ETHIOPIAN FOOD AND DRUG AUTHORITY

Guideline for Good Laboratory Practice

Document No.: **EFDA/GDL/062** **Version No:** **001**

Date of approval: **02 Sept 2024** **Date of First issue:** **04 Sept 2024**

Document History

Version No.	Reason for Amendment	Effective Date
001	New Version	04 Sept 2024

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ACKNOWLEDGEMENT

The Ethiopian Food and Drug Authority (EFDA) would like to acknowledge and express its appreciation to the U. S. Pharmacopeial Convention Promoting the Quality of Medicines Program (USP/PQM) for the financial and technical support delivered in the preparation of this Guideline.

The Authority would also like to give special acknowledgement to TWG members, all participants of guideline enrichment workshop and other experts for their unreserved effort to bring this document to reality.

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ABBREVIATIONS/ACRONYMS

CRO	Contract Research Organization
EFDA	Ethiopian Food and Drug Authority
GCP	Good Clinical Practice
GCLP	Good Clinical Laboratory Practice
GLP	Good Laboratory Practice
IRERC	Institutional Research Ethics Review Committee
PQM	Promoting the Quality of Medicines
QA	Quality Assurance
QAP	Quality Assurance Program
QAU	Quality Assurance Unit
SOP	Standard Operating Procedure
USP	U. S. Pharmacopeial Convention
WHO	World Health Organization

FORWARD

Preclinical research is simply, any research about a drug or treatment for a disease that occurs before it is tested by human volunteers. This encompasses everything from experiments to investigate the causes of the disease to testing potential treatments in animals, and everything in between. It is extremely important that any treatment that reaches human trials be vetted by quality preclinical research. However, there are concern about the safety and efficacy of drugs and pre-clinical research processes among members of medical profession, scientific community, regulatory authorities and the public. Therefore, any drug that makes it to a human trial must have a good reason to be there – strong, well-researched evidence based on principles of Good Laboratory practice that it has the potential for efficacy and safety in humans.

Recognizing this, the Food and Medicine Administration Proclamation No. 1112/2019 Article 27, sub-article 9 stated that, in approving investigation-medicinal products or medical device, the executive organ may require submission of laboratory experiment and animal testing data to determine its safety.

I have no doubt that with the unwavering government leadership, the commitment of the scientific community and all stakeholders the implementation of guideline will ensure compliance with the principles for Good Laboratory and guarantee having data generated under the GLP principles.

Finally, I would like to take this opportunity to acknowledge and express my appreciation to the U. S. Pharmacopeial Convention Promoting the Quality of Medicines Program (USP/PQM) for the financial and technical support; and to all those experts who have directly or indirectly extended their helping hands in the preparation of this guideline.

I also call upon interested parties to continue their support by forwarding their comments and suggestions to the EFDA P.O. Box 5681 Addis Ababa, Ethiopia., Tel.251-115524122, e-mail: contactefda@efda.gov.et.

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1. INTRODUCTION

Good Laboratory Practice guideline of the WHO, defined Good Laboratory Practice (GLP) as "a quality system concerned with the organizational process and the conditions under which nonclinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported." According to Article 27, sub-article 9 of Ethiopian Food and Medicine Administration Proclamation No.1112/2019 stated that, in approving investigation-medicinal products or medical device, the executive organ may require submission of laboratory experiment and animal testing data to determine its safety. Article 15 sub-article 9 of clinical trial directive No. 964/2023 also stated that all equipment used at the clinical trial shall be calibrated and conform to GLP. The purpose of these Principles of GLP is thus to promote the development of quality test data and to provide a managerial tool to ensure a sound approach to the management, including conduct, reporting and archiving, of laboratory studies.

The principles of GLP may be considered as a set of criteria to be satisfied as a basis for ensuring the quality, reliability and integrity of studies, the reporting of verifiable conclusions, and the traceability of data. Consequently, the Principles require institutions to allocate roles and responsibilities to improve the operational management of each study, and to focus on those aspects of study execution (planning, monitoring, recording, reporting, archiving) which are of special importance for the reconstruct ability of the whole study. Since all these aspects are of equal importance for compliance with the principles of GLP, there cannot be any possibility of using only a choice of requirements and still claiming GLP compliance. No test facility may thus rightfully claim GLP compliance if it has not implemented, and if it does not comply with, the full array of GLP rules. Irrespective of the place of study conduct, the GLP Principles generally apply to the relevant studies planned and conducted in a manufacturer's laboratories, at a contract or subcontract facility or in a university or governmental laboratory.

2. SCOPE

The principles of GLP guideline should be applied to the non-clinical safety testing of test items contained in pharmaceutical products, cosmetic products, food additives and traditional medicine. These test items are frequently synthetic chemicals, but may be of natural or biological origin and, in some circumstances, may be living organisms. The purpose of testing these test items is to obtain data on their properties and/or their safety with respect to human health and/or

the environment. Non-clinical safety studies covered by the Principles of GLP include work conducted in the laboratory. Unless specifically exempted by national legislation, these principles of GLP apply to all non-clinical safety studies required by regulations for the purpose of registering or licensing pharmaceuticals, food, cosmetic products, traditional medicines and similar products. In general, the GLP requirements for non-clinical laboratory studies conducted for safety evaluation in the field of drug safety testing cover the following classes of studies:

1. Single dose toxicity or repeated dose toxicity (sub-acute and chronic).
2. Reproductive toxicity (fertility, embryo-fetal toxicity and teratogenicity, peri-/post-natal toxicity).
3. Mutagenic potential and/or carcinogenic potential.
4. Toxicokinetic (pharmacokinetic studies which provide systemic exposure data).
5. Pharmacodynamic studies designed to test the potential for adverse effects (safety pharmacology).
6. Local tolerance studies, including photo-toxicity, irritation and sensitization studies, and testing for suspected addictivity and/or withdrawal effects of drugs.

The principles defined in this framework are also be applied equally to the analysis of a blood sample for routine safety screening of volunteers (hematology/biochemistry) as to pharmacokinetics or even the process for the analysis of ECG traces. The types of facilities undertaking analyses of clinical samples may include pharmaceutical company laboratories, Contract Research Organizations (CROs), central laboratories, pharmacogenetic laboratories, hospital laboratories, clinics, Investigator sites and specialized analytical services.

3. OBJECTIVES

The objectives of this guideline are: ·

1. To provide a framework that allows for the reconstruction of the studies, ensuring that all procedures and results can be traced and verified.
2. To establish clear roles and responsibilities for all personnel involved in the study, ensuring overall accountability.
3. To standardize procedures and practices across laboratories to ensure consistency in the conduct of studies.

