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# CURRENT GOOD LABORATORY PRACTICES IN PHARMA INDUSTRY

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## ABSTRACT

Good Laboratory Practice (GLP) is a quality system concerned with the organizational process and conditions, under which a study is planned, performed, monitored, recorded, archived and reported. The role of GLP is the development of quality test data, mutual acceptance of data avoids duplication of data, avoids technical barriers to trade and also protection of human health and the environment. GLP is sometimes confused with the standards of laboratory safety like wearing safety goggles. GLP is a regulation that was created by the FDA (United states food and drug administration) in 1978. FDA decided to do an in-depth investigation on 40 toxicology labs. The principles of GLP are complied with a sufficient number of qualified personnel, appropriate facilities, equipment and materials are available. Records of qualifications, job descriptions, training and experience of personnel are maintained. It involves a number of good practices in the QC laboratory which are to be undertaken to carry out ananalysis with a defined degree of accuracy and precision. GLP and cGMP regulations have a significant impact on the daily operation of an analytical laboratory. GLP was altered to protect the integrity and quality of laboratory data used to back up a product application.

**KEYWORDS:** Regulatory Authorities, Quality Control, 21 CFR.

## INTRODUCTION

In the early 70's FDA (United States Food and Drug administration) have realized cases of poor laboratory practice throughout the United States. FDA decided to check over 40

toxicology labs in-depth. They revealed lot dishonest activities and a lot of poor lab practices. Examples of some of these poor lab practices found were equipment not been calibrated to standard form, therefore giving wrong measurements, incorrect or inaccurate accounts of the actual lab study and incompetent test systems.GLP is one of the crucial code which is essential for the development and design of pharmaceutical products. GLP is the part of quality standards as required by the market authorization. The principle of GLP ensures the generation of high quality and reliable test data related to the safety of industrial chemicals, pesticides, pharmaceuticals, food and feed additives, cosmetics etc in the framework of harmonizing testing procedures for the mutual acceptance of data**.** Good planning is the greater half of success. With a perfect propose in mind and a well figured out and defined testing procedure is it achiavable to acquire an evaluable outcome of a study. GLP places a high degree of reliance upon creating and following a pre- defined study plan.

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. Hence GLP aims to decrease the occurrence of mistakes or mix-ups through large and specific labelling requirements. The registered information can be provided by demonstrating the application of the correct item in the stated amounts to the pertinent test systems. The aim of GLP will be to give enough information about the GLP in details with the test facility organisation and personel, the facilities of quality assurance programme, test system, archive and waste disposal, apparatus, material, and reagents, physical, chemical, biological test systems, receipt, handling, sampling and storage and characterisation of the test and reference items, standard operating procedures, performance of the study, reporting of study results, storage and retention of records and materials.

**WHY GLP?**

1. Development of quality test data
2. Mutual acceptance of data
3. Avoid duplication of data
4. Avoid technical barriers to trade
5. Protection of human health and the Environment

**THE PRINCIPLES OF GOOD LABORATORY PRACTICE**

1. Test facility management
2. Quality assurance programme

3. Meeting the requirements of the test facility
4. Equipment
5. Receipt, handling, sampling and storage
6. Standard operating procedures.
7. Performance of the study.
8. Reporting of study results
9. Storage and retention of records and materials.

**1. Test facility management**

Test facility means the persons, premises and operational units that are necessary for conducting the non-clinical health and environmental safety study.The term "test facility" may include several "test sites", at one or more geographical locations, where phases or components of a single overall study are conducted and does not only include buildings, rooms and other premises, but that it includes also the people who are working there and are liable for performing these studies. Properties of biological test systems are generally more complex and mutable than the ones of physical/chemical test systems. Hence biological test systems need very careful characterisation in order to guarantee the quality and integrity of the data derived from them. The outcome of a study may be influenced by the state and condition of the test system at the time of the study which has special importance with regard to the reconstructability. The GLP Principles, in uttering the requirements for the accommodation and siting of these systems, for their maintenance and utilization, and for the associating documentation, aims at supplying the essential basis for confidence into the results obtained from biological test systems. A test item should only be used in studies if it can safely be regarded as being in its pure, unspoilt and not decomposed. Any change in the properties of the test item may lead to spurious and erroneous results, and to wrong interpretations of the effects the test item is supposed to have produced. Stability testing will lead to the definition of a time interval within which the test item will stay in this state, and as a result "expiry" or "re-analysis" dates have to be mentioned on the label of the test item container. With this necessity GLP aims to reduce the possibility that an item will be used in a study which does no longer correspond to the item that had been intended for testing. The aim of any safety testing is to analyze possible effects of the test item on the test system. Therefore, the effects observed in any test system should be traceable to the application of the item which was the designated subject of the study.

