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Unit III — Quality Control and Good Laboratory Practices

Pills & Python Notes

From-zero teaching standard: every technical term is defined before use.

Syllabus coverage: Unit III (10 hours)

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CHAPTER 5: QC TESTS FOR FORMULATIONS, RAW MATERIALS AND PACKAGING MATERIALS

Unit III (10 hours)

1. Learning Objectives

After studying this chapter, you will be able to:

1. Define in-process QC and finished-product QC, and explain why both are needed.
2. List the in-process and finished-product QC tests for tablets and capsules.
3. List the QC tests for ointments, creams, ophthalmic and parenteral preparations.
4. Explain the QC tests for raw materials and describe how raw materials are sampled.
5. Describe the QC tests for glass and plastic containers, rubber closures and secondary packaging materials.

2. Definitions

- Quality Control (QC): Checking and testing materials and products at different stages to make sure they meet the required standards.
- In-process QC (IPQC): Tests done during manufacturing. Example: checking tablet weight while tablets are being made on the machine.
- Finished-product QC: Tests done on the final packed product before it is released to the market. Example: testing the packed tablet strip for assay and dissolution.
- Raw material: Any substance used to make the medicine — the active drug and the excipients (helper substances like binders, fillers, preservatives).
- Packaging material: Anything that holds or protects the medicine — bottles, vials, blister packs, rubber stoppers, cartons.
- Sterility test: A test to prove that a product has NO living microorganisms (bacteria or fungi) in it.
- Pyrogen test / Bacterial endotoxins test: Tests to check that an injectable product does not contain fever-causing substances (pyrogens / endotoxins).
- Certificate of Analysis (COA): A written document from the supplier showing that a batch of material passed all the required tests.

> **NOTE**
>
> Caution on exact limits: Pharmacopoeial limits are updated in new editions. In this chapter, test values are given as commonly taught values. Always confirm against the current pharmacopoeial edition / current guidelines before quoting a limit in an exam answer that asks for "as per IP".

3. Terminology (Word Bank)

Term	Simple meaning
Disintegration	How fast a tablet or capsule breaks into small pieces in water or stomach-like fluid
Dissolution	How fast the drug dissolves and comes out of the tablet/capsule into a liquid
Friability	How much a tablet chips or breaks when it is tumbled/rolled — a measure of tablet strength
Hardness	How much pressure a tablet can bear before it crushes
Assay	The measured amount of drug in the product, usually shown as a percentage of what is written on the label
Content uniformity	Check that every single tablet/capsule contains nearly the same amount of drug
Weight variation	Check that every single tablet/capsule weighs nearly the same
Sterility	Complete absence of living microorganisms
Endotoxin	A poison-like substance released from dead bacteria that causes fever; tested by the LAL test
LAL test	Limulus Amoebocyte Lysate test — a test using a substance from horseshoe-crab blood that detects bacterial endotoxins
LOD (Loss on Drying)	Amount of water (and volatile matter) lost when a material is heated and dried
Extractables / Leachables	Chemicals from packaging that can come out into the medicine
Hydrolytic resistance	How well a glass container resists giving out alkali (dissolving) into water/medicine
Fragmentation (closure)	Test to check that a rubber stopper does not break into small pieces when a needle passes through it
Self-sealability	The ability of a rubber closure to close itself after a needle is removed, so air and germs cannot enter
Sub-visible particles	Very small particles in an injection that cannot be seen with the naked eye but can be counted by a machine
Osmolality	A measure of how "concentrated" a liquid is — important so injections do not damage blood cells
Viscosity	How thick a liquid or cream is — how slowly it flows
Spreadability	How easily an ointment or cream spreads on the skin
Extrudability	How easily an ointment comes out of its tube when squeezed

Term	Simple meaning
Preservative efficacy	Proof that the preservative added to the product actually kills or stops the growth of microbes
Sampling	Taking a small, representative portion of a large batch for testing
Approved vendor	A supplier who has been checked and approved by the company's QA department

4. Explanations

4.1 Why do we need both in-process and finished-product QC?

Think of it this way: in-process QC is like tasting the curry while it is cooking — if it needs more salt, you can add it now. Finished-product QC is like tasting the curry after it is served — if something is wrong now, the whole dish is wasted.

- In-process QC finds problems early, when they can still be corrected. It saves time, money and materials.
- Finished-product QC is the final gate. Only batches that pass are released for sale. This protects the patient.

4.2 QC tests for tablets

In-process tests (during tablet manufacturing):

- Weight check: Tablets are weighed at regular intervals while the compression machine is running. If tablets become too heavy or too light, the machine is adjusted immediately.
- Hardness test: A tablet is crushed between two jaws of a hardness tester. Commonly taught range: hard enough to survive handling, commonly expressed as a few kg/cm² (confirm the exact target from the product specification).
- Thickness: Measured with a caliper or micrometer. Thickness must stay uniform, otherwise tablet weight and appearance vary.
- Friability: Tablets are tumbled in a rotating drum. Commonly taught limit: not more than 1% weight loss. This proves tablets will not chip during packing and transport.
- Disintegration: Tablets are placed in a basket that moves up and down in water at body temperature (37°C). Commonly taught times: uncoated tablets within about 15 minutes, film-coated within about 30 minutes, sugar-coated within about 60 minutes (confirm against the current pharmacopoeial edition).

Finished-product tests (on the final packed tablets):

- Description: Colour, shape, size, markings — tablets must look as specified.
- Identification: Test to prove the drug present is the correct drug.
- Assay: Commonly taught acceptance: 90–110% (or the range given in the monograph) of the labelled amount (confirm against the current monograph).
- Uniformity of dosage units: Two ways are commonly taught —
  - Weight variation test: used when the drug is a large part of the tablet weight. Commonly taught limits for uncoated tablets: average weight up to 80 mg → ±10%;

80–250 mg → ±7.5%; above 250 mg → ±5%. Not more than 2 tablets out of 20 may be outside the limit, and none may be beyond double the limit.

- Content uniformity test: used when the drug is a small part of the tablet weight. The drug content of each of 10 tablets is measured; commonly taught limits: each within 85–115% of the average (confirm against the current pharmacopoeial edition).

- Dissolution: Tablets are stirred in a vessel of warm fluid using a paddle or basket apparatus. The amount of drug released is measured over time. Commonly taught requirement: a specified percentage (the "Q value", commonly 75% or 80%) must be released within 45 minutes (confirm against the current monograph).
- Disintegration: Same test as in-process, done again on the finished pack.
- Related substances / impurities: Check that unwanted chemicals formed during manufacturing or storage are within limits.
- Microbial limits: Check that the number of microbes is below the allowed limit.

4.3 QC tests for capsules

In-process tests:

- Fill weight of contents: Capsules are opened and the powder/granule fill is weighed at intervals. Fill weight must be uniform.
- Shell integrity: Empty and filled capsule shells are checked for cracks, dents, dents at the joint, and proper locking of cap and body.
- Disintegration: Commonly taught: hard gelatin capsules within about 30 minutes, soft gelatin capsules within about 60 minutes (confirm against the current pharmacopoeial edition).

Finished-product tests:

- Description: Colour and size of the capsule shell, markings.
- Identification and assay: Same purpose as in tablets.
- Uniformity of dosage units: Weight variation of contents (hard capsules) or content uniformity (for low-dose drugs).
- Dissolution: Very important for capsules, because the shell must first open and the fill must then release the drug.
- Disintegration: Repeated on finished packs.
- Moisture content: Capsule shells contain water; too much or too little moisture makes them soft or brittle. Commonly taught: checked by LOD or Karl Fischer (confirm limits from the product specification).
- Microbial limits: Required as for tablets.

