PharmacoLearn

MRA101T Good Regulatory Practices, M.Pharm Semester 1

Unit 2: Good Laboratory Practices

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2.1 What GLP is, and what it is not

Good Laboratory Practice (GLP) is a quality system for the organisational process and conditions under which **nonclinical health and environmental safety studies** are planned, performed, monitored, recorded, archived and reported. Its territory is the safety study: the toxicity, mutagenicity and related experiments whose results a regulator reads when deciding whether a substance may proceed toward humans. GLP does not judge whether the science is clever; it guarantees that the study was done as described, by identifiable people, with calibrated equipment, under written procedures, leaving a complete record from which the work can be reconstructed years later by someone who was never in the building. Two distinctions examiners insist on: GLP is not GCP (which governs human trials), and GLP is not laboratory accreditation for routine analysis (which is the territory of ISO/IEC 17025, met in section 2.8); a clinical pathology result inside a GLP study follows GLP, a hospital laboratory follows its own systems, and confusing the three settings loses marks and, in industry, audits.

2.2 Why GLP exists: the IBT scandal and the 1978 rule

GLP was written in response to fraud, not error. In the 1970s, investigations of **Industrial Bio-Test Laboratories (IBT)**, then the largest independent toxicology laboratory in the United States, found studies that had been fabricated, altered or so carelessly run that hundreds of safety studies supporting marketed products could not be relied on. The scandal's lesson was structural: a sponsor's data package could look perfect while the underlying work was worthless, because nothing required the raw work to be kept, checked or reconstructable. The FDA answered with the **GLP final rule of 1978**, codified at **21 CFR Part 58** and effective in 1979, imposing organisation, personnel, facility, documentation and quality assurance requirements on nonclinical laboratory studies. The **OECD** followed with its **Principles of Good Laboratory Practice (1981)**, and built around them the system of **Mutual Acceptance of Data (MAD)**: a study done under OECD GLP in one member country must be accepted for assessment in the others, ending duplicate animal testing across borders. India operates a national GLP compliance monitoring programme aligned to OECD (section 2.8). Every clause of Part 58 can be traced to an IBT era failure: animals replaced without record, dead animals written up as completing studies, raw data that did not exist.

2.3 The US FDA GLP regulations: Subparts A to K

The syllabus requires the regulations as a structure: **21 CFR Part 58, Subpart A to Subpart K**. The map is:

Subpart	Title and core content
A	General provisions: scope, definitions, applicability to studies supporting FDA applications
B	Organization and personnel: management duties, the study director, the quality assurance unit, personnel qualifications and training
C	Facilities: suitable size and construction, separation of functions, animal care, storage, handling areas
D	Equipment: design, maintenance, calibration, standard operating procedures for equipment, records
E	Testing facilities operation: standard operating procedures, reagent and solution labeling, animal care
F	Test, control, and reference substances: characterization, handling, storage, distribution, labeling and accountability

Subpart	Title and core content
G	Protocol for and conduct of a nonclinical laboratory study: the written protocol, its required elements, conduct to protocol, changes recorded
H and I	Reserved
J	Records and reports: the final report, approval statements, storage and retrieval of records and specimens, retention periods, archives
K	Disqualification of testing facilities: grounds, notice, hearing, consequences and reinstatement

Subparts B, G and J carry the system's heart. **Subpart B** creates the two people on whom everything hangs (section 2.4). **Subpart G** makes the **protocol** sovereign: a study is a written plan approved before work begins, and every departure from it is a recorded amendment or deviation, never a silent adjustment, so that the final report can be checked against the intention. **Subpart J** makes the study permanent: raw data, specimens and the signed final report are archived and retrievable for defined periods (in the FDA scheme, at least five years after submission of results in an application, or longer where the application is approved), because a safety study may be re-read a generation later when a harm appears.

2.4 The people of GLP: management, study director, quality assurance unit

GLP distributes responsibility in a triangle that examiners love. **Testing facility management** owns the organisation: it appoints the study director, provides the quality assurance unit, facilities, staff and resources, and is answerable for the facility's overall GLP compliance. The **study director** is the single point of control for one study: the individual responsible for its overall conduct and its final report, who approves the protocol, ensures procedures are followed and data recorded, judges deviations, and signs the report as a true account. One study, one named director: this rule exists because the IBT failures thrived where responsibility was everyone's and therefore no one's. The **quality assurance unit (QAU)** is the independent inspectorate inside the facility: a person or people, separate from study conduct, who inspect studies at critical phases, audit the final report against raw data, and maintain a signed **quality assurance statement** in the report listing what was inspected and when, and what was reported to management and the study director. A QAU that reports to the study director it inspects would fail the regulation; its independence is the system in miniature.

