Almustansiriyah University
College of pharmacy

Dosage Form Design & Drug Delivery

Chapter-3

Current Good Manufacturing Practices

Fifth Stage

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Msc Drug Delivery

Current Good Manufacturing Practise (cGMP)

- ***GMP*** *regulations established by FDA to ensure that minimum standards are present for drug product quality in the U.S.*
- *They apply to domestic and to foreign suppliers and manufacturers whose bulk components and finished pharmaceutical products are imported, distributed, or sold in this country.*

TOPICAL OUTLINE OF CURRENT GOOD MANUFACTURING PRACTICE REGULATIONS

A. General Provisions
B. Organization and Personnel
- Responsibilities of quality control unit
- Personnel qualifications
- Personnel responsibilities
- Consultants

C. Buildings and Facilities
- Design and construction features
- Lighting
- Ventilation, air filtration, air heating and cooling
- Plumbing
- Sewage and refuse
- Washing and toilet facilities
- Sanitation
- Maintenance

D. Equipment
- Equipment design, size, and location
- Equipment construction
- Equipment cleaning and maintenance
- Automatic, mechanical, and electronic equipment
- Filters

E. Control of Components and Drug Product Containers and Closures
- Receipt and storage of untested components, drug product containers, and closures
- Testing and approval or rejection of components, drug product containers, and closures
- Use of approved components, drug product containers, and closures
- Retesting of approved components, drug product containers, and closures
- Rejected components, drug product containers, and closures
- Drug product containers and closures

F. Production and Process Controls
- Written procedures; deviations
- Charge-in of components
- Calculation of yield
- Equipment identification
- Sampling and testing of in-process materials and drug products
- Time limitations on production
- Control of microbiological contamination
- Reprocessing

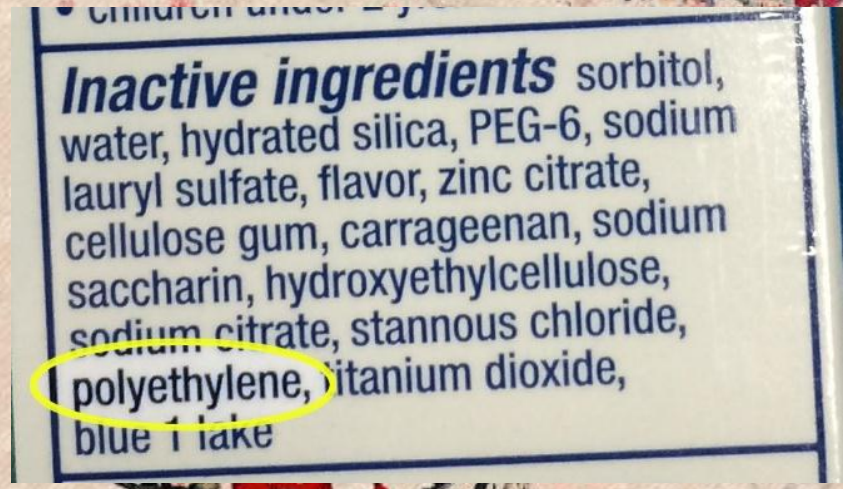
G. Packaging and Labeling Control
H. Holding and Distribution
I. Laboratory Controls
J. Records and Reports
K. Returned and Salvaged Drug Products
- Returned drug products
- Drug product salvaging

cGMP for Finished Pharmaceuticals

Common terms used in these regulations are defined as :

- ***Active pharmaceutical ingredient (API):*** *Any component have pharmacologic activity in diagnosis, cure, mitigation, treatment or prevention of disease.*
- ***Certification:*** *Documented testimony by qualified authorities that a system qualification, calibration, validation, or revalidation has been performed appropriately and that the results are acceptable*

