ROLE OF GLP (GOOD LABORATORY PRACTICE) IN GOOD CLINICAL PRACTICE: ENSURING SAFETY

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ABSTRACT: Continuous quality improvement strategy through regulatory guidelines like (GLP) could serve as a key for error minimization. GLP is an easily understandable for any organization staff and internationally accepted quality system to improve the quality and maintain the quality. GLP has become a compulsory in the laboratories and other organization which are involved in clinical research particularly it serves as a solid standard for registration and regulatory research settings. GLP work as a helpful tool in ensuring laboratory staff integrity, data reliability, sensitivity and test specificity. GLP describes good practices for non-clinical lab studies that support research or marketing approvals for FDA-regulated products. GLP was initially adopted by USA as US-FDA-GLP and was accepted by OECD and without modifying the essence of US-FDA-GLP, GLP was practiced globally. In this review, we discuss Introduction to GLP, Objective of GLP, Basic requirement of GLP, Strength and Weakness of GLP, Discussion and Conclusion.

Key Words: GLP; Good Laboratory Practice; Good Clinical Practice

INTRODUCTION:
Good laboratory practice including principles that are intended to assure the quality and integrity of non-clinical laboratory studies that are intended to support research or marketing permits for products regulated by government agencies. GLP in general symbolizes the “good practices” which need to be used in the laboratory, the purpose of which is testing the physical, chemical and microbial testing of materials as applicable and to avoid threat or hazardous to human. [1]

The term “Good Laboratory Practice” was first officially used in the year 1972 in New Zealand Testing Laboratory, where the development and maintenance of Good Laboratory Practice in testing was made mandatory for registration of a “Testing Laboratory”. [2]

A number of countries require manufactures of industrial chemicals, pesticides, pharmaceuticals, veterinary drugs, cosmetic products, food products, feed additives, etc., to establish through data that use of these products do not pose any hazards to human health and the environment. [3]

Non-hazardous nature needs to be established through studies and data, which will be examined by the regulatory authorities of the concerned countries. [4]

Good Laboratory Practice is a system, which has been evolved by Organization for Economic Cooperation and Development (OECD) used for achieving the goals. [5]

In 1981, the Organization for Economic Cooperation and Development (OECD) published GLP Principles. [6]

After the “Thalidomide” disaster the regulatory requirements for “Safety and Testing” of pharmaceutical were tightened all over the world especially in contract research organizations. [7]

In India National GLP Compliance Monitoring Authority was established by the Department of Science & Technology, Government of India, with the approval of the Union Cabinet on April 24, 2002.

OBJECTIVES OF GLP:
The objective of GLP is to provide a framework for quality system under which laboratory studies are planned, performed, monitored, recorded, reported and achieved. [8]

Some other objectives are:

- Adopt good and safe operating procedure and recording system.
- To promote the development of quality test data.
- Comparable quality of test data to avoid duplicative testing.
- To avoid the creation of technical barrier to trade.
- Prevent human error in the performance of the job.
- Prevent equipment error in measurement.
• Prevent unsafe and hazardous acts which could affect individuals.
• Improve the protection of human health and the environment.
• Improve efficient performance of the job

Accuracy, Precision and Sensitivity these three objectives of GLP make a work errorless and safe. [9]
The GLP Principles lead to,[10]

 Limit waste resources.
 Ensure high quality of results.
 Ensure comparability of results.
 Promote mutual recognition of result.