4.4 QC tests for ointments and creams (semisolid preparations)

- Description: Colour, texture, smell, and absence of lumps.
- Homogeneity: The cream/ointment must be smooth — no gritty particles when rubbed between fingers. For suspension-type products, particle size is checked.
- Identification and assay: Proof of correct drug and correct amount.
- pH: Important for creams and emulsions because the pH of the skin is mildly acidic; wrong pH can irritate the skin (commonly taught: compare with the product specification).

- Viscosity: Measured with a viscometer. The product must be thick enough to stay on the skin but not so thick that it cannot be squeezed out.
- Spreadability: Measured in-process — how easily a measured amount spreads between two glass plates under a fixed weight.
- Extrudability (tube test): How easily and uniformly the ointment comes out when the tube is squeezed.
- Fill weight / net content: Each tube must contain at least the labelled amount.
- Leaker test: Tubes are checked for leaks (commonly taught: kept under defined conditions and checked for oozing product).
- Microbial limits and preservative efficacy: Because water-containing creams can grow microbes, both the number of microbes and the working of the preservative are tested.
- Uniformity of mass of delivered doses: For metered-dose containers, each delivered dose must be uniform.

4.5 QC tests for ophthalmic preparations (eye drops, eye ointments)

The eye is very sensitive, so these tests are extra strict:

- Sterility: Eye products MUST be sterile — no microbes allowed at all.
- Clarity / absence of particles: Eye drops must be clear and free from visible particles; any particle can scratch the eye.
- pH: The eye tolerates a pH close to tears (commonly taught target near neutral pH, about 7.4; confirm from the product specification).
- Osmolality: The solution should be close to the salt concentration of tears, otherwise it stings.
- Viscosity: Some drops are made slightly thick so they stay longer in the eye — viscosity is checked.
- Assay and identification: Correct drug, correct strength.
- Content uniformity / uniformity of delivered dose: Each drop or single-dose unit must deliver the same amount.
- Particle size: For eye suspensions, particles must be very fine and uniform so they do not irritate.
- Leaker test and net content: For single-dose and multi-dose containers.
- Preservative content: If a multi-dose bottle contains a preservative, its amount is checked, and preservative efficacy is proven.

4.6 QC tests for parenteral preparations (injections)

Injections go directly into the blood or tissues, so their tests are the strictest of all:

- Description / clarity: The solution must be clear and free from visible particles when viewed against black and white backgrounds.
- Identification and assay: Correct drug, correct strength.
- pH: Checked and compared with the specification.

- Particulate matter (sub-visible particles): Invisible tiny particles are counted by a machine. Commonly taught limits (confirm against the current pharmacopoeial edition): not more than a defined number of particles ≥10 micrometres and ≥25 micrometres per container.
- Sterility: Absolute requirement — injections must be sterile.
- Bacterial endotoxins (LAL test): Even dead bacteria release endotoxins that cause fever, so every batch of injection is tested for endotoxins.
- Volume in container (extractable volume): The vial/ampoule must deliver at least the labelled volume.
- Colour: Compared with a reference — colour change can mean degradation.
- Osmolality: Important for large-volume injections so blood cells are not damaged.
- Uniformity of dosage units: For powders for injection.
- Water content and reconstitution time: For freeze-dried (lyophilized) powders — the powder must dissolve quickly and completely when the diluent is added.
- Container closure integrity (CCI): Proof that the sealed container does not leak — commonly taught method: dye ingress test.
- Preservative/antioxidant content: If added, the amount is checked.

4.7 QC of raw materials

Every raw material is tested before it is allowed into manufacturing:

1. Sampling: A small representative sample is taken from the consignment. Commonly taught rule for how many containers to sample: $\sqrt{n} + 1$ (where n = number of containers) — for example, from 16 drums, sample $\sqrt{16} + 1 = 5$ drums. Sampling is done with clean, dedicated sampling tools, and each sampled container is labelled.
2. Identity test: Proves the material is what the label says (e.g., chemical tests, IR spectrum, melting point).
3. Assay: Measures the purity/strength — commonly taught: must be within the monograph range, commonly 98–102% for many pure substances (confirm against the current monograph).
4. Tests for impurities: Limit tests for chlorides, sulfates, heavy metals, arsenic — unwanted chemicals must be below limits.
5. Loss on drying (LOD) / water content: Too much water can spoil the material or affect weighing.
6. Ash values (for herbal/mineral materials): Total ash, acid-insoluble ash — show the material is clean and not adulterated.
7. Particle size: Important for drugs that must dissolve well.
8. Microbial limits: Especially for natural and excipient materials.
9. Solubility, melting range, specific optical rotation: Physical checks that confirm identity and purity.
10. Vendor approval: Materials are bought only from approved vendors who supply a COA; the QC department re-tests before use.

4.8 QC of packaging materials

Glass containers:

- Hydrolytic resistance test: Glass is classified into Types I, II and III. Type I (borosilicate) is the most resistant and is used for injections; the test measures how much alkali the glass releases into water.
- Test for arsenic: Glass must not release arsenic into the medicine.
- Thermal shock test: The container must not crack when moved between hot and cold.
- Internal pressure test: Bottles must withstand pressure without bursting.
- Light transmission test: Amber glass for light-sensitive drugs must block the required amount of light.

Plastic containers:

- Clarity and appearance: No defects, correct colour and shape.
- Water vapour permeability: Plastic bottles must not let too much moisture pass through (important for tablets).
- Extractables/leachables: Chemicals from the plastic must not migrate into the medicine beyond limits.
- Collapsibility: For squeezable containers.

Rubber closures (stoppers):

- Fragmentation test: A needle is pushed through the stopper several times; the stopper must not break into fragments that could fall into the medicine.
- Self-sealability test: After the needle is removed, the stopper must close by itself so that air and microbes cannot enter.
- Penetrability (piercing force): The force needed to push a needle through must not be too high.
- Water extractables: The stopper is boiled in water and the extract is tested for turbidity, colour, pH change, UV absorbance and residue on evaporation — all must be within limits.
- Sterility and depyrogenation: Stoppers for injections are sterilised and made pyrogen-free before use.

Secondary packaging materials (cartons, labels, leaflets):

- Board strength: Bursting strength and stiffness of the carton board (commonly taught: measured in standard units and compared with the specification).
- GSM (grams per square metre): The thickness/weight of the paper or board.
- Print quality: Text must be sharp, legible and correctly aligned; colours must match the approved shade.
- Correctness of printed matter: Batch number, manufacturing/expiry date, MRP, and statutory details must be printed correctly — wrong printing is a common cause of product recall.

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5. Classifications

5.1 Types of QC tests by stage

1. In-process QC (IPQC): done during manufacturing — weight, hardness, thickness, friability, disintegration, fill weight, pH, viscosity, spreadability.

2. Finished-product QC: done on the packed product — description, identification, assay, uniformity of dosage units, dissolution, disintegration, sterility, endotoxins, particulate matter, microbial limits, related substances.

5.2 Classification of dosage forms by strictness of QC

1. Non-sterile solid dosage forms (tablets, capsules): weight, content, dissolution, disintegration, microbial limits.
2. Non-sterile semisolids (ointments, creams): homogeneity, pH, viscosity, spreadability, microbial limits, preservative efficacy.
3. Sterile preparations (ophthalmic, parenteral): ALL the above-type tests PLUS sterility, endotoxins/pyrogens, particulate matter, container integrity — because they enter the eye or the body directly.

5.3 Classification of packaging materials

1. Primary packaging: touches the medicine directly — glass bottles, vials, ampoules, plastic bottles, rubber stoppers, blister foil, tubes.
2. Secondary packaging: does not touch the medicine — cartons, labels, package inserts/leaflets, shrink wrap.