4. To provide a reliable basis for assessing the safety of new compounds, including pharmaceuticals, chemicals and other products.

4. DEFINITION

- **Batch:** means a specific quantity or lot of a test item or reference item produced during a defined cycle of manufacture in such a way that it could be expected to be of a uniform character and should be designated as such.
- **Experimental starting date** means the date on which the first study specific data is collected.
- **Good Laboratory Practice (GLP):** is a quality system concerned with the organizational process and the conditions under which nonclinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.
- **Good Clinical Laboratory Practice (GCLP):** applies those principles established under GLP for data generation used in regulatory submissions relevant to the analysis of samples from a clinical trial. At the same time, it ensures that the objectives of the GCP principles are carried out. This ensures the reliability and integrity of data generated by analytical laboratories
- **Principal Investigator (PI):** means an individual who, for a multi-site study, acts on behalf of the Study Director and has defined responsibility for delegated phases of the study. The Study Director's responsibility for the overall conduct of the study cannot be delegated to the Principal Investigator(s); this includes approval of the study plan and its amendments, approval of the final report, and ensuring that all applicable Principles of Good Laboratory Practice are followed.
- **Master schedule** means a compilation of information to help assess workload and track studies at a test facility**.**
- **Quality Assurance Program (QAP):** means a defined system, including personnel, which is independent of study conduct and is designed to assure test facility management of compliance with principles of GLP.
- **Raw data:** means all original test facility records and documentation, or verified copies thereof, which are the result of the original observations and activities in a study. Raw

data also may include, for example, photographs, microfilm or microfiche copies, computer readable media, dictated observations, recorded data from automated instruments, or any other data storage medium that has been recognized as capable of providing secure storage of information for a period.

- **Reference item ("control item"):** means any article used to provide a basis for comparison with the test item.
- **Sponsor:** means an entity which commissions, supports and/or submits a non-clinical safety study.
- **Study Director** means the individual responsible for the overall conduct of the non-clinical health and environmental safety study.
- **Standard Operating Procedures (SOPs):** means documented procedures which describe how to perform tests or activities normally not specified in detail in study plans or test guidelines.
- **Short-term study:** means a study of short duration with widely used, routine techniques
- **Study plan** means a document defining the objectives and experimental design for the study and including any amendments**.**
- **Study initiation date** means the date the Study Director signs the study plan.
- **Study completion date** means the date the Study Director signs the final report.
- **Specimen:** means any material derived from a test system for examination, analysis, or retention.
- **Test item** means an article that is the subject of a study.
- **Test facility** means the persons, premises and operational unit(s) necessary for conducting the non-clinical safety study**.** For multi-site studies, conducted at more than one site, the test facility comprises the site where the Study Director is located and all individual test sites, which individually or collectively can be considered test facilities. Test facility include trial facilities for clinical research.
- **Test site** means the location(s) at which a phase(s) of a study is conducted.
- **Test facility management** means the person(s) who has the authority and formal responsibility for the organization and functioning of the test facility according to these principles of Good Laboratory Practice.

- **Test site management (if appointed):** means the person(s) responsible for ensuring that the phase(s) of the study, for which he is responsible, are conducted according to these principles of GLP.
- **Test system** means any biological, chemical or physical system or a combination thereof used in a study.
- **Vehicle:** means any agent which serves as a carrier used to mix, disperse, or solubilize the test item or reference item to facilitate the administration/application to the test system.

5. ROLE AND RESPONSIBILITIES OF STAKEHOLDERS

5.1. SPONSOR

5.1. 1 The sponsor should understand the requirements of the principles of GLP, particularly those related to the responsibilities of the test facility management and the Study Director/Principal Investigator.

5.1. 2 The sponsor should ensure that the test facility can conduct the study in compliance with GLP.

5.1. 3 The sponsor monitors contracted laboratories prior to the initiation of as well as during the study in accordance with their nature, length and complexity to ensure that its facilities, equipment, SOPs and personnel are according to GLP. If the test facility is in the national GLP compliance monitoring program, the Ethiopian national accreditation services may also be contacted to determine the current GLP compliance status of the test facility.

5.1. 4 The sponsor ensures adequate communication links exist between his/her representatives and all parties conducting a study (in case of several studies in single package), such as the Study Director, Quality Assurance Unit (QAU) and test facility management.

5.1. 5 If the test item is supplied by the sponsor, there should be a mechanism, developed in co-operation between the sponsor and the test facility, to verify the identity of the test item subject to the study and to ensure that there is no mix-up of test items.

5.1. 6 The study plan should also be approved by the test facility management and the sponsor.

5.1. 7 The sponsor should inform the test facility of any known potential risks of the test item to human health or the environment as well as any protective measures which should be taken by test facility staff.

5.1. 8 The sponsor should mention in the final report if the characterization data is not disclosed to the contracted test facility.

5.1. 9 The sponsor makes the decision on the scientific validity of the final report, based on the outcome of the studies, whether to submit a test item for registration to a regulatory authority.

5.2. TEST FACILITY MANAGEMENT

Each test facility management should ensure that these Principles of GLP are complied with, in its test facility. At a minimum it should:

5.2. 1 Ensure that a statement exists which identifies the individual(s) within a test facility who fulfills the responsibilities of management as defined by these principles of GLP.

5.2. 2 Ensure that enough qualified personnel, appropriate facilities, equipment, and materials are available for the timely and proper study.

5.2. 3 Ensure the maintenance of a record of the qualifications, training, experience and job description for each professional and technical individual.

5.2. 4 Ensure that personnel clearly understand the functions they are to perform and, where necessary, provide training for these functions.

5.2. 5 Ensure that appropriate and technically valid SOPs are established and followed and approve all original and revised SOPs.

5.2. 6 Ensure that there is a Quality Assurance Program with designated personnel and assure that the quality assurance responsibility is being performed in accordance with these principles of GLP.

5.2. 7 Ensure that for each study an individual with the appropriate qualifications, training, and experience is designated by the management as the Study Director before the study is initiated. The replacement of the Study Director should be done according to established procedures and should be documented.

5.2. 8 Ensure, in a multi-site study, that, if needed, a Principal Investigator is designated, appropriately trained, qualified and experienced to supervise the delegated phase(s) of

the study. The replacement of a Principal Investigator should be done according to established procedures and should be documented.

5.2. 9 Ensure documented approval of the study plan by the Study Director.

5.2. 10 Ensure that the Study Director has made the approved study plan available to the Quality Assurance personnel.

5.2. 11 Ensure the maintenance of an historical file of all Standard Operating Procedures.

5.2. 12 Ensure that an individual is identified as responsible for managing the archive(s).

