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## GOOD MANUFACTURING PRACTICE FOR PHARMACEUTICAL PRODUCTS

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### Abstract

A manufacturing authorization holder is responsible for producing pharmaceuticals in a way that is appropriate for the intended purpose, complies with marketing authorization standards, and does not jeopardize patient safety by subpar quality, safety, or efficacy. Senior management bears the responsibility for achieving this quality target, which calls on the involvement and dedication of employees across numerous departments and levels of the organization, as well as suppliers and distributors. To consistently achieve the quality objective, a thorough system of quality assurance that incorporates good manufacturing practices—and, by extension, quality C and quality risk management—must be created and implemented appropriately. Its efficacy ought to be tracked and thoroughly documented. Every component of the quality assurance systems needs to have enough staff, appropriate and sufficient space, equipment, and facilities, as well as knowledgeable individuals. The holder of the manufacturing authorization for the authorized person is subject to additional legal obligations.

### KEY WORDS:

Good Manufacturing Practices, pharmaceutical industry, quality, regulatory authorities, security and effectiveness

### Introduction

The portion of quality assurance known as "good manufacturing practice" (GMP) is responsible for making sure a product is consistently made to the acceptable standard for the use for which it is designed. GMP mandates that all facilities must be available and that the production process be thoroughly described before it is started. In actuality, this means that employees need to be properly taught, that the right materials be used, that the right facilities and equipment be used, that approved procedures be followed, that acceptable and transport facilities be made accessible, and that the right records be kept.

The quality of pharmaceutical products depends on the degree of care taken in their preparation. Final checks carried out on the finished products are useful in confirming that the correct ingredients have been used and that the materials have been correctly processed. It is however essential that proper in-process control is exercised and that it is adequately documented to provide reliable evidence that the correct

procedures have been followed. The need for GMP is recognized throughout the world. More than 20 countries have issued their own GMP guidelines

## Required

The following are the purposes of the Good Manufacturing Practices:

- (i) Raw materials used in the production of pharmaceuticals must be genuine, meet quality standards, and be free of contaminants.
- (ii) The production procedure is followed exactly as directed to uphold standards.
- (iii) Sufficient quality control procedures are implemented and
- (iv) The produced medication meets the required quality standards and is approved for sale.
- (v) To accomplish the aforementioned goals, every license must develop techniques and procedures for adhering to the established medication manufacturing process. These should be recorded in a manual and maintained for inspection and reference. G.M.P. does not apply to educational institutions or recognized, certified vaidyas, Siddhas, or Hakeems who make their medications to give to patients and do not sell them on the open market.

## World Health Organization (WHO) GMP:-

The World Health Organization (WHO) explains good manufacturing practice as "the fact part of quality assurance that assures that the goods are consistently created and monitored according to the quality ideals applicable to their intended use and are required by market approval"

All facets of the manufacturing process are included by GMP, including defined manufacturing processes, critical manufacturing steps, suitable areas for production, storage, and conveyance, qualified and experienced personnel for production and quality control, adequate laboratory facilities, approved written guidelines and instructions, records suggesting the conclusion of all steps in defined procedures, full product traceability in batch rewards and delivery records, and systems for recall and complaint investigation.

## GMP Requirements For Premises And Materials For Pharmaceutical Products

### 1. General requirements:

**1.1. Location and surroundings:** The factory building or buildings used in the manufacture of drugs have to be in a location that inhibits the risk of contamination from other sources, such as open sewers and drains, bathrooms available to the public, or any other factory the fact that gives noxious or disagreeable fumes, stains, high soot, dust, smoke, chemical, or biological emissions.

**1.2. Buildings and Premises:** The factory's building(s) must be planned, constructed modified, and kept up to date with a variety of manufacturing procedures so as for the production of medications in a clean and safe environment. They have to comply with the requirements outlined in the 1948 Factories Act (63 of 1948).

The areas used for production, processing, warehousing, packaging, labeling, and testing must be:

- (i) compatible with each other manufacturing operations that might use place in the same or nearby section;
- (ii) adequate to enable personnel movement and equipment placement in an orderly and logical manner;
- (iii) Designed/constructed/maintained to prevent entry of insects, pests, birds, vermin, and rodents. Interior surface (walls, floors, and ceilings) shall be smooth and free from cracks, and permit easy cleaning, painting, and disinfection;

(iv) When recommended for the processes and dosage forms being produced, air conditioning. The manufacturing and dispensing spaces must have sufficient natural light, efficient ventilation, air control systems, and, if necessary, Air Handling Units to maintain the humidity and temperature required for the particular product. These constraints must be suitable for the kind of medication and the intended use. They must also be appropriate for the comfort of those who wearing protective gear, handling items, and doing tasks inside of them in connection to the outside world. These regions must be frequently checked for conformity with the requirements;

(v) outfitted with a drainage system, by the guidelines for the different product categories, that must be large enough and constructed in a way that inhibits backflow and/or keeps rats and insects out of the building.