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6. Diagrams (describe so they can be drawn)

Diagram 1 — The two gates of QC.

Draw a factory line with three boxes: "Raw materials → Manufacturing → Finished pack". Put a gate (a checkpoint barrier) labelled "In-process QC" in the middle of manufacturing, and a second gate labelled "Finished-product QC" after packing, before "Market". Add a small dustbin icon labelled "Rejected batch" under each gate. Caption: "Problems caught early at Gate 1 save the batch; Gate 2 protects the patient."

Diagram 2 — Disintegration vs dissolution.

Draw two beakers side by side. Left beaker: a tablet breaking into small chunks, labelled "Disintegration = breaking into pieces (physical)". Right beaker: the chunks dissolving into a clear solution with arrows showing drug molecules spreading, labelled "Dissolution = drug dissolving into liquid (chemical)". Caption: "Disintegration is breaking; dissolution is dissolving. A tablet can disintegrate but still dissolve slowly."

Diagram 3 — Glass types for containers.

Draw three bottles: Type I labelled "Borosilicate — most resistant — for injections", Type II labelled "Treated soda-lime — for aqueous products", Type III labelled "Soda-lime — for dry powders, non-aqueous products". Caption: "Higher hydrolytic resistance = safer for sensitive medicines."

Diagram 4 — Rubber stopper: fragmentation vs self-sealability.

Draw a rubber stopper with a needle passing through it. On the left, show tiny rubber bits falling into a vial below, crossed out in red, labelled "Fragmentation — must NOT happen". On the right, show the needle removed and the hole closing by itself, ticked in green, labelled "Self-sealability — MUST happen".

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7. Flowcharts

Flowchart 1 — Raw material approval flow.

```
Supplier sends material + COA
↓
QC takes samples (√n + 1 rule)
↓
Identity + Assay + Impurity tests + LOD + Microbial limits
↓
Pass? ──No──→ REJECT, inform purchase dept, do not use
│ Yes
↓
APPROVED → "Released" label → material moves to manufacturing
```

Flowchart 2 — Tablet QC journey.

```
Compression running
↓ IPQC: weight, hardness, thickness checked every 30 min
↓ Problem found? → adjust machine, segregate tablets made in between
↓
Coating / packing
↓
Finished-product QC: description, assay, uniformity, dissolution,
disintegration, related substances, microbial limits
↓
All pass? → Batch released to market
Any fail? → Batch rejected / investigated (deviation report)
```

