressure generating pumps are used to pass liquid containing the sample mixture and the mobile phase through a column filled with solid adsorbent material leading to the separation of sample components.

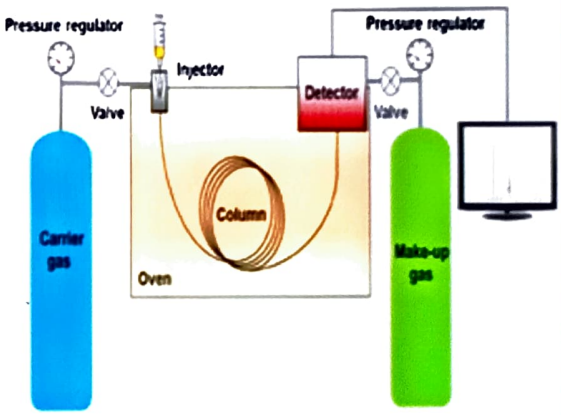


➢ APPLICATIONS:

- As HPLC is carried out under high pressure, it provides high degree of separation and resolution.
- Mobile phase composition can be varied at any time which can affect the complete separation of phytoconstituents which is not possible in HPTLC.
- Column temperature can be controlled accurately which can affect the separation and resolution of separated phytoconstituents.
- Detection of impurities in pharmaceutical industries.
- Quantity of sample required for analysis is very less (up to nanogram).

❖ GAS CHROMATOGRAPHY (GC):

- Gas chromatography (GC) is another type of analytical technique used for separating, characterization, quantization and identification of volatile compounds.
- It can be used in many different fields such as; pharmaceuticals, cosmetics and even for environmental toxins.



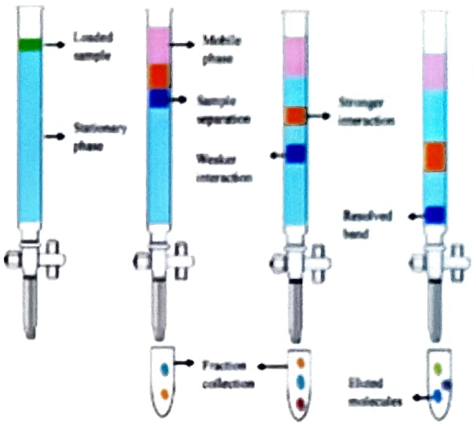
- In GC, the mobile phase is an inert gas such as; helium or nitrogen or hydrogen.

➢ APPLICATIONS:

- GC can be used to determine the identity of herbal products containing complex mixtures of similar compounds.
- It is most suitable for the separation and analysis of volatile compounds such as; essential oils and fatty oils.
- It is used in the analysis of foods like; carbohydrates, proteins, lipids, vitamins, steroids, drug, pesticide residues and trace elements.

- It serves both qualitative and quantitative purposes.
- It is used in analysis of **dairy product for rancidity.**

❖ COLUMN CHROMATOGRAPHY (CC):

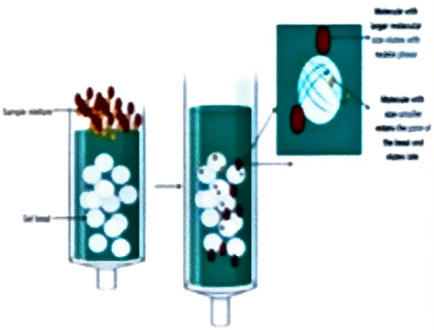


- **Column chromatography** is a separation technique in which, the substances to be separated are introduced onto the top of a column packed with the **solid adsorbent.**
- The mobile phase is then loaded at **the top of the column** and is allowed to flow down slowly and continuously through the column.
- The components with **lower adsorption and affinity** to the stationary phase travel faster when compared to the greater adsorption and affinity with the stationary phase.

