



GOOD LABORATORY PRACTICE FOR NATIONAL PHARMACEUTICAL CONTROL LABORATORIES

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GOOD LABORATORY PRACTICE
CONTENTS

	PAGE
SECTION ONE: INTRODUCTION	1
1. Scope.	
1.2 Definitions of Terms	
SECTION TWO: GOOD LAB. PRACTICE PRINCIPLES	6
1. Test Facility Organization and Personnel:	6
1.1 Management's Responsibilities.	
1.2 Study Director's Responsibilities.	
1.3 Personnel Responsibilities.	
2. Q. A. Program:	9
2.1 General.	
2.2 Responsibility of Q. A. Personnel.	
3. Facilities:	11
3.1 General.	
3.2 Test System Facilities.	
3.3 Facilities for Handling test and Reference Substances.	
3.4 Archive Facilities.	
3.5 Waste Disposal.	
3.6 Animal Care Facilities.	
3.7 Animal Supply Facilities.	

4. Equipment, Reagents and Animals:	14
4.1 Equipment.	
4.2 Reagents & Solutions.	
4.3 Animal Care.	
5. Test and Reference Substance:	18
5.1 Receipt, Handling, Sampling and Storage.	
5.2 Characterization.	
6. Standard Operating procedures:	19
6.1 General.	
6.2 Applications.	
7. Performance of the Study:	21
7.1 Study plan (Protocol).	
7.2 Content of the Study Plan.	
7.3 Conduct of the Study.	
8. Records and Reports:	23
8.1 Reporting of Study results.	
8.2 Content of the Final Report.	
8.3 Storage and Retention of Records and Materials.	
SECTION THREE: INSPECTION AND AUDITS	28
1. Pre-inspection.	
2. Conduct and operation of inspection.	
SECTION FOUR: GLP GUIDELINES-CHECKLIST	43
REFERENCES.	58

GOOD LABORATORY PRACTICE FOR NATIONAL PHARMACEUTICAL CONTROL LABORATORIES

SECTION 1: INTRODUCTION

1. SCOPE:-

- These principles of Good Laboratory Practice should be applied to testing of pharmaceutical products to obtain data on their properties and/or their safety with respect to human health or the environment.
- Studies covered by Good Laboratory Practice also include work conducted in field studies.
- These data would be developed for the purpose of meeting regulatory requirements.

2. DEFINITIONS OF TERMS

2.1 Good Laboratory Practice

Good Laboratory Practice (GLP) is concerned with the organizational process and the conditions under which laboratory studies are planned, performed, monitored, recorded, and reported.

2.2 Terms Concerning the Organization of a Test Facility

- **Test facility** means the persons, premises, and operational unit(s) that are necessary for conducting the study.
- **Study director** means an individual who is designated by the management responsible for the overall conduct of the study and in

charge of the technical advice on the study, the analysis and interpretation of the result, and the record and report of the study.

- **Sponsor** means a person (s) or entity who commissions and/or supports a study.
- **Quality Assurance Programme** means an internal control system designed to ascertain that the study is in compliance with these principles of good laboratory practice.
- **Standard Operating Procedures (SOPs)** means written procedures which describe how to perform certain routine laboratory tests or activities normally not specified in detail in study plans or test guidelines.
- **Laboratory** means a test facility which conducts or which intends to conduct safety studies.
- **Premises** in relation to a laboratory, includes field sites at which safety studies are conducted.
- **Monitoring authority** means any national conducts or which is responsible (either solely or jointly with other such authorities) for monitoring adherence to the principles of good laboratory practice.
- **Regulatory authority** means any national authority with legal responsibility for aspects of the control of chemicals, biological and pharmaceutical products.

- **Regulatory study** means a non-clinical experiment or set of experiments.
 - In which a substance is examined to evaluate its safety with respect to human health, animal health or the environment.
 - In relation to which a Community provision provides for the application of the principles of good laboratory practice in respect of that experiment or set of experiments.
- **Testing facility management** means an individual responsible for the overall operation of a testing facility.
- **Quality assurance unit** which is a part of a testing facility, means any person or organizational element in order to perform duties related to quality assurance of a study.
- **Archives** mean a facility for the storage and retrieval of protocols, specimens, raw data, documentation records and final reports.
- **Master schedule sheet** means a document indexed by a test substance containing the test system, nature of study, date study was initiated, current status of each study, name of the sponsor, name of the study director, and status of the final report on all studies conducted at the test facility.