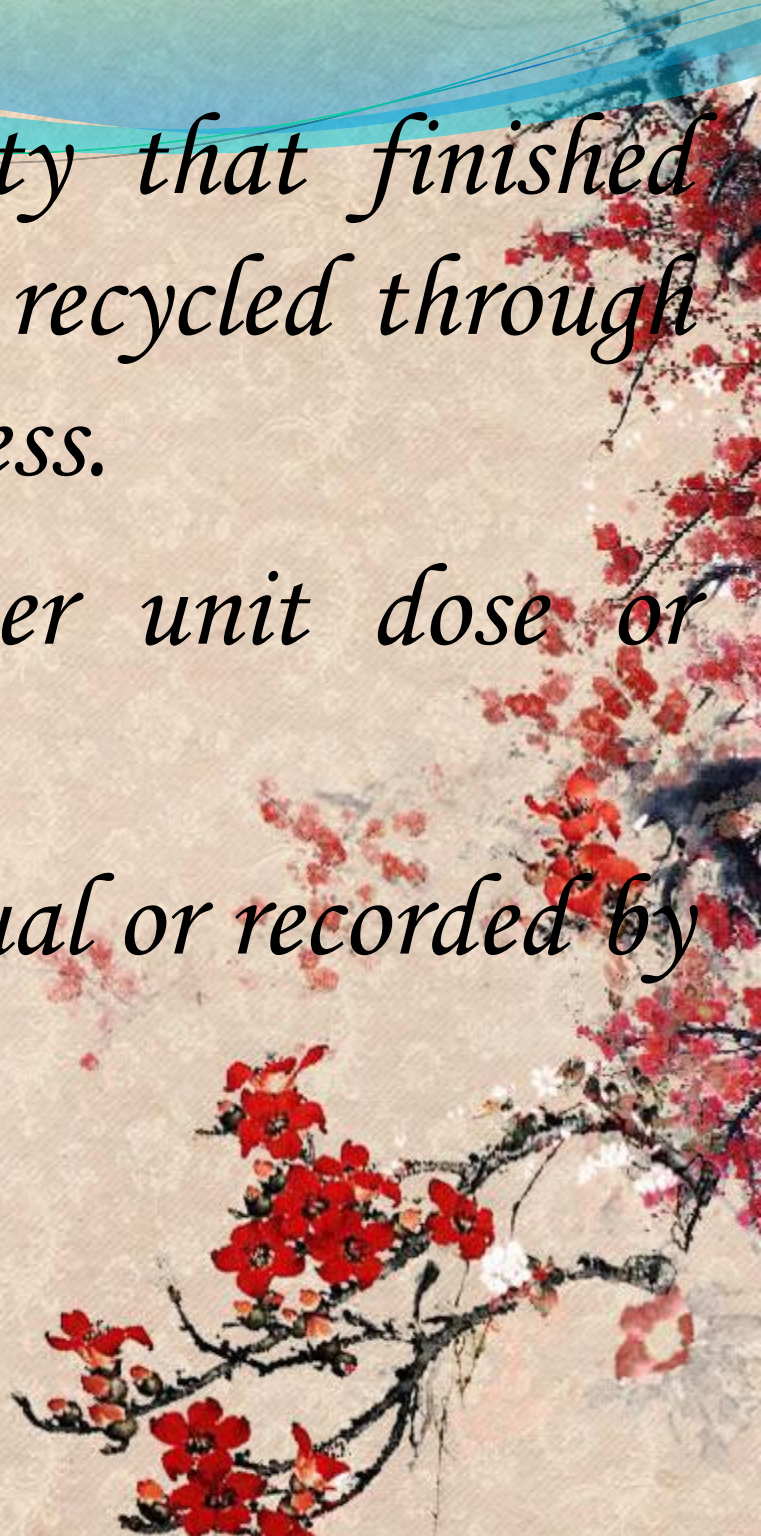
- ***Compliance:*** *manufacturer acting in accordance with prescribed regulations, standards, and practices.*
- ***Component:*** *Any ingredient used in manufacture of drug product*
- ***Drug product:*** *Finished form that contains active drug and inactive ingredients.*



- ***Lot:*** *A batch or any portion of a batch having uniform specified quality and a distinctive identifying lot number.*
- ***Lot number, control number, or batch number:*** *combination of letters, numbers, or symbols from which the complete history of manufacture, processing, packaging, holding, and distribution of a batch or lot of a drug product may be determined.*

- ***Quality assurance:*** *all evidence needed that activities relating to quality are being performed adequately.*
- ***Quality control:*** *process through which industry measures actual quality performance, compares it with standards, and acts on the difference.*
- ***Quality control unit:*** *organizational element designated by a firm to be responsible for work related to quality control.*

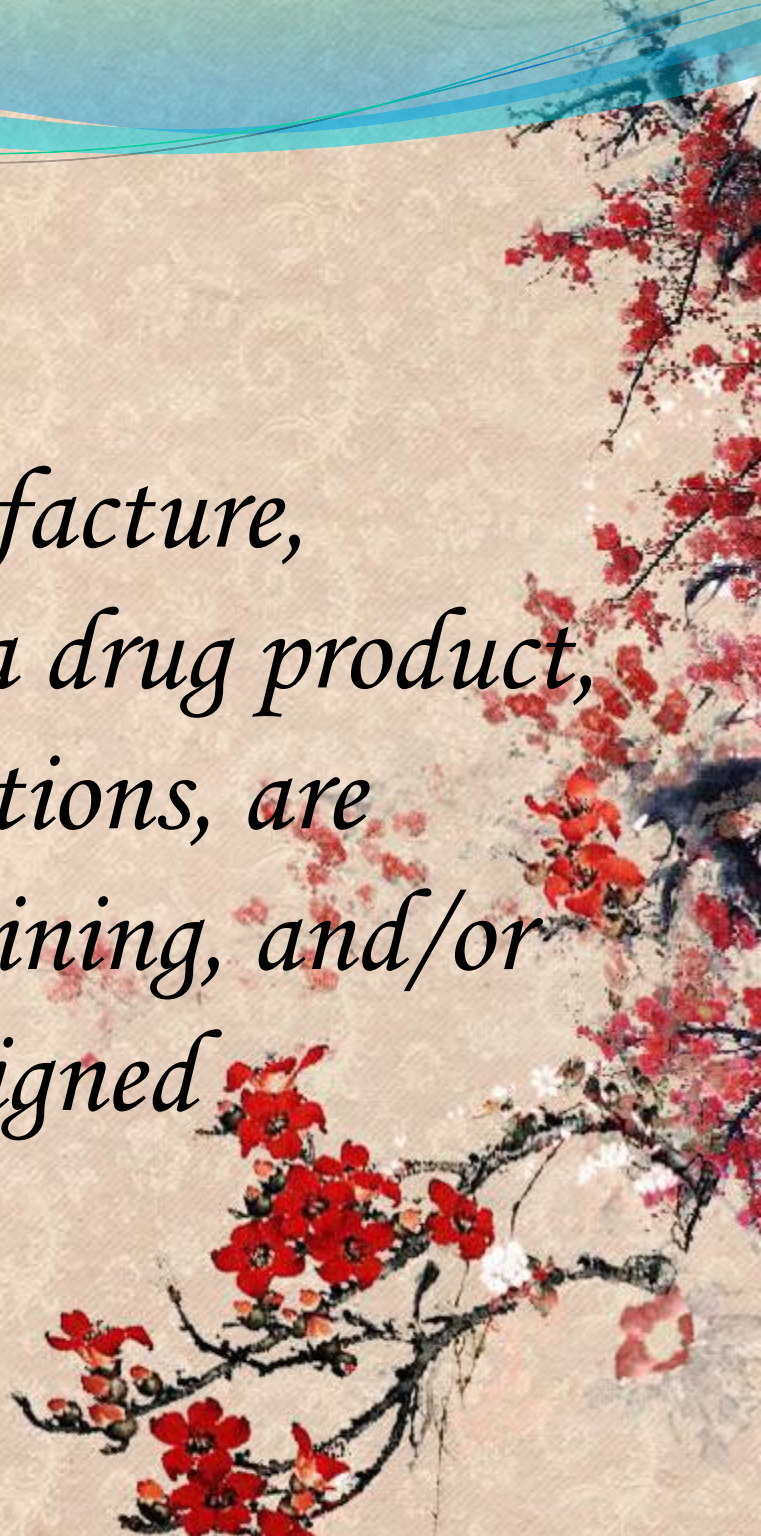
- ***Reprocessing:*** *recycling the activity that finished product or any of its components is recycled through all or part of the manufacturing process.*
- ***Strength:*** *concentration of drug per unit dose or volume.*
- ***Verified:*** *Signed by a second individual or recorded by automated equipment.*



