DRUGS AND COSMETICS ACT

Contents of this chapter

- Definitions
- Administration of the act and rules
- Provisions related to Import
- Provisions related to Manufacture
- Provisions related to Sale
- Labeling and Packaging
- Schedules to the act and rules

Learning Objectives

- At the end of this lecture, student will be able to
  - Discuss the Provisions of GMP related to manufacture of drugs and pharmaceuticals
  - Explain the GMP guidelines
  - Explain the principles of Schedule M
  - Discuss Explain the principles of Schedule M II

Schedule M

Good Manufacturing Practices (GMP)

Guidelines are meant to assure the quality of drugs.

Draft of GMP was prepared in 1975 & finalized & implemented in 1988

Part I deals with Good manufacturing practices relating to factory premises.

Part II deals with plant & equipment for the manufacture of drugs.

GMP Guidelines

GMP as per Schedule “M”

www.cdsco.nic.in

GMP as per WHO

www.who.int

GMP as per MCA now known as MHRA

www.mca.gov.uk

GMP as per TGA

www.tga.gov.au

GMP as per US FDA

www.fda.gov

GMP as per ICH guidelines

www.ich.org

GMP

GMP in solid dosage forms

GMP in semisolid dosage forms

GMP in Liquid orals

GMP in Parenterals Production

GMP in Ayurvedic medicines

GMP in Bio technological products

GMP in Nutraceuticals and cosmeceuticals

GMP in Homeopathic medicines

Principles of GMP

1. Design and construct the facilities and equipments properly
2. Follow written procedures and Instructions
3. Document and validate work
4. Monitor facilities and equipment
5. Write step by step operating procedures and work on instructions
6. Design, develop and demonstrate job competence
7. Protect against contamination
8. Control components and product related processes
9. Conduct planned and periodic audits

10 Attributes of a Good Document

1. Accurate
2. Clear
3. Complete
4. Consistent
5. Indelible
6. Legible
7. Timely
8. Direct
9. Authentic
10. Authorized

Schedule M - cGMP for Finished Pharmaceuticals

1. General Provision
2. Organization & Personnel
3. Building & Facilities
4. Equipment
5. Control of Components & Drug Product Containers & Closures
6. Production & Process Control
7. Packaging & Labeling Control
8. Handling & Distribution
9. Laboratory Control
10. Records & Reports
11. Returned & Salvaged Drugs

Factory Premises

General Requirements

Location of **factory & its surroundings** should ensure freedom from contamination due to sewage drain, etc & obnoxious odors or fumes, or large quantity of soot, dust or smoke.

Factory building should be constructed to ensure production of drugs under hygienic conditions.

Operations such as manufacturing, processing, packing labeling & testing should be carried out in such a way that mix up & cross contamination are prevented.

Premises should be constructed and maintained as to prevent entry of insects & rodents, Interior surface should be smooth & free from cracks & permit easy cleaning disinfection. Adequate lighting, ventilation & humidity must be maintained. Drainage systems should be underground, the sanitary fitting & electrical fixtures in the manufacture area must be concealed. Water used must be free of pathogenic micro organisms and of drinkable quality. Waste water should be treated before disposal.

There should be a validated system for the treatment of **water** so as to produce purified water confirming to IP specification. Water should be stored in tanks and freedom from microbial growth must be ensured. The tanks should be cleaned periodically and the records should be maintained.

Provisions should be made for the roper storage of the **materials awaiting disposal**. The disposal of sewage and effluents shall be as required under the Environmental Pollution control board while all biomedical waste must be destroyed as per the rules of Biomedical Waste Management and Handling rules.

Warehousing Area

Adequate areas shall be designed & provided with proper bins, racks & platforms for the storage and warehousing of all materials & products, machine & equipment's etc. Warehousing area must be clean, dry & maintained within acceptable temperature limits. Storage areas should have appropriate house keeping & rodents, pests & vermin control procedures & records should be maintained.

Active raw materials and excipients must require separate sampling and warehousing area.