➢ APPLICATIONS:

- Column chromatography is used to **isolate active ingredients.**
- It is very helpful in separating compound mixtures.
- It is used to determine drug **estimation from drug formulations.**
- Column chromatography has wider choice of mobile phase.
- **Automation is possible.**
- Used to isolate metabolites from biological fluids.
- It is used to remove impurities.

❖ GEL PERMEATION CHROMATOGRAPHY:



- Gel permeation chromatography is also called as **gel filtration or size exclusion chromatography.**
- It is a separation technique in which the **separation is based on the analyte molecular sizes** since the gel behaves like a molecular sieve.
- In gel permeation chromatography, the **stationary phase is a porous matrix** made up of compounds like; **cross- linked polystyrene, dextran, polyacrylamide gels, agarose gels, etc.**
- The molecules in the sample are pumped through specialized columns containing such microporous packing material (gel).

➢ APPLICATIONS:

- The gel permeation chromatography technique is used for the separation of **proteins, polysaccharides, enzymes and synthetic polymers.**
- Can be used to determine the **quaternary structure of purified proteins**.
- Separation of **sugar, proteins, peptides, rubbers** and others on the basis of their size.
- There is no sample loss. Only small amount of mobile phase is required.

❑ PREPARATION OF DOCUMENTS FOR NEW DRUG APPLICATION AND EXPORT REGISTRATION

- For decades, the regulation and control of new drugs in the United States has been based on the **New Drug Application (NDA).** Since **1938**, every new drug has been the subject of an **approved NDA before US commercialization.**
- The New Drug Application (NDA) is the vehicle through which drug sponsors such as; **organizations, pharmaceutical companies** formally propose that the FDA approve a new Phytopharmaceuticals for sale and marketing.
- In India, the traditional herbal medicines such as; **Ayurveda, Siddha and Unani (ASU)** are usually considered safe because of their long history of use. As such, no safety and efficacy studies are required for marketing approval, as per the **Drugs and Cosmetics Act of 1940.**

❖ Preparation of Documents for New Drug Application (NDA) in India

- When any pharmaceutical company in India wants **to manufacture or import a new Phytopharmaceutical drug,** it has to apply to seek permission from the licensing authority, **Drug Controller General of India** (DCGI) by submitting the data as given in Schedule Y of Drugs and **Cosmetics, Act 1940 and Rules 1945.**
- To prove its **efficacy and safety** in Indian population, it has to conduct clinical trials in accordance with the guidelines specified in Schedule Y and submit the report of such **clinical trials in specified format to FDA.**

- In addition to general regulatory requirements for an NDA, **non-clinical pharmacology/toxicology studies, clinical evidence of efficacy and safety for botanical drugs,** there are special requirements to ensure the safety and quality of botanicals as follows:
  - Description of product and documentation of prior human experience.
  - Description of **botanical raw materials** used and known active constituents or chemical constituents.

Quality control:

- Botanical raw materials.
- Botanical drug substance and drug product: Identity, chemical characterization, **manufacturing processes, biological assay, specifications**, stability, current good manufacturing practices and environmental assessment.

Evidence to ensure therapeutic consistency:

- Botanical raw material control test
- Quality control by chemical test(s) and manufacturing control
- **Biological assay**
- **Clinical data:** Dose-response data and multiple batch clinical data.

✓ In India, **ASU drugs** have been under the purview of the Department of AYUSH and regulatory requirements for phytopharmaceuticals are under purview of the **Central Drugs Standards Control Organization (CDSCO).**