Organization and personnel

- Deals with the responsibilities of the quality control unit, employees, and consultants. The regulations require that a quality control unit have the authority and responsibility for all functions that may affect product quality. This includes accepting or rejecting product components, product specifications, finished products, packaging, and labeling

- *All personnel engaged in the manufacture, processing, packing, or holding of a drug product, including those in supervisory positions, are required to have the education, training, and/or experience needed to fulfill the assigned responsibility.*



Equipments

- Each piece of equipment must be :appropriate design and size to facilitate use, cleaning, and maintenance.
- equipment's surfaces and parts must not interact with processes or product's surfaces compounds so not affect purity, strength, or quality.
- Standard operating procedures must be written and followed for proper use, maintenance, and cleaning of each piece of equipment.

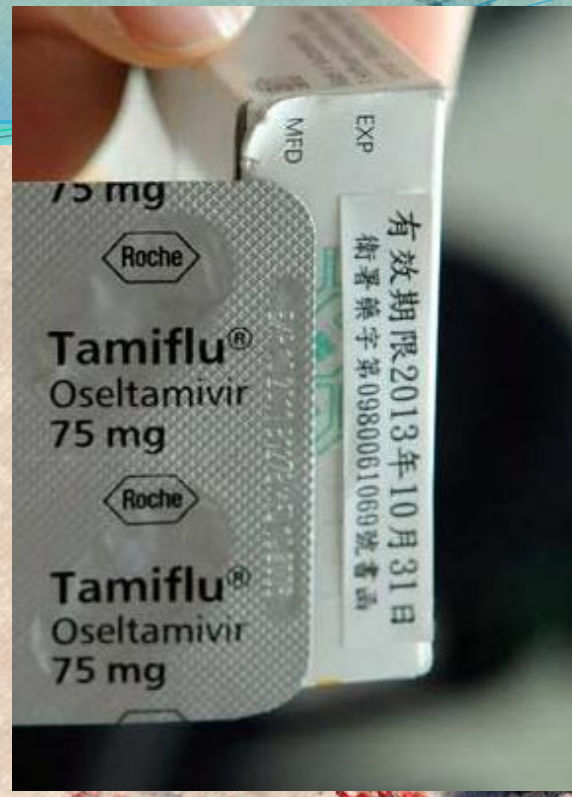
Control of Components, Containers and Closure

- Bulk pharmaceutical chemicals, containers, and closures must meet the exact physical and chemical specifications established with the supplier at the time of ordering
- Raw materials are quarantined until they are verified through representative sampling and careful qualitative and quantitative analysis. The quality control unit approves and releases for use in manufacture only those that meet the specifications

Production and process control

- *Written procedures are required to ensure that drug products have correct identity, strength, quality, and purity. In-process samples taken from production batches periodically for product control.*

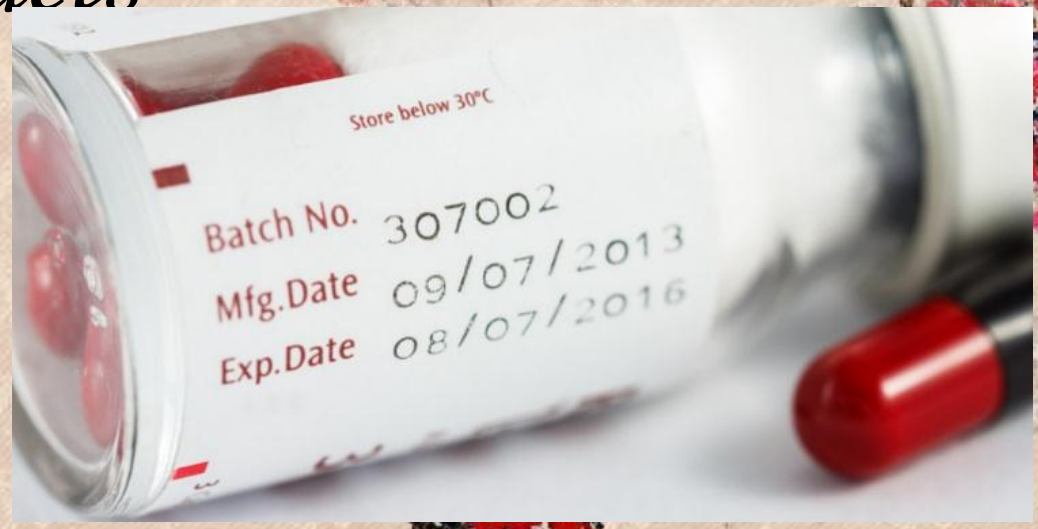
Packaging and labelling control



- *Written procedures are required for the identification, storage, handling, sampling, and testing of drug product and issuance of labeling and packaging materials.*

