Current GMP

- cGMP regulations are established by FDA
- It contains minimum requirements for the methods, facilities and controls used in manufacturing, processing and of a drug product packing .
- The regulations make sure that a product is safe for use, and that it has the ingredients and strength it claims to have.
- The approval process for new drug and generic drug marketing applications includes a review of the manufacturer's compliance with the c GMP
- FDA can issue a warning letter or initiate other regulatory actions against a company that fails to comply with the regulations

CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS

- **Subpart A--General Provisions**
  - § 211.1 - Scope.
  - § 211.3 - Definitions.
- **Subpart B--Organization and Personnel**
  - § 211.22 - Responsibilities of quality control unit.
  - § 211.25 - Personnel qualifications.
  - § 211.28 - Personnel responsibilities.
  - § 211.34 - Consultants.
- **Subpart C--Buildings and Facilities**
  - § 211.42 - Design and construction features.
  - § 211.44 - Lighting.
  - § 211.46 - Ventilation, air filtration, air heating and cooling.
  - § 211.48 - Plumbing.
  - § 211.50 - Sewage and refuse.
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  - § 211.56 - Sanitation.
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- **Subpart D--Equipment**
  - § 211.63 - Equipment design, size, and location.
  - § 211.65 - Equipment construction.
  - § 211.67 - Equipment cleaning and maintenance.
  - § 211.68 - Automatic, mechanical, and electronic equipment.
  - § 211.72 - Filters.
- **Subpart E--Control of Components and Drug Product Containers and Closures**
  - § 211.80 - General requirements.
  - § 211.82 - Receipt and storage of untested components, drug product containers, and closures.
  - § 211.84 - Testing and approval or rejection of components, drug product containers, and closures.
  - § 211.86 - Use of approved components, drug product containers, and closures.
  - § 211.87 - Retesting of approved components, drug product containers, and closures.
  - § 211.89 - Rejected components, drug product containers, and closures.
  - § 211.94 - Drug product containers and closures.

- **Subpart F--Production and Process Controls**

§ 211.100 - Written procedures; deviations.
§ 211.101 - Charge-in of components.
§ 211.103 - Calculation of yield.
§ 211.105 - Equipment identification.
§ 211.110 - Sampling and testing of in-process materials and drug products.
§ 211.111 - Time limitations on production.

- § 211.113 - Control of microbiological contamination.

§ 211.115 - Reprocessing.

- **Subpart G--Packaging and Labeling Control**

§ 211.122 - Materials examination and usage criteria.
§ 211.125 - Labelling issuance.
§ 211.130 - Packaging and labelling operations.
§ 211.132 - Tamper-evident packaging requirements for over-the- counter (OTC) human drug products.

- § 211.134 - Drug product inspection.

§ 211.137 - Expiration dating.

- **Subpart H--Holding and Distribution**
  - § 211.142 - Warehousing procedures.
  - § 211.150 - Distribution procedures.
- **Subpart I--Laboratory Controls**
  - § 211.160 - General requirements.
  - § 211.165 - Testing and release for distribution.
  - § 211.166 - Stability testing.
  - § 211.167 - Special testing requirements.
  - § 211.170 - Reserve samples.
  - § 211.173 - Laboratory animals.
  - § 211.176 - Penicillin contamination.
- **Subpart J--Records and Reports**
  - § 211.180 - General requirements.
  - § 211.182 - Equipment cleaning and use log.
  - § 211.184 - Component, drug product container, closure, and labeling records.
  - § 211.186 - Master production and control records.
  - § 211.188 - Batch production and control records.
  - § 211.192 - Production record review.
  - § 211.194 - Laboratory records.
  - § 211.196 - Distribution records.
  - § 211.198 - Complaint files.

- **Subpart K--Returned and Salvaged Drug Products**
  - § 211.204 - Returned drug products.
  - § 211.208 - Drug product salvaging.

General provisions scope and definitions

- The regulations in this part contain the minimum current good manufacturing practice for preparation of drug products for administration to humans or animals.
- The cGmp regulations pertain to drug products
- The requirements in these regulations should not be enforced to OTC drugs if they are ordinarily marketed
- Definitions
- Active ingredient
- Batch wise control
- Compliance
- Master record

Organisation and personnel

- It deal with the responsibilities of a quality control unit
- The applications and responsibilities of QA should be in written form
- Adequate laboratory facilities for testing and approval of components
- Personnel qualifications
- Each person engaged in the supervising, manufacture, processing, packing, or holding of a drug product shall have education, training, and experience.
- There shall be an adequate number of qualified personnel .