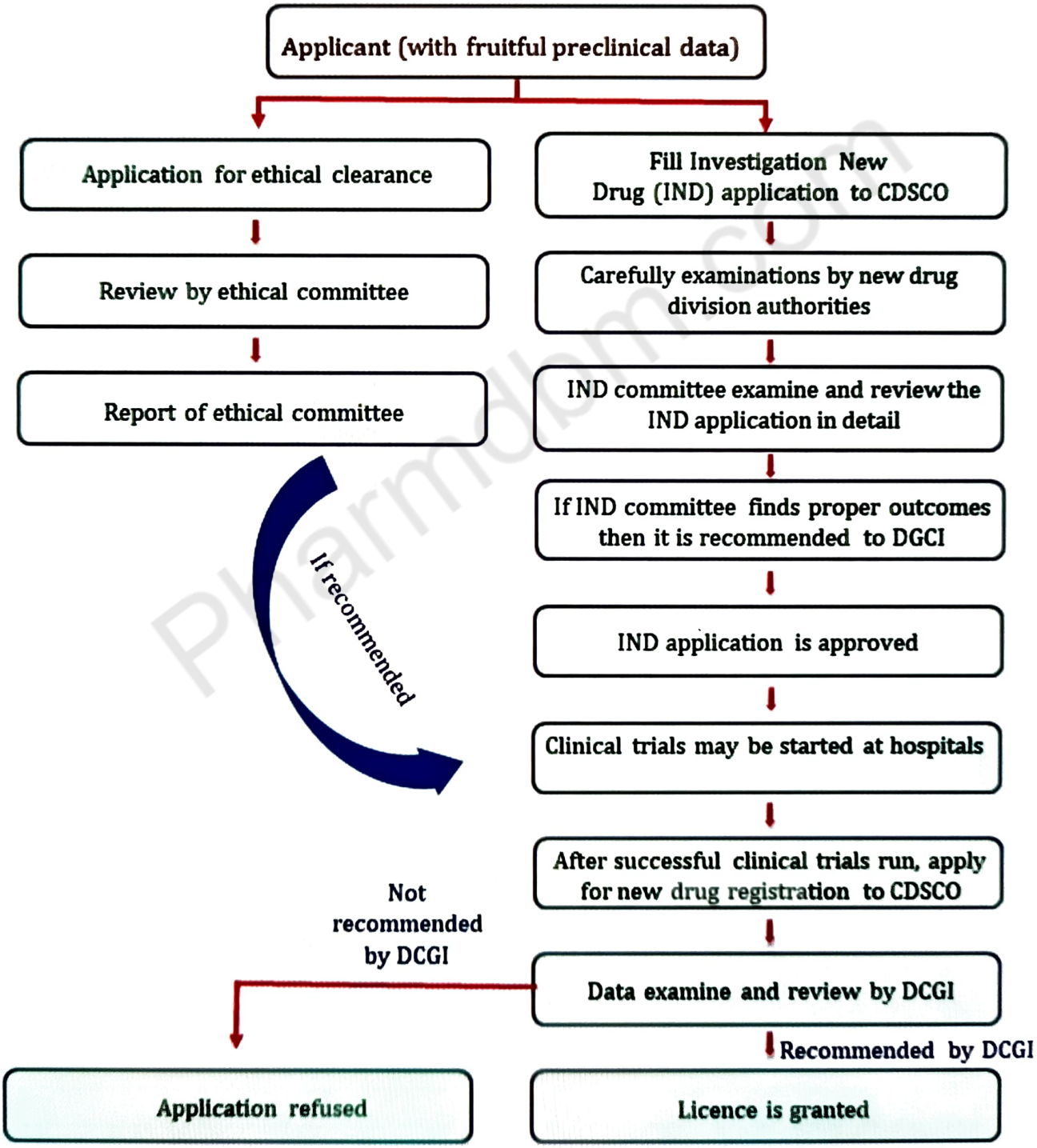
✓ For phytopharmaceutical drug, there is a lot of stress on:

- Available information on the plant, formulation and route of **administration, dosages and therapeutic class** for which it is indicated and the claims to be made for the **phytopharmaceutical and supportive information** from published literature on safety and efficacy and human or clinical pharmacological information.
- Data generated on:
  - **Identification, authentication and source of the plant** used for extraction and fractionation.
  - Process for extraction and subsequent **fractionation and purification.**
  - Formulation details of the phytopharmaceutical drug.