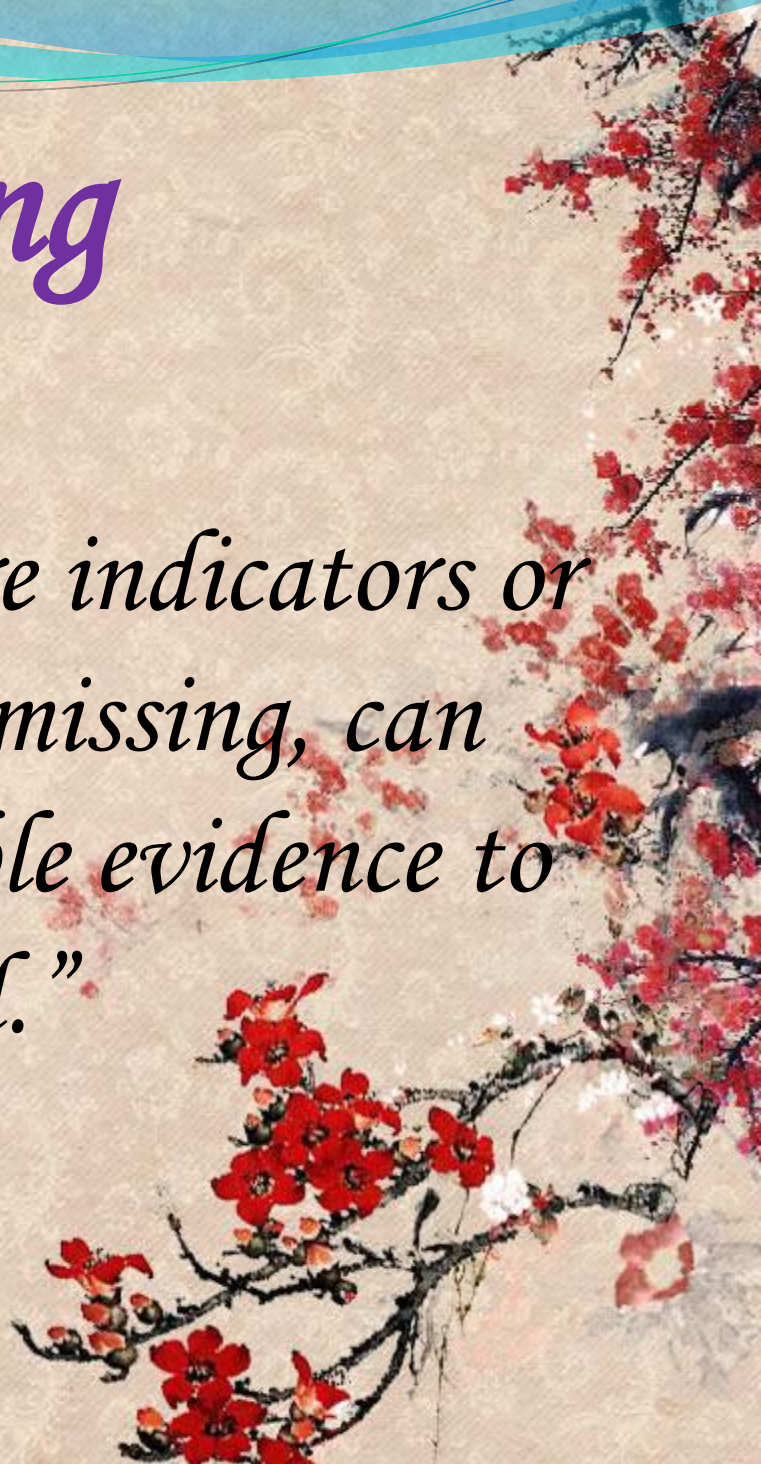
Expiration Date

- To ensure that a drug product meets standards of identity, strength, quality, and purity at time of use.
- Except from this requirement are homeopathic drug products, allergenic extracts