Flowchart 3 — Sterile product (injection) QC gates.

```
Vial filling → IPQC: fill volume, seal integrity
↓
Sterilisation → IPQC: steriliser cycle records checked
↓
Finished-product QC: clarity → pH → particulate matter →
sterility → endotoxin (LAL) → extractable volume → CCI
↓
ALL must pass → release. Even ONE failure → whole batch rejected.
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8. Infographic Concept Box

INFOGRAPHIC CONCEPT

 THE QC PYRAMID — "Test early, test finally, test everything sterile hardest"

 BASE (widest): Raw materials + packaging — test identity, purity, strength of every material before use.

 MIDDLE: In-process checks — weight, hardness, pH, viscosity checked while making; fix problems now, not later.

 TOP (narrowest): Finished product — final proof: assay, uniformity, dissolution.

 ABOVE THE PYRAMID: Sterile products — everything above PLUS sterility + endotoxins + particles. The stricter the product, the taller the testing tower.

One-line memory hook: "Catch it in the kitchen (IPQC), not on the dining table (finished QC)."

9. Comparison Tables

Table 1 — In-process QC vs finished-product QC

Point	In-process QC (IPQC)	Finished-product QC
When	During manufacturing	After packing, before release
Purpose	Catch and correct problems early	Final proof the batch is safe and effective
Action on failure	Adjust the process, segregate affected units	Reject or investigate the whole batch
Examples	Tablet weight, hardness, thickness; fill weight of capsules; pH and viscosity of creams	Assay, dissolution, sterility, endotoxins, uniformity of dosage units

Table 2 — QC tests across dosage forms (finished product)

Test	Tablets	Capsules	Ointments / Creams	Ophthalmic	Parenteral
Description	✓	✓	✓	✓	✓
Identification	✓	✓	✓	✓	✓
Assay	✓	✓	✓	✓	✓
Uniformity of dosage units	✓	✓	(delivered dose, if metered)	✓ (delivered dose)	✓ (powders)
Dissolution	✓	✓	–	–	–
Disintegration	✓	✓	–	–	–
Friability	✓ (IPQC)	–	–	–	–
pH	–	–	✓ (creams)	✓	✓
Viscosity / spreadability	–	–	✓	✓ (some drops)	–
Homogeneity	–	–	✓	–	–

Test	Tablets	Capsules	Ointments / Creams	Ophthalmic	Parenteral
Sterility	–	–	–	✓	✓
Endotoxins (LAL)	–	–	–	–	✓
Particulate matter	–	–	–	✓ (no visible particles)	✓
Microbial limits	✓	✓	✓	– (must be sterile)	– (must be sterile)
Preservative efficacy	–	–	✓	✓ (multi-dose)	✓ (multi-dose)
Container integrity	–	–	✓ (leaker test)	✓ (leaker test)	✓

Table 3 — Packaging material tests

Material	Key tests
Glass containers	Hydrolytic resistance (Types I/II/III), arsenic test, thermal shock, internal pressure, light transmission
Plastic containers	Appearance, water vapour permeability, extractables/leachables, collapsibility
Rubber closures	Fragmentation, self-sealability, penetrability, water extractables (turbidity, colour, pH, UV, residue), sterility/depyrogenation
Secondary packaging	Bursting strength, GSM, print quality and shade, correctness of printed matter (batch no., dates, MRP)

10. Examples

1. Tablet weight variation in action: A paracetamol tablet is labelled 500 mg of drug in a 650 mg tablet. During compression, the operator weighs 20 tablets: the average is 650 mg, so the allowed range (above 250 mg → ±5%) is 617.5–682.5 mg. Two tablets weigh 690 mg — outside the limit. The operator adjusts the machine and segregates the tablets made since the last good check.
2. Dissolution failure: A batch of tablets passes assay (correct drug amount) but fails dissolution — only 40% dissolves in 45 minutes instead of the required Q value. The tablets look fine and contain the right drug, but in the patient's body the drug would not be released properly. The batch is rejected.
3. Friability catch: During IPQC, tablets lose 1.8% weight in the friability drum (limit: not more than 1%). The batch would have arrived at pharmacies as chipped, broken tablets — so the granulation formula is corrected before packing.
4. Rubber closure fragmentation: A stopper lot fails the fragmentation test — needle punctures produce rubber bits. If used, these bits could fall into the injection vial. The entire lot of stoppers is rejected and returned to the vendor.

5. Glass type mistake: An acidic injection is packed in Type III glass instead of Type I. Over months, alkali leaches from the glass, the pH rises, and the drug degrades. Correct glass selection (Type I for injections) prevents this.
6. Secondary packaging error: A batch of cartons is printed with the wrong expiry date. The medicine inside is perfect, but the batch cannot be sold — it must be repacked with corrected cartons, after QA approval and documentation.

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11. Analogies

- IPQC vs finished QC = cooking vs serving: Tasting the curry while cooking (IPQC) lets you fix the salt; tasting after serving (finished QC) only tells you the dish is ruined. Good cooks — and good manufacturers — taste while cooking.
- Dissolution test = sugar in tea: Drop a sugar cube in cold tea and it sits there; stir it in hot tea and it disappears fast. The dissolution test is the "stirring in hot tea" check — it proves the drug will actually come out of the tablet in the body.
- Sterility + endotoxin tests = double lock on a door: Sterility proves no living germs are inside (lock 1). The endotoxin test proves no dead-bacteria poison is inside either (lock 2). An injection needs both locks.
- Sampling $\sqrt{n} + 1$ = tasting from several pots: If a caterer makes 16 pots of dal, you don't taste just one — you taste a few pots spread across the batch ($\sqrt{16} + 1 = 5$ pots) to be sure all are good.
- Rubber stopper = self-healing door: A good stopper is like a door with a spring — the needle opens it, and when the needle leaves, the door closes by itself (self-sealability). A bad stopper is like a door that breaks into splinters (fragmentation).

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12. Pharmacy Relevance

- Every medicine you will ever dispense passed through these QC gates. When a patient asks "is this tablet safe?", the honest technical answer is: it passed IPQC during manufacture and finished-product QC before release.
- As a pharmacist in industry, you may work in QC — running dissolution, HPLC assays, sterility tests — or in QA — approving vendors, releasing batches, investigating failures.
- In a hospital or retail pharmacy, QC knowledge helps you spot problems: chipped tablets, leaking tubes, cloudy eye drops, cracked vials — and know they must be reported, not dispensed.
- Pharmacovigilance starts with QC awareness: if a product looks, smells or behaves wrong, it may be a quality defect — report it through the proper channel.

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13. India Context

- Indian manufacturers follow the Indian Pharmacopoeia (IP) for QC test methods and limits; products for export may also be tested as per the USP, BP or EP, as required by the importing country.
- The CDSCO (Central Drugs Standard Control Organisation) is India's drug regulator; state drug control departments inspect manufacturing sites and draw market samples for testing at government laboratories.

- India is one of the world's largest suppliers of generic medicines ("pharmacy of the world") — this position exists because Indian QC laboratories consistently prove that generics match the quality of the original brands.
- Schedule M of the Drugs and Cosmetics Rules lays down Good Manufacturing Practices for Indian factories, including requirements for QC laboratories, equipment calibration and batch testing.
- Government drug testing laboratories (such as the Central Drugs Laboratory, Kolkata, and state drug testing labs) re-test market samples; batches failing these tests are recalled.

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14. Key Points

1. QC has two stages: in-process (during manufacture) and finished-product (before release).
2. Tablets/capsules: weight variation or content uniformity, assay, dissolution, disintegration, friability (tablets), microbial limits.
3. Ointments/creams: homogeneity, pH, viscosity, spreadability, extrudability, fill weight, microbial limits, preservative efficacy.
4. Ophthalmic and parenteral products must be sterile; parenterals additionally need endotoxin testing and particulate matter control.
5. Disintegration = breaking into pieces; dissolution = drug dissolving out. Both are needed for solid oral dosage forms.
6. Raw materials are sampled (commonly taught $\sqrt{n} + 1$ rule) and tested for identity, assay, impurities, LOD and microbial limits before use; only approved vendors are used.
7. Glass is tested for hydrolytic resistance (Types I, II, III); rubber closures for fragmentation, self-sealability and extractables; secondary packaging for strength, GSM and print correctness.
8. One failed critical test (e.g., sterility of an injection) = whole batch rejected.

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15. Common Confusions

1. Disintegration vs dissolution: Disintegration is the tablet breaking into granules; dissolution is the drug molecules dissolving into the liquid. A tablet may disintegrate fast but dissolve slowly (e.g., if the drug itself is poorly soluble).
2. Weight variation vs content uniformity: Weight variation assumes that if each tablet weighs the same, each contains the same drug — valid only when the drug is a large fraction of tablet weight. Content uniformity actually measures drug in each unit — needed for low-dose drugs.
3. Sterility vs microbial limits: Sterility means ZERO microbes (for injections, eye products). Microbial limits mean microbes are allowed but only below a small number (for tablets, creams).
4. Pyrogen test vs endotoxin (LAL) test: Both check for fever-causing substances. The LAL test is the modern laboratory method using horseshoe-crab blood extract; the older rabbit pyrogen test is now rarely used.
5. Primary vs secondary packaging: Primary touches the medicine (bottle, stopper, blister); secondary does not (carton, label, leaflet). A "leaker test" applies to primary packs (tubes, vials); "bursting strength" applies to secondary cartons.

6. LOD vs water content: Loss on drying measures all volatile matter lost on heating (water + solvents); Karl Fischer water content measures only water.

16. Common Mistakes

1. Writing that "dissolution and disintegration are the same test" — they are different apparatus, different purposes.
2. Claiming friability is a finished-product test — it is mainly an in-process test done during/after compression.
3. Forgetting sterility for ophthalmic products — students remember it for injections but eye products must be sterile too.
4. Mixing up Type I, II, III glass — remember: Type I (borosilicate) is best and is used for injections.
5. Writing "microbial limit test" for injections — injections need sterility (zero microbes), not limits.
6. Quoting exact pharmacopoeial numbers from memory in exams without checking — limits change between editions; write "as per the current IP monograph" when unsure.