- The manufacturing process of formulation.
- **Stability data.**

✓ The new phytopharmaceuticals regulation permits the development of the drug-using advanced techniques of solvent **extraction, fractionation, potentiating steps, modern formulation development, etc.**

✓ After **NDA approval from CDSCO**, the marketing status of the new phytopharmaceutical drug would be like that of a new chemical entity-based drug.



Flow Chart Showing Drug Approval Process in India

❖ Preparation of Documents for Export Registration

- **Introduction:** A manufacturer holding **valid license copy in Form-25 and Form-28** can obtain No Objection Certificate from Zonal/Sub Zonal offices of **Central Drugs Standard Control Organization (CDSCO)** for export purpose only for approved/unapproved new/banned drug from India.
- **Purpose:** Requirement for the common submission format for issuance of No Objection Certificate for export of approved/unapproved new drugs/banned drugs from India. This document is made as per guidelines issued by the **Ministry of Health and Family Welfare** for Export purpose and **Rule 94 of the Drugs and Cosmetic Act, 1940.**
- The following documents are required to be submitted in the following manner and order for issue of the No Objection Certificate for export of drugs from India:

1. **Covering Letter:** The covering letter is an important part of the application and should **specify the intent of the application**. The list of documents that are being submitted as well as any other **important and relevant information** may be provided in the covering letter.
2. **Purchase order:** Order from the foreign buyer either in the name of manufacturer or in the name of **trader mentioning** list of products to be exported clearly indicating name of the drug, dosage form, composition and **strength, packet size** duly signed by the competent authority with specific destination point of the importing country.
3. **Manufacturing License:** License issued by the **State Licensing Authority** should been closed along with each application for the required location to manufacture the drug for **export purpose.**
4. **Performa Invoice:** A copy of the Performa invoice from the importing country should accompany with the application for import of unapproved **Active Pharmaceutical Ingredients**, used in the drug formulation, it should be duly signed by the competent authority.
5. **Registration Certificate:**

- A copy of registration certificate from the specific importing country along with composition and strength of the drug should accompany with the

and strength of the drug should accompany with the application.

- Registration certificate should be provided in the name of the manufacturer.

➢ Rules Related to Export of Drugs from India:

A. Rule 94: Packing and labeling of drugs other than Homeopathic Medicines

i. Labels on **packages or containers of drugs** for export should be adapted to meet the specific requirements of the law of the country to which the drug is to be exported.

- **Name of the drug,**
- **The name, address** of the manufacturer and the number of the license under which, the drug has been manufactured,
- **Batch or lot number,**
- **Date of expiry, if any.**

ii. Each consignment of export should be accompanied by requisite import license from the importing country.

iii. A No Objection Certificate should be obtained from the **Drugs Controller,** India for export of each consignment.

iv. A No Objection Certificate should be obtained from the **Narcotic Commissioner of India,** Gwalior for export of each consignment of the drug.

V. **The provisions of Rules 96 to 101 inclusive**, should not apply to medicine made up ready for treatment, whether after or without dilution, which is supplied on the prescription of a **registered practitioner provided** that the medicine is labelled with the following particulars:

- The name and address of the supplier,
- The name of the patient and the quantity of the medicine,
- The number representing serial number of the entry in the prescription register,
- The dose, if the medicine is for internal use,
- The words - **FOR EXTERNAL USE ONLY** should be printed on the label if the medicine is for external application.

B. Rule 95: Prohibition of sale or distribution unless labelled

Subject to the other **provisions of these rules**, no **person** should sell or distribute any drug (including a patent or proprietary medicine) unless it is labelled.

C. Rule 96: Manner of Labeling

The following particulars should be either **printed or written in indelible ink** and should appear in a **conspicuous manner** on the label of the innermost container of any drug and on every other covering in which, the container is packed, namely:

i. **The name of the drug**
ii. **For drugs included in the Schedule F or Schedule F (1),** the name was given therein.
iii. **For drugs included in the Pharmacopoeias** and official compendia of drug standards prescribed in Rule 124.