(vi) To prevent dust collection, the walls and floors of the areas where medication manufacturing is done must be free of cracks and open joints. Open channels should be avoided in manufacturing areas, and where they are present, they should be shallow. These need to be smooth, washable, covered, and able to be cleaned and disinfected quickly and efficiently. The inside surfaces are not allowed to shed debris. The premises' cleaning and painting history must be kept on file regularly.

**1.3 Water system:** To create purified water that complies with pharmacopoeial specifications, a validated system must be in place for treating water that is obtained from one's own or any other source and making it drinkable in line with standards established by the Bureau of Indian Standards or Local Municipality, as applicable. Only the operations that call for potable water—such as washing and cleaning—may employ the purified water that has been created in this way. Water must be kept in tanks that prevent microbial growth and do not negatively impact the water's quality. Periodically, the licensee must clean the tank and keep records of the cleaning.

**1.4 Disposal of waste:-**(i) The Factory's sewage and effluents (solid, liquid, and gas) must be disposed of by the Environment Pollution Control Board's guidelines.

(ii) By the Bio-Medical Waste (Management and Handling) Rules, 1996, all biomedical waste must be eliminated.

(iii) Extra care must be exercised when storing and discarding medications that are rejected. For each garbage disposal, records must be kept.

(iv) Measures for the appropriate and secure storage of waste items while they wait to be disposed of must be taken. By federal and state laws, flammable items, hazardous materials, and toxic chemicals must be stored in appropriately constructed, enclosed spaces.

**2. Warehousing Area:-** Enough space must be planned to accommodate the adequate and organized storage of a variety of materials and goods, including machine and equipment spare parts, change items, bulk and finished goods, intermediates, products in quarantine, rejected, returned, or recalled goods, and starting and packaging materials.

Good storage conditions must be ensured by the design and adaptation of warehousing areas. They must be kept dry, clean, and within reasonable temperature ranges. If certain storage conditions (such as temperature and humidity) are needed, they must be supplied, tracked, and documented. Storage areas must maintain proper housekeeping practices, as well as processes and records for controlling rodents, bugs, and vermin. There must be adequate platforms, bins, and racks for material storage. Materials and goods must be shielded from bad weather by receiving and dispatching bays.

These spaces must be clearly defined while maintaining a quarantine status within a warehouse or store through distinct, designated storage rooms. Any method that takes the place of the physical quarantine must provide a comparable level of segregation assurance. Only those who are allowed may enter these locations.

The warehouse space must provide a dedicated sample area for active raw ingredients and excipients. If sampling is carried out at another location, care must be taken to avoid cross-contamination, contamination, and confusion.

### 3. Production Area:

1. The production area should be planned to facilitate production in a logical sequence of operations and ideally in a single flow.
2. Different, independent facilities must be made available for the production of biological preparations including live microorganisms or sensitive medicinal goods like penicillin to reduce the possibility of cross-contamination. Manufacturing powerful and contaminating goods like beta lactum, sex hormones, and cytotoxic compounds must be done in separate, specialized facilities.
3. To prevent cross-contamination and reduce the possibility of any production or control measures being overlooked or applied incorrectly, working and in-process space must be sufficient to allow for the logical and orderly placement of materials and equipment as well as the mobility of workers.
4. To prevent recesses from being created, pipework, electrical fittings, ventilation holes, and similar service lines must be built, fixed, and installed. The nature of the supply and the direction of the flow must be recognized or indicated, and service lines should ideally be distinguished by color.

### 4. Ancillary places:

Refreshment and rest places need to be kept apart from other locations. The manufacturing and storage sectors cannot be reached directly from these sites.

The number of customers must be accommodated and easily accessible restrooms, laundry, and changing areas must be provided. Male and female restrooms must be kept apart and not be connected to the production or storage areas. Written guidelines for disinfecting and sanitizing these locations must be provided.

Workshops for maintenance must be kept apart from areas used for production. Tools, spares, and altered components must always be housed in designated rooms or lockers when they are kept in the manufacturing area. Before being brought into the manufacturing areas, tools and spare parts intended for usage in sterile areas must be cleaned.

Animal housing places need to be kept apart from other locations. The additional specifications for animal housing are outlined in the Drugs and Cosmetics Rules, 1945 Rule 150-C(3), which will be enacted for manufacturing purposes.

### 5. Area of Quality Control:

1. The manufacturing regions must not have any influence over the Quality Control Laboratories. Each of the following areas needs to be set off specifically: biological, microbiological, radioisotope, and physico-chemical. Sensitive and complex instruments used for analysis must have a dedicated instrument room with enough space.
2. The layout of Quality Control Laboratories must be suitable for the tasks that will be performed there. It is necessary to allow enough room to prevent confusion and cross-contamination. Reference standards, reagents, test samples, retained samples, and records must all have adequate and appropriate storage space.

3. The appropriateness of the building materials and ventilation shall be considered in the laboratory's design. Testing sections for microbiology, radioisotopes, and biology must have their air-handling systems and other necessities. Water of suitable quality must be regularly supplied to the laboratory for cleaning and testing needs.