Regular checks should be made to ensure adequate steps taken against spillage, breakage and leakage of containers.

Production Area

Should be designed to allow the production preferably in uni-flow & with logical sequence of operations.

The equipment's and materials must be placed orderly & the movement of personnel must be restricted to avoid cross contamination.

Separate dedicated self containing facilities should be made available for the production of sensitive pharmaceutical products like penicillin or biological preparations with live microorganisms.

Pipe works, electrical fittings, ventilations, openings & similar service lines must be designed to avoid creation of recesses.

Service lines shall preferably identified by colors & nature of supply and direction of flow shall be indicated.

Quality control area

Should be independent of production area & divided to separate sections for physio-chemical, biological, microbiological & radio isotope analysis.

Laboratories shall be designed to avoid mix-ups and cross-contamination. Separate instrument room with adequate area shall be provided for sensitive & sophiscated instruments employed for analysis.

Suitable storage space shall be provided for test samples, retained samples, reference standards, reagents & records.

Personnel

Manufacture/testing shall be conducted under the direct supervision of competent technical staff & head of quality control laboratory shall be independent of manufacturing unit.

Personnel in quality control and quality control operations shall be suitably qualified & experienced & appropriate training must be given to them in the duties & responsibilities assigned to them.

Health, Clothing & Sanitation of workers

All personnel coming to contact with products & raw materials should be free from contagious diseases & should undergo periodic health check up. Just before entry to manufacturing area, room with facility for personnel cleanliness should be provided.

Prior to employment, personnel shall undergo medical examination & shall be free from TB, skin and other communicable/contagious diseases.

Periodical medical examination at least once an year may be necessary.

All persons prior to & during the employment shall be trained in practices that ensure personnel hygiene.

Persons handling beta lactam antibiotics shall be tested for penicillin sensitivity before employment and those handling sex hormones, cytotoxic substances & other potent drugs shall be periodically examined for adverse effects.

Direct contact shall be avoided b/w unprotected hands of personnel 7 raw materials, intermediate, or finished unpacked products.

All persons should wear clean body coverings.

Smoking, eating, drinking, chewing or keeping plants or food & personnel medicines shall not be permitted in production, laboratory storage & other areas.

Ancillary Areas

Rest & refreshment rooms should be separate & should not lead directly to the manufacturing area.

Facilities for changing, storing of clothes & for washing & toilet purposes should be provided and must be adequate for the number of users.

Sanitation in Manufacturing premises:

Manufacturing area should not be utilized for any other purposes & should be maintained clear & in orderly manner free from accumulated waste, dust, debris etc. A routine sanitation program must be exercised.

Production areas shall be well lit, particularly where visual online controls are carried out.

Raw Materials: All raw materials must be:

Purchased from approved sources under valid purchase vouchers, possibly from producers directly.

Identified & their containers examined for damage& assigned control number.

There shall be separate areas for materials **under test**, **approved** & **rejected raw materials.**

All incoming materials shall be quarantined immediately after receipt.

Materials must be stored in such a way that **first in/first expiry**, **first out** principle can be applied.

Only raw materials released by QC department & which are within their shelf life shall be used.

Sterile Products

Separate enclosed areas provided with air locks, dust free, ventilated with air supply through HEPA filters are recommended.

Routine microbial counts of area are necessary during manufacturing operation.

Design of area must avoid possibility of mix up between sterile & non sterile products.

Access to manufacturing area must be restricted to authorized personnel only.

Working Space

Adequate working space & adequate room for orderly placement of equipment & materials should be provided to eliminate mix up between different drugs & cross contamination.

Medical Services: Manufacturer must provide facilities for

Adequate facilities for first aid.

Medical examination of workers at time of employment & periodic check up there after once in a year.

Facilities for vaccination or other exigencies.

Equipment: Equipment used for manufacture must be constructed, designed, installed & maintained to:

Achieve operational efficiency to attain the desired quality.

Prevent physical, chemical or physiochemical change through surface contact.