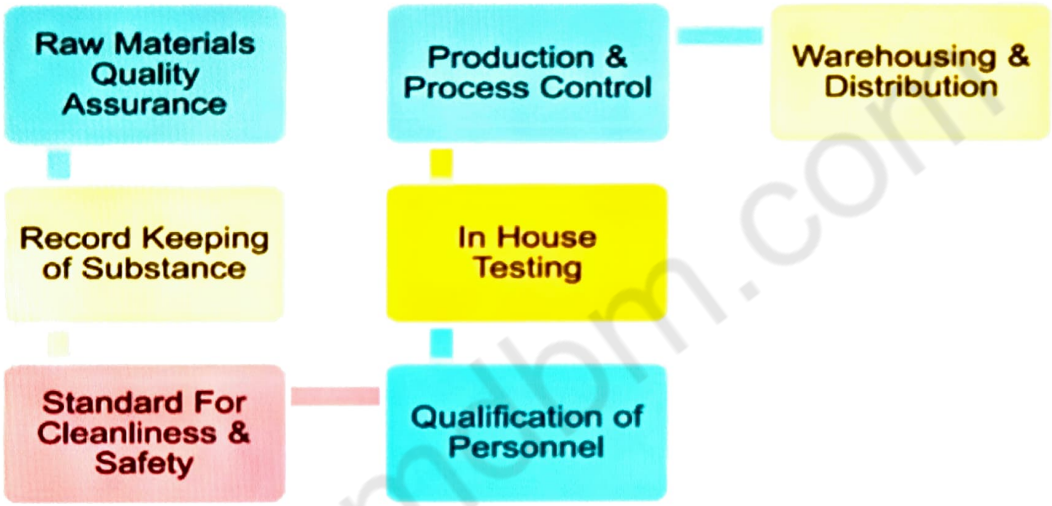
➢ Guidelines for the Export of Drug issued by Ministry of Health and Family Welfare:

During the issue of NOC's for the manufacturing of new drug solely forexport, the following conditions should be taken into consideration:

1. The application should provide **copy of valid export order and NOC** will be issued on a case by case basis against each such order.
2. The applicant should **identify the premises** where, the drug will be **manufactured for export**.
3. The applicant should mention whether the batch to be exported has undergone **Quality control testing** or should be tested at the destined site.
4. The applicant should make available for **inspection of the appropriate authorities.**
5. The applicant should **ensure the physical destruction of all unexported quantity of drugs.**
6. The applicant should ensure that the drug for which, NOC has been given should cease to be manufactured or exported if the drug is prohibited in future in the country or in the importing country.

❑ GMP REQUIREMENTS AND DRUGS AND COSMETICS ACT PROVISIONS

Good Manufacturing Practices (GMP) comes in **Schedule M in Drugs and Cosmetics Act 1940 and Rules 1945.** GMPs are the requirements that the drug and **methods/control/facilities** used in their **manufacturing, processing and packaging** conforms to practice that will assure the **safety and efficacy of the product**. GMPs include a set of practices that ensure quality at every level of operation in industry. It takes into consideration the following aspects:



Flow Chart Showing Different Levels of Operation in an Industry that Ensures Quality

❖ Different parts of GMP are:

1. **General provisions:** The regulation in this part **contains the minimum cGMP** for preparation of drug products for administration to human beings or animals.
2. **Organization and personnel:** The establishment and maintenance of a **satisfactory system of quality assurance** and the correct manufacture of quality products relies upon people. which are the responsibility of the manufacturer.

- Important personnel includes; the head of Production, the **head of Quality Control, and the head of Engineering.**
- The manufacturer should provide training for all the personnel.
- All personnel should **receive medical examination** upon recruitment.