5.2. 13 Ensure the maintenance of a master schedule.

5.2. 14 Ensure that test facility supplies meet requirements appropriate to their use in a study.

5.2. 15 Ensure for a multi-site study that clear lines of communication exist between the Study Director, Principal Investigator(s), the Quality Assurance Program(s) and study personnel.

5.2. 16 Ensure that test and reference items are appropriately characterized.

5.2. 17 Establish procedures to ensure that computerized systems are suitable for their intended purpose and validated, operated and maintained in accordance with these Principles of Good Laboratory Practice.

5.2. 18 The management should be asked to produce certain documents, such as:

A. Floor plans

B. Facility management and scientific organization charts.

C. CVs of personnel involved in the type(s) of studies selected for the study audit.

D. List(s) of on-going and completed studies with information on the type of study, initiation/completion dates, test system, method of application of test substance and name of study director.

E. Staff health surveillance policies.

F. Staff job descriptions and staff training program and records.

G. An index to the facility's standard operating procedures (SOPs).

H. Specific SOPs as related to the studies or procedures being inspected or audited.

I. List(s) of the study directors and sponsors associated with the study(ies) being audited.

J. The inspector should check.

1) Lists of on-going and completed studies to ascertain the level of work being undertaken by the test facility.
2) The identity and qualifications of the study director(s), the head of the quality assurance unit and other personnel.
3) Existence of SOPs for all relevant areas of testing.

When a phase(s) of a study is conducted at a test site, test site management (if appointed) will have the responsibilities as defined above with the following exceptions.

5.2.9 Ensure documented approval of the study plan by the Study Director.

5.2.10 Ensure that the Study Director has made the approved study plan available to the Quality Assurance personnel.

5.2.15 Ensure for a multi-site study that clear lines of communication exist between the Study Director, Principal Investigator(s), the Quality Assurance Program(s) and study personnel.

5.2.7 Ensure that for each study an individual with the appropriate qualifications, training, and experience is designated by the management as the Study Director before the study is initiated. The replacement of the Study Director should be done according to established procedures and should be documented.

5.3 STUDY DIRECTOR

The Study Director represents the single point of study control with ultimate responsibility for the overall scientific conduct of the study. Unless responsibility for the proper conduct of a study is assigned to one person, there is a potential for personnel to receive conflicting instructions, which can result in poor implementation of the study plan. There can be only one Study Director for a study at any given time. Although some of the duties of the Study Director can be delegated, as in the case of a subcontracted study, the ultimate responsibility of the Study Director as the single central point of control cannot. In this regard, the Study Director assures us that the scientific, administrative and regulatory aspects of the study are controlled. In general, the Study Director is responsible for the scientific conduct of a study and can confirm its compliance with the principles of GLP. So, the director has the following responsibilities.

5.3. 1 The Study Director must request, and coordinate resources provided by management, such as personnel, equipment and facilities, to ensure they are adequate and available as scheduled for the proper conduct of the study.

5.3. 2 The Study Director is usually the scientist responsible for study plan design and approval and overseeing data collection, analysis and reporting.

5.3. 3 The Study Director is responsible for drawing the final overall conclusions from the study. As the lead scientist, the Study Director must coordinate with other study scientists, and/or Principal Investigator(s) keeping informed of their findings during the study and receiving and evaluating their respective individual reports for inclusion in the final study report.

5.3. 4 The Study Director is responsible for ensuring that the study is carried out in accordance with the Principles of GLP, which require the Study Director's signature on the final study report to confirm compliance with the GLP Principles.

5.3. 5 Approval of the study plan which is prepared before study initiation by dated signature.

5.3. 6 For a multi-site study, the study plan should identify and define the role of any Principal Investigator(s) and any test facilities and test sites involved in the conduct of the study.

5.3. 7 The Study Director should take responsibility for the study by dated signature of the study plan, at which stage the study plan becomes the official working document for that study (study initiation date).

5.3. 8 The Study Director should also ensure that the study plan has been signed by the sponsor and the management.

5.3. 9 Before the study initiation date, the Study Director should make the study plan available to Quality Assurance (QA) staff to verify that it contains all information required for compliance with the GLP Principles.

5.3. 10 Before the experimental starting date of the study, the Study Director should ensure that copies of the study plan are supplied to all personnel involved in the study; this should include Quality Assurance (QA) staff.

5.3. 11 The Study Director ensures that the procedures laid down in the study plan, including amendments, are followed and all data generated during the study are fully documented. Specific technical responsibilities may be delegated to competent staff and need to be documented.

5.3. 12 The Study Director overviews the study procedures and data to ensure that the procedures laid down in the study plan are being followed and that there is compliance with the relevant

SOPs and should include computer generated data. To demonstrate this, the type and frequency of the reviews should be documented in the study records.

5.3. 13 All decisions that may affect the study's integrity should be approved by the Study Director.

5.3. 14 The Study Director should ensure that the data generated is fully and accurately documented and that it has been generated in compliance with GLP Principles.

5.3. 15 For data recorded electronically onto a computerized system, he/she should ensure that computerized systems are suitable for their intended purpose, have been validated, and are fit for use in the study.

5.3. 16 The final report of a study should be produced as a detailed scientific document outlining the purpose of the study, describing the methods and materials used, summarizing and analyzing data generated, and stating the conclusions drawn.

5.3. 17 If the Study Director is satisfied that the report is a complete, true and accurate representation of the study and its results, then and only then, should the Study Director sign and date the final report to indicate acceptance of responsibility for the validity of the data. He should also assure himself that there is a QA statement and that any deviations from the study plan have been noted.

5.3. 18 On completion (including termination) of a study, the Study Director is responsible for ensuring that the study plan, final report, raw data and related material are archived promptly. The final report should include a statement indicating where all the samples of test and reference items, specimens, raw data, study plan, final report and other related documentation are to be stored. Once data is transferred to the archives, the responsibility for it lies with management.

5.3. 19 In the event of sub-contracting, where parts of any study are contracted out, the Study Director (and QA staff) should have knowledge of the GLP compliance status of that facility. If a contract facility is not GLP compliant, the Study Director must indicate this in the final report.

5.4 PRINCIPAL INVESTIGATOR

In multi-site studies which involve work at more than one test site and the Study Director cannot exercise immediate supervision, study procedures may be controlled by an appropriately trained, qualified and experienced member of the staff, called the PI. He is responsible for the conduct of

certain defined phases of the study in accordance with the applicable Principles of Good Laboratory Practice, acting on behalf of the Study Director.

5.5 STUDY PERSONNEL

5.5. 1 All personnel involved in the study's conduct must know those parts of the Principles of GLP which are applicable to their involvement in the study.