4. Examining Quality The laboratory will be separated into areas for chemical, microbiological, and, if necessary, biological testing. These must have enough space for both primary installation and auxiliary uses. When deemed required, the microbiology department will feature setups like airlocks and a laminar airflow workstation.

## **6. Employees:**

1. The manufacturing process must be carried out directly under the guidance of qualified technical personnel who have real-world experience with the applicable dosage form and/or active pharmaceutical products.

2. The leader of the Quality Control Laboratory must be separate from the production line. The licensee's full-time personnel who possess the necessary technical skills will oversee the testing directly.

3. Appropriately skilled and experienced personnel must be used in Quality Assurance and Quality Control procedures.

4. Technical and Quality Control employees must have clearly defined written responsibilities that they must adhere to.

5. The number of employees must be sufficient and directly related to the volume of work.

6. The license holder is responsible for making sure that all employees in the production area or the Quality Control Laboratories get training relevant to the responsibilities and duties that have been delegated to them, as per written instruction. They will receive frequent in-service training.

## **7. Workers' Clothing, Sanitation, and Health:**

7.1. Employees handling beta-lactam antibiotics must undergo a Penicillin sensitivity test before work, and those handling cytotoxic chemicals, sex hormones, and other strong medications must undergo routine examinations for side effects. For health reasons, these employees should be rotated out of these areas (unless they work in facilities designated for that purpose).

7.2. All employees must pass a medical examination, which includes an eye exam, and be free of skin, skin, and other infectious or communicable diseases before being hired. After that, they ought to have routine medical examinations—at the very least, once a year. There must be documentation kept on file. To determine the health status of employees engaged in various activities, the licensee must offer the services of a licensed physician.

7.3. Everyone must get training in procedures that guarantee employee cleanliness both before and during work. Everyone involved in the production operations must maintain a high standard of personal cleanliness. Change rooms and other key sites will have instructions to this effect posted.

7.4. Until his condition is determined to be no longer a risk, no one displaying a visible illness or open lesions that could negatively impact the quality of products is permitted to handle starting materials, packaging materials, in-process materials, or medication products.

7.5. Every employee must be directed to notify their immediate supervisor of any illness or unusual health condition so that the proper steps can be taken.

## 8. Manufacturing Operations and Controls:-

8.1. All production processes must be managed by technical personnel who are currently licensed by the regulating body. Every crucial step in the procedure concerning the choice, measurement, and weighing of raw material addition at different phases must be carried out by qualified workers under the close supervision of authorized technical professionals. The product name, batch number, batch size, and manufacturing stage must be prominently labeled on the inside of all vessels and receptacles used for the production and storage of the product during the various stages of manufacturing.

8.2.1 The licensee must use the necessary air-handling system, pressure difference, segregation, status marking, and cleaning to prevent the mixing and cross-contamination of drug material and drug product (from ambient dust). Standard Operating Procedures and related documentation must be kept up to date.

8.2.2. The licensee is responsible for making sure that sensitive medications, such as sex hormones, beta-lactam antibiotics, and cytotoxic compounds, are processed in isolated production areas or segregated portions of the building that have their air handling unit and appropriate pressure differentials. Enough maintenance and service documents must attest to the successful segregation of these regions.

8.2.3. Materials that are under process must be clearly labeled to indicate their status to avoid confusion during the production phases. Every piece of production-related equipment must be labeled with its present condition.

8.2.4. Packaging lines must be sufficiently separated from one another and autonomous. Before the closing hour, it must be made sure that any packaging leftovers, such as labels, cartons, and caps, are removed.

8.2.5. Measures must be made to guarantee that the workspace, packing lines, printing machines, and other equipment are clear of any products, materials, or spills before packaging activities start. The line clearance must be completed by the relevant checklist and documented.

8.2.6. The accuracy of any printing, whether done separately or during packaging (such as batch numbers or expiration dates), must be double-checked regularly. All printing, including overprinting, requires written permission.

## 9. Hygiene in the Production Facilities:

9.1 The manufacturing area must be kept clean and organized, devoid of collected trash, dust, debris, and other materials of a similar nature. There must be a recognized cleaning protocol followed.

9.2 No material shall be stored in the manufacturing areas other than that which is being processed. It is not to be utilized as a public route.

9.3. A regular sanitation schedule that is created, followed, accurately documented, and includes the following information

- designated cleaning zones and cleaning schedules;
- the cleaning process to be followed, together with the tools and supplies needed; and
- Those tasked with overseeing and managing the cleaning process.

9.4 Enough working and in-process storage space must allow for the logical and orderly arrangement of materials and equipment to minimize the possibility of cross-contamination between various pharmaceutical products or their components and to reduce the possibility of any manufacturing or control steps being overlooked or applied incorrectly.

9.5. Production spaces must have adequate lighting, especially in places where visual online controls are used.

## 10. Raw Materials:

10.1. The licensee must maintain records by Schedule U and retain an inventory of all raw materials to be utilized at any point during the drug-making process.