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<tr>
<th>GLP is needed for:</th>
<th>GLP is not needed for:</th>
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<td>• Non clinical safety studies of development of drugs.</td>
<td>• Basic research</td>
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<td>• Agriculture pesticide development.</td>
<td>• Studies to develop new analytical methods.</td>
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<td>• Development of toxic chemicals.</td>
<td>• Chemical tests use derive the specification of a marketed food product.</td>
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<td>• Food control (food additives).</td>
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<td>• Test of substance with regards to explosive hazards</td>
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❖ STRENGTH IN GLP:

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<th>Insist Verifiability (Audit)</th>
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<td>Insist Documentation Actions</td>
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<td>Same standards worldwide</td>
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❖ WEAKNESS OF GLP:

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<th>Does not take regard for scientific content</th>
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<td>Does not consider further steps along the reporting chain</td>
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<td>Tends to over-elaborate technical details</td>
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<td>Focus only on testing chemicals</td>
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BASIC REQUIREMENT FOR GLP:

I. **Instrumentation Calibration:**
   - Calibration calendar will be maintained for all the QC instruments.[11]
   - The instrument will be tagged with the tags sowing the instrument details such as instrument ID and instrument name and will carry a label indicating its calibration status.
   - The instrument and glassware calibration will be carried out as per SOP.

II. **Reagent/ Materials Certification:**
   - Container for laboratory reagents/materials must be labeled with information such as date received, date opened, preparation date, expiration time, use before etc.[12]
   - All the reagents or materials will be stored at its specified storage condition.[13]
   - All the volumetric glassware used must be calibrated; the apparatus and material used in test should not interfere adversely with the test system.
   - There will be a list of all the chemicals and reagents, which should be displayed on the respective rack.
   - All the cupboards and drawers should be numbered, list of materials kept inside each cupboard and drawer should be maintained.[14]
   - Use the protective gloves, masks during reagent preparation and standardization.[15]

III. **Analyst Certification:**
   - All analyst working in the QC lab should be educated and qualified analysts.
   - Test is invalid if unqualified analyst has carried it out.[16]

IV. **Lab Facilities Certification:**
   - The QC lab is independent of the manufacturing area.[17]
   - Separate Area will be provided for physico-chemical and microbiological analysis.
   - QC lab will be design appropriately to carry out the operation.[18]
   - Sufficient space will be provided for storage of test sample, reference samples, reference standard, reagents, media and records.[19]

V. **Documentation:**
   - At a minimum QC department should have the following documents:
     a) Specification
     b) Sampling Procedures
     c) Standard Operating Procedure
     d) Method of analysis
     e) Analytical work sheet an records
   - All the documents will be stored in secured manner.
   - All the activity performed will be documented.[20]

VI. **Recording of Activity in log book:**
   - For each laboratory instruments, drying oven, microbiological incubator or autoclave there shall be a logbook to record the complete list of activities involving the laboratory instrument.[21]
     For example:
     a) Calibration
     b) Maintenance
     c) Testing
     d) Vendor Activities
     e) Relocation
   - The laboratory instrument/equipment logbook entries shall contain sufficient detail to enable complete, accurate and timely assessment of impact to testing activity in the event of an investigation.[22]

VII. **Cleaning of laboratory and Clean rooms:**
   - There will be a cleaning schedule for the QC lab.
   - The cleaning will be done according to schedule.[23]
   - The cleaning will be done with RO or WFI water and qualified cleaning agent.[24]
   - There will be restricted entries into the clean room.[25]

VIII. **Cleaning of Glassware, Plastic ware and others:**
   - All the new and old glassware and plastic ware will be cleaned as per SOP.
The cleaned glassware will be labeled and will be kept at the specified space. Every time use clean glassware for testing. For BET and microbiological work use depyrogenated and sterilized glassware respectively. Before use, check the glassware/ laboratory ware for its cleanliness as it does not have any brown spot, residue or visible traces. And if found, then do not use it, and send it back for washing.

IX. Handling of Spillage and Handling of Waste:
- There will be discard procedure for every type of waste generated in the QC lab.
- Handle the spilled material in a manner to avoid contact with skin.
- Handle volatile, fumes producing material in the fume hood chamber.
- Discard the cytotoxic waste as per the procedure mentioned in related SOP.