5.5. 2 Study personnel will have access to the study plan and appropriate SOP applicable to their involvement in the study. It is their responsibility to comply with the instructions given in these documents. Any deviation from these instructions should be documented and communicated directly to the Study Director, and/or if appropriate, the Principal Investigator(s).

5.5. 3 All study personnel are responsible for recording raw data promptly and accurately and in compliance with these principles of GLP and are responsible for the quality of their data.

5.5. 4 Study personnel should exercise health precautions to minimize risk to themselves and ensure the study's integrity. They should tell the appropriate person any relevant known health or medical condition so they can be excluded from operations that may affect the study.

5.6 QUALITY ASSURANCE UNIT

The QAU (Quality Assurance Unit – the group of persons with a set of defined duties, mostly of an audit and control nature) is part of this total quality assurance process. The QAU's mandated role is that of an independent witness of the whole pre-clinical research process and its organizational framework. To be effective, QAU must have access to staff documents and procedures at all levels of the organization and be supported by a motivated top management.

5.6. 1 QAU reviews the protocol for completeness and clarity. At some laboratories, the QAU also signs the protocol – but this signature is not mandatory.

5.6. 2 QA should review all studies, from planning, through inspecting of ongoing studies, to reporting and archiving of documentation.

5.6. 3 The QAU receives and maintains a copy of all protocols with any subsequent amendments.

5.6. 4 QAU should review SOPs and signs to indicate that the SOP is GLP compliant, complete, clear and not in conflict with other SOPs that exist on the research site – this is not a mandatory duty.

5.6. 5 QAU must be aware of all planned studies and must have a copy of, or direct access to, the master schedule sheet (MSS – a list of all studies at the facility).

5.6. 6 The QAU plans the inspections and audits considered necessary to support the study, if necessary, with input from the Study Director. There are arguments for and against performing unannounced QA inspections, but usually inspections and audits are planned with the study director or his representative.

5.6. 7 The QAU should maintain its own inspection and audit plans.

5.6. 8 The QAU performs three types of audits/inspections:

A. Study-based inspections/audits.

B. Facility/systems-based inspections/audits.

C. Process-based inspections/audits.

5.6. 9 QA may also inspect contractors and suppliers.

5.6. 10 Promptly report any inspection results in writing to the management and to the Study Director, and to the Principal Investigator(s) and the respective management, when applicable.

5.6. 11 Prepare and sign a statement, to be included with the final report, which specifies types of inspections and their dates, including the phase(s) of the study inspected, and the dates inspection results were reported to management and the Study Director and Principal Investigator(s), if applicable. This statement would also confirm that the final report reflects the raw data.

5.6. 12 The head of the QAU should be asked to demonstrate the systems and methods for QA inspection and monitoring of studies, and the system for recording observations made during QA monitoring.

6. PRINCIPLES OF GOOD LABORATORY PRACTICE

Good laboratory practice, applied in whatever the industry targeted, stresses the importance of the following main points:

1. Resources: Organization, personnel, facilities, equipment.
2. Rules: Protocols, Standard Operating Procedures, concept of the Study Director as the pivotal point of study control.
3. Characterization: Test items, test systems.
4. Documentation: Raw data, final report, archives.

5. Quality assurance: Independence from study conduct.

Although most GLP guidelines apply formally only to nonclinical safety studies, general principles of GLP in this guideline should also be followed during the bio-analytical part of BE studies.

6.1 ORGANIZATION AND PERSONNEL

6.1.1 ORGANIZATION STRUCTURE

GLP regulations require the research organization's structure and the research personnel's responsibilities to be clearly defined. The test facility must have sufficient qualified personnel, staff resources and support services for the variety and number of studies undertaken; the organizational structure is appropriate; and management has established a policy regarding training and staff health surveillance appropriate to the studies undertaken in the facility to perform the tasks required in a timely and GLP compliant way.

The responsibilities of all personnel should be defined and recorded in job descriptions, and their qualifications and competence defined in training and education records. GLP attaches considerable importance to staff qualifications and to internal and external training given to personnel to maintain levels of excellence. A point of major importance in GLP is the position of the Study Director, who is the pivotal point of control for the whole study. This individual will have to assume full responsibility for the GLP compliance of all activities within the study. She/he will have to assert this at the end of the study in a dated and signed compliance statement. She/he has therefore to be aware of all occurrences that may influence the quality and integrity of the study, to judge their impact and to institute corrective actions, as necessary.

6.1.2 TRAINING AND QUALIFICATION

Management is responsible for overall organization of the test facility. With respect to personnel, this organization is usually reflected in the organization chart. This is often the first document requested by authority to obtain an idea of how the facility functions. GLP requires personnel to have the competence (education, experience, training) necessary to perform their functions. Personnel competence is reflected in job descriptions, curricula vitae (CVs) and training records. These documents should be defined in SOPs, regularly updated, and verified in QA audits. The contents of job descriptions should correspond to the qualifications as described in the CV. In addition, they should be:

1. Updated at a minimum required interval (fixed by an SOP).
2. Signed by the person occupying the post and by at least one appropriate member of management supervising the post.
3. Rules of delegation should be defined at the test facility. Tasks can be delegated, but the final responsibility remains with the person who delegates the task.
4. A review of all job descriptions annually, or in the event of any reorganization, helps a facility's management to ensure that their organization is coherent.
5. A procedure should ensure that CVs:
    a. Exist for all personnel in a standard approved format.
    b. Are kept up to date.
    c. Exist in required languages (local and sometimes English for regulatory submissions).
    d. Are carefully archived to ensure historical reconstruction.

All staff should have a CV. Even if some staff do not have extensive qualifications, they will have professional experience which should be listed in their CV.

It is usual to include in a CV:

1. Name, age, sex of the person.
2. Education, including diplomas and qualifications awarded by recognized institutions.
3. Professional experience both within the institution and before joining it.
4. Publications.
5. Membership of associations.
6. Languages spoken.

Finally, training records complement CVs and job descriptions. GLP explicitly requires that all personnel understand GLP, its importance, and the position of their own job within GLP activities. Training must be formally planned and documented. New objectives and new activities always involve some training. Training systems are usually SOP-based. A new SOP therefore requires new certification of the personnel involved. Some companies have advanced training schemes linking training to motivation, professional advancement and reward. The training system will have elements common to all GLP management systems i.e. it will be formal, approved, documented to a standard format, described in a SOP, and with historical reconstruction possible through the archive.

6.2 FACILITIES

GLP principles emphasize that facilities must be sufficient and adequate to perform the studies. The facilities should be spacious enough to avoid problems such as overcrowding, cross contamination or confusion between projects. Utilities (water, electricity etc.) must be adequate and stable.