10.2 All arriving materials must be placed in quarantine as soon as they are received or processed. The 'first in/first expiry' - 'first-out' principle of batch segregation and stock rotation requires that all materials be stored in an orderly and suitable manner. Every shipment of supplies must be examined to make sure it matches the order that was placed.

10.3 All arriving items must be bought from authorized vendors with current purchase coupons. Whenever feasible, raw materials have to be acquired straight from the manufacturers.

10.4 Each consignment must be examined upon receipt, and authorized staff—who may include members of the quality control department—must verify that each container has a sealed and intact package. Containers that are damaged must be recognized, noted, and kept apart.

10.5. If multiple batches are included in a single delivery of material, each batch will be treated as an independent batch for testing, sampling, and release.

10.6. The storage area's raw materials must have the proper labels. Labels must prominently display the following information:- the product's designated name, the batch number, the manufacturer's name, address, and internal code reference, if applicable; - the contents' status (e.g., in quarantine, being tested, released, accepted, or refused); - the manufacturing date, expiry date, and re-test date.

10.7. Appropriate, distinct spaces with equipment and arrangements for the "under test," "approved," and "rejected" materials must be provided. Products and materials must be stored, when needed, in a dry, clean, and organized manner with controlled humidity and temperature.

10.8. The containers used to collect the samples must be identified.

10.9 Only raw materials that are within their shelf life and have been approved by the quality control department may be utilized. It will be made sure that the formulation product's shelf life does not surpass that of the active raw materials it contains.

10.10 Care must be taken to make sure that all raw material containers are positioned on elevated platforms or racks rather than on the ground.

## 11. EQUIPMENT:-

11.1. The location, design, construction, adaptation, and maintenance of equipment must be tailored to the specific tasks that need to be completed. To prevent cross-contamination, dust or dirt buildup, and any other negative impact on product quality, the equipment's layout and design must minimize error risk and enable efficient cleaning and maintenance. Every piece of equipment must, if needed, come with a log book.

11.2. In the raw material stores, production, and in-process control operations, balances and other measuring instruments with the proper range, accuracy, and precision must be available. These instruments must be calibrated and checked regularly in compliance with Standard Operating Procedures and records kept.

11.3. No piece of the production machinery that comes into contact with the product can be unduly reactive, additive, or adsorptive to limit the product's quality.

11.4. Non-toxic/edible grade lubricants are needed to be used whenever feasible to prevent undetected contamination, and equipment should be maintained such that lubricants do not contaminate the items being produced.

11.5. Defective equipment must be fully tagged or removed from the production and quality control areas.

## **12. DOCUMENTATION AND RECORDS:-**

Since documentation is a crucial component of the quality assurance system, it must address every facet of good manufacturing practices (GMP). Its goals are to establish the requirements for all raw materials, manufacturing processes, and quality control; to guarantee that all manufacturing staff members are equipped with the knowledge required to determine whether or not to release a drug batch for sale, and to create an audit trail that will enable the tracking down of any suspected defective batch.

12.1. Where relevant, documents that are developed, prepared, reviewed, and managed must adhere to these guidelines.

12.2 Appropriate and authorized individuals must approve, sign, and date documents.

12.3. Title, type, and purpose of documents must be specified. They must be easily verifiable and arranged in an organized manner. Document copies must be readable and clear. Records must be updated and examined regularly. Any changes made to a document's entry must be dated and signed.

12.4. Information can be captured by electronic data processing systems or other dependable methods; however, comprehensive operating procedures and master formulas for the system in use must also be provided in hard copy to enable verification of the accuracy of the records. Authorized individuals are required to enter or alter data in the computer whenever documentation is processed using electronic data processing techniques. A record of the additions and removals must exist. Passwords and other restrictions will be used to limit access, and the accuracy of key data entering will be verified by a third party. Electronically stored batch records must have a reliable backup. Every important piece of information must be easily accessible for the duration of retention.

## **13. LABELS AS WELL AS OTHER PRINTED MATTER:**

Labels are a must for identifying medications and how to use them. The printing must be done legibly and with vibrant colors. The product's label must include all required information about it.

13.1. The proper labels must be on all equipment and containers. To indicate a product's status (e.g., under test, approved, passed, rejected), different colored labels must be used.

13.2. Product leaflets about various products should be kept apart to prevent the possibility of confusion in printed packaging materials.

13.3. The licensee's quality control department has to check all labels for glasses, cartons, and boxes, as well as all circulars, inserts, and leaflets, before releasing them.

13.4. The licensee shall ensure that samples are taken from the bulk and that they have been accurately tested, approved, and released by the quality control personnel before packaging and labeling a given batch of a drug.

13.5. For each shipment received, records of receipt of all labeling and packaging materials must be kept, indicating receipt, control reference numbers, and whether the shipment was accepted or rejected. Labels and packaging materials that are damaged or not in use must be disposed of and documented.



## 14. QUALITY ASSURANCE:-

This is a broad idea that encompasses all factors that either separately or jointly affect a product's quality. It is the culmination of all the preparations done to guarantee that the goods are of the caliber necessary for the purposes for which they are intended.