## 2. Quality assurance programme

Quality control is the process, procedures and authority used to accept or reject all components, drug product containers, closures, in-process materials, packaging material, labeling and drug products and the authority to review production records to assure that no errors have occurred, that they have been fully investigated. The quality and reliability of test data count on the state and condition of the test system which is used in its production. This is meant to be the control of a number of technical features and specifications which are needed to ensure the integrity of the system and the quality of the data generated. In a study for compliance with GLP, the most important aspects may be characterised as "suitability", "capacity" and "integrity" (OECD, 1998). "Trust is Good, Control is Better" says an old proverb. The quality which is supposed to be achieved in GLP is not a quality which can be controlled by easy, numerical or other means, but it is the şcontrol over the intrinsic quality of a test facility and its studies. Only through this independence a reliable assurance of the studies inherent quality that can be achieved.

### 3. Meeting the requirements of the test facility

The GLP principles do not address the question of the specific requirements for the location of an archive, except that it should be "of suitable size, construction and location to meet requirements". Therefore there is complete freedom for every test facility to define the location of its archives and to designate the proper locations for each type of materials to be stored.Before they can be considered as GLP compliant General Requirements Facilities need to conform to a number of general rules. The facilities should be designed for the best suitability to the studies that are to be performed within. Some comfort for the employees comes of course with all the requirement of study quality, which means that the people working in a facility should certainly have sufficient room to move around in order to be able to perform the duties which the study calls for, and to perform them in a manner compatible with the quality, integrity and validity of the study. Handling and disposal of wastes should be carried out in such a way as not to risk the integrity of studies. This includes provision for appropriate collection, storage and disposal facilities, and decontamination and transportation procedures. This policy is to assure that reagents used are specified in the standard operating procedure. Purchasing and testing should be handled by a quality assurance program. Reagents and solutions should be labeled, deteriorated or outdated reagents and solutions should not be used. The opening date should be recorded. They should be stored under ambient temperature and the expiration date should be considered(Lori et al , 2009).The equipments should be appropriately designed, adequate throughput capacity, appropriately located and routinely maintained & calibrated.

### 4. Equipment

Equipment, including validated computerised systems, used for the generation, storage and recovery of data, and for controlling environmental factors relevant to the study should be suitably located and of appropriate design and adequate capacity. Equipment records should include: name of the equipment and manufacturer, model or type for identification, serial number, date equipment was received in the laboratory, copy of manufacturers operating instruction(s). Equipment used in a study should be periodically inspected, cleaned, maintained, and calibrated according to Standard Operating Procedures. Records of these activities should be maintained. Calibration should be traceable to national or international standards of measurement. Instrumentation validation is a process necessary for any analytical laboratory. Equipment used for the generation of physical/chemical data should be suitably located and of proper design and adequate capacity. The integrity of the

physical/chemical test systems should be ensured. Appropriate conditions should be established and maintained for the storage, housing, handling and care of biological test systems, in order to ensure the quality of the data. Standardization, calibration, and verification are the definitions which have particular importance for the equipments. The difference between those should be well understood and performed by the laboratory personnel: Verification is the external check of equipment accuracy. It is the check balance accuracy against weights at laboratory.

**5. Receipt, handling, sampling and storage**

Sampl e tracking vary among laboratories. Receipt, handling, sampling and storage should be prepared appropriately. Records including test item and reference item characterisation, date of receipt, expiry date, quantities received and used in studies should be maintained. Handling, sampling, and storage procedures should be identified in order that the homogeneity and stability are assured to the degree possible and contamination or mixup are precluded (Seiler, 2005). They should maintain the unmistakable connection between a set of analytical data and the samples from which they were obtained. Original source of samples must be recorded and unmistakably connected with the set of analytical data (Cobb, 2007). Records including test item and reference item characterisation, date of receipt, expiry date, quantities received and used in studies should be maintained. While receipt and storage involves mainly the handling of closed containers, the opening of such a container exposes the test item to the facility environment and leads consequently to the possibility of contamination of either the test item or the environment. Moreover, the greater the number of different test items to be performed, the greater the danger that somebody would. Therefore, work in the special area where test items are mixing with the vehicle, it should be made

compulsory that only one test item would be present in that area at any one time. Special attention has to be given to such areas where test, control and reference items are prepared for in vitro studies.