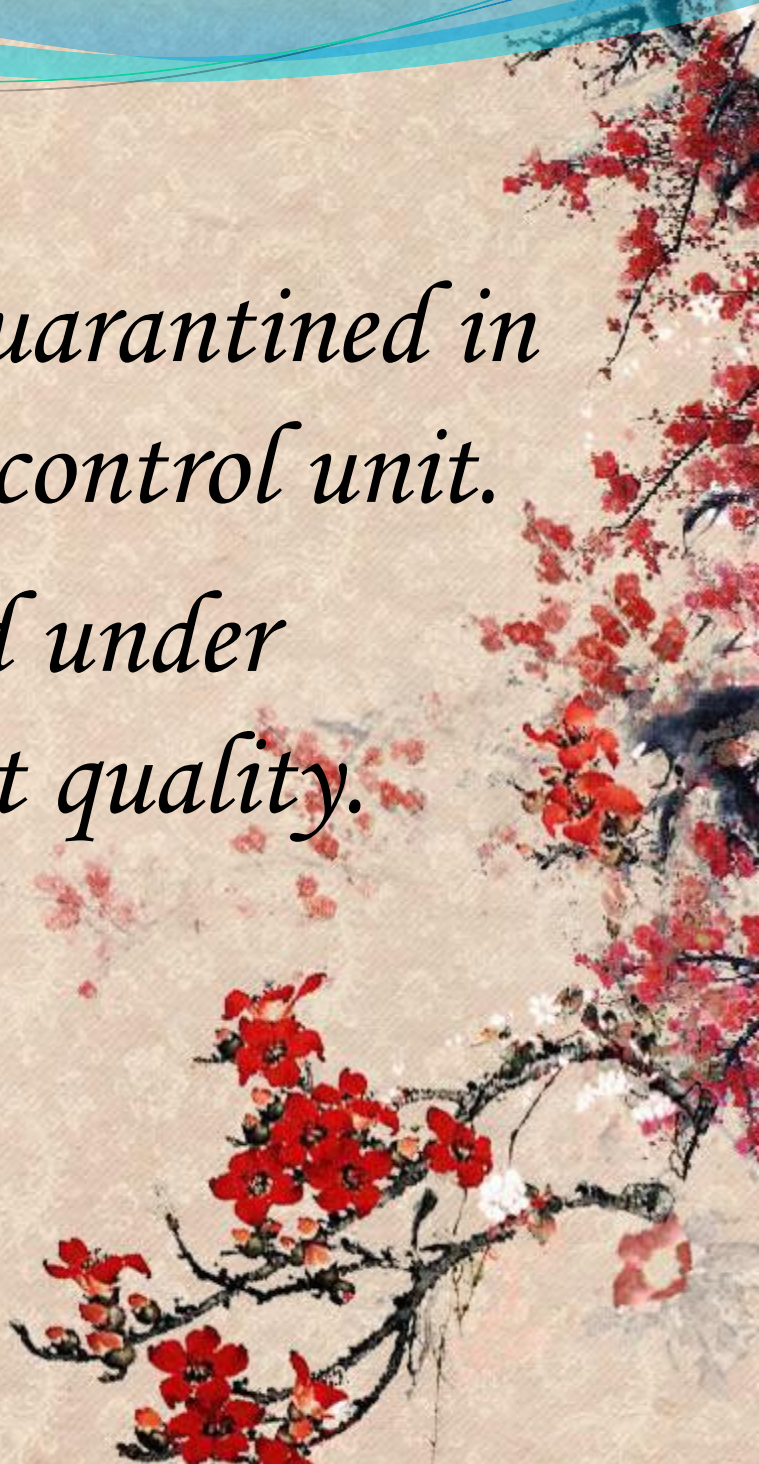
Tamper-Evident Packaging

It is defined as "one having one or more indicators or barriers to entry which, if breached or missing, can reasonably be expected to provide visible evidence to consumers that tampering has occurred."



Holding and Distribution

- *Finished pharmaceuticals must be quarantined in storage until released by the quality control unit.*
- *Products must be stored and shipped under conditions that do not affect product quality.*

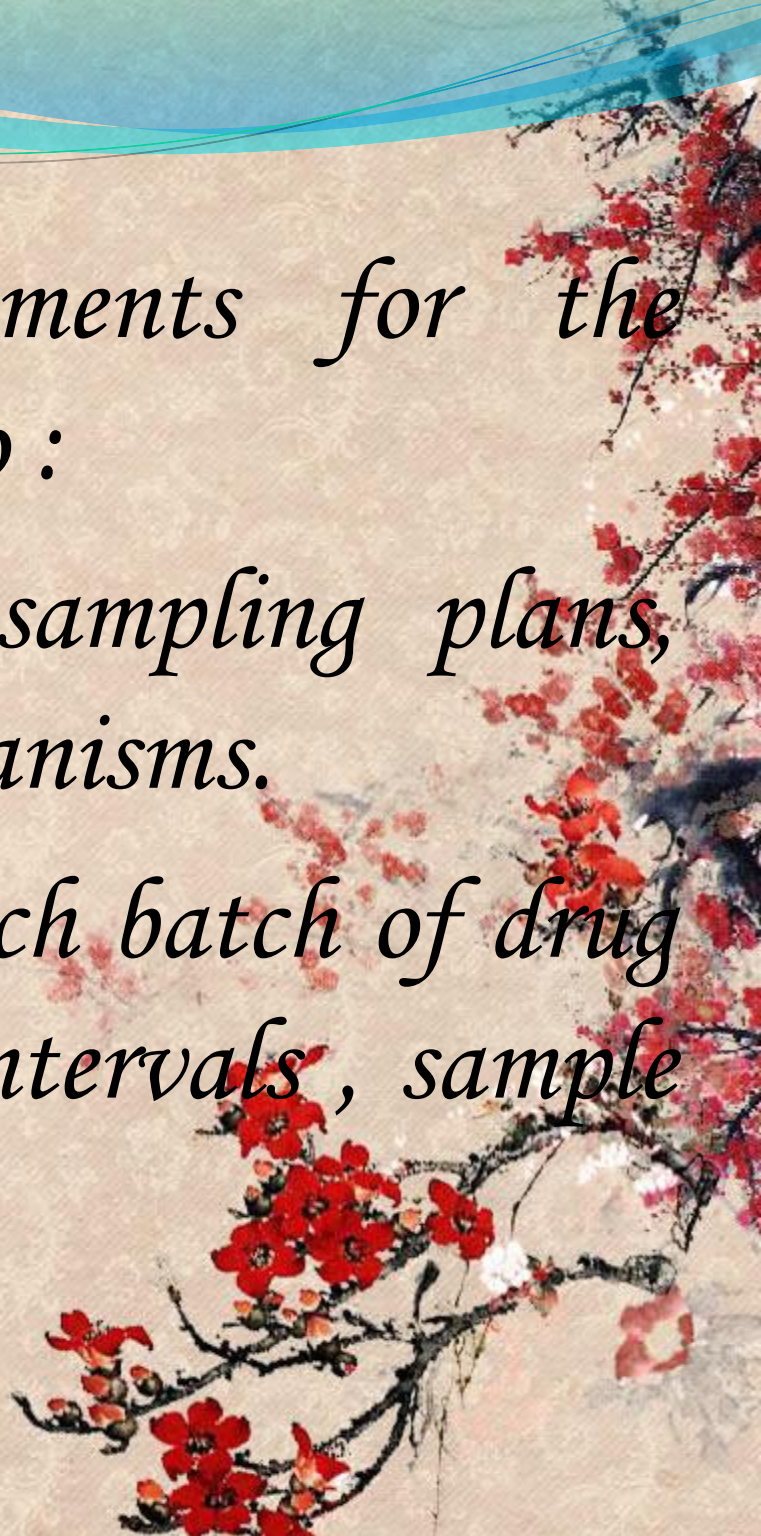


LABORATORY CONTROLS

- *Laboratory controls are requirements for the establishment of and conformance to :*