17. Mnemonics

- Tablet finished-product tests — "A DUDI FIRM": Assay, Description, Uniformity of dosage units, Dissolution, Identification, Friability (IPQC), Impurities (related substances), R (disintegration — "bReaking"), Microbial limits. (Read as "a duddy firm makes tablets.")
- Sterile product extra tests — "SEP": Sterility, Endotoxins, Particulate matter. (Every injection needs SEP.)
- Packaging tests — "Glass, Plastic, Rubber, Carton": Glass → hydrolytic resistance; Plastic → permeability; Rubber → fragmentation + self-sealability; Carton → bursting strength + print.
- Raw material testing order — "SIAIL": Sampling → Identity → Assay → Impurities → LOD/water.

18. Exam Summary

QC is done at two stages: in-process (during manufacture, to correct problems early) and finished-product (before release, the final gate). Tablets and capsules are tested for description, identification, assay, uniformity of dosage units (weight variation or content uniformity), dissolution, disintegration, and microbial limits; tablets additionally for friability and hardness in-process. Ointments and creams are tested for homogeneity, pH, viscosity, spreadability, extrudability, fill weight and preservative efficacy. Ophthalmic and parenteral preparations must be sterile; parenterals also require bacterial endotoxin (LAL) testing, particulate matter control, extractable volume and container closure integrity. Raw materials are sampled (√n + 1 rule) and tested for identity, assay, impurities, LOD and microbial limits, and bought only from approved vendors. Packaging QC covers glass (hydrolytic resistance, Types I/II/III), plastic (permeability, extractables), rubber closures (fragmentation, self-sealability, extractables) and secondary packaging (bursting strength, GSM, print correctness).

19. One-Minute Revision

- Two QC stages: in-process (fix early) + finished product (final gate).
- Tablets/capsules: assay, uniformity, dissolution, disintegration, microbial limits.
- Creams: homogeneity, pH, viscosity, spreadability, preservative efficacy.
- Eye + injections: must be STERILE; injections also need endotoxin (LAL) + particle tests.
- Disintegration = breaking; dissolution = dissolving.
- Raw materials: sample (√n+1) → identity → assay → impurities → LOD.
- Glass Type I = best, for injections. Rubber: no fragmentation, must self-seal.

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20. Exam Questions

Short-answer questions

1. Define in-process QC and finished-product QC. Give two examples of each for tablets.
2. What is the difference between disintegration and dissolution? Why are both tested?
3. List the finished-product QC tests for capsules.
4. Why must ophthalmic preparations be sterile? List four QC tests for eye drops.
5. What is the LAL test? Why is it done on parenteral preparations?
6. Explain the √n + 1 sampling rule with an example.
7. Differentiate between Type I, Type II and Type III glass.
8. What are fragmentation and self-sealability tests for rubber closures?
9. List four tests for secondary packaging materials.
10. What is the difference between weight variation and content uniformity tests?

Long-answer questions

1. Describe the in-process and finished-product QC tests for tablets in detail.
2. Explain the QC tests for parenteral preparations. Why are they stricter than tablet tests?
3. Describe the QC tests for raw materials from sampling to approval, including vendor qualification.
4. Discuss the QC tests for packaging materials: glass containers, plastic containers, rubber closures and secondary packaging.

MCQs (with answer key)

1. Which test measures how fast the drug dissolves out of a tablet?

a) Friability b) Hardness c) Dissolution d) Disintegration — Answer: c

2. Friability of tablets is mainly a —

a) Finished-product test b) In-process test c) Raw material test d) Packaging test — Answer: b

3. Which glass type is preferred for parenteral preparations?

a) Type III b) Type II c) Type I d) Ordinary soda glass — Answer: c

4. The LAL test detects —

a) Living bacteria b) Bacterial endotoxins c) Fungal spores d) Viruses — Answer: b

5. If a consignment has 25 containers of raw material, how many are commonly sampled (√n + 1 rule)?

a) 5 b) 6 c) 25 d) 26 — Answer: b (√25 + 1 = 6)

6. Which test is NOT required for an injection?

a) Sterility b) Endotoxin test c) Dissolution d) Particulate matter — Answer: c

7. Self-sealability is a test for —

a) Glass vials b) Rubber closures c) Cartons d) Aluminium tubes — Answer: b

8. Spreadability is an in-process test for —

a) Tablets b) Capsules c) Ointments/creams d) Injections — Answer: c

9. GSM is a quality parameter of —

a) Rubber stoppers b) Carton board/paper c) Glass bottles d) Plastic bottles — Answer: b

10. Content uniformity test is preferred over weight variation when —

a) The tablet is very large b) The drug content per unit is low c) The tablet is coated d) The drug is highly soluble — Answer: b

Viva questions

1. Why do we do IPQC if finished-product testing exists?
2. Your tablet batch passes assay but fails dissolution — will you release it? Why?
3. Why is the endotoxin test needed even when the sterility test passes?
4. What would happen if an injection were packed in Type III glass?
5. How do you check that a rubber stopper lot is safe for injectable vials?
6. A carton has the wrong expiry date printed but the medicine is fine — can it be sold? What should be done?

Application-based questions

1. During compression, 20 tablets are weighed: average 400 mg, two tablets weigh 368 mg and 372 mg. Using the commonly taught weight variation limits, decide whether the batch portion passes, and state your next action as the IPQC chemist. (Confirm limits against the current pharmacopoeial edition.)
2. A cream batch shows good assay but the preservative efficacy test fails. Explain the risk to the patient and recommend a corrective action.
3. You receive 49 drums of an excipient from a new supplier with a COA. How many drums will you sample, and list the tests you will perform before approving the material.

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21. References

- Godfrey, A. B. and Juran, J. M. Juran's Quality Handbook. McGraw-Hill.
- OPPI. Quality Assurance Guide.
- WHO. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials.

CHAPTER 6: GOOD LABORATORY PRACTICE (GLP)

Unit III (10 hours)

1. Learning Objectives

After studying this chapter, you will be able to:

1. Define GLP and explain its purpose and scope.
2. Describe the organisation of a GLP testing facility and the roles of management, the study director and the QA unit.
3. List the GLP requirements for facilities and equipment.
4. Explain the ALCOA principles of good documentation.
5. Describe the handling of reference standards (test and reference items).
6. Outline testing facility operations, records, reports and archives.
7. Explain how and why a testing facility can be disqualified under GLP.

2. Definitions

- GLP (Good Laboratory Practice): A set of principles that ensure non-clinical safety studies are planned, performed, monitored, recorded, archived and reported properly and honestly.
- Non-clinical safety study: A laboratory or animal study done to check whether a drug or chemical is safe — done before the drug is tested in humans. (Clinical trials in humans follow GCP, not GLP.)
- Testing facility: The laboratory/organisation (including buildings, people and equipment) where the GLP study is conducted.
- Study director: The single scientist who is fully responsible for one GLP study from start to finish.
- Quality Assurance (QA) unit: An independent team inside the testing facility that inspects studies and audits records to check GLP compliance. It must be independent of the scientists doing the study.
- SOP (Standard Operating Procedure): A written step-by-step instruction for doing a routine task (e.g., "how to calibrate a balance").
- Raw data: The original, first-recorded observations of a study — e.g., the actual readings written in the lab notebook, instrument printouts, photographs.
- Study plan (protocol): The written plan of the study, approved before the study starts — what will be done, how, and by whom.
- Final report: The complete written account of the study: what was planned, what was done, what was found, and what it means.
- Archive: The secure storage place where raw data, reports, samples and records are kept safely for years after the study ends.
- Reference standard (test item / reference item): The substance being tested (test item) and the substance it is compared with (reference item). Both must be properly identified, labelled and stored.

NOTE

Caution: GLP principles are issued by the OECD and adopted by national authorities with their own notification numbers and retention periods. Exact clause numbers, inspection procedures and archive periods in this chapter are described as commonly taught; confirm against current guidelines/notifications.

3. Terminology (Word Bank)

Term	Simple meaning
OECD	Organisation for Economic Co-operation and Development — the body that published the international Principles of GLP
MAD	Mutual Acceptance of Data — OECD system under which GLP study data generated in one member country is accepted by others
NGCMA	National GLP Compliance Monitoring Authority — India's authority (under the Department of Science and Technology) that grants GLP certification to Indian test facilities
Test system	The animal, plant, cells or other biological/chemical system on which the test item is studied
Test item	The drug/chemical being tested for safety
Reference item	A known substance used for comparison with the test item
Vehicle	The liquid used to dissolve or suspend the test item for dosing (e.g., water, oil)
Deviation	Any departure from the study plan or SOPs — must be recorded with reason
Audit	A systematic check of records and activities by the QA unit
Inspection	A visit by the QA unit (or regulators) to watch the study being performed and check compliance
Disqualification	Official removal of a testing facility's GLP compliance status when it seriously violates GLP
ALCOA	Attributable, Legible, Contemporaneous, Original, Accurate — the principles of trustworthy records
Calibration	Checking and adjusting an instrument against a known standard so its readings are correct
Chain of custody	The documented record of who handled a sample, when, and where — so nothing is mixed up or tampered with

4. Explanations

4.1 General provisions — what GLP is and why it exists

Before a new drug is given to humans, it is tested in laboratories and animals for safety (toxicity studies). Regulators must be able to TRUST these safety results — because human lives will depend on them.

GLP is the rulebook that makes safety-study data trustworthy. It answers one question: "Can we believe this study?" GLP ensures that:

- the study was properly planned (study plan),