**6. Standard Operating Procedures (SOP)**

According to EPA(Environmental Protection Agency) GLP regulations, "Raw data" means any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. Logbooks for recording temperatures or equipment use, repair, and maintenance, field or laboratory notebooks, forms for field or laboratory observations, training reports, computer printouts, recorded data from automated instrument are examples of raw data. It's so hard and not necessary for anyone remember all these details and that's one of the functions of the Standard Operating Procedures (SOPs).

In FDA it is said that: "If it is not documented, it did not happen!" or, it's a rumor!" GLPs SOPs Can't do Guarantee "good science", guarantee good documentation, replace common sense, prevent all mistakes (Cobb, 2007). SOPs are written procedures for a laboratories program. They are approved protocols indicating test objectives and methods. Standard Operating Procedures are intended to ensure the quality and integrity of the data generated by the test facility. Revisions to Standard Operating Procedures should be approved by test facility management (OECD, 1998). They define how to carry out protocol-specified activities. SOPs are most often written in a chronological listing of action steps. They are written to explain how the procedures are supposed to work SOP of routine inspection,

cleaning, maintenance, testing and calibration, actions to be taken in response to equipment failure, analytical methods, definition of raw data, keeping records, reporting, storage, mixing, and recovery of data. (Standard Operating Procedures should have been written and approved by test facility management that are intended to ensure the quality and integrity of the data generated by that test facility. Revisions to Standard Operating Procedures should be approved by test facility management. Each separate test facility unit or area should have at once available current Standard Operating Procedures relevant to the activities being performed therein. Published text books, analytical methods, articles and manuals may be used as supplements to these Standard Operating Procedures. Deviations from Standard Operating Procedures related to the study should be documented and should be acknowledged by the Study Director and the Principal Investigator(s). SOPs are written, approved procedures that describe routine activities that are specific for daily operations at each facility. SOPs should allow appropriately qualified personnel to perform a procedure once trained. The details given under each heading are to be considered as illustrative examples. Room preparation and environmental room conditions for the test system, procedures for receipt, transfer, proper placement, characterisation, identification and care of the test system, test system preparation, observations and examinations, before, during and at the conclusion of the study, handling of test system individuals found in a severe position or dead during the study, collection, identification and handling of specimens ,siting and placement of test systems in test conspiracy should be reviewed

**7. Performance of the study**

Performance of the Study should be monitorized carefully. All the standards supplied by the GLP should be followed from the beginning of the study to the end by the final report. For

each study, a written plan should exist prior to the initiation of the study (Seiler, 2005). The study plan should contain the following information: Identification of the study, the test item and reference item, information concerning the sponsor and the test facility, dates, test methods, issues (where applicable) and records. (OECD, 1998).

**8. Reporting of study results**

All studies generate raw data that are the original data gathered during the conduct of a procedure. They are essential for the reconstruction of studies and contribute to the traceability of the events of a study. Raw data are the results of the experiment upon which the conclusions of the study will be based. Some of the raw data may be used directly, and some of them will be treated statistically. The results and their interpretations provided by the scientist in the study report must be a true and accurate reflection of the raw data.

**9. Storage and retention of records and materials**

Storage and retention of records and materials should be prepared appropriately. The following should be retained in the archives for the period specified by the appropriate authorities : the study plan, raw data, samples of test and reference items, specimens, and the final report of each study records of all inspections performed by the Quality Assurance Programme, as well as master schedules, records of qualifications, training, experience and job descriptions of personnel; records and reports of the maintenance and calibration of apparatus; validation documentation for computerised systems. In the absence of a necessitated retention period, the final arrangement of any study materials should be documented.