written specifications, standards, sampling plans, test procedures and other such mechanisms.

The specifications, which apply to each batch of drug product, include sample size, test intervals , sample storage and stability testing



RECORDS AND REPORTS

- Name and strength of the product
- Dosage form
- Quantitative amounts of components.
- Complete manufacturing and control procedures
- Equipment used

- *In-process controls*
- *Sampling and laboratory methods and assay results*
- *Calibration of instruments*
- *Distribution records*
- *Dated and employee-identified records*

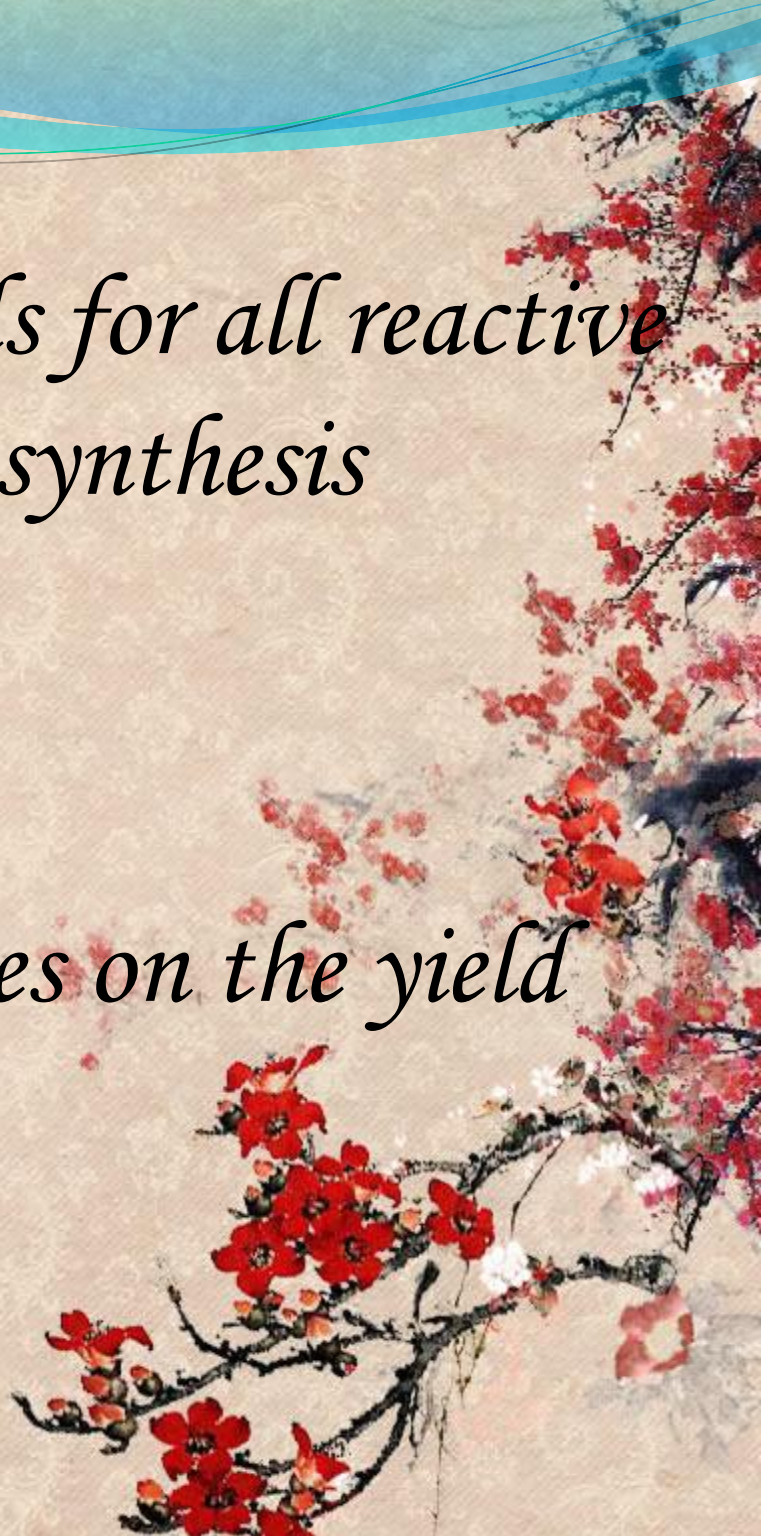
All records must be made available at the time of inspection by FDA officials.

