What is Good Laboratory Practice?

The late 1970s witnessed the introduction of Good Laboratory Practice (GLP) requirements into the regulatory framework as an apparent response to misconduct in pharmaceutical companies and their contract research and development (R&D) facilities. GLP aims to control the approaches used by scientists that test potential medications' (and other chemical or biological entities') safety. The safety of pharmaceuticals is a major concern due to the apparent possible effects on individuals recruited for clinical trials and patients taking medication. GLP is considered a way to make sure that researchers don't fabricate or alter safety data, and that experiments are properly managed and carried out, which significantly raises the likelihood of obtaining reliable experimental data.

The term GLP is most commonly associated with the pharmaceutical industry and the required non-clinical animal testing that must be performed before approval of new drug products. However, GLP also covers a wide range of other non-pharmaceutical items, such as food packaging, medical equipment, food additives, colour additives, and food contamination thresholds.

GLP is a formal regulation created by the USFDA as these regulations were proposed on November 19, 1976, and designated as a new part of Chapter 21 of the Code of Federal Regulations (CFR) as 21 CFR Part 58 in 1979. In 1981 an organization named OECD (Organization for Economic Cooperation and Development) produced GLP principles that are international standards. GLP in OECD principles is defined as “a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported”.

Objectives of GLP

1. GLP makes sure that the data submitted are a true reflection of the results obtained from the studies.

2. GLP makes sure that the data is traceable.

3. Promotes international acceptance of tests.

The GLP laws assist researchers in carrying out their work following their pre-established plans and standardized procedures by laying out the guidelines for good practice. The scientific or technological content of the research programs is not covered by the regulations. Furthermore, they do not seek to evaluate the studies' scientific merit.

All GLP texts, irrespective of their origin, stress the importance of the following five points:

1. **Resources**: organization, personnel, facilities and equipment

2. **Characterization**: test items and test systems

3. **Rules**: study plans (or protocols) and written procedures

4. **Results**: raw data, final report and archives

5. **Quality assurance**

Principles of Good Laboratory Practice (GLP)

Figure: Principles of GLP; Image: Ajmal Aseem/BiotechReality.com

Resources

Organization, personnel, facilities, and equipment

GLP Standards mandate that R&D personnel's roles and the organization's structure be made explicit. GLP also emphasizes that there should be enough employees to complete the necessary jobs. Staff training and credentials need to be specified and recorded as well. The regulations place a strong emphasis on the necessity of having enough space and tools to carry out the studies. All of the devices must have to be operational. A stringent certification, calibration, and maintenance program needs to be implemented to guarantee this.

Organization and personnel

The entire structure of the testing facility must be specified with GLP. An organization chart is typically used for this. To get an overview of how the facility works, inspectors often begin by seeking this document. Occasionally, the organizational chart is included in a quality manual or other document that outlines the structure and functions of the organization. They are supplemented by more detailed information which may be incorporated into the following documents relating to each individual:

- **Curriculum vitae**
- **Training records**
- **Job description.**

Taken as a whole, these three documents satisfy the GLP mandate that records be kept proving staff members possess the skills, knowledge, background, and training required to carry out their duties. SOPs should specify the format and content of these documents, and QA audits should routinely validate their accuracy.

Facilities and equipment

According to GLP, facilities must be built, sized, and located appropriately to fulfil study criteria and reduce disruptions that could compromise the study's validity. They have to be planned so that there is enough space between the different research tasks. These specifications are meant to guarantee that insufficient facilities won't jeopardize the study. The facility management is responsible for determining what is sufficient, and this will vary depending on the type of research being done.

Adequate equipment must be provided in order to conduct a study effectively. Everything should be suitable for the purpose for which it was designed. The sort of study and its goals determine what equipment is appropriate for a particular investigation. The only way to figure out suitability is to take the equipment's performance into account. Evaluating the equipment's suitability is a scientific problem that the research director will assess. To prove that some equipment is reliable, proper testing or even formal authorization must be performed. This frequently applies to analytical equipment. All equipment, whether technically qualified or not, needs to be maintained and calibrated to guarantee accurate functioning. The calibration is typically dependent on the standards being utilized.

Characterization

Test items and Test systems

A thorough understanding of the materials used for the study is crucial to carry out the research accurately. To assess the characteristics of pharmaceutical compounds in non-

clinical investigations, further details regarding the test item and the test system, which is typically an animal or plant, to which the test item is to be given are necessary.