6.2.1 BUILDINGS

Test facilities should be of suitable size, construction and location to meet the requirements of the study and to minimize disturbances that could interfere with the study. They should be designed to provide an adequate degree of separation of the diverse elements of the study.

These requirements are to ensure the study is not compromised due to inadequate facilities. It is important to fulfill the requirements of the study and carefully consider whether the objectives of the study can be achieved using the facilities available. Separation ensures that disturbances are minimized and that different activities do not interfere with one another or adversely affect the study. This can be achieved by:

A. Physical separation, e.g. walls, doors, filters or separate cabinets or isolators. In new buildings, or those recently renovated, separation will be part of the design.
B. Organizational separation, e.g. carrying out different activities in the same area but at different times, allowing for cleaning and preparation between operations, maintaining separation of staff, or by establishing defined work areas within a laboratory.

As an illustration of the GLP principles involved, the following shall be considered:

A. Pharmacy and dose mixing areas: concerned with test material control and mixing with vehicles. The same considerations would apply to other areas such as analytical or histopathology laboratories.
B. Animal facilities.
C. Laboratory biosafety and GLP.

A. PHARMACY AND DOSE MIXING AREAS

The Pharmacy and Dose Mixing area is a laboratory zone dealing with test item workflow: receipt, storage, dispensing, weighing, mixing, dispatch to the animal house and waste disposal.

Size: The area should be adequate to accommodate the number of staff working in it and allow them to carry on their work without the risk of getting in one another's way or of mixing up different materials. Each operator should have a workstation sufficiently large to enable him/her

to carry out the operation efficiently. To reduce the chance of mix-up of materials or of cross-contamination, there should also be a degree of physical separation between the workstations. The pharmacy is a sensitive area, and access to such facilities should be restricted to limit the possible contamination of one study or compound by another.

CONSTRUCTION: The zone must be built of materials that allow easy cleaning and that are not likely to allow test materials to accumulate and contaminate one another. There should be a ventilation system that provides airflow away from the operator through filters which both protect personnel and prevent cross-contamination. Most modern dose mix areas are now designed in a "box" fashion, each box having an independent air system.

ARRANGEMENT: There should be separate areas for storage of test items under different conditions. storage of control items, handling of volatile materials, weighing, mixing of different dose formulations, e.g. in the diet or as solutions or suspensions, storage of prepared dose formulations, cleaning equipment, offices and refreshment rooms, changing rooms.

B. ANIMAL FACILITY

The facility should be designed and operated to minimize environmental variables' effects on the animal. Consideration should also be given to measures which prevent the animal from encountering disease, or with a test item other than the one under investigation. Requirements will differ depending on the studies' nature and duration. The risks of contamination can be reduced by a "barrier" system, where all supplies, staff and services cross the barrier in a controlled way, as well as by providing "clean" and "dirty" corridors for the movement of new and used supplies.

A well-designed animal house would maintain separation by providing areas for: different species, different studies, quarantine, changing rooms, receipt of materials, storage, cleaning equipment, necropsy, laboratory procedures, utilities and waste disposal. The building and its rooms should provide enough space for animals and studies to be separated and to allow the operators to work efficiently.

The environment and control system should maintain the temperature, humidity and airflow at the defined levels depending on the species concerned. The surfaces of walls, doors, floors and ceilings should be constructed to allow for easy and complete cleaning, and there should be no gaps or ledges where dirt and dust can build up, or where water will collect, for instance on

uneven floors. Sensible working procedures reduce potential danger to the study from outside influences and maintain a degree of separation between activities. Adequate separation can be achieved by:

1. Minimizing the number of staff allowed to enter the building.
2. Restricting entry into animal rooms.
3. Organizing workflow to move clean and dirty materials around the facility at different times of day.
4. Requiring staff to put on different clothing in different zones within the facility.
5. Ensuring that rooms are cleaned and sanitized regularly, particularly between studies.

C. LABORATORY BIOSAFETY AND GLP

Originally, GLP regulations were intended for toxicity testing only and were reserved for laboratories undertaking animal studies for pre-clinical work. Establishment of GLP is mandatory to evaluate safety or toxicity of products intended to undergo clinical trials. Laboratories should have the required facility to handle biological or chemical agents based on their potential to cause harm to humans, animals, and the environment.

6.3 EQUIPMENT, APPARATUS, MATERIAL, AND REAGENT

6.3.1 All equipment must be in working order; a program of validation/qualification, calibration and maintenance attains this. For the proper conduct of the study, appropriate equipment of adequate capacity must be available. All equipment should be suitable for its intended use, and it should be properly calibrated and maintained to ensure reliable and accurate performance. Records of repairs and routine maintenance and of any non-routine work should be retained.

SUITABILITY: Deciding on the suitability of equipment is a scientific responsibility and is usually defined in SOPs.

CALIBRATION: All equipment, whether it is used to generate data (e.g. analytical equipment or balances), or to maintain standard conditions (e.g. refrigerators or air conditioning equipment), should work to fixed specifications. Verification should be performed at a frequency that allows action to be taken in time to prevent any adverse effect on the study should it be discovered that the equipment is not operating within specifications.

MAINTENANCE: The requirement that equipment be properly maintained is based on the assertion that this ensures the constant performance of equipment to specifications and that it

reduces the likelihood of an unexpected breakdown and consequent loss of data. Maintenance may be carried out in two quite distinct ways:

A. Preventive maintenance: when parts are changed regularly based upon the expected life of the part concerned. Planned maintenance of this type may be a useful precaution for large items of equipment or items that do not possess suitable backup or alternatives.
B. Curative maintenance: when repairs are made in the case of a fault being detected.

Back-up for vital equipment should be available whenever possible as well as back-up in the event of service failures, such as power cuts. A laboratory should be able to continue with essential services to prevent animals or data being lost, and studies irretrievably affected. Early warning that equipment is malfunctioning is important; hence the checking interval should be assigned to assure this. Alarms are valuable, particularly if a problem occurs when staff are not present in the laboratory.

6.3.2 Apparatus, including validated computerized systems, used for the generation, storage and

retrieval of data, and for controlling environmental factors relevant to the study should be suitably located and of appropriate design and adequate capacity.

6.3.3 Apparatus 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, where appropriate, be traceable to national or international standards of measurement.

6.3.4 Apparatus and materials used in a study should not interfere adversely with the test systems.

6.3.5 Chemicals, reagents, and solutions should be labeled to indicate identity (with concentration if appropriate), expiry date and specific storage instructions. Information concerning source, preparation date and stability should be available. The expiry date may be extended based on documented evaluation or analysis.