- Direct contact should be avoided between the operator's hands and the exposed product.
- Personnel should be instructed to use the **hand washing facilities**.

3. Building and Facilities:

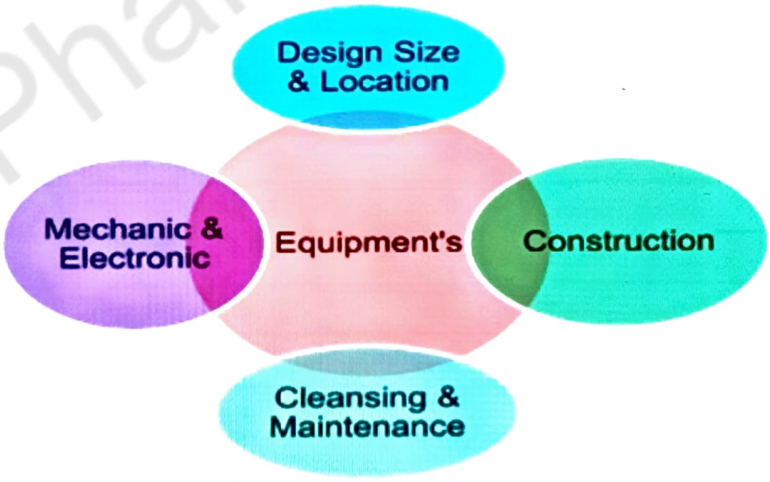
Building and Facilities Requirement under GMP

Building Requirements	Facilities Requirement under GMP
Premises	Premises must be located, designed, constructed, adapted and maintained to suit the operations to be carried out.
Design and construction features	The building should have adequate space for orderly placement of equipments and materials to prevent mix-up. It should be designed in such a way to facilitate cleaning, maintenance and proper operation. Temperature and humidity control should be provided
Lighting	Adequate lighting should be provided in all the areas.
Ventilation, Air filtration	Air ventilation system should be provided. Equipment for control over pressure, microorganism, dust, humidity and temperature should be provided.
Plumbing	Potable water should be supplied. Drains should be of adequate size and preventive measures should be taken to prevent back siphonage.
Sewage and refuse	Sewage waste and other refused material from building and intermediate premises should be disposed off in a safe and sanitary manner.
Washing and toilet facilities	Suitable washing facilities should be provided including: hot and cold water, soap or detergent, air drier, towel and clean toilet facilities easily accessible to working area
Sanitation	Any building used in manufacturing, processing, packing or holding of a drug product should be maintained in a clean and sanitary condition.

Maintenance	• The building should be maintained in a good state. • Steps should be taken in order to **prevent the entry of unauthorized people.** • Weighing of starting materials should be carried out in a separate weighing room designed for that use. • Segregated areas should be provided for the **storage of rejected, recalled or returned materials or products**. • Highly active (controlled) materials or products should be stored in safe and secure areas. • Quality control laboratories should be separated from production areas. • Rest and refreshment rooms should be separate from other areas

4. Equipments:

Equipments 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**, the buildup of dust or dirt.



5. Control of components, drug product containers and closures:

- There should be written procedures describing in **details of receipt, identification,storage, handling, sampling, testing and approval or rejection** of components and drug product **containers and closures.**
- It should be **clean and sterilized**.

6. **Production and process control:**

- There should be written **procedure for production and process control** designed to assure that the drug products have the **identity, strength, quality and purity** that they are represented to possess.
- To assure the **batch uniformity and integrity of drug products,** written procedures have to be established to monitor the output and to validate the performance of the **manufacturing process responsible for causing variability.**

7. **Packaging and labeling control:**

- Labeling and packaging materials should be **examined or tested upon receipt** and before use in **packaging or labeling of drug products.**
- Records should be maintained for each shipment.
- Packaged and labelled products have to be examined after **finishing the operations** to **assure that containers and packages** in the lot have the correct label.