ADDITIONAL cGMP REQUIREMENTS

Active Pharmaceutical Ingredients and Exciepients

the quality of any finished pharmaceutical product depends on the quality of the various components, including the active ingredients and pharmaceutical excipients, as they, too, are components of finished pharmaceutical products, must be produced in accordance with cGMP standards

- *Specifications and analytical methods for all reactive and nonreactive components used in synthesis*
- *Critical chemical reaction steps*
- *Handling of chemical intermediates*
- *Effect of scale-up of chemical batches on the yield*



- *Quality of the water systems*
- *Solvent handling and recovery systems*
- *Analytical methods to detect impurities or chemical residues and the limits set*
- *Stability studies of the bulk pharmaceutical chemical*

Clinical Trial Materials

- *This applies to both the production of the APIs and investigational drug products.*
- *As the clinical trials progress from Phase 1 to Phase 2, the processes are being characterized and refined, and during Phase 3 they are expected to meet all regulatory requirements.*

Biologics

Medical Devices

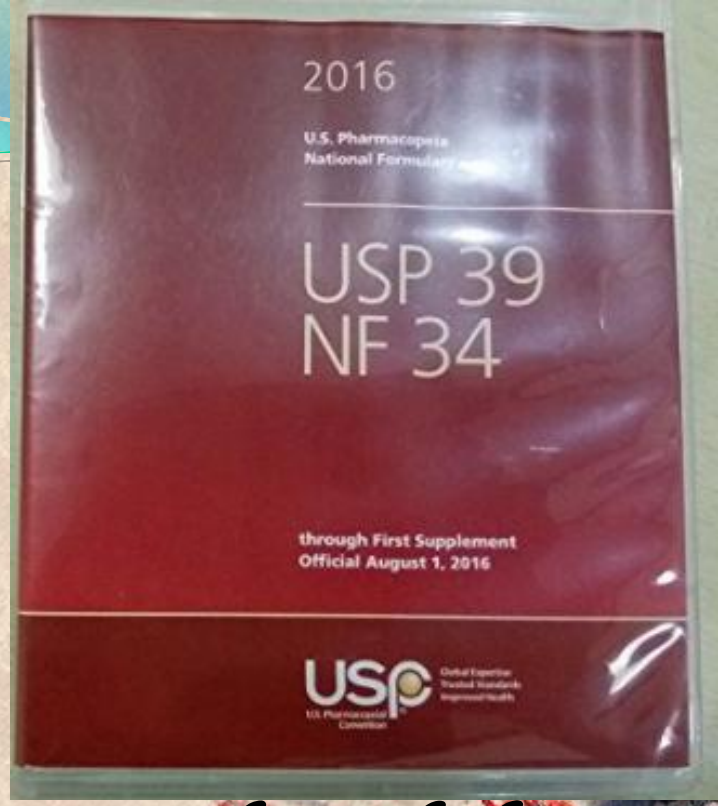
- *Devices are approved for marketing when shown to be safe and effective through premarket approval.*
- *Medical devices are subject to the reporting of adverse events, to recall, and to termination of approval.*

Current good compounding practices (cGCP)

A number of reasons have been presented for the increase in preparing patient-specific medications, including the following:

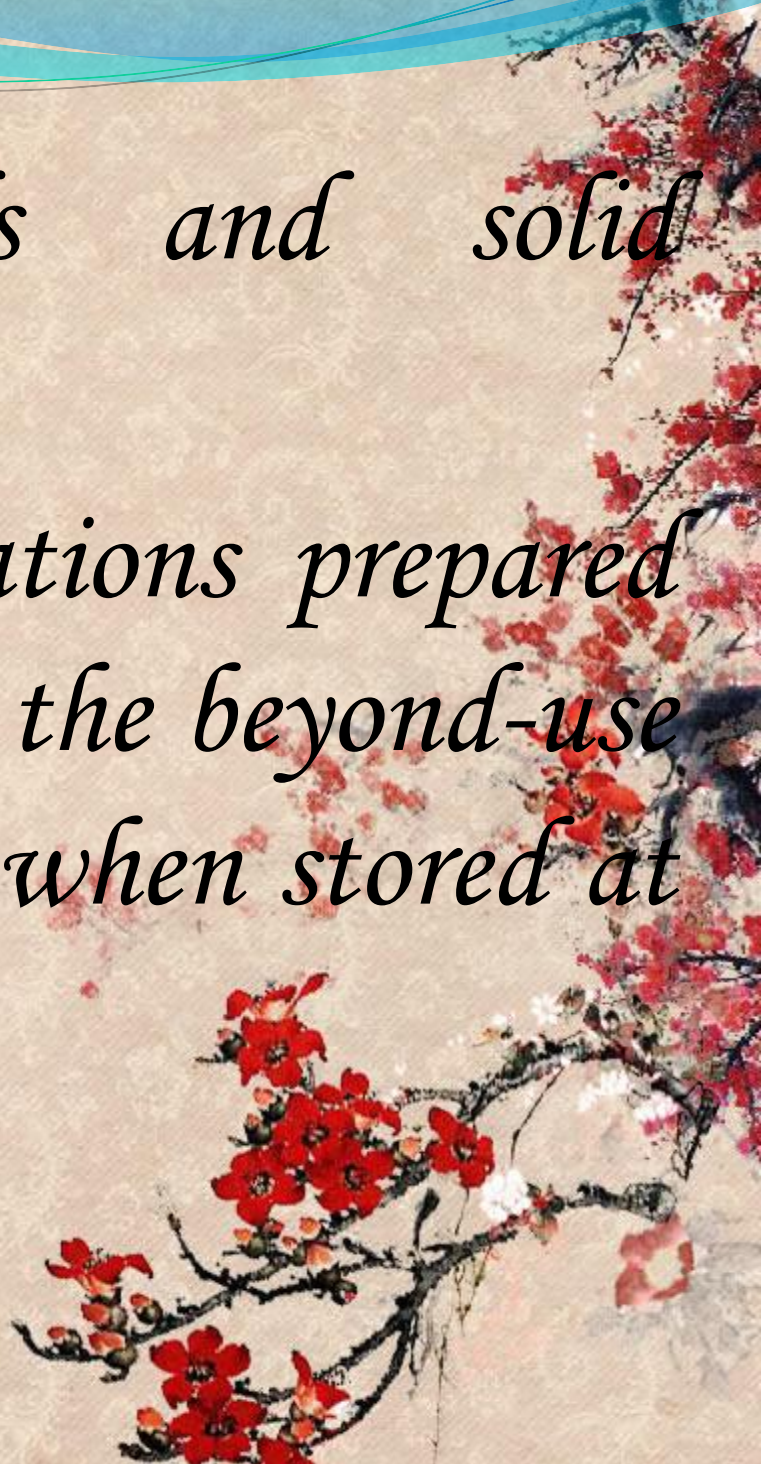
1. *Many patients need drug dosages or strengths that are not commercially available.*
2. *Many patients need dosage forms are not commercially available.*
3. *Many patients are allergic to excipients in commercially available products.*
4. *Children's medications must be prepared as liquids, flavoured to enhance compliance.*
5. *Some medications are not very stable and require preparation and dispensing every few days.*