14.1. The quality assurance system suitable for the production of pharmaceuticals must guarantee:

The requirements of good manufacturing practice (henceforth referred to as GMP) and other related codes, such as those of good laboratory practices (henceforth referred to as GLP) and good clinical practices (henceforth referred to as GCP), are taken into consideration during the design and development of pharmaceutical products.

Adequate preparations are made to guarantee that the right starting and packaging materials are manufactured, supplied, and used. Enough controls are applied to bulk, intermediate, and starting materials plus to other process validations, calibrations, and controls. The final product is processed and checked correctly, following established protocols. Before authorized persons certify that each production batch has been produced and controlled in compliance with the specifications of the label claim and any other provisions relevant to the production, control, and release of pharmaceutical products, the pharmaceutical products are not released for sale or availability.

## 15. SELF INSPECTION AND QUALITY AUDIT:-

For the express purpose of improving a system, it may be helpful to establish a self-inspection team and augment it with a quality audit procedure.

15.1. The concept of self-inspection shall be used to assess the manufacturer's adherence to GMP in all facets of production and quality control. The manufacturer will put together a group of impartial, skilled, and experienced individuals from both inside and outside the organization to audit the application of the developed methodology and procedures. The process for conducting a self-inspection must be recorded, along with the findings, recommendations for corrective action, and an efficient program for monitoring the results. Adoption of the corrective action recommendations is required.

15.2. The program's objective is to identify inadequacies in the application of Good Manufacturing Practices and suggest the required remedial measures. Regular self-inspections as well as one-time ones, such as in response to product recalls repeated rejections, or the announcement of a licencing authority inspection, are required. All recommendations for corrective action must be carried out by the team in charge of self-inspection, which should be made up of individuals qualified to assess GMP implementation objectively.

15.3 The following must be included in the written instructions for self-inspection:

- The buildings, which include the staff quarters.
- Upkeep of structures and machinery.
- Storage of both raw materials and completed goods.
- Instruments.
- In-process and production controls.
- Quality assurance.
- Record-keeping.
- Hygiene and sanitation.
- Instrument or measurement system calibration.

- Recall actions.
- Management of complaints.
- The outcomes of earlier self-inspections and any remedial actions completed.

## 16. QUALITY CONTROL SYSTEM:

Quality control deals with sampling, requirements, testing, documentation, and release procedures. It makes sure that the relevant and necessary tests are conducted and that neither materials nor products are made available for use or sale until their quality is deemed acceptable. It is not limited to laboratory operations; rather, it will be considered in all choices about the product's quality. It will be made sure that all quality control procedures are followed consistently and successfully. Other responsibilities for the department as a whole include developing, assessing, validating, and putting into practice all quality control procedures and methods.

16.1. Each manufacturing facility must set up a quality control laboratory run by knowledgeable and experienced personnel.

16.2 There are four categories for testing in the quality control laboratory: chemical, instrumentation, microbiological, and biological. When producing radioactive material, separate provisions should be made for testing.

16.3. A sufficient space with the necessary storage conditions must be offered to store reference samples. Reference samples must be examined, maintained, and stored by the quality control division.

16.4. Standard operating procedures must be accessible for the sampling, testing, and inspection of intermediate and bulk finished goods, packing materials, and raw materials. They should also be available for environmental condition monitoring when needed.

16.5. All materials, products, reagents, and solvents must have approved and current specifications, which must include tests for identity, content, purity, and quality. These will include guidelines for the use of reagents, solvents, and water in analyses.

16.6. Until a batch of the product has been certified by the designated person or people that it complies with the established standards, it cannot be made available for purchase or use.

16.7. Reference/retained samples from each batch of manufactured products must be kept in a quantity that is at least twice as large as the amount of drug needed to conduct all tests, except the pyrogen/bacterial endotoxin test, which is conducted on both the manufactured product and the active material. Within three months of the expiration date, the retained product must be stored in either its final or simulated pack.

16.8. The evaluation of records related to completed goods must take into account all pertinent information, such as the manufacturing conditions, the outcomes of in-process testing, the manufacturing (including packaging) documentation, the finished product's compliance with specifications, and a final pack inspection. The person in charge of production should sign assessment records.

- printed material specimen;
- instructions for sampling and testing, or a link to the procedures;
- storage circumstances; and - the longest storage time before retesting.

## 17. SPECIFICATION:-

17.1. About packaging and raw materials: They must contain the following: the internal code reference and specified name;

a mention of a pharmacopoeial monograph, if any;

- specifications, both quantitative and qualitative, together with acceptability bounds;
- the original manufacturer of the material and their name and address, if applicable; An example of printed content;
- instructions for testing and sampling, or a list of steps;
- storage circumstances; and - the longest storage time before retesting.

### 17.2. Regarding Product Closures and Containers:

17.2.1. All use-related containers and closures must meet pharmacopoeial standards. Strict adherence to the recommended cleaning, sterilization, and testing protocols, sample sizes, specifications, and validated test methods are required to guarantee that the drug is not reactive, additive, adsorptive, or leachable to a degree that would materially compromise its quality or purity. Used or second-hand closures and containers are not permitted.

