Unit-3

Pharmaceutical Quality Assurance

B.Pharma 6th Sem Notes

Unit: 3

- **Quality Control:** Quality control test for containers, rubber closures and secondary packing material
- **Good Laboratory Practices:** General Provisions, Organization and Personnel, Facilities, Equipment, Testing Facilities Operation, and Control Articles, Protocol for Conduct of a Nonclinical Laboratory Study, Records and Reports, Disqualification of Testing Facilities.

Quality Control (QC)

Definition

Quality Control is a part of Pharmaceutical Quality Assurance that deals with **sampling, testing, specification, documentation, and release procedures** to ensure that **raw materials, packaging materials, in-process materials, and finished products** meet the required quality standards.

In pharmaceutical industries, **packaging materials** play a critical role in maintaining the **identity, strength, quality, and purity** of the drug product. Therefore, quality control testing of **containers, rubber closures, and secondary packaging materials** is essential.

Quality Control Tests for Pharmaceutical Packaging Materials

Quality Control Tests for Containers

Pharmaceutical containers are used to store and protect drug products from **environmental, chemical, and biological contamination**.

Types of Containers

- Glass containers
- Plastic containers
- Metal containers

A. Quality Control Tests for Glass Containers

1. **Hydrolytic Resistance Test**
   - Determines resistance of glass to water attack.
   - Glass is classified as **Type I, II, and III**.
   - Measures amount of alkali released from glass.
2. **Thermal Shock Test**
   - Evaluates resistance of glass to sudden temperature changes.
   - Containers are heated and rapidly cooled to observe cracking or breakage.
3. **Internal Pressure Test**
   - Checks mechanical strength of glass containers.
   - Internal pressure is applied until container breaks.
4. **Light Transmission Test**
   - Determines ability of glass to protect light-sensitive drugs.
   - Amber glass should reduce UV and visible light transmission.
5. **Annealing Test**
   - Checks internal stresses in glass.
   - Polarized light is used to detect strain patterns.

B. Quality Control Tests for Plastic Containers

1. **Extractables and Leachables Test**
   - Ensures no harmful substances migrate into the drug product.
2. **Permeability Test**
   - Measures permeability to water vapor, gases, and solvents.
3. **Compatibility Test**
   - Confirms no interaction between plastic and drug formulation.
4. **Clarity and Transparency**
   - Ensures absence of turbidity or discoloration.
5. **Mechanical Strength Test**
   - Resistance to cracking, breaking, and deformation.

Quality Control Tests for Rubber Closures

Rubber closures (stoppers) are used to seal vials, bottles, and infusion containers.

A. Physical Tests

1. **Fragmentation Test**
   - Determines tendency of rubber to fragment when pierced by a needle.
   - Ensures fragments do not contaminate the product.
2. **Self-Sealing Test**
   - Checks ability of closure to reseal after needle puncture.
   - Important for multi-dose vials.
3. **Penetrability Test**
   - Measures force required to pierce the rubber closure.
   - Ensures ease of injection.
4. **Hardness Test**
   - Ensures rubber elasticity and flexibility.

B. Chemical Tests

1. **pH Change Test**
   - Measures change in pH when rubber is in contact with water.
2. **Extractable Substances Test**
   - Detects soluble substances released from rubber.
3. **Heavy Metals Test**
   - Ensures absence of toxic metals like lead, cadmium, and mercury.
4. **Volatile Sulphides Test**
   - Confirms no sulphur compounds are released.

C. Biological Tests

1. **Sterility Test**
   - Ensures closures are free from microorganisms.
2. **Pyrogen Test**
   - Confirms absence of fever-producing substances.

3. **Cytotoxicity Test**
    - Ensures material is safe for biological use.

Quality Control Tests for Secondary Packaging Materials

Secondary packaging protects the **primary container** and provides **information, identification, and branding**.