Prevent contact of any substances required for operation of equipment's such as lubricants.

Facilitate thorough cleaning whenever necessary.

Minimize any contamination of any drugs and their containers during manufacture.

Master Formula Records: The Licensee ‘d maintain master formula records relating to all manufacturing procedures for each product. The master formula record shall give:

Patent or proprietary name of product along with generic name. strength & dosage form

Description of final containers, packaging materials. Labels & closures to be used.

Identity, quality & quantity of each raw materials to be used.

Description of all equipment's & vessels & the size used in the process.

Manufacturing & control instructions along with parameters for critical steps such as mixing, drying, blending, sieving, sterilizing the product.

Theoretical yield to be expected from the formulation

Detailed instructions & precautions to be taken in manufacture, storage of drugs & of semi-finished products & the requirements in process quality control tests & analysis to be carried out during each stage of manufacture.

Batch Manufacturing Records: Licensee ‘d maintain batch manufacturing records for each batch of drugs as per Schedule U. it ‘d provide complete account of manufacturing history of each batch showing that it has been manufactured, tested & analyzed in accordance with manufacturing procedures & written instructions as per master formulae.

Manufacturing Operations & Control: All manufacturing operations must be carried out under the supervision of competent technical staff. Critical steps in the process related to selection, weighing & measuring of raw materials must be done under the direct supervision of competent technical staff.

Product containers & closures: ‘d comply with Pharmacopoeial requirements. Suitable test methods, cleaning & sterilization procedures ‘d be used to assure that components, closures & other component part of drug packages are suitable & they are not reactive, additive, absorptive, or leach to an extent that significantly affects the quality or purity of the drug.

Labels & other printed materials: Printed labels & packaging materials including leaflets ‘d be handles & accounted to ensure that they do not become intermixed. Prior to issue, they should be examined & released as satisfactory for use by quality control personnel.

Distribution of Records: Records for the distribution of each batch of drug should be maintained in order to facilitate prompt & complete recall of the batch if necessary.

Quality control system: Principal duties of quality control department are:

Prepared detailed Instruction for carrying out each tests & analysis.

To release or reject i) each batch of raw material, ii) semi-finished products if necessary, iii) packaging & labeling materials & final containers, iv) each batch of finished products ready for distribution.

Evaluate adequacy of conditions under which raw materials, semi-finished products & finished products are stored.

Evaluate quality & stability of finished products.

To establish, & when necessary revise, procedure & specifications.

To examine returned products as to whether such products ‘d be released, reprocessed or destroyed.

Schedule M Part II
Plant & Equipment

Recommends the requirements of plant & equipment for the manufacture of drugs under the following sections.

i) Ointments, emulsions, lotions & suspensions, ii) syrups, elixirs & solutions, iii)pills, compressed tablets & hypodermic needles, iv) Powders, v) Hard gelatin capsules, vi) surgical dressings other than absorbent cotton, vii) Eye ointments,, eye lotions & other preparations for external use, viii) pessaries & suppositories, ix) inhalers, x) repacking of drugs, xi) Parenteral preparations.

Summary

- Location of factory & its surroundings should ensure freedom from contamination due to sewage drain, etc & obnoxious odors or fumes, or large quantity of soot, dust or smoke.
- Factory building should be constructed to ensure production of drugs under hygienic conditions
- Should be designed to allow the production preferably in uni-flow & with logical sequence of operations.
- The equipment's and materials must be placed orderly & the movement of personnel must be restricted to avoid cross contamination
- All manufacturing operations must be carried out under the supervision of competent technical staff. Critical steps in the process related to selection, weighing & measuring of raw materials must be done under the direct supervision of competent technical staff
- Printed labels & packaging materials including leaflets ‘d be handles & accounted to ensure that they don not become intermixed. Prior to issue, they should be examined & released as satisfactory for use by quality control personnel.
- Records for the distribution of each batch of drug should be maintained in order to facilitate prompt & complete recall of the batch if necessary.

Thank You

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