17.2.2. The written cleaning schedule must be set up and adhered to whenever bottles are used. Bottles that are not dried after washing should be rinsed with either distilled water or de-ionized water.

17.3. For in-process and bulk products: Material, intermediate, and bulk product specifications must be provided. It is necessary to authenticate the specifications.

17.4. Regarding Finished Products: The following are acceptable requirements for finished products:

- the code reference and the product's designated name.
- the pharmacopoeial reference and the formula, or a reference to both.
- guidelines for testing and sampling or a list of steps.
- an explanation of the package information and dosage form.
- the acceptance thresholds for release, along with the qualitative and quantitative requirements.
- the storage circumstances and safety measures, if any, and
- the longevity.

17.5. To get the closures and containers ready: The machinery, equipment, and space needed to prepare containers and closures for various dosage forms and drug categories are not included in the requirements listed in the Schedule. The requirements of each licensee in this regard will be taken into consideration when evaluating the suitability and sufficiency of the machinery, equipment, and premises.

## 18 MASTER FORMULA RECORDS:

For every product and batch size that needs to be produced, there must be Master Formula records about all manufacturing processes. The head of production and quality control, as well as other qualified technical staff, will prepare and approve these. The product's name and the product reference code that corresponds to its specifications are required to be included in the Master Formula.

- the product's patent or proprietary name, combined with its generic name; a description of the product's dosage form, strength, composition, and batch size; and more.
- the name, amount, and reference number of every starting material that will be utilized. Bring up any material that could "disappear" during processing.
- an explanation of the anticipated final yield, along with any applicable acceptable bounds, and any pertinent intermediate yields.
- an explanation of the processing location and the main pieces of equipment that will be utilized.
- the procedures, or references to the procedures, to be followed to prepare the crucial equipment, such as assembly, cleaning, calibration, and sterilization.
- thorough instructions for processing in steps with an indication of how long each step takes.
- the limitations and instructions for in-process controls.
- the specifications for the products' storage conditions, including the labeling, the container, and any special storage needs that may apply.
- any extra safety measures that need to be taken.
- packing information and labels on specimens.

## 19 PACKAGING RECORDS:-

Every product,

together with the size and kind of the pack, must have approved packing instructions. These must mention or contain any of the following: -

brand name of the item. An explanation of the composition, strength, and dosing form.

The dimensions of the pack, as indicated by the quantity, weight, or volume of the goods in the ultimate receptacle.

comprehensive inventory of all the packing supplies needed for a typical batch size, including amounts, sizes, and types, each packaging's code or reference number according to its requirements substance. Reprocessing the pertinent printed package items and samples indicating where The product's batch number and expiration date have been applied. extra safety measures are to be taken, Including a thorough inspection of the apparatus and surrounding area to determine the line clearance before the start of operations. An explanation of the packaging process, mentioning any noteworthy ancillary businesses and equipment that will be employed. Information about in-process controls and guidelines for sampling as well as approval. After the packing and labeling process is finished, a reconciliation must be determined by dividing the total number of labeled units, packaging units issued, and labeled units packaged, with extras either destroyed or returned. Any notable or peculiar disparity in the figures shall be thoroughly examined before the release of the last batch.

## 20. BATCH PACKAGING RECORDS:-

20.1. For each processed batch or piece of a batch, a batch packaging record needs to be maintained. The relevant portions of the packaging instructions will serve as the foundation for it, and the process of producing these records will be planned to prevent transcription errors.

20.2. Before packaging absorption starts, it is necessary to verify and certify that there are no outdated goods, files, or supplies on the workstations that are needed for The planned packing practices and the neatness and compatibility of the equipment.

## 21. BATCH PROCESSING RECORDS:-

21.1 Every product must have a batch processing record. It will be based on the pertinent sections of the Master Formula that is now in approval. To prevent transcribing errors, the process used to prepare the records that are part of the Master Formula must be carefully thought out.

21.2. Examine every industrial location before beginning any procedure to make sure that the The workstation and equipment are free of earlier goods. This needs to be recorded and captured.

21.3. The following details must be noted at the moment each action is performed during processing. and the individual in charge of the processing procedures must date and sign the document:

- (a) The product's name;
- (b) The batch number being manufactured;
- (c) the times and dates of the start, crucial intermediate stages, and the product's completion, creation,
- (d) initials of the managers of several key production steps, and if appropriate, of the the individual who verified each of these operations,
- (e) the quantities of each initial component as well as the batch number and/or analytical control number material's true heft

## 22. STANDARD OPERATING PROCEDURES (SOPS) AND RECORDS, REGARDING:-

22.1. Materials Received:

22.1.1. Written standard operating procedures and documentation must be kept for each delivery of primary, printed, and raw packaging materials.

22.1.2. The receipts' records must contain

- (a) Number of containers
- (b) the receipt date
- (c) The name of the source and/or manufacturer
- (d) The batch or reference number of the manufacturer
- (e) the total amount received, the number of containers, and the amount inside each container
- (f) following receipt, the control reference number assigned

(g) Any further pertinent remarks or details.