- done by trained people (personnel),
- with working instruments (equipment),
- in suitable buildings (facilities),
- everything was written down honestly at the time it happened (raw data, ALCOA),
- an independent team double-checked it (QA unit),
- and everything is stored safely for future inspection (archive).

Scope (commonly taught): GLP applies to non-clinical safety studies — such as toxicity, mutagenicity and safety pharmacology studies — whose data are submitted to regulators. It does NOT apply to clinical trials in humans (those follow GCP — Good Clinical Practice) and not to basic exploratory research.

Simple idea: GLP does not judge whether the science is brilliant. It guarantees the study was honestly planned, properly done, fully recorded and independently checked.

4.2 Organisation and personnel

A GLP testing facility must have a clear organisation with defined responsibilities:

- Test facility management: Appoints the study director, ensures enough qualified staff, proper facilities and equipment, approves SOPs, and ensures the QA unit is independent and effective. Management is ultimately answerable for GLP compliance.
- Study director: ONE scientist is named study director for each study. He/she approves the study plan, supervises the work, ensures deviations are documented, signs the final report, and takes overall responsibility. There is only one captain per ship — one study director per study.
- Principal investigator (multi-site studies): If parts of a study are done at another site, a principal investigator supervises that part and reports to the study director.
- Quality Assurance unit: A team independent of the study scientists. It inspects ongoing studies, audits the final report against raw data, and reports findings directly to management. QA does not do the study — it watches the study.
- Personnel: Every person must be qualified by education/training/experience for their job, must be trained in GLP and relevant SOPs, must have a written job description, and training records must be kept.

4.3 Facilities and equipment

Facilities (buildings and rooms):

- The facility must be of suitable size and design — separate areas for receiving test items, dosing animals, laboratories, and archives, so that materials do not get mixed up or contaminated.
- Animal houses must have controlled temperature, humidity and light, with quarantine areas for new animals.
- Storage areas must protect test items, reference items and samples from deterioration (e.g., refrigerators, locked cupboards for controlled substances).
- There must be proper waste disposal so hazardous material does not contaminate studies.
- Archives must be secure, fire-safe and access-controlled.

Equipment:

- Every instrument (balances, pH meters, HPLCs, refrigerators) must be suitable for its job — this is called qualification.
- Instruments must be calibrated regularly against known standards, and maintained as per schedule.
- Calibration and maintenance records must be kept — an uncalibrated balance makes all weighing data untrustworthy.
- Any equipment found faulty must be labelled "out of service" and not used until repaired and re-qualified.

4.4 ALCOA principles — the heart of good documentation

Regulators trust data only if it follows ALCOA. Each letter is a promise:

- A — Attributable: It must be clear WHO recorded the data and WHEN. Every entry is signed/initialled and dated. No anonymous data.
- L — Legible: The record must be readable — clear handwriting, permanent ink, no scribbles. If nobody can read it, it is useless.
- C — Contemporaneous: Recorded AT THE TIME the work was done, not days later from memory. Date and time of observation = date and time of recording.
- O — Original: The FIRST recording is the raw data. If data is copied to another sheet, the original is still kept. Photocopies are not originals.
- A — Accurate: The record must be true, complete and without errors. Mistakes are corrected with a single line through the error, the correct value written beside it, signed and dated — never hidden with whitener or overwriting.

Commonly taught extensions add: Complete, Consistent, Enduring, Available — records must be whole, written the same way every time, stored to last for years, and retrievable when an inspector asks.

Simple idea: Write it so that a stranger, ten years later, can reconstruct exactly what you did — that is ALCOA.

4.5 Reference standards (test items and reference items)

- Every test item and reference item must be properly identified (name, batch/lot number, purity, composition) and characterised before the study.
- Containers must be labelled with identity, expiry/retest date and storage conditions.

- Items must be stored under the specified conditions (temperature, light, humidity) so they do not degrade.
- A record of receipt, handling, sampling and disposal (chain of custody) must be kept — who took how much, when, and for what.
- Stability of the test item under storage and test conditions must be known, so the study result is not blamed on a degraded sample.

4.6 Testing facility operations

- SOPs: Every routine activity must have a written, approved SOP — from cleaning glassware to operating the HPLC to handling animals. Staff must follow the current approved version; old versions are removed from use.
- Study plan: Before the study starts, a written plan is prepared and approved (signed) by the study director and QA-verified. It describes the objective, test system, doses, schedule, methods and responsibilities.
- Conduct of the study: The study is performed exactly as per the study plan and SOPs. Any deviation (change from the plan) is documented immediately with the reason, and assessed for its effect on the study.
- QA inspections: The QA unit inspects critical phases of the study while it is running, and audits the draft final report by comparing it with raw data.

4.7 Records and reports

- Raw data: All original observations — lab notebooks, instrument printouts, photographs, animal observation sheets. Raw data must follow ALCOA and must never be thrown away or altered.
- Final report: Signed by the study director, it contains: the study plan details, what was done, results, discussion, conclusions, QA statement (confirming inspections and audits were done), and any deviations. It must be a true reflection of the raw data.
- Archives: After the study, the study plan, raw data, final report, samples of test items and specimens are kept in the archive under secure, controlled conditions. Commonly taught retention: for a defined number of years after the study or after regulatory submission (confirm the exact period against current guidelines/notifications). Archived material must be retrievable — an archive nobody can search is not an archive.
- Records of personnel (CVs, training, job descriptions), equipment (calibration, maintenance) and SOPs (all versions) are also archived.

4.8 Disqualification of testing facilities

GLP compliance is monitored by inspections (in India, by NGCMA; internationally, by regulators such as the US FDA under its GLP regulations). Commonly taught sequence when serious non-compliance is found:

1. Inspection findings: Inspectors record violations — e.g., fabricated data, missing raw data, uncalibrated equipment, no independent QA, untrained staff.
2. Show-cause / proposed disqualification: The facility is informed of the findings and given a chance to respond or correct them.
3. Hearing: The facility may present its case before a final decision.

4. Disqualification: If violations are serious (especially data integrity failures), the facility's GLP compliance status is withdrawn/disqualified. Studies from a disqualified facility are not accepted by regulators — meaning the sponsor must repeat the safety studies, at huge cost and delay.
5. Reinstatement: The facility may reapply after correcting all deficiencies and demonstrating compliance.

Simple idea: Disqualification is the "licence cancelled" punishment of the GLP world — it happens when a facility cannot be trusted with safety data.

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5. Classifications

5.1 The pillars of GLP (commonly taught grouping)

1. Organisation & personnel — right people, clear responsibilities.
2. Facilities & equipment — right place, right instruments, calibrated.
3. Characterisation of test items — know what you are testing.
4. Rules for study conduct — SOPs, study plan, documented deviations.
5. Records, reports & archives — ALCOA data, true final report, secure storage.
6. Independent QA — the watchdog that checks all of the above.

5.2 Types of studies under GLP vs outside GLP

Under GLP	NOT under GLP
Non-clinical safety/toxicity studies for regulatory submission	Clinical trials in humans (follow GCP)
Mutagenicity and safety pharmacology studies for regulators	Basic exploratory/academic research
Environmental safety studies of chemicals	Manufacturing QC testing (follows GMP)

5.3 Types of QA activity in a GLP facility

1. Study-based inspection: QA watches a particular study's critical phases.
2. Facility-based inspection: QA checks general areas — archives, equipment calibration, animal house.
3. Process-based inspection: QA checks a repeated process (e.g., weighing, dosing) across studies.
4. Report audit: QA compares the final report line-by-line with raw data before it is signed.

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6. Diagrams (describe so they can be drawn)

Diagram 1 — The GLP trust chain.

Draw five links of a chain: "Study plan → Trained people → Calibrated equipment → ALCOA records → Independent QA check". Below the chain write: "If ANY link breaks, the data cannot be trusted." Caption: "GLP is a chain — only as strong as its weakest link."

Diagram 2 — Organisation chart of a GLP testing facility.

Draw boxes: at the top "Test Facility Management". Below it, three separate boxes side by side: "Study Director (runs the study)", "Study Personnel (do the work)", "QA Unit (independently checks)". Draw a thick wall between QA Unit and the other two boxes, labelled "INDEPENDENT — QA never does the study it inspects". Caption: "QA must be separate from the scientists it audits."

Diagram 3 — ALCOA star.

Draw a five-pointed star. At each point write one letter and word: A-Attributable (who/when), L-Legible (readable), C-Contemporaneous (at the time), O-Original (first record), A-Accurate (true). In the centre write "TRUSTWORTHY DATA". Caption: "Every record must earn all five points of the star."

Diagram 4 — Archive room.

Draw a locked room with shelves of labelled boxes ("Study 101 — raw data", "Study 102 — specimens"), a fire extinguisher, and a register book at the door labelled "Access log — who entered, when". Caption: "Archives: secure, organised, retrievable — for years."

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7. Flowcharts

Flowchart 1 — Life of a GLP study.