2.3 Terms Concerning the Study

- **Study** means an experiment or set of experiments in which a test substance is examined to obtain data on its properties and/or its safety with respect to human health and the environment.
- **Study plan** means a document which defines the entire scope of the study.
- **Test system** means any animal, plant, microbial, as well as other cellular, sub-cellular, chemical, or physical system or a combination thereof used in a study.
- **Protocol** means a document established in each study which is to ensure that the study methods and operating procedures required to attain the intended purpose of the study will be authentically adopted.
- **Experimental starting date** means the date on which the first study specific data are collected.
- **Experimental completion date** means the last date on which data are collected from the study.
- **Raw data** means any laboratory worksheets, notes, unretouched records, or exact transcripts thereof, etc. which record original observations and activities in a study and are necessary for the reconstruction and evaluation of the report of that study photographs, microfilm copies, computer printouts, magnetic media, including

dictated observations, and recorded data from automated instruments, etc. may be included.

- **Final report** means a record which is prepared finally to compile the result of the study conducted in the testing facility.

2.4 Terms Concerning the Test Substance

- **Test substance** means a chemical substance or a mixture which is under investigation.
- **Reference substance (control substance)** means any well defined chemical substance or any mixture other than the test substance used to provide a basis for comparison with the test substance.
- **Batch** means a specific quantity or lot of a test or reference substance 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.
- **Vehicle (carrier)** means any agent which serves as a carrier used to mix. Disperse or solubilise the test or reference substance to facilitate the administration the test system.
- **Sample** means any quantity of a test or reference substance.
- **Specimen** means any material derived from a test system for examination, analysis, or storage.

SECTION II:

GOOD LABORATORY PRACTICE PRINCIPLES

1. TEST FACILITY ORGANIZATION AND PERSONNEL

1.1 Management's responsibilities

1. Test facility management should ensure that the principles of good laboratory practice are complied with in the test facility.
2. At minimum it should:
 - a. Ensure that qualified personnel, appropriate facilities, equipment, and materials are available.
 - b. Maintain a record of the qualifications, training, experience and job description for each professional and technical individual.
 - c. Ensure that personnel clearly understand the functions they are to perform and, where necessary, provide training for these functions.
 - d. Ensure that health and safety precautions are applied according to national and/or international regulations.
 - e. Ensure that appropriate standard operating procedures are established and followed.
 - f. Ensure that there is a quality assurance programme with designated personnel.
 - g. Where appropriate, agree to the study plan in conjunction with the sponsor.
 - h. Ensure that amendments to the study plan are agreed upon and documented.

- i. Maintain copies of all study plans.
- j. Maintain a historical file of all standard operating procedures.
- k. For each study ensure that a sufficient number of personnel is available for its timely and proper conduct.
- l. For each study designate an individual with the appropriate qualifications, training, and experience as the study director before the study is initiated. If it is necessary to replace a study director during a study, this should be documented.
- m. Ensure that an individual is identified as responsible for the management of the archives.

1.2 Study Director's Responsibilities

- 1. The study director has the responsibility for the overall conduct of the study and for its report.
- 2. These responsibilities should include, but not be limited to, the following functions:
 - a. Should agree to the study plan.
 - b. Ensure that the procedures specified in the study plan are followed, and that authorization for any modification is obtained and documented together with the reasons for them.
 - c. Ensure that all data generated are fully documented and recorded.
 - d. Sign and date the final report to indicate acceptance of responsibility for the validity of the data and to confirm compliance with these principles of good laboratory practice.

- e. Ensure that after termination of the study, the study plan, the final report, raw data and supporting material are transferred to the archives.

1.3 Personnel Responsibilities

1. Each individual engaged in the conduct of or responsible for the supervision of a nonclinical laboratory study shall have education, training, and experience, or combination thereof, to enable that individual to perform the assigned functions.
2. Each testing facility shall maintain a current summary of training and experience and job description for each individual engaged in or supervising the conduct of a nonclinical laboratory study.
3. There shall be a sufficient number of personnel for the timely and proper conduct of the study according to the protocol.
4. Personnel shall take necessary personal sanitation and health precautions designed to avoid contamination of test and control articles and test systems.
5. Personnel engaged in a nonclinical laboratory study shall wear clothing appropriate for the duties they perform. Such clothing shall be changed as often as necessary to prevent microbiological, radiological, or chemical contamination of test systems and test and control articles.
6. any individual found at any time to have an illness that may adversely affect the quality and integrity of the nonclinical laboratory study shall be excluded from direct contact with test systems, test and control articles and any other operation or function that may adversely affect the study until the condition is corrected. All personnel shall be instructed to report to their immediate

supervisors any health or medical conditions that may reasonably be considered to have an adverse effect on a nonclinical laboratory study.