6.4 TEST SYSTEMS

Test systems are the tools with which the purpose of the study, the search for, and the investigation of, effects produced by a test item, or the elucidation of its properties can be fulfilled. Test systems may therefore be “any biological, chemical or physical system or a combination thereof used in a study”. Since the test systems are the instruments for the

generation of the safety data, documented evidence for their adequacy and integrity, as well as their properties must be provided to ensure the scientific validity of the studies conducted.

6.4.1 PHYSICAL/CHEMICAL

6.4.1.1 Apparatus used for the generation of physical/chemical data should be suitably located and of appropriate design and adequate capacity.

6.4.1.2 The integrity of the physical/chemical test systems should be ensured.

6.4.2 BIOLOGICAL

6.4.2.1 Proper conditions should be established and maintained for the storage, housing, handling and care of biological test systems to ensure the quality of the data.

6.4.2.2 Newly received animals, plants and other test systems should be isolated until their health status has been evaluated. If any unusual mortality or morbidity occurs, this lot should not be used in studies and, when appropriate, should be humanely destroyed. At the experimental starting date of a study, test systems should be free of any disease or condition that might interfere with the purpose or conduct of the study. Test systems that become diseased or injured during a study should be isolated and treated, if necessary, to maintain the study's integrity. Any diagnosis and treatment of any disease before or during a study should be recorded.

6.4.2.3 Records of source, date of arrival, and arrival condition of test systems should be maintained.

6.4.2.4 Biological test systems should be acclimatized to the test environment for an adequate period before the first administration/application of the test or reference item.

6.4.2.5 All information needed to properly identify the test systems should appear on their housing or containers. Individual test systems that are to be removed from their housing or containers during the conduct of the study should bear appropriate identification, wherever possible.

6.4.2.6 During use, housing or containers for test systems should be cleaned and sanitized at appropriate intervals. Any material that encounters the test system should be free of contaminants at levels that would interfere with the study. The bedding for animals should be changed as required by sound husbandry practice. The use of pest control agents should be documented.

6.4.2.7 Test systems used in field studies should be located to avoid interference in the study from spray drift and from past usage of pesticides.

6.5 TEST AND REFERENCE ITEMS

The term test item "means an article that is the subject of a study", as it is expressed in the concise definition of the OECD Principles. This test item may be anything from a pure chemical substance to a complex preparation, a device or an organism, of which the properties regarding safety aspects are to be evaluated.

6.5.1 RECEIPT, HANDLING, SAMPLING AND STORAGE

6.5.1.1 Records including test item and reference item characterization, date of receipt, expiry date, batch number, quantities received and used in studies should be maintained.

6.5.1.2 Handling, sampling, and storage procedures should be identified so that homogeneity and stability are assured, and contamination or mix-ups are precluded.

6.5.1.3 The storage container(s) should carry identification information, expiration dates and specific storage instructions.

6.5.2 CHARACTERIZATION

6.5.2.1 Each test and reference item should be appropriately identified (e.g., code, Chemical Abstracts Service Registry Number [CAS number], name, biological parameters).

6.5.2.2 For each study, the identity, including batch number, purity, composition, concentrations, or other characteristics to appropriately define each batch of the test or reference items should be known.

6.5.2.3 In cases where the test item is supplied by the sponsor, there should be a mechanism, developed in co-operation between the sponsor and the test facility, to verify the identity of the test item subject to the study.

6.5.2.4 The stability of test and reference items under storage and test conditions should be known for all studies.

6.5.2.5 If the test item is administered or applied in a vehicle, the homogeneity, concentration and stability of the test item in that vehicle should be determined. For test items used in field studies (e.g., tank mixes), these may be determined through separate laboratory experiments.

6.5.2.6 A sample for analytical purposes from each batch of test items should be retained for all studies except short-term studies.

6.6 PROTOCOL AND WORKING PROCEDURES

6.6.1 STANDARD OPERATING PROCEDURES (SOPS)

6.6.1.1 A test facility should have written Standard Operating Procedures 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.

6.6.1.2 Each separate test facility unit or area should have immediately available current Standard Operating Procedures relevant to the activities being performed therein. Published textbooks, analytical methods, articles and manuals may be used as supplements to these Standard Operating Procedures.

6.6.1.3 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), as applicable.

6.6.1.4 Standard Operating Procedures should be available for, but not be limited to, the following categories of test facility activities.

- SOP for receipt, identification, labeling, handling, sampling and storage of Test and Reference Items.
- SOP for apparatus use, maintenance, cleaning and calibration.
- SOP for Validation, operation, maintenance, security, change control and back-up Computerized Systems.
- SOP for Preparation and labeling of materials, reagents and solutions.
- SOP for record keeping reporting, storage, and retrieval.
- SOP for coding of studies, data collection, preparation of reports, indexing systems, handling of data, including the use of computerized systems.
- SOP for room preparation and environmental room conditions for the test system.
- SOP for procedures for receipt, transfer, proper placement, characterization, identification and care of the test system.
- SOP for test system preparation, observations and examinations, before, during and at the conclusion of the study.
- SOP for handling of test system individuals found moribund or dead during the study.

- SOP for collection, identification and handling of specimens including necropsy and histopathology.
- SOP for siting and placement of test systems in test plots.
- SOP for operation of Quality Assurance personnel in planning, scheduling, performing, documenting and reporting inspections.

6.6.2 PROTOCOL OR STUDY PLAN

The protocol is the central document through which the study director communicates the objectives and conduct of the study to the study staff and to third parties (such as the quality assurance unit [QAU] or the study sponsor). In the case of a study performed by a contract research organization (CRO), the protocol may also be contractual. The protocol contains the overall experiment plan with time frame, a description of the study design with methods and materials and the responsibilities of the scientific staff concerned.

The study plan or protocol outlines the design and conduct of the study and provides evidence that the study has been properly thought through and planned: the principal steps of studies conducted in compliance with GLP are thus described in the study protocol. The protocol must be approved by the Study Director, by dated signature, before the study starts. Alterations to the study design can only be made through formal amendment procedures. All this will ensure that the study can be reconstructed at a later point in time. The GLP Principles list the essential elements to be included in a study protocol.

CONTENT OF THE PROTOCOL

The protocol's content is designed to meet the scientific requirements of the study and to comply with GLP.

IDENTIFICATION:

The study identification number, or the number attributed to the protocol, must provide a means of uniquely identifying the study in the records of the laboratory and of confirming the identity of all data generated during the study. There are no set rules for the system to use for identification.