```
Study plan written → approved by Study Director → QA verifies
↓
Study performed exactly as per plan + SOPs
(QA inspects critical phases; deviations recorded with reasons)
↓
Raw data collected (ALCOA) → draft final report written
↓
QA audits report against raw data → corrections if needed
↓
Study Director signs final report (+ QA statement attached)
↓
Everything archived securely for the retention period
```

Flowchart 2 — Handling a deviation.

```
Deviation from study plan/SOP noticed
↓
Record immediately: what happened, when, who found it
↓
Study Director assesses: does it affect study validity?
┌──────┴──────┐
Minor Major → corrective action + may need plan amendment
↓
Document reason + corrective/preventive action → QA informed
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Flowchart 3 — Disqualification pathway.

```
Regulatory inspection → serious GLP violations found
↓
Facility notified (proposed disqualification) → chance to respond
↓
Hearing
↓
Decision: ──Compliant──→ continue (with corrections)
──Serious violation──→ DISQUALIFIED
↓
Studies not accepted by regulators → sponsor must repeat studies
↓
Reinstatement only after full correction + re-inspection
```

8. Infographic Concept Box

INFOGRAPHIC CONCEPT

□ GLP IN ONE PICTURE — "The 5 Promises of Trustworthy Safety Data"

□ 1. PLAN IT — written, approved study plan before starting.

□□ 2. STAFF IT — one study director, trained people, independent QA.

□ 3. EQUIP IT — suitable facility, calibrated instruments, controlled storage.

✍ 4. WRITE IT (ALCOA) — attributable, legible, contemporaneous, original, accurate — at the time it happens.

□ 5. KEEP IT — true final report + secure archive for years.

⚠ Break the promises → inspection → hearing → DISQUALIFICATION → studies rejected.

One-line memory hook: "Plan it, staff it, equip it, write it right, keep it locked."

9. Comparison Tables

Table 1 — GLP vs GMP vs GCP

Point	GLP	GMP	GCP
Full form	Good Laboratory Practice	Good Manufacturing Practice	Good Clinical Practice
Applies to	Non-clinical safety studies (lab/animal)	Manufacturing of medicines	Clinical trials in humans
Main question	"Can we believe this safety data?"	"Is every batch made correctly?"	"Are trial volunteers protected and data reliable?"
Key person	Study director	Production/QA heads	Principal investigator
Records focus	Raw data + ALCOA + archive	Batch records + QC data	Case report forms + consent

Table 2 — QA unit vs study personnel

Point	QA unit	Study personnel
Role	Independently inspect and audit	Plan and perform the study

Point	QA unit	Study personnel
Reports to	Test facility management (directly)	Study director
Does the experiment?	No — never	Yes
Checks	Critical phases, final report vs raw data, SOP compliance	Day-to-day study conduct as per plan

Table 3 — Raw data vs final report

Point	Raw data	Final report
What	Original first recordings (notebooks, printouts)	Complete written account of the study
When created	During the study (contemporaneous)	After the study ends
Changes allowed	Corrections only by single-line strike-through, signed/dated	Amendments with documented reason
Signed by	Person who recorded (attributable)	Study director (+ QA statement)
Storage	Archived securely for the retention period	Archived with raw data

10. Examples

1. Study director in action: A 90-day toxicity study of a new tablet is running. The study director approves the study plan, checks weekly progress, and when a dosing error occurs on day 40, documents the deviation, assesses that it does not invalidate the study, informs QA, and records corrective training — all before signing the final report.
2. ALCOA violation: A technician weighs animals on Monday but writes the weights in the notebook on Friday "from memory". This breaks Contemporaneous — the data is no longer trustworthy, and QA will flag it as a GLP deviation.
3. Correction the right way: A pH reading of 7.4 is wrongly written as 7.9. The technician draws a single line through 7.9, writes 7.4 beside it, signs and dates the correction. This is the correct ALCOA way — no whitener, no overwriting, no tearing the page.
4. Calibration saves a study: A balance used for weighing test item doses is found overdue for calibration. QA stops the study dosing until the balance is calibrated and the earlier weighings are verified — because uncalibrated equipment makes dose data unreliable.
5. Archive retrieval: Five years after a study, a regulator asks for the raw data of a toxicity study. The archivist finds the labelled boxes within an hour using the archive index — this is why "Available/retrievable" is part of good record-keeping.
6. Disqualification consequence: A testing facility is disqualified after inspectors find fabricated animal observation data. The drug sponsor's safety data is rejected by regulators, and the entire toxicity study must be repeated at another GLP-certified facility — costing crores of rupees and delaying the drug by years.

11. Analogies

- GLP = CCTV for science: Just as CCTV cameras make everyone in a shop behave honestly, GLP's rules (written plans, witnessed records, independent QA) make sure study data is honest — because everything is recorded and checkable.
- Study director = ship's captain: Many sailors work the ship, but one captain is responsible for the voyage. In a GLP study, many scientists work, but one study director owns the study.
- QA unit = cricket umpire: The umpire does not bat or bowl — he watches the game and calls fouls. QA does not do the study — it watches and reports deviations.
- Raw data = original land documents: A photocopy of a property paper is not proof of ownership; only the original registered document counts. Similarly, only the original first recording counts as raw data.
- Archive = bank locker: You keep property papers in a bank locker — safe from fire, theft and damage, and you can take them out when needed. Study records go to the archive for the same reasons.
- Disqualification = driving licence cancelled: A driver who repeatedly breaks traffic rules loses the licence. A facility that breaks GLP trust loses its GLP status.

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12. Pharmacy Relevance

- Every medicine you dispense was approved partly on the basis of GLP safety studies. GLP is the reason regulators trust that "this drug is safe enough to test in humans."
- As a pharmacist in industry, you may work in non-clinical departments, QA, or regulatory affairs — where you will write or review study plans, handle deviations, and face GLP inspections.
- In regulatory affairs, you will compile safety data dossiers; knowing GLP tells you which studies regulators will accept (GLP-compliant) and which they will reject.
- Even in community pharmacy, GLP awareness answers the patient's deeper question — "how do we know this new drug is safe?" — with the real story of tested, recorded, audited safety data.

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13. India Context

- NGCMA (National GLP Compliance Monitoring Authority), under the Department of Science and Technology, Government of India, grants GLP certification to Indian test facilities after inspection.
- India is adherent to the OECD Mutual Acceptance of Data (MAD) system for GLP — safety data generated in NGCMA-certified Indian laboratories is accepted by regulators of other OECD countries, which strongly supports India's pharmaceutical and chemical industries.
- CDSCO expects non-clinical safety data submitted for new drug approval in India to come from GLP-compliant studies.
- Many Indian contract research organisations (CROs) earn international business specifically because they hold NGCMA GLP certification — GLP compliance is a business advantage, not just a rule.

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14. Key Points

1. GLP = principles ensuring non-clinical safety studies are planned, performed, recorded, checked and archived honestly.
2. GLP covers lab/animal safety studies for regulators — NOT clinical trials in humans (GCP) and NOT manufacturing (GMP).
3. One study director per study; QA unit must be independent of the study team.
4. Facilities must be suitable and separated; equipment must be qualified, calibrated and maintained with records.
5. ALCOA: Attributable, Legible, Contemporaneous, Original, Accurate (plus complete, consistent, enduring, available).
6. Test and reference items must be identified, labelled, properly stored, with chain-of-custody records.
7. Work follows approved SOPs and the study plan; deviations are recorded with reasons and assessed.
8. Raw data + final report + specimens are archived securely for the retention period and must be retrievable.
9. Serious violations → inspection findings → hearing → disqualification; studies from disqualified facilities are rejected.