Types of Secondary Packaging

- Cartons
- Labels
- Leaflets
- Corrugated boxes

A. Tests for Cartons

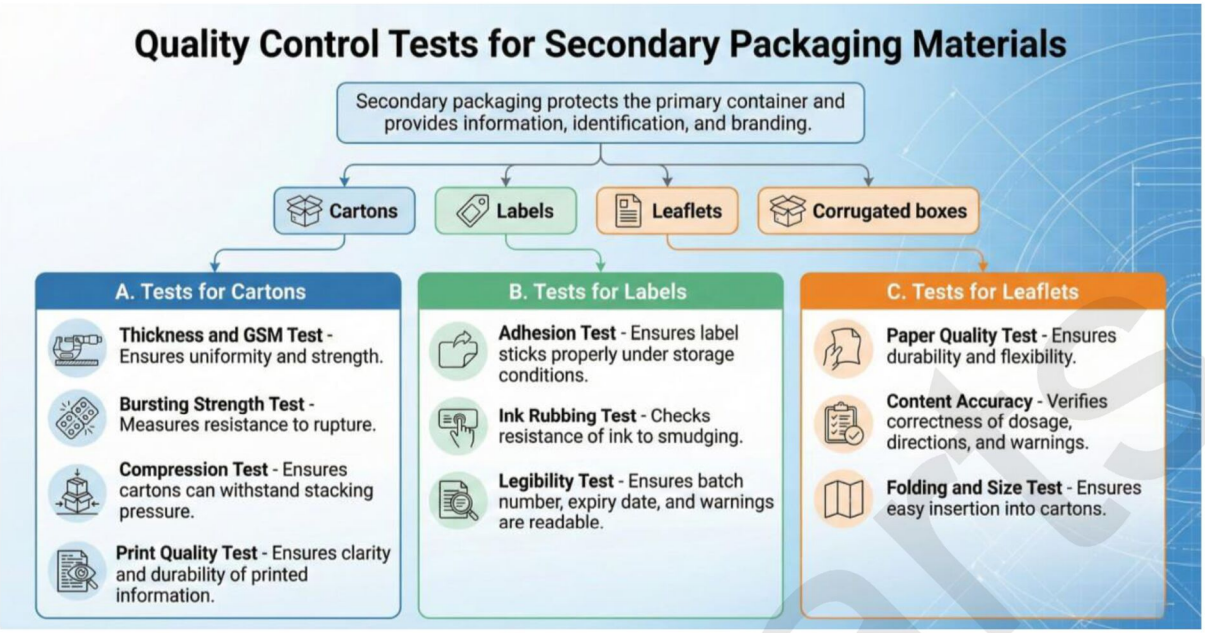
1. **Thickness and GSM Test**
    - Ensures uniformity and strength.
2. **Bursting Strength Test**
    - Measures resistance to rupture.
3. **Compression Test**
    - Ensures cartons can withstand stacking pressure.
4. **Print Quality Test**
    - Ensures clarity and durability of printed information.

B. Tests for Labels

1. **Adhesion Test**
    - Ensures label sticks properly under storage conditions.
2. **Ink Rubbing Test**
    - Checks resistance of ink to smudging.
3. **Legibility Test**
    - Ensures batch number, expiry date, and warnings are readable.

C. Tests for Leaflets

1. **Paper Quality Test**
    - Ensures durability and flexibility.
2. **Content Accuracy**
    - Verifies correctness of dosage, directions, and warnings.
3. **Folding and Size Test**
    - Ensures easy insertion into cartons.



Importance of QC Testing of Packaging Materials

- Maintains **drug stability and safety**
- Prevents **contamination and interaction**
- Ensures **patient safety**
- Complies with **GMP and regulatory guidelines**
- Enhances **product shelf life**

Good Laboratory Practices (GLP):

Introduction to Good Laboratory Practices (GLP)

Good Laboratory Practices (GLP) are a **set of rules and guidelines** that ensure laboratory work is **planned, performed, monitored, recorded, and reported properly**.
The main aim of GLP is to ensure that **laboratory data is accurate, reliable, reproducible, and traceable**.

GLP is mainly applied in:

- Quality Control laboratories
- Research and development laboratories
- Pharmaceutical testing laboratories
- Chemical and biological testing labs

Objectives of GLP

The main objectives of GLP are:

- To ensure **accuracy and reliability of test results**
- To maintain **uniformity and consistency** in laboratory work
- To prevent **errors, mix-ups, and data manipulation**
- To ensure **proper documentation and traceability**
- To improve **confidence in laboratory results**
- To support **regulatory acceptance** of laboratory data

General Provisions (GLP)

General provisions describe the basic rules and principles that must be followed to ensure that laboratory work is **accurate, reliable, and acceptable**.

Points:

- All laboratory activities must be conducted according to **Good Laboratory Practices (GLP)**.
- Laboratory studies should be **properly planned, performed, monitored, recorded, and reported**.
- Written **Standard Operating Procedures (SOPs)** must be available and followed.
- All data generated in the laboratory must be:
  - Accurate
  - Complete
  - Legible
  - Traceable
- Proper **documentation and record maintenance** is mandatory.
- Any deviation from SOPs must be:
  - Documented
  - Justified
  - Approved by authorized personnel
- GLP ensures **data integrity**, which means data should not be altered or falsified.

Organization and Personnel

Proper organization and qualified personnel are essential for effective implementation of GLP.

Organization:

- The laboratory should have a **clearly defined organizational structure**.
- Duties and responsibilities of all staff should be **clearly documented**.
- There should be:
  - Laboratory Head
  - Analysts / Technicians
  - Quality Assurance (QA) personnel

Personnel:

- Laboratory personnel must be:
  - Appropriately **qualified**
  - Adequately **trained**
  - Experienced for assigned tasks
- Initial and periodic **training programs** should be conducted.
- Training records must be **maintained and updated**.
- Personnel should follow:
  - Personal hygiene practices
  - Laboratory safety rules
- Access to laboratory areas should be **restricted to authorized personnel only**.