22.1.3 Written standard operating procedures must be in place for the internal labeling, storage, and quarantine of packing, starting, and other items as needed.

22.1.4. Standard Operating Procedures must be made available for every piece of equipment and instrument. and these need to be positioned close to the relevant equipment and instruments.

22.2. Prototyping:

22.2.1 Written Standard Operating Procedures must be in place for sampling, and these should comprise the someone(s) with permission to collect the samples.

### **23. REFERENCE SAMPLES:-**

23.1. Each lot of every active ingredient, in a quantity sufficient to carry out all the tests, except sterility and pyrogens/Bacterial Endotoxin Test, shall be retained for 3 months after the date of expiry of the last batch produced from that active ingredient.

23.2. Samples of finished formulations shall be stored in the same or simulated containers in which the drug has been marketed.

### **24. REPROCESSING AND RECOVERIES:-**

24.1. Written protocols that outline the parameters and restrictions of recurring chemical processes must be developed and authorized by the Quality Assurance Department in cases where reprocessing is required. This reprocessing needs to be verified.

24.2 Should the product batch require reprocessing, the method needs to be approved and documented. The reasons for the need for reprocessing will be investigated, and suitable corrective action will be implemented to stop recurrence. The batch that has been reprocessed will have its stability assessed.

24.3. Product residue can be recovered, if allowed, by adding it to later batches of the product and keeping track of it in the master production and control records.

### **25. DISTRIBUTION RECORDS:-**

25.1. It must be confirmed that a drug batch has passed the required testing, acceptance, and discharge by quality control personnel before it gets distributed or shipped. Pre-dispatch inspections must be carried out periodically on every shipment to ensure that only the correct items are delivered. After the batch is released for distribution, there have to be clear guidelines for the storage and storage of large volume parenteral, if they are to be kept. Distribution centers have to perform routine audits of their warehousing processes and keep evidence of them. It is necessary to create established processes for product holding. Records designed for distribution must be kept under certain rules. so that the finished batch of aTo enables timely and thorough recall of the batch, if and when appropriate, the medicine can be tracked down to the retail level.

25.2 Records intended for distribution must be kept according to certain rules. To enable a timely and thorough recall of the batch, should the need arise, a drug's completed batch can be traced back to the retail level.

## 26. VALIDATION AND PROCESS VALIDATION:-

26.1. Validation studies must be carried out by the established protocols and are a crucial component of good manufacturing practices. These will consist of testing, cleaning, and processing validation methods.

26.2. It is required to compile, document, and preserve a written report that summarizes the findings and conclusions of the recorded data.

26.3 Processes and procedures must be created based on validation studies, and they must go through periodic revalidation to make sure they continue to be able to produce the desired results. Validation of critical processes must be done both proactively and retrospectively.

26.4. When any new master formula or method of preparation is adopted, steps shall be taken to demonstrate its suitability for routine processing. The defined process, using the materials and equipment specified shall be demonstrated to yield a product consistently of the required quality.

26.5. Significant changes to the manufacturing process, including any change in equipment or materials that may affect product quality and/or the reproducibility of the process, shall be validated.

## 27. PRODUCT RECALLS:-

27.1. In the shortest amount of time possible, a rapid and efficient procedure for recalling faulty items must be developed to promptly notify all relevant suppliers, distributors, and stockists, all the way up to the retail level. In this sense, the licensee may employ print as well as electronic media.

27.2. For the licensee's products to be effectively recalled, a documented protocol in the form of a Standard Operating Procedure must be in place. Recall procedures must be able to start quickly to efficiently reach every level of the distribution chain.

27.3. The individuals named for recalls must have easy access to the distribution records.

27.4. A final report that includes a reconciliation of the product amounts that were delivered and recovered must be recorded by the designated person.

27.5. The recall arrangements' efficacy will be periodically assessed.

27.6. Until a final decision is made regarding them, the recalled items must be kept apart in a safe segregated location.

## GMP IN THE MANUFACTURING OF PHARMACEUTICALS

### ORAL LIQUIDS (SYRUPS, ELIXIRS, EMULSIONS AND SUSPENSIONS):-Note :

When manufacturing (syrups, elixirs, emulsions, and suspensions), compliance with the General Requirements outlined in Good Manufacturing Practises for Premises and Materials for Pharmaceutical Products is required. Apart from these prerequisites, the subsequent Particular Requirements must also be adhered to, specifically:

#### 1 Building And Equipment:

1.1. The building and its furnishings must be planned, built, and maintained to accommodate the production of oral liquids. The production area's layout and design must work to reduce the possibility of mix-ups and cross-contamination.

1.2. A double-door air-lock facility should be used for access into the manufacturing area. It must be rendered fly-proof by using an air curtain or a flycatcher.

1.3. Drainage must have appropriate traps, be of a suitable size, have no open channels, and be designed to stop backflow. Shallow drains are required to make cleaning and disinfection easier.