ENSURING SAFETY:
- The principles of GLP aim to ensure and promote safety, consistency, high quality, and reliability of chemicals in the process of non-clinical and laboratory testing. But GLP is not limited only to chemicals.
- Five ways safe and effective laboratory design impact Health, Safety and Productivity:

1. Lab user’s need are fulfilled.
   - To design a lab that supports both safety and productivity, the design team must start by determining specifications, such as how people will use the lab (including what materials or processes will be used), how many people will be working there, what their roles are, and how much space is needed. This ensures that everything included in the design will serve a purpose in supporting lab users' productivity. As a result, workers will have the equipment and materials they need to carry out their tasks.

2. The probability of everyday accidents decreases.
   - Many accidents are caused by human error or bad luck – but improper design does increase the probability of negative incidents. In addition to putting people at the risk of harm, these incidents ultimately decrease productivity, as they hinder the researchers’ ability to work. Hazards in the lab can range from fires to falls to eye damage and beyond, all of which can both harm lab users and shut down or delay work. A lab designed for safety makes these accidents less likely. When users have adequate workspaces and aisles between them, they won’t bump into each other; sprinkler systems can extinguish fires before they spread; and chemical spills and other hazards can be contained quickly, efficiently, and with minimal harm when appropriate warning systems and cleaning materials are available.

3. The layout will be suitable for activities in the lab.
   - A well-designed lab’s layout provides appropriate storage, equipment, and workspaces. For example, simple cabinets may be adequate for electronics, but chemicals often require more complex storage spaces. By providing the appropriate accommodations, it becomes less likely that lab space will be wasted. In addition, lab users can avoid storing supplies in places that block exits
or cause other dangerous conditions. For example, potentially hazardous materials and equipment should be stored and used in lab zones away from heavy traffic flow and ventilation sources that cause disruptive airflows.

4. **Users can focus on their task instead of worrying about emergencies.**
   - When designing a lab, it is crucial to include vital safety features, such as biosafety cabinets, fire protection, detection systems, emergency showers & eye wash stations. When users know these features are easily available, they can focus on performing their research with a greater measure of security regarding their health and safety & thus be more productive. In addition, labs should have easy-to-access, well-marked exits so that researchers can get out quickly and safely in case of an emergency or accident.
   - To further enhance safety, designers should include ventilation systems based on users' activities. All labs should have ventilation systems to control the temperature and keep the space comfortable, especially as research shows that optimal workplace temperatures can increase productivity, no matter the work environment. In addition, when hazardous materials are being used, ventilation systems should be more advanced and may require features such as chemical fume hoods to control potential exposure and capture contaminants in laboratory air.

5. **The lab can be adapted for future research needs.**
   - It is important to get a sense of how research efforts in the lab might change in the future – even five or more years out. A design with some flexibility built in will allow you to include features that lab users might not need now, but could benefit from later, such as more and/or moveable workbenches or advanced ventilation for chemical work.

**DISCUSSION:**

- Standard Steps required for accurate Testing according GLP are as follow:
  - For achieving accurate results qualified analyst are necessary and they should perform every testing without any human error.
  - Good Laboratory Practice (GLP) requirements based on this fundamental scientific principles and practices, are indispensable for providing scientific confidence in studies conducted for chemical safety determination.[32]
  - To achieve accurate results, testing done with cleaned and sterilized glassware, labelled solvents.[33]
  - After testing, the solvent stored in its storage condition according to SOP.
  - GLP differs from other quality systems in aspects that are important not only for the traceability of data but especially for the full reconstructability of the study, there are certain co-occurrences between GLP and other quality systems like accreditation schemes.[34]
  - The principles of good laboratory practice (GLP) is to support the development of quality and validity of test data used for determining the safety of chemicals and chemicals product. [35]
CONCLUSION:

- Implementation of GLP should start from top level management and investigators.
- Organization also spend some amount of fund to implement GLP for safety purpose and long term benefit of organization itself.
- If one person in top management is aware of GLP or trained on GLP so it is easy to implement GLP in organization for top management.
- GLP training is not 1 time training event, the training of GLP give to the whole organization periodically.

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