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15. Common Confusions

1. GLP vs GMP vs GCP: GLP = safety studies in lab/animals; GMP = manufacturing; GCP = clinical trials in humans. Students often mix GLP and GMP — remember "L = Laboratory".
2. QA unit vs QC: QA (in GLP) is the independent team that audits the study; QC is laboratory testing of products. Both check quality, but in completely different settings.
3. Study director vs principal investigator: One study = one study director (overall in charge). In multi-site studies, each remote site has a principal investigator who reports to the study director.
4. Raw data vs final report: Raw data is the original observation recorded during the study; the final report is the interpreted account written afterwards. QA audits the report AGAINST the raw data.
5. Deviation vs violation: A deviation is any departure from the plan/SOP, recorded honestly with reason (allowed, if assessed). A violation/fraud is hiding or fabricating data (never allowed — can lead to disqualification).
6. Contemporaneous vs accurate: Contemporaneous = recorded at the time; accurate = recorded truthfully. A record can be prompt but wrong, or true but written late — ALCOA demands both.

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16. Common Mistakes

1. Writing "GLP applies to clinical trials" — it does not; clinical trials follow GCP.
2. Saying the QA unit "does the study" — QA only inspects and audits; it must stay independent.
3. Describing data correction with whitener/overwriting — the only correct method is single-line strike-through with signature and date.

4. Forgetting the archive — students describe the study but omit that raw data, reports and specimens must be securely stored for years.
5. Confusing test item with reference item — test item = the substance under investigation; reference item = the known comparator.
6. Quoting exact archive retention years or guideline clause numbers from memory — these vary by authority and notification; write "as per current guidelines/notifications".

17. Mnemonics

- ALCOA: "All Lab Clerks Observe Accuracy" — Attributable, Legible, Contemporaneous, Original, Accurate.
- GLP pillars — "PETS RA": Personnel & organisation, Equipment & facilities, Test item characterisation, Study conduct (SOPs + plan), Records/reports/archives, Assurance (independent QA).
- Study life — "Plan-Do-Check-Keep": Plan (study plan) → Do (perform as per SOPs) → Check (QA audit) → Keep (archive).
- Disqualification ladder — "I-H-D": Inspection findings → Hearing → Disqualification.
- GLP/GMP/GCP — "Lab, Mill, Man": Laboratory safety studies = GLP; manufacturing mill = GMP; trials in man = GCP.

18. Exam Summary

GLP (Good Laboratory Practice) is the set of principles that makes non-clinical safety-study data trustworthy for regulators — it covers lab and animal safety studies, not clinical trials (GCP) or manufacturing (GMP). A GLP testing facility needs clear organisation: management accountable for compliance, one study director per study, trained personnel with job descriptions, and an independent QA unit that inspects studies and audits reports against raw data. Facilities must be suitable and separated, and equipment qualified, calibrated and maintained with records. All records must follow ALCOA — Attributable, Legible, Contemporaneous, Original, Accurate. Test and reference items must be identified, labelled, properly stored with chain-of-custody records. Studies run per approved SOPs and the study plan; deviations are documented and assessed. Raw data, the signed final report (with QA statement) and specimens are kept in a secure archive for the retention period and must be retrievable. Serious non-compliance leads through inspection findings and a hearing to disqualification — after which the facility's studies are not accepted by regulators. In India, NGCMA grants GLP certification, and India participates in the OECD MAD system.

19. One-Minute Revision

- GLP = trust rules for lab/animal safety studies (not human trials, not manufacturing).
- One study director per study; QA watches but never does the study.
- Facilities suitable; equipment calibrated; records ALCOA.
- Test items: identified, labelled, stored right, chain of custody.
- SOPs + study plan → do it → record deviations → QA audits → archive.
- Serious fraud → inspection → hearing → DISQUALIFICATION → studies rejected.
- India: NGCMA certifies; OECD MAD accepts Indian GLP data abroad.

20. Exam Questions

Short-answer questions

1. Define GLP. What is its purpose and scope?
2. Differentiate between GLP, GMP and GCP.
3. Who is a study director? List his/her key responsibilities.
4. Why must the QA unit be independent of the study team?
5. Expand ALCOA and explain each term with one example.
6. What is the correct way to correct an error in a GLP raw-data record?
7. List the GLP requirements for equipment.
8. What is a study plan? What does it contain?
9. What is an archive? Why must archived material be retrievable?
10. Explain the disqualification of a testing facility in brief.

Long-answer questions

1. Describe the organisation and personnel requirements of a GLP testing facility, including the roles of management, study director and QA unit.
2. Explain the ALCOA principles of documentation with examples. What happens when they are violated?
3. Describe testing facility operations under GLP: SOPs, study plan, conduct of study, deviations, and QA inspections.
4. Discuss records, reports and archives under GLP, and explain the process and consequences of disqualification of a testing facility.

MCQs (with answer key)

1. GLP applies to —

a) Clinical trials in humans b) Non-clinical safety studies c) Tablet manufacturing d) Hospital pharmacy — Answer: b

2. In a GLP study, overall responsibility lies with the —

a) QA auditor b) Study director c) Archivist d) Animal caretaker — Answer: b

3. The QA unit must be —

a) Part of the study team b) Independent of the study team c) Headed by the study director d) Optional — Answer: b

4. "C" in ALCOA stands for —

a) Complete b) Certified c) Contemporaneous d) Controlled — Answer: c

5. The correct way to correct an error in raw data is —

a) Use whitener and rewrite b) Tear the page and rewrite c) Single line through the error, correct value beside it, signed and dated d) Overwrite the wrong figure — Answer: c

6. Which is NOT part of ALCOA?

a) Attributable b) Legible c) Approved d) Accurate — Answer: c

7. In India, GLP certification to test facilities is granted by —

a) CDSCO b) NGCMA c) IPC d) ICMR — Answer: b

8. Raw data means —

a) The final report b) The original first-recorded observations c) A photocopy of the notebook d) The published paper — Answer: b

9. Disqualification of a testing facility means —

a) Temporary holiday b) Withdrawal of GLP compliance status; its studies are not accepted c) Change of study director d) Shifting to a new building — Answer: b

10. The OECD system under which GLP data from one country is accepted by others is called —

a) MAD b) SAD c) GLP-Plus d) TRIPS — Answer: a

Viva questions

1. Why does GLP exist? Whose lives depend on GLP data?
2. Can the study director also head the QA unit? Why not?
3. Your balance calibration is overdue by a week — can you continue weighing test items? What should you do?
4. A technician recorded Monday's observations on Friday. Which ALCOA principle is broken, and why does it matter?
5. What is the difference between a deviation and data fabrication?
6. Why would a regulator reject an entire safety study from a disqualified facility?

Application-based questions

1. During a 28-day toxicity study, the animal house temperature exceeds the specified range for 6 hours due to a power failure. As study director, describe step-by-step how you handle this under GLP.
2. A QA auditor finds that the final report states "no mortality observed" but the raw animal-observation sheets record two deaths. Explain the auditor's next actions and the possible consequences for the facility.
3. A CRO wants international clients for its toxicity studies. Explain what GLP certification it needs in India, who grants it, and why OECD MAD membership matters to its business.

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21. References

- Weinberg, S. Good Laboratory Practice Regulations. Marcel Dekker.
- WHO. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials.
- OPPI. Quality Assurance Guide.

UNIT IV: Documentation, Complaints and Product Recall