The test item could be a biological material, an extraction from plant tissue, a pesticide, a food additive, a vaccination, an industrial chemical, or an active ingredient in one of these products. The analytical profile of the test item—such as its chemical identity, impurity, solubility, stability, etc.—is most commonly used to sum up it. It is crucial to preserve the test item from contamination by pathogens, dust, water, and other external causes, as well as from cross-contamination from other chemicals (or even the same chemical from a different batch), to prevent mixing up problems and producing erroneous findings. Therefore, to comply with the GLP Principles, appropriate arrangements must be made for the test item's receipt and storage.

Before delivering the test item to the test system, it is often formulated. As a result, GLP also mandates that the testing facility follow precise formulation protocols to ensure that the same technique is applied consistently and results in the same concentrations. To avoid confusion between formulations, cross-contamination, and pollution, safety measures must be applied again. An animal, a plant, a bacterium, an isolated organ, a field or other ecosystem, analytical tools, etc. could all serve as the test system. The GLP standards are not as exact as those for the test item since the characterization of the test system can differ significantly.

Rules

Study plans (or protocols) and written procedures (SOP)

Documents that have been authorized by management must specify the institute's guidelines for organizing and carrying out GLP investigations. Prescriptive documents are those that specify who is responsible for what, when, how, and where.

There are two main types of prescriptive documents:

- The protocol (study plan), outlines the design and conduct of the study as well as its expected time period.
- The standard operating procedures (SOP), offer comprehensive guidelines for carrying out each technical procedure and guaranteeing that the study, its surroundings, and its data are well-organized.

Protocol (study plan)

Prescriptive documents that govern and validate the conduct of scientific experiments ought to be present in the laboratory. These documents' objectives are to:

• Describe general policies, decisions, and principles governing how the research centre operates;

• Define the experimental design for particular studies;

• Instruct staff about how to carry out routine operations;

A description of the study design, including materials and procedures, the general experiment plan, and the roles and duties of the participating scientific staff are all included in the protocol. Since the protocol serves as the primary method of communication with research staff, it should be clearly planned and written so that everyone can understand it.

Standard operating procedures (SOP)

For GLP compliance to be successful, a solid SOP framework must be implemented. Additionally, it's frequently regarded as the most significant and time-consuming compliance activity. Standardized, approved documented working procedures are necessary for excellent management and classical quality assurance methodologies, even in the absence of GLP laws. The following are necessary for the successful implementation of SOPs: -

- A sound SOP management system to guarantee that current SOPs are available in the appropriate location;
- SOP-based education and training of personnel to ensure that the procedures are performed in the same way by all personnel;
- Sustained and enthusiastic support from all levels of management with a commitment to establishing SOPs as an essential element in the organization and culture of the laboratory.

Results

Raw data, final report and archives

Data are produced during the study's experimental phases. These statistics are reported by the study director in the study report's discussion and conclusion sections. The experiment's result is the report and the data that goes with it. As soon as the findings are made available to the public, usually through publication, they are incorporated into the scientific body of knowledge. The data must be accurate, complete, and securely stored given the possible significance of the knowledge gained from the research.

Raw data are defined as original results recorded during the study.

The raw data should include: “WHAT was done”; “HOW it was done”; “WHEN the work was performed” and “WHO performed the work”.

The ***final study report*** is the responsibility of the study director, and must include the following contents:

- Information on sponsor and test facility.
- Experimental starting and completion dates.
- Objectives and procedures stated in the protocol (including the changes).
- Description of materials and test methods.
- A Quality Assurance Program statement.
- Storage (specimens, reference items, raw data and final report).

The ***archives*** should be viewed as more than just a location for collecting and preserving old documents. It is a secure repository of priceless data. Additionally, it serves as a hub for the distribution and compilation of summary documents and is a crucial instrument for reconstructing earlier research projects.

Quality assurance (QA)

GLP outlines the minimal standards for quality control required to guarantee the reliability of experimental findings. The group of people with specific responsibilities known as the quality assurance unit (QAU) assures management that all of the quality procedures put in place in an organization function as intended. Being an impartial observer of the entire preclinical research process and its institutional environment is the core purpose of Quality Assurance. Preclinical research must go through all stages of evaluation by QA, from planning to reporting to record archiving, in order to adhere to GLP Principles.

For QA to be successful, it needs top management that is driven and has access to staff papers and procedures at all organizational levels. Facility management should have access to QA audit files, but not outside legal entities or regulatory bodies. QA reviews the protocol for completeness and clarity. QA has the responsibility of reviewing SOPs.