USP-NF formulary



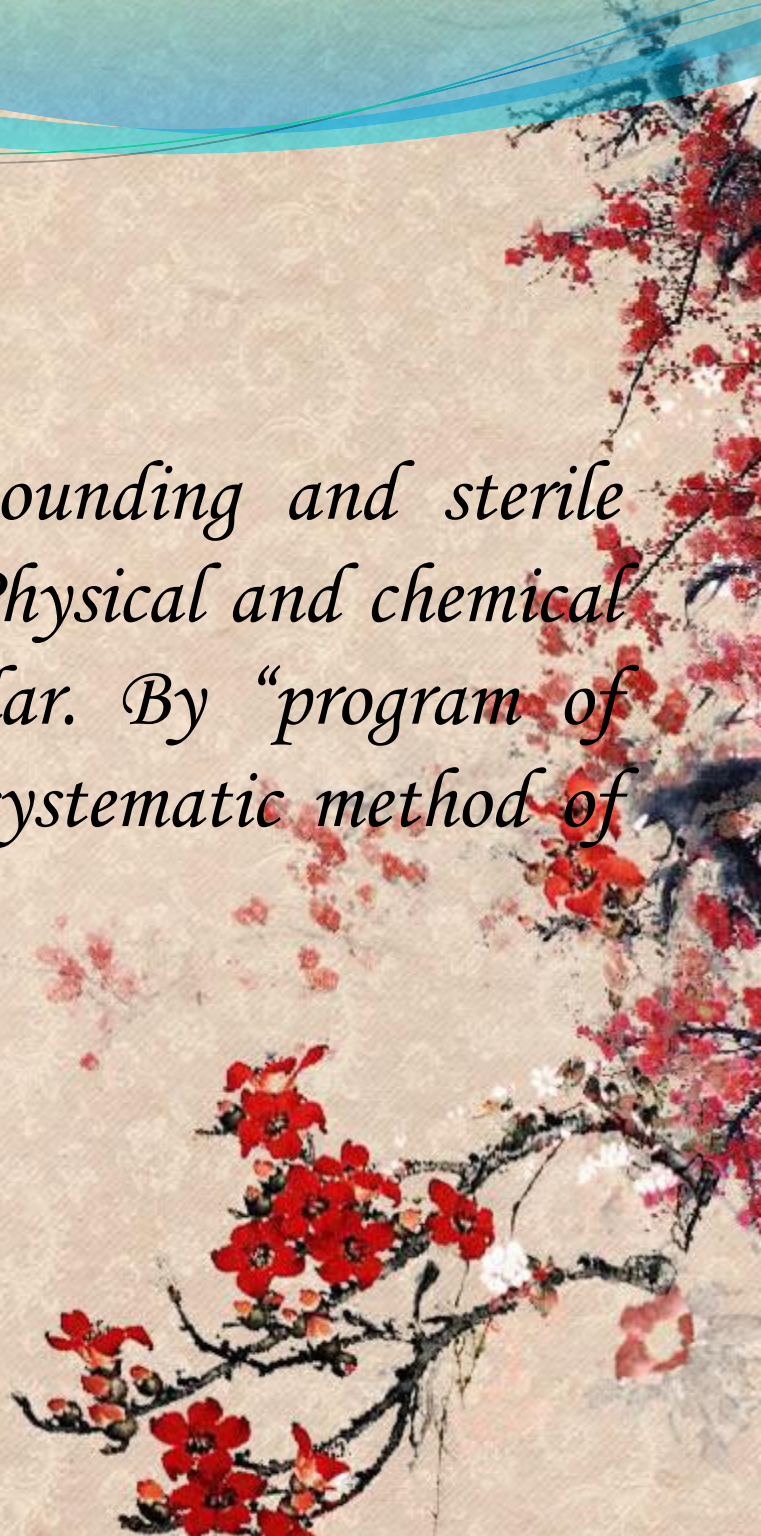
The stability includes packaging, sterility, and stability criteria and guidelines for assigning beyond-use dates

1. *For non aqueous liquids and solid formulations:*
2. *For water-containing formulations prepared from ingredients in solid form, the beyond-use date is not later than 14 days when stored at cold temperatures.*



- *3. For all other formulations, use date is not later than intended duration of therapy or 30 days.*

The main difference between non-sterile compounding and sterile compounding is the requirement for sterility. Physical and chemical properties should be the same or quite similar. By "program of sterility testing," it is meant that there is a systematic method of periodically testing compounded preparations.



References

- *Ansel's pharmaceutical dosage forms and drug delivery systems , eighth edition*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