## UTILITY AND IMPORTANCE OF GLP FOR IMPLEMENTATION and MAINTENANCE OF GMP IN LABORATORY

**1. Laboratory Infrastructure**

Modern Quality Control Laboratory should have following sections:

A. General Chemical Laboratory: It should be well ventilated well lit and preparable air conditioned to maintain a temperature of 27°C± 1° C

B. Instrument Room: The temperature should be 25°C± 1°

C and RH of 45± 5% in this area. It should have a centrally regulated constant supply voltage of 230 volts ± 1% and a frequency of 27Hz± 3%. There should be separate room for housing semi micro and microbalances.

C. Microbiological Laboratory: The laboratory must be air conditioned, preferably with an AHU suitable filter (5 micron or less), For units having both sterile and nonsterile products there should be two aseptic zones having class 1,000 area with LAF and entry through graded air zones, one for inoculation and culture transfer and one for sterility testing. For units having only non-sterile products, one aseptic zone must be there.

D. Hot zone: This zone should have proper ventilation system and it consists of antoclaves, hot air oven, muffle furnance, furne cupboard etc.

E. package Material Testing Section: It should have adequate space, furniture and fixtures, required equipments and instruments etc.

F. Retained Sample Area: Proper temperature control is must in this area and this should be provided for storage and preservation.

G. Cleaning Area: Suitable facilities like running hot and cold water, purified water, different cleaning agents etc. Should be essential for this area. H. Storage area for laboratory chemicals, glass apparatus and miscellaneous items: Proper temperature control is required for this area.

I. Others: The suitable arrangements are required for Q.C. lab in different section such as vaccum, compressed air, nitrogen, potable water, purified water, ultra-pure water etc.

**2. Reference Standard and Reference Microbial Cultures**

The primary reference standards for active and inactive bulk drugs are to be procured periodically and these standards are to be preserved properly (i.e. temp, RH etc). Reference microbial cultures are to be procured from the standard institutions whenever required. These culture are to be maintained properly in the microbial lab as per instructions from the suppliers or as per pharmacopoeia.Proper documentation also required for this case.

**3. Use of Analytical Reagents and Chemicals**

They should be of analytical reagents and grades of suitable manufacturer. Documentation is crucial code in this case.

**4. Use of Volumetric Glasswares**

The all volumetric glasswares should be of two grades which are used in the laboratory. Class A are to be used for work of the highest accuracy like standardization of volumetric solutions and class B for routine work.

**5. Preparation of Standard Solutions and Reagent**

All standard solutions, reagents must have proper labels indicating name, strength, date of preparation, date of expiry and storage conditions.

**6. Calibration of Equipments and Instruments**

Calibration is the comparison of the performance of a measuring equipment/instrument with that of standard equipment/instrument. It may be divided into three categories:

a. Calibration by external agency: e.g. Pressure gauge, thermo dials, glass thermometers, wet and dry bulb hygrometers, balances etc.

b. Calibration in the laboratory: e.g. UV Vis Spectrophotometer, Polarimeter etc.

c. Calibration in the laboratory with the help of external agency: e.g. HPLC, particle counters etc.

**7. Validation of Analytical Procedure**

The various aspects are accuracy, precision, specificity, linerity and range, limit of detection, limit of quantitation, robustness, ruggedness etc.

**8. Training**

All laboratory personnel i.e. managers, supervisory staff, analyst, technical helpers etc. should have regular training and updation. Training may be two types. The first type namely formal training which included analytical chemistry, statistical techniques, microbial techniques, instrumental techniques, electronic data processing, documentation etc. The second type namely informal training which involves laboratory skills and manipulations, records of training etc.

**9. Documentation and Records**

The following documents and records are included:

- Specification
- Test procedure
- Standard operation
- Certificate of Analysis with relevant test protocols
- Sample Register.
- Register for records.
- Registered for retained samples (Both finishedproducts and active raw materials).

- Records pertaining to the preparation of solutions of reference standards, volumetric solutions and other reagents.
- Log book instruments and equipments.

**10. Safety**

The uses of mask, gloves, face shields, aprons, gumboots etc. Should be compulsory in the handling of corrosive chemicals. There should be adequate fire fighting arrangements in the laboratory and personnel should be given proper training for fire fighting.

## CONCLUSION

A final report should be prepared after the completion of each laboratory activity. The final report should be signed and dated by the laboratory director to indicate acceptance of responsibility for the validity of the data. The extent of compliances with the principles of good laboratory practice should be indicated. GLP is specific to the nonclinical health and environmental safety studies, it covers physical and chemical test systems, and gives emphasis to biological test systems**.**

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