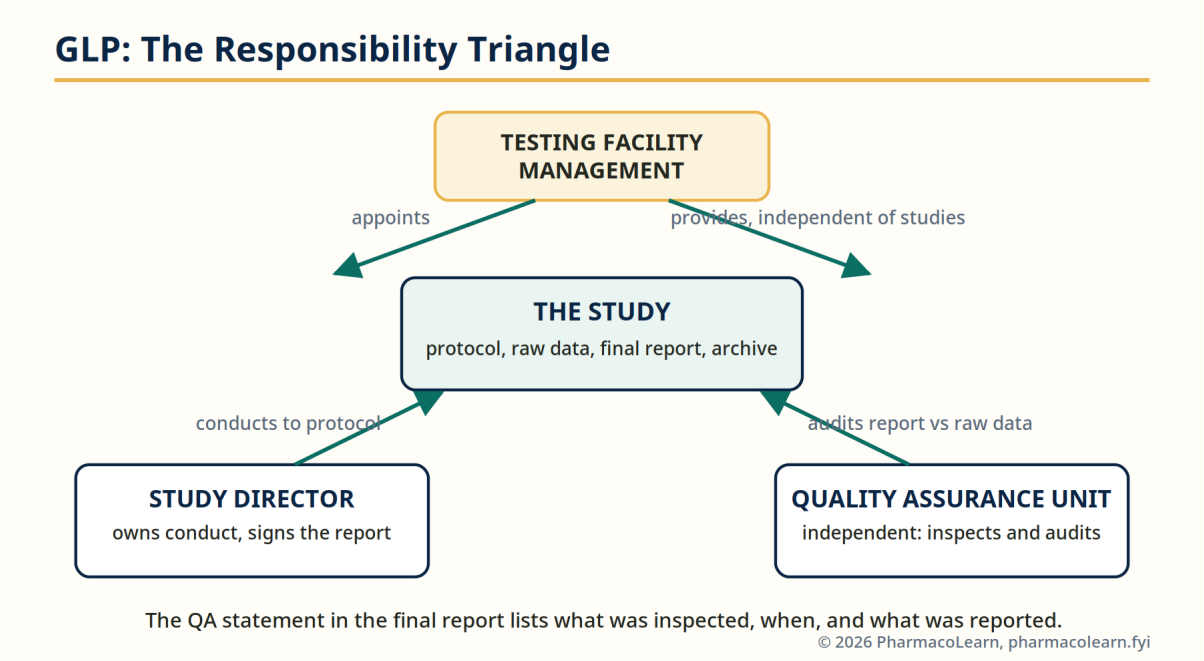

Figure: Management, the study director and the quality assurance unit: three corners of GLP responsibility, joined by the protocol and the archived record.

2.5 Documentation in GLP

Documentation is where GLP becomes visible. The system runs on **standard operating procedures (SOPs)** for every recurring operation, held controlled and available at the point of use, with deviations documented; on **raw data**, defined as the original records and certified copies from which results are computed, recorded promptly, legibly and indelibly, with corrections made by single line strike through, initialled and dated, never obliterated; and on the **final report**, which carries the study director's signed statement of compliance and the QAU statement, and must allow the study to be reconstructed. Around these sit the supporting records: training files, equipment calibration and maintenance logs, animal receipt and husbandry records, test item characterization and accountability, and the **archives**, secure, indexed, access controlled rooms or systems with a designated archivist, because a record that cannot be found is legally a record that does not exist. The objectives of this subject name **good documentation practice** as one of the practices to be mastered; in truth it is the common solvent of all four practices in this course, and Unit 3 shows what happens to it when the paper becomes electronic.

2.6 Controlling the GLP inspection process

A GLP facility will be inspected: by the FDA under its Bioresearch Monitoring (BIMO) programme, by the national GLP monitoring authority, and by sponsors placing studies. **Controlling the inspection process** means running the facility so that an inspection is a demonstration, not a discovery. Its elements are practical and examinable: a standing state of readiness (current SOP index, training records, calibration status, archive index, all retrievable within hours); an **inspection host** procedure naming who receives inspectors, escorts them, logs every request and provides copies under control; **front room and back room** discipline, in which requests are answered from a managed document room while subject experts are prepared before they meet inspectors; complete and honest answers, because inspectors forgive findings and do not forgive concealment; and a managed response afterward, in which observations (in the FDA system, recorded on Form FDA 483) receive a prompt written reply with corrective and preventive actions. Facilities fail inspections less often for bad science than for bad control: studies they cannot reconstruct, QA statements they cannot support, archives they cannot search. The inspection is the audit of the system of section 2.7 by an outsider, and the same rules win both.

2.7 Audit under GLP: goals of the laboratory quality audit, and audit tools

The **laboratory quality audit** is the QAU's own instrument, and its goals are worth listing as the syllabus frames them: to verify that studies comply with GLP, the protocol and SOPs; to verify that the final report accurately and completely reflects the raw data; to detect systemic weaknesses (a recurring deviation, an untrained operator, a drifting instrument) before a regulator does; and to give management an evidence based picture of the facility's compliance health. Audits divide by object: **study based** audits inspect a live study at critical phases; **facility based** audits examine the systems (archives, animal house, calibration programme) across studies; **process based** audits follow one procedure end to end; and the **report audit**, the line by line comparison of report against raw data, is the last internal gate before a report leaves. The **audit tools** are correspondingly concrete: approved **checklists** built from the regulation, protocol and SOPs; the master schedule of studies; sampling plans for records; interview technique; and the audit trail through documents, in which every number in a report is chased to its raw datum. Findings are classified, reported to the study director and management, answered with corrective action, and followed up: an audit without follow up is theatre, a point MRA102T develops for GMP audits.