7. Personnel should exercise safe working practice. Chemicals should be handled with suitable caution until their hazards (s) has been established.
8. Personnel should exercise health precautions to minimize risk to themselves and to ensure the integrity of the study.
9. Personnel known to have a health or medicinal condition that is likely to have an adverse effect on the study should be excluded from operations that may affect the study.

2. QUALITY ASSURANCE PROGRAMME

2.1 General

- The test facility should have a documented quality assurance programme to ensure that studies performed are in compliance with these principles of good laboratory practice.
- The quality assurance programme should be carried out by an individual or by individuals designated by and directly responsible to management and who are familiar with the test procedures.
- This individual (s) should not be involved in the conduct of study being assured.
- This individual (s) should report any findings in writing directly to management and to the study director.

2.2 Responsibilities of the Quality Assurance Personnel

The responsibilities of the quality assurance personnel should include, but not be limited to, the following functions:

1. Maintain a copy of a master schedule sheet of all studies conducted at the testing facility.
2. Maintain copies of all protocols pertaining to studies for which the unit is responsible.
3. Inspect each phase of a study periodically and maintain written and properly signed or sealed records of each periodic inspection showing the nature of inspection, findings, problems recorded, action reinspection, etc.
4. Immediately report any significant problems which are likely to affect the quality and integrity of the study found during the course of an inspection to the management and the study director.
5. Periodically submit to management and the study director written status reports on each study, noting any problems and the corrective actions taken.
6. Assure that revisions of the standard operating procedures or of the protocol were approved by the management and documented and that deviations from the standard operating procedures were approved by the study director and documented.
7. Prepare documents in writing the responsibilities and procedures applicable to the quality assurance unit, the records maintained by the quality assurance unit, and the method of indexing such records and maintain the documents.

8. Ascertain that the study plan and standard operating procedures are available to personnel conducting the study.
9. Ensure that the study plan and standard operating procedures are followed by periodic inspections of the test facility and/or by auditing the study in progress. Records of such procedures should be retained.
10. Promptly report to management and the study director unauthorized deviations from the study plan and from standard operating procedures.
11. Review the final reports to confirm that the methods, procedures, and observations are accurately described, and that the reported results accurately reflect the raw data of the study.
12. Prepare and sign a statement, to be included with the final report, which specifies the dates inspections were made and the dates any findings were reported to management and to the study director.

3. FACILITIES

3.1 General

- The test facility should be of suitable size, construction and location to meet the requirements of the study and minimize disturbances that would interfere with the validity of the study.
- The design of the test facility should provide an adequate degree of separation of the different activities to assure the proper conduct of each study.

3.2 Test System Facilities

- The test facility should have a sufficient number of rooms or areas to assure the isolation of test systems and the isolation of individual projects, involving substances known or suspected of being biohazardous.
- Suitable facilities should be available for the diagnosis, treatment and control of diseases, in order to ensure that there is no unacceptable degree of deterioration of test systems.
- There should be storage areas as needed for supplies and equipment. Storage areas should be separated from areas housing the test systems and should be adequately protected against infestation and contamination. Refrigeration should be provided for perishable commodities.

3.3 Facilities for Handling Test and Reference Substances

- To prevent contamination or mix-ups, there should be separate areas for receipt and storage of the test and reference substances, and mixing of the test substances with a vehicle.
- Storage areas for the test substances should be separate from areas housing the test systems and should be adequate to preserve identity, concentration, purity, and stability, and ensure safe storage for hazardous substances.

3.4 Archive Facilities

Space should be provided for archives for the storage and retrieval of raw data, reports, samples, and specimens.

3.5 Waste Disposal

- Handling and disposal of wastes should be carried out in such a way as not to jeopardize the integrity of studies in progress.
- The handling and disposal of wastes generated during the performance of a study should be carried out in a manner which is consistent with pertinent regulatory requirements. This would include provision for appropriate collection, storage, and disposal facilities, decontamination and transportation procedures, and the maintenance of records related to the preceding activities.

3.6 Animal Care Facilities

- A testing facility shall have a sufficient number of animal rooms or areas, as needed, to assure proper:
 - Separation of species or test systems.
 - Isolation of individual projects.
 - Quarantine of animals.
 - Routine or specialized housing of animals.
- A testing facility shall have a number of animal rooms or areas separate from those described in previous paragraph of this section to ensure isolation of studies being done with test systems or test and

control articles known to be biohazardous, including volatile substances, aerosols, radioactive materials, and infectious agents.