Personnel responsibilities

- Personnel engaged in the manufacture, processing, packing, or holding of a drug product shall wear clean clothing appropriate for the duties they perform.
- Protective apparel, such as head, face, hand, and arm coverings, shall be worn as necessary to protect drug products from contamination.
- Personnel shall practice good sanitation and health habits.
- Only personnel authorized by supervisory personnel shall enter those areas of the buildings and facilities designated as limited-access areas.
- Any person shown at any time (either by medical examination or supervisory observation) to have an apparent illness or open lesions shall be excluded from direct contact to components.

Buildings and facilities

- Any building or buildings used in the manufacture, processing, packing, or holding of a drug product shall be of suitable size, construction and location to facilitate cleaning, maintenance, and proper operations.
- Any such building shall have adequate space for the orderly placement of equipment and materials to prevent mix ups between different components.
- Operations shall be performed within specifically defined areas of adequate size. There shall be separate or defined areas or such other control systems.

Facilities to be provided

- Floors, walls, and ceilings of smooth, hard surfaces that are easily cleanable
- An air supply filtered through high-efficiency particulate air filters under positive pressure, regardless of whether flow is laminar or nonlaminar
- A system for monitoring environmental conditions
- A system for cleaning and disinfecting the room and equipment to produce aseptic conditions
- A system for maintaining any equipment used to control the aseptic conditions
- Adequate lighting .
- Adequate ventilation.
- Potable water shall be supplied under continuous positive pressure in a plumbing system free of defects that could contribute contamination to any drug product

- Air filtration systems, including pre filters and particulate matter air filters, shall be used.
- Sewage, trash, and other refuse in and from the building and immediate premises shall be disposed of in a safe and sanitary manner
- Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a clean and sanitary condition.
- Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a good state of repair.

Equipment

- Equipment used shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.
- Equipment shall be constructed so that surfaces that contact components, in-process materials, or drug products shall not be reactive, additive, or absorptive.
- Equipment and utensils shall be cleaned, maintained, and, as appropriate for the nature of the drug, sanitized and/or sterilized at appropriate intervals to prevent malfunctions or contamination.

Types of equipments

- Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily.
- Appropriate controls shall be exercised over computer or related systems.
- Filters for liquid filtration used in the manufacture, processing, or packing of injectable drug products intended for human use shall not release fibers into such products.

Control of components and drug product containers and closures

- There shall be written procedures describing in sufficient detail the receipt, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures.
- Bagged or boxed components of drug product containers, or closures shall be stored off the floor and suitably spaced to permit cleaning and inspection
- Upon receipt and before acceptance, each container or grouping of containers of components, drug product containers, and closures shall be examined visually for appropriate labelling as to contents, container damage or broken seals, and contamination

- Each lot of components, drug product containers, and closures shall be withheld from use until the lot has been sampled, tested, or examined, as appropriate, and released for use by the quality control unit.
- Representative samples of each shipment of each lot shall be collected for testing or examination
- At least one test shall be conducted to verify the identity of each component of a drug product.
- Containers and closures shall be tested for conformity with all appropriate written specifications
- Standards or specifications, methods of testing, and, where indicated, methods of cleaning, sterilizing, and processing to remove pyrogenic properties shall be written and followed for drug product containers and closures

Production and process controls

- There shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they possess or are represented to possess
- Written production and process control procedures shall be followed.
- The batch shall be formulated with the intent to provide not less than 100 percent of the labelled or established amount of active ingredient.

- Weighing, measuring, or subdividing operations for components shall be adequately supervised. Each container of component dispensed to manufacturing shall be examined by a second person
- Actual yields and percentages of theoretical yield shall be determined at the conclusion .
- All compounding and storage containers, processing lines, and major equipment used during the production of a batch of a drug product shall be properly identified .
- To assure batch uniformity and integrity of drug products, written procedures shall be established and followed that describe the in-process controls, and tests, or examinations to be conducted .
- Written procedures shall be established and followed prescribing a system for reprocessing batches that do not conform to standards or specifications.