8. **Holding and Distribution:**

- **Warehouse procedure include:** Storage of drug products under appropriate conditions of **temperature, humidity and light** so that, the identity, purity of drug products are not affected.
- **Distribution procedure include:** Oldest approved stock of drug product is distributed first. Distribution of each lot of drug product can be readily determined to **facilitate its recall if necessary.**

9. **Laboratory Control:**

- Laboratory control should include; **appropriate specifications, standards, sampling plans and test procedures** designed to assure that **components, drug product containers, closures,** in-process materials conform to appropriate standards of identity, strength, quality and purity.

10. **Records and Reports:**

- Production, quality control and distribution records are required to be maintained and should be retained for at **least 1 year** after the expiration of the batch.
- All maintained records should be available for **authorized inspection.**

❖ Quality Assurance (QA):

- Quality Assurance (QA) testing is an activity to **ensure that an organization is providing** the best possible product to customers. QA focuses on improving processes to deliver quality products to the customer.
- Quality assurance has a defined cycle called **PDCA (Plan-Do-Check-Act).**
- The phases of this cycle are:

➢ **Plan:** Organization should plan and **establish the process related objectives** and determine the processes that are required to **deliver a high quality end product.**

➢ **Do:** Development and testing of processes and also "do" changes in the processes.

➢ **Check:** **Monitoring of processes, modify the processes** and check whether it meets the predetermined objectives.

➢ **Act:** Implement actions that are necessary to achieve improvements in the processes.

The system of quality assurance suitable to the manufacture of the pharmaceutical product should ensure that:

- **Production and quality control** operations are properly documented.
- Managerial responsibilities are specified in job descriptions.
- **Calibration and validation are carried out.**
- Finished products are correctly processed and checked.
- There must be procedure for **self-inspection.**
- **Deviations are reported, investigated and documented.**

➢ Quality Assurance in production consists of the following steps:

1. **General requirements:** Handling of materials and products such as; receipt, sampling, storage should be done in accordance with a written procedure.
2. **Prevention of cross-contamination and bacterial contamination in production:** Protective clothes should be worn, provided with appropriate **air lock and pressure** differentials.

3. **Processing operations:** Intermediate and bulk products: In-process control and environmental control.
4. **Packaging operation:** Filling, sealing, printing, embossing should be distinct and resistant to fading or erasing.

❖ Quality Audit:

- Quality audit is the process of **regular examination of a quality system** carried out by an **internal or external quality auditor or an audit team.**
- This helps to determine if the pharmaceutical industry complies with the defined quality system processes and can involve **procedural or results-based assessment criteria.**
- Quality audit consists of:
  - **Preparing a list of items** (procedures, equipment set-ups, quality records, measurements, etc.)
  - Checking and going to the areas responsible for these items for an **actual check or audit of these items.**

➢ Types of Quality Audit

➢ Objectives of Auditing:

1. To determine the **conformity or non-conformity of the quality system.**
2. To determine the effectiveness of the **implemented quality system.**
3. To provide audit team with an opportunity to improve the quality system.
4. To meet the **regulatory requirements.**
5. To permit listing of audited organizations in a register.

➢ Steps to perform a Quality Audit:

1. To plan and **prepare for the audit.**
2. To **arrange and announce for the audit.**

3. To **arrive at the site of the audit**, meet people and explain the purpose.
4. To perform a quality audit.
5. **Informal oral report finding.**
6. A formal report with recommendation.
7. Finally to follow up the deficiencies.

➢ Standard Operating Procedure (SOP) for Auditing:

Every pharmaceutical company prepares a Standard Operating Procedure (SOP) for auditing which includes:

1. Information regarding the **company policy pertaining to auditing.**
2. Composition of auditing team.
3. **Scope of audit.**
4. Selected area subjected to auditing.
5. **Frequency of auditing.**
6. Written reports on audits including their distribution.
7. Corrective actions of deficiencies.