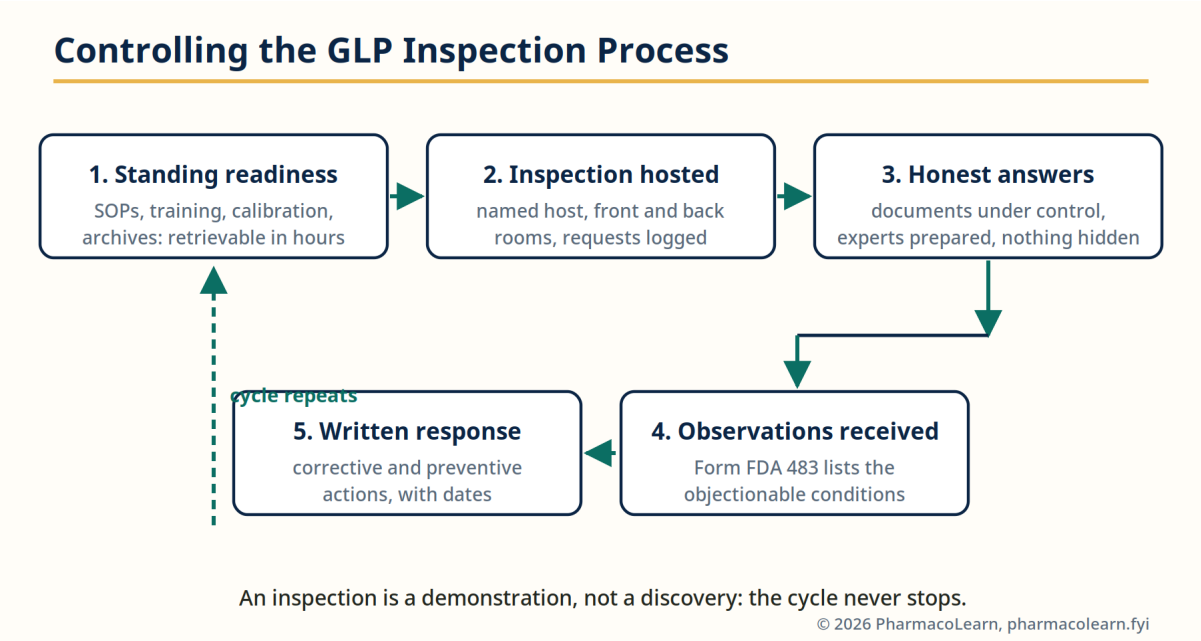

Figure: Inspection readiness as a continuous cycle: readiness, hosting, honest answers, written response, corrective action, and readiness again.

2.8 ISO and QCI: the Indian and international standards layer

Two standard systems border GLP and appear in the syllabus beside it. **ISO/IEC 17025** sets general requirements for the competence of testing and calibration laboratories: management requirements and technical requirements (personnel, accommodation, methods and validation, equipment, traceability, sampling, handling of items, quality assurance of results, reporting). It accredits the competence of routine laboratories; it is not GLP, and a 17025 accredited laboratory is not thereby GLP compliant, but the two overlap in equipment, calibration and documentation discipline, and many facilities hold both. In India, accreditation and monitoring run through the **Quality Council of India (QCI)**, the national accreditation body, whose board **NABL** (National Accreditation Board for Testing and Calibration Laboratories) accredits laboratories to ISO/IEC 17025, while India's **National GLP Compliance Monitoring Authority (NGCMA)**, under the Department of Science and Technology, inspects and certifies GLP test facilities against the OECD principles and represents India in the OECD MAD system, which India joined as a full adherent in 2011. For the examination, the chain to remember is: OECD principles define GLP, NGCMA certifies Indian facilities against them, MAD makes their studies acceptable abroad, QCI and NABL run the parallel 17025

accreditation world.

2.9 The future of GLP regulations

GLP is a mature system changing at its edges, and the syllabus asks where it is going. Four directions are visible. **Computerization** is the deepest: electronic raw data, laboratory information systems and automated instruments have moved the old paper concepts (original record, certified copy, archive) into systems governed by Part 11 and its international equivalents, which is why Unit 3 exists. **Multi site studies**, in which one study is split across facilities and countries, have forced the roles of principal investigator and lead QA and OECD guidance on remote conduct. **Data integrity** has become the organising anxiety of all the good practices, expressed in principles such as ALCOA and its extensions (records attributable, legible, contemporaneous, original, accurate, and also complete, consistent, enduring and available). And **scope pressure** grows as new study types (in vitro methods, in silico toxicology, organ on chip systems) ask whether and how GLP should cover work that has no animal house at all. The principles have survived every technology change since 1978 unchanged in substance, because they were written about honesty and reconstruction rather than about paper; that is the sentence with which to close an examination answer on GLP's future.

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