1.4. After each manufacturing step, the production space needs to be thoroughly cleaned and sanitized.

## **2. Purified Water:-**

2.1. The used purified water's chemical and microbiological purity must be defined and regularly checked. According to IP 1996's Appendix 12.5, the microbiological examination must test for the absence of pathogens and cannot be greater than 100 cfu/ml.

2.2. The purified water system should be operated and maintained by a documented method. It is important to take precautions against the possibility of microbial growth by using suitable techniques such as UV treatment, heat treatment, recirculation, and sanitizing agents. Following any chemical cleaning the water system after sanitization is necessary to make sure the sanitizing substance has been completely removed.

## **3. Manufacturing:**

3.1. To prevent product contamination, manufacturing staff are required to wear clothing that does not shed fibers.

3.2. Items that are prone to fiber loss, such as wooden pallets or gunny sacks, should not be brought into areas where products or cleaned containers are visible.

3.3. During filling, care must be given to preserve the homogeneity of the emulsion by using the proper emulsifier and stirrer for the suspensions. Processes for mixing and filling must be defined and closely watched. To guarantee that the product is consistently homogeneous throughout the filling process, extra attention must be given at the start of the process, following any interruption that may have caused a pause, and after the operation.

3.4. An air supply that has passed through five-micron filters is required for the primary packing area. The area's temperature cannot rise over 30 degrees Celsius.

3.5. The maximum storage time and circumstances must be indicated in the Master Formula in cases when the bulk product is not packaged right away. A product's maximal storage time during the bulk stage has to be verified.

## **4. EXTERNAL PREPARATIONS (CREAMS, OINTMENTS, PASTES, EMULSIONS, LOTIONS, SOLUTIONS, DUSTING POWDERS AND IDENTICAL PRODUCTS):-**

Note: When manufacturing topical products, or external preparations (such as creams, ointments, pastes, emulsions, lotions, solutions, dusting powders, and similar products used for external applications), the general requirements listed in Good Manufacturing Practises for facilities and materials for pharmaceutical products must be followed. Apart from these prerequisites, the subsequent particular conditions must also be adhered to, specifically:

1. An appropriate airlock must be used as the entryway to the area where topical goods are prepared. Installing interlocutors outside the airlock is required.

2. This production area's air must be air-conditioned and pass through a minimum of 20 air filters. The space has to have ventilation.



3. An exhaust system with the necessary capacity must be installed in the area to efficiently remove smoke, fumes, vapors, and floating dust particles.
4. The machinery must be built and maintained in a way that keeps any foreign materials or lubricants from unintentionally contaminating the product.
5. When cleaning or drying the process equipment or accessories, no rags or dusters may be used.
6. Purified Water IP is the required water for compounding.
7. Powders must be properly sieved before use, if at all.
8. Using steam, gas, electricity, solar energy, etc., automobiles and abases such as petroleum jelly must be heated in a separate mixing area in appropriate stainless steel containers.

## 5. METERED-DOSE INHALERS (MDI):-

Note: When producing Metered-Dose-Inhalers (MDI), facilities and materials must adhere to the General Requirements listed in Good Manufacturing Practises for pharmaceutical goods. Apart from these prerequisites, the subsequent Particular Requirements must also be adhered to, specifically:

The general manufacturing process for metered-dose inhalers must be carried out in a way that minimizes the risk of particle and microbiological contamination. It is crucial to guarantee the bulk product's and the component's quality. When drugs are suspended, the uniformity of the suspension must be determined.

## 6. Equipment:-

- 6.1. Closed system equipment is required for manufacturing. Stainless steel is required for the supply lines and the vessels.
- 6.2. The department must have labeling machines, spray testing equipment, and appropriate check weights.
- 6.3. Upon receipt and regularly after that, all equipment must be properly calibrated and have its performance verified.

## 7. Manufacture:

- 7.1. A master formula record that has been authorized must be used in the production of metered dosage inhalers. To eliminate particles, all propellants, liquids, and gases must be filtered via 2-micron filters.
- 7.2. Compressed air that has been adequately filtered through a 0.2-micron filter is required to clean the primary packing material. When necessary, the compressed air's humidity will be regulated.
- 7.3. The valves must be handled carefully, and once they have been de-carbonized, they must be stored in the filling room in hygienic, closed containers.
- 7.4 The bulk of suspensions must be constantly agitated.

## 8. Documentation:-

- 8.1. The documentation of production records must include the extra information listed below in addition to the usual good manufacturing practices (1) Humidity and temperature in the production zone.  
(2) Periodically filled formulation weights.

(3) Records of refusals made throughout the online check-weighing process.

(4) Documentation of spray testing rejections.

## CONCLUSION:

The conditions upheld during the manufacturing process determine the pharmaceutical product's quality and purity. Strict adherence to exacting standards observed throughout the production process is required by the Good Production Process (GMP) concept. This guarantees the caliber of the ultimate result. Therefore, GMP is crucial to producing high-quality goods and preventing access to the counterfeit medication market.

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