TITLE AND STATEMENT OF PURPOSE:

It is important to state why a study is being performed. A study must be planned and designed in advance.

IDENTIFICATION OF TEST (AND CONTROL) ITEMS

This includes not only the chemical name and/or code number of the test item but also its specifications or characterizations or details about how these will be determined if they are not yet available. The protocol must also detail any control materials to be used in addition to the vehicle.

NAME OF SPONSOR AND ADDRESS OF TEST FACILITY:

The sponsor and the test facility may or may not be the same company. The protocol should indicate where the test is to be done and include the address of any consultants involved. The name of the sponsor should also be included.

NAME OF STUDY DIRECTOR AND OTHER RESPONSIBLE PERSONNEL:

The name of the study director must be included in the protocol. It is good practice to identify any other responsible scientists who will contribute significantly to the study. Most laboratories include the names of scientists who will be responsible for the interpretation of the data generated under their responsibility (e.g. pathologists, clinical pathologists). For contracted studies, it is usual to include the name of the monitor or contact person for the sponsor.

PROPOSED DATES:

The proposed dates for the study are the start and finish dates (corresponding to the date when the protocol is signed and the date when the report is signed by the study director) and the experimental dates. These correspond to the dates when the first and last experimental data are collected. To help study personnel perform their work, the protocol may include a more detailed time plan. This may be produced separately.

6.7 PERFORMANCE OF THE STUDY

Conducting studies according to the rules of GLP will be the final effort needed to place a test facility under the realm of the GLP Principles. The GLP Compliance Monitoring Authorities will in most cases insist on the presentation of some GLP studies before a final judgement on the compliance of the respective test facility can be made.

A unique identification should be given to each study. All items concerning this study should carry this identification. Specimens from the study should be identified to confirm their origin. Such identification should enable traceability, as appropriate for the specimen and study.

6.7.1 The study should be conducted in accordance with the study plan.

6.7.2 All data generated during the study should be recorded directly, promptly, accurately, and legibly by the individual entering the data. These entries should be signed or initialed and dated.

6.7.3 Any change in the raw data should be made so as not to obscure the previous entry, should indicate the reason for change and should be dated and signed or initialed by the individual making the change.

6.7.4 Data generated as a direct computer input should be identified at the time of data input by the individual(s) responsible for direct data entries. Computerized system design should always provide for the retention of full audit trials to show all changes to the data without obscuring the original data. It should be possible to associate all changes to data with the persons having made those changes, for example, by use of timed and dated (electronic) signatures. Reason for changes should be given.

6.8 REPORTING OF STUDY RESULTS

Laboratories should have descriptive documents describing what happened during the experimentation. The records are the qualitative and quantitative results of the study. The Study Director uses the records as the basis for the scientific interpretation of the study. This interpretation and accurate data representation will be incorporated into the final report of the study. The authorship of the final report is the responsibility of the Study Director. At study completion, all the documents, both prescriptive and descriptive, are archived so that when necessary full study reconstruction will be possible through examining the archived material.

6.8.1 CARRYING OUT PROCEDURES AND RECORDING OBSERVATIONS

Before any procedure is conducted in a study, the Study Director will have ensured that:

- Enough adequately trained and experienced staff are available.
- Staff have read and understood the protocol and a copy is present at the site where the procedures will be performed.
- SOPs are available in the work areas.
- Necessary equipment and supplies are available.
- Data recording forms are available in the work area.

Before starting any procedure requiring equipment of any kind, the operator should check that the equipment is in working order. The operator should ensure that such checks have been done with reference to the appropriate logbook or equipment label.

6.8.2 RECORDS AND RECORDING

Making a record is essential for complete reconstruction of the study. Records must not only contain the data generated, but also prove that all the required procedures were correctly carried out at the correct time. If raw data is lost, or a complete record has not been made, the study validity may be seriously compromised.

Raw data, also called source data, are essential for the reconstruction of studies and contribute to the traceability of the events of a study. They are the results of the experiment on which the study's conclusions will be based. Some of the raw data will be treated statistically, while others may be used directly. Whatever the case, the results and their interpretations provided by the scientist in the study report must be a true and accurate reflection of the raw data. The data should therefore indicate:

WHAT was done: A description of the technique's conduct, including the results of the observation or measurement, and demonstrating that the actions required by the protocol were done.

HOW it was done: The data should indicate that they were collected and recorded in accordance with the methods set out in the SOPs and Protocol or indicate where there were deviations from these instructions.

WHEN the work was performed: A demonstration of compliance with the schedule defined in the protocol. This is done by recording the date and, if necessary, the time that the procedure was conducted. For certain procedures (for example sampling in a toxicokinetic study) very exact timing is necessary and the data must demonstrate that the schedule was strictly followed.

WHO performed the work: The data should clearly identify who was responsible for carrying out the procedure and recording the data. If more than one person is involved in a procedure, this should be recorded in the data and identified the responsibilities of each. All data generated during the conduct of a study should be identified and recorded directly, promptly, accurately, legibly and indelibly by the person entering the data, and be signed or initialed, and dated. Any changes should be made so as not to obscure the previous entry and should indicate the reason for such a change. The person making the change must sign and date it.

Identified: The study number, animal number, etc. must be recorded with the data to ensure that data mix-ups do not occur. The parameter evaluated must be identified.

Directly: Since the first written records are considered to constitute the raw data and must be retained, records should not be made on scraps of paper and then transcribed into a final form. When data is acquired directly by computer, the raw data is considered an electronic medium. For data derived from equipment, the raw data may be a direct print out (or trace) or in an electronic form.

Promptly: Data must be recorded as the operation is done. It is not acceptable to make the record sometime after the task has been completed.

Accurately: This is most important as accuracy underpins the scientific interpretation and integrity of the study.

Legibly: Data that cannot be read are useless and records that are difficult to decipher raise doubts as to their credibility.

Indelibly: Use indelible and waterproof ink; ballpoint pens are well suited for the purpose. Check the robustness of machine-print outs. Some print disappears quickly (or becomes totally black) as is the case with light-sensitive printouts from thermo-printers. In this case, take an authorized (signed and dated) photocopy for storage.

Signed: Accountability is one of the basic tenets of GLP, hence the need for a record of who did every job on a study.

Dated: The date of each signature demonstrates that the procedure was conducted and recorded at the correct point in the study.

Reasons for corrections: Records may require alteration from time to time, but a clear audit trail is needed showing why a change was carried out, when and by whom. Data should be recorded in a logical way, and duplication should be avoided wherever possible. A clear structure for the study file, defined upfront, helps to organize and archive the documents as they are produced in real-time, preventing loss and facilitating reference between records.