Packaging and labelling control

- There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labelling and packaging materials.
- Records shall be maintained for each shipment received of each different labelling and packaging material indicating receipt, examination or testing, and whether accepted or rejected.
- Any labelling or packaging materials meeting appropriate written specifications may be approved and released for use.
- Labels and other labelling materials for each different drug product, strength, dosage form, or quantity of contents shall be stored separately with suitable identification

- Printing devices on, or associated with, manufacturing lines used to imprint labelling upon the drug product unit label or case shall be monitored to assure that all imprinting conforms to the print specified in the batch production record.
- Labelling materials issued for a batch shall be carefully examined for identity and conformity to the labelling specified in the master or batch production records
- Identification and handling of filled drug product containers that are set aside and held in unlabelled condition for future labelling operations to preclude mislabelling of individual containers, lots, or portions of lots .
- *Requirements for tamper-evident package*- Each manufacturer and packer who packages an OTC drug product (except a dermatological, dentifrice, insulin, or lozenge product) for retail sale shall package the product in a tamper-evident package, if this product is accessible to the public while held for sale.

- *Request for exemptions from packaging and labelling requirements.*
- Packaged and labelled products shall be examined during finishing operations to provide assurance that containers and packages in the lot have the correct label
- To assure that a drug product meets applicable standards of identity, strength, quality, and purity at the time of use, it shall bear an expiration date determined by appropriate stability testing
- New drug products for investigational use are exempt from the requirements of this section, provided that they meet appropriate standards or specifications as demonstrated by stability studies during their use in clinical investigations.

Holding and distribution

- Storage of drug products should be under appropriate conditions of temperature, humidity, and light.
- A procedure whereby the oldest approved stock of a drug product is distributed first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.
- A system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary

Laboratory controls

- Laboratory controls shall include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labelling, and drug products conform to appropriate standards of identity, strength, quality, and purity.
- For each batch of drug product, there shall be appropriate laboratory determination of satisfactory conformance.
- Any sampling and testing plans shall be described in written procedures that shall include the method of sampling and the number of units per batch to be tested.

- The accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented
- Drug products failing to meet established standards or specifications and any other relevant quality control criteria shall be rejected
- There shall be a written testing program designed to assess the stability characteristics of drug products.
- An adequate number of batches of each drug product shall be tested to determine an appropriate expiration date and a record of such data shall be maintained
- For each batch of drug product purporting to be sterile and/or pyrogen-free, there shall be appropriate laboratory testing to determine conformance to such requirements

- An appropriately identified reserve sample that is representative of each lot in each shipment of each active ingredient shall be retained
- Animals used in testing components, in-process materials, or drug products for compliance with established specifications shall be maintained and controlled in a manner that assures their suitability for their intended use
- If a reasonable possibility exists that a non-penicillin drug product has been exposed to cross-contamination with penicillin, the non-penicillin drug product shall be tested for the presence of penicillin

Records and reports

- A written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed
- The identity and quantity of each shipment of each lot of components, drug product containers, closures, and labelling; the name of the supplier; the supplier's lot number etc must be recorded
- An individual inventory record of each component, drug product container, and closure and, for each component, a reconciliation of the use of each lot of such component.
- To assure uniformity from batch to batch, master production and control records for each drug product, including each batch size thereof, shall be prepared, dated, and signed

- Batch production and control records shall be prepared for each batch of drug product produced.
- All drug product production and control records, including those for packaging and labelling, shall be reviewed and approved by the quality control unit.
- Laboratory records shall include complete data derived from all tests necessary to assure compliance with established specifications and standards
- Distribution records shall contain the name and strength of the product and description of the dosage form, name and address of the consignee, date and quantity shipped, and lot or control number of the drug product

Returned and salvaged drug products

- Drug products that have been subjected to improper storage conditions including extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace
- Records of returned drug products shall be maintained and shall include the name and label potency of the drug product dosage form, lot number (or control number or batch number), reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned drug product

Reference

- www.fda.gov
- Ansels textbook of pharmaceutical dosage forms and drug delivery systems

Thank you