Facilities

Laboratory facilities should be designed to ensure **safe, efficient, and contamination-free operations**.

Requirements:

- Laboratory premises should be:
  - Clean
  - Well ventilated
  - Adequately lighted
- The layout should allow:
  - Smooth workflow
  - Prevention of cross-contamination
- Separate areas should be provided for:
  - Sample receipt
  - Sample testing
  - Storage of chemicals and reagents
  - Instrument rooms (if required)
- Environmental conditions such as:
  - Temperature
  - Humidity
  - Cleanliness

  must be controlled and monitored.
- Safety facilities such as:
  - Fire extinguishers
  - Emergency exits
  - First aid kits

  should be available and easily accessible.

Equipment

Equipment plays a critical role in generating **accurate and reproducible results**.

Equipment Requirements:

- Equipment should be:
  - Suitable for intended use
  - Properly installed
  - Maintained in good working condition
- Each instrument must undergo:
  - **Calibration**
  - **Qualification**
  - **Preventive maintenance**
- Written information should be available for:
  - Operating procedures
  - Cleaning methods
  - Maintenance schedules
- Equipment should have:
  - Unique identification number
  - Calibration status label
- Records must be maintained for:
  - Calibration
  - Maintenance
  - Repairs
- Defective equipment should be:
  - Clearly labeled
  - Removed from use until repaired

Testing Facilities Operation

Testing facility operation refers to the **day-to-day working of the laboratory** according to GLP principles.

Points:

- All laboratory activities must be conducted as per **approved Standard Operating Procedures (SOPs)**.
- Work should be **planned, supervised, and documented properly**.
- Proper coordination must exist between:
  - Study director
  - Laboratory staff
  - Quality Assurance (QA) unit
- Unauthorized personnel should not be allowed inside testing areas.
- Housekeeping and sanitation must be maintained regularly.
- Any deviation from SOPs must be:
  - Documented
  - Investigated
  - Approved by authorized personnel

Purpose:
To ensure laboratory work is **consistent, controlled, and reproducible**.

Control Articles

Control articles are **substances used for comparison** during laboratory testing.

Types of Control Articles:

- **Positive control:** Produces a known response
- **Negative control:** Produces no response
- **Vehicle control:** Contains solvent without active substance

GLP Requirements:

- Control articles must be:
  - Properly identified
  - Labeled clearly
  - Stored under suitable conditions
- Label should include:
  - Name of control article
  - Batch or lot number
  - Expiry date
  - Storage conditions
- Records of receipt, handling, and usage must be maintained.
- Control articles must not be contaminated or mixed up.

Protocol for Conduct of a Non-Clinical Laboratory Study

A protocol is a **written study plan** that describes how a non-clinical laboratory study will be conducted.

Contents of a Study Protocol:

- Title and objective of the study
- Name of:
  - Study director
  - Testing facility
- Description of:
  - Test and control articles
  - Test system used
- Experimental design
- Method of data collection and analysis
- Type and frequency of observations
- Statistical methods (if applicable)

GLP Requirements:

- Protocol must be:
  - Written

  - Approved
  - Dated and signed before study starts
- Any changes must be made through:
  - Protocol amendments
  - Proper authorization

Records and Reports

Documentation is the **most critical part of GLP**.

Records:

- Raw data must be:
  - Accurate
  - Legible
  - Permanent
- Records include:
  - Laboratory notebooks
  - Instrument printouts
  - Calibration records
  - SOPs
- Corrections must:
  - Not erase original data
  - Be signed and dated

Reports:

- Final report should include:
  - Study objectives
  - Methods used
  - Results obtained
  - Conclusions
  - Deviations (if any)
- Reports must be:
  - Signed by study director
  - Reviewed by QA unit
- Records and reports must be **stored safely** for the required retention period.

Purpose:
To maintain **data integrity, traceability, and regulatory acceptance**.

Disqualification of Testing Facilities

Disqualification occurs when a testing facility **fails to comply with GLP requirements**.

Reasons for Disqualification:

- Falsification or manipulation of data
- Repeated violation of SOPs
- Poor documentation practices
- Inadequate QA supervision
- Use of unqualified personnel
- Failure to correct previously reported deficiencies

Consequences:

- Rejection of laboratory data by regulatory authorities
- Suspension or cancellation of laboratory approval
- Loss of credibility and regulatory trust

Prevention:

- Regular internal audits
- Continuous training of staff
- Strict adherence to GLP guidelines
- Effective QA monitoring
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