6.8.3 THE STUDY REPORT

The Study Director must ensure that the study report describes the study accurately. The Study Director is responsible for the scientific interpretation included in the study report and is also responsible for declaring to what extent the study was conducted in compliance with the GLP Principles.

The report of the study, approved by the Study Director, contains an account of the practical conduct of the study, any deviations from the intended course of action, tabulated results, a

presentation of the significant features and results of the experiment, a critical discussion and a conclusion. When the report relates to a multi-site study, the Principal Investigator's contribution about the phase concerned may be appended to the report or incorporated into the body of the report. In either case, the Study Director takes responsibility for the entire report, including the scientific interpretation and the GLP compliance of the work. There are also specific elements required by GLP which must be in the study report:

- Name and address of test facility.
- Dates of start and finish of experimental work.
- Name of Study Director.
- Study objectives.
- Details of test item(s) and vehicle(s).
- Description of test system.
- Details of dosing, route and duration.
- Results.
- Statistics.
- Discussion.
- References.
- GLP Compliance Statement from Study Director.
- QA statement of Inspections/Audits
- Signed/dated reports from responsible scientists.

"The report should fully and accurately reflect the raw data..." This means that everything which happened during the study should be reported, but does not necessarily mean that every, single item of raw data must be included in the report. The report should certainly include any aspects where the study conduct deviated from that laid down in the protocol or SOPs, whether this is considered to have impacted on the study integrity or not.

The report may include input from experts other than the Study Director, such as specialists within the laboratory or from outside, consultants or Sponsor. These may be included and signed by those specialists. Data supplied from outside sources should comply with GLP. If this is not the case, then this should be identified in the Study Director's statement.

After the report has been drafted it will pass through a review stage and a QA audit. During this, modifications may be made to the report, but any alterations made must be agreed and accepted by the Study Director. The process of review and approval is designed to ensure that the report, when finalized, is unlikely to require modification: after finalization this can only be achieved by writing a formal amendment, approved and signed by the Study Director, which identifies the changes made with a reason for each.

6.9 STORAGE AND RETENTION OF RECORDS AND MATERIALS

A study may have to be reconstructed many years after it has ended. Thus, the storage of records must enable their safekeeping for long periods of time without loss or deterioration and, preferably, in a way which allows quick retrieval. To promote safe storage of precious data, it is usual practice to restrict access to archive facilities to a limited number of staff and to record the documents logged in and out. Even if access is restricted to certain staff, records are also kept of the people entering and leaving the archives. At the end of every study, all data should be collected with the study plan and final report and combined into a single package of information – the study file. The study file should then be formally archived to guarantee the data and study's integrity. The archiving process is of such importance that GLP requires the test facility management to formally designate an archivist; this named person should be included in the organizational chart and have appropriate qualifications and training.

When multi-site studies are performed, a decision must be taken about the location(s) where data from the geographically separate test sites will be archived. There are no set rules about this, though most facilities like to centralize the data at a single site. However, the place(s) where the archives are located must be given in the final study report and it should also be defined ahead of time in the study plan. The following should be retained in the archives for the period specified by the appropriate bodies:

a) The study plan, raw data, samples of test and reference items, specimens, and the final report of each study
b) Records of all inspections performed by the Quality Assurance Program, as well as master schedules
c) Records of qualifications, training, experience and job descriptions of personnel.
d) Records and reports of the maintenance and calibration of apparatus.
e) Validation documentation for computerized systems.

f) The historical file of all Standard Operating Procedures.

g) Environmental monitoring records.

6.9.1 "WHEN" AND BY "WHOM" ARE ARCHIVES SUBMITTED?

The Study Director or his designer is responsible for verifying the completeness of the collation/inventory and presenting all study relevant materials to the Central Archive. This is required soon after final report approval. If archival requirements are not followed, the Central Archive may refuse to accept the submission.

6.9.2 TERM OF STORAGE

The retention period shall be based on the data retention policy of the authority. Often, however, because reports may be needed for other purposes, the period of retention may exceed these. Each event of archive destruction must, therefore, be treated on a case-by-case basis. This policy reflects the varying retention schedules required by different GLP texts, coupled with the possible internal need to consult old data for product improvement/liability or scientific reasons. Therefore, laboratories impose strict destruction policies. When a space problem arises, very old holdings and abandoned projects belonging to chemical families holding no current interest may be destroyed upon justification and written authorization of upper management. If a company goes out of business, product license holders should be notified, and archival responsibility transferred.

6.9.3 HOW" ARE HOLDINGS SUBMITTED AND STORED?

All records and material transferred to the Archives should be personally transported by designated persons. The originals of all documents should be submitted. All material submitted should be accompanied by a document submission form and the record should be stored in;

1. Securely: Only authorized personnel are permitted.
2. Fire, pests and vandalism protection.
3. Under conditions which minimize deterioration:
4. Blocks sealed; tissues wrapped in preservative-soaked gauze on heat sealed bags, slides cover slipped, etc.
5. Computer backups are maintained in the security cabinet.

6.9.4 INDEXING

As rapid retrieval may be necessary, it is good practice to impose a rigorous system of indexing archived material. This is often computerized and provides complete and quick retrieval starting from any one of the indexed parameters.

6.9.5 RETRIEVAL FROM ARCHIVES

Once an item has become an official Central Archives holding, the original should be subject to restricted access. It can be examined in situ with formal authorization but only within the Central Archives area, and in the presence of the archivist. Photocopies may be provided upon request.

Removal of original holdings from the Central Archive will be allowed only under exceptional circumstances when justified and authorized in writing by upper management. The history of each holding must be documented.

7. REFERENCE

1. Handbook for Good Laboratory Practice, quality practices for regulated non-clinical research and development, UNDP/WORLD BANK/WHO, Special Program for Research and Training in Tropical Disease (TDR).
2. OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring Number 1 OECD Principles on Good Laboratory Practice (as revised in 1997).
3. ICH Harmonized Tripartite Guideline Safety Pharmacology Studies for Human Pharmaceuticals S7A Current Step 4 version dated 8 November 2000.
4. Good Laboratory Practice – the Why and the How Riedtwil, June 2000 Jürg P. Seiler, Switzerland.
5. Good Clinical Laboratory Practice (GCLP) Special Program for Research & Training in Tropical Diseases (TDR) sponsored by UNICEF/UNDP /World Bank /WHO.
6. Training Manual, Good Laboratory Practice (GLP), WHO Special Program for Research and Training in Tropical Diseases 2008, Second Edition.

8. LIST OF WORKSHOP PARTICIPANTS

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Dr. Abule Takele	Secretary of National Research Ethics Review Board (NRERB)	Ministry of Education
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