- Separate areas shall be provided, as appropriate, for the diagnosis, treatment, and control of laboratory animal diseases. These areas shall provide effective isolation for the housing of animals either known or suspected of being diseased, or of being carriers of disease, from other animals.
- When animals are housed, facilities shall exist for the collection and disposal of all animal waste and refuse or for safe sanitary storage of waste before removal from the testing facility. Disposal facilities shall be so provided and operated as to minimize vermin infestation, odors, disease hazards, and environmental contamination.

3.7 Animal Supply Facilities

There shall be storage areas as needed, for feed, bedding, supplies, and equipment. Storage areas for feed and bedding shall be separated from areas housing the test systems and shall be protected against infestation or contamination. Perishable supplies shall be preserved by appropriate means.

4 EQUIPMENT, REAGENTS AND ANIMALS

4.1 Equipment

A. Equipment Design

Equipment used in the generation, measurement, or assessment of data and equipment used for facility environmental control shall be of appropriate design and

adequate capacity to function according to the protocol and shall be suitably located for operation, inspection, cleaning, and maintenance.

B. Maintenance and Calibration of Equipment

- Equipment shall be adequately inspected, cleaned, and maintained. Equipment used for the generation, measurement, or assessment of data shall be adequately tested, calibrated and/or standardized.
- The written standard operating procedures shall set forth in sufficient detail the methods, materials, and schedules to be used in the routine inspection, cleaning, maintenance, testing, calibration, and/or standardization of equipment, and shall specify, when appropriate, remedial action to be taken in the event of failure or malfunction of equipment. The written standard operating procedures shall designate the person responsible for the performance of each operation.
- Written records shall be maintained of all inspection, maintenance, testing, calibrating and/or standardizing operations. These records, containing the date of the operation, shall describe whether the maintenance operations were routine and followed the written standard operating procedures. Written records shall be kept of nonroutine repairs performed on equipment as a result of failure and malfunction. Such records shall document the nature of the defect, how and when the defect was discovered, and any remedial action taken in response to the defect.

4.2 Reagents and Solution:

All reagents and solutions in the laboratory areas shall be labeled to indicate identity, titer or concentration, storage requirements, and expiration date. Deteriorated or outdated reagents and solutions shall not be used.

4.3 Animal Care

- There shall be standard operating procedures for the housing, feeding, handling, and care of animals.
- All newly received animals from outside sources shall be isolated and their health status shall be evaluated in accordance with acceptable veterinary medical practice.
- At the initiation of a nonclinical laboratory study, animals shall be free of any disease or condition that might interfere with the purpose or conduct of the study. If, during the course of the study, the animals contract such a disease or condition, the diseased animals shall be isolated, if necessary. These animals may be treated for disease or signs of disease provided that such treatment does not interfere with the study. The diagnosis, authorizations of treatment, description of treatment, and each date of treatment shall be documented and shall be retained.
- Warm-blooded animals, excluding suckling rodents, used in laboratory procedures that require manipulations and observations over an extended period of time or in studies that require the animals to be removed from and returned to their home cages for any reason (e.g. cage cleaning, treatment, etc), shall receive appropriate identification. All information

needed to specifically identify each animal within an animal-housing unit shall appear on the outside of that unit.

- Animals of different species shall be housed in separate rooms when necessary. Animals of the same species, but used in different studies, should not ordinarily be housed in the same room when inadvertent exposure to control or test articles or animal mix up could affect the outcome of either study. If such mixed housing is necessary, adequate differentiation by space and identification shall be made.
- Animal cages, racks and accessory equipment shall be cleaned and sanitized at appropriate intervals.
- Feed and water used for the animals shall be analyzed periodically to ensure that contaminants known to be capable of interfering with the study and reasonably expected to be present in such feed or water are not present at levels above those specified in the protocol. Documentation of such analyses shall be maintained as raw data.
- Bedding used in animal cages or pens shall not interfere with the purpose or conduct of the study and shall be changed as often as necessary to keep the animals dry and clean.
- If any pest control materials are used, the use shall be documented. Cleaning and pest control materials that interfere with the study shall not be used.

5 TEST AND REFERENCE SUBSTANCES

5.1 Receipt, Handling, Sampling and Storage.

- Records including substance characterization, date of receipt, quantities received, and used in studies should be maintained.
- Handling, sampling, and storage procedures should be identified in order that the homogeneity and stability is assured to the degree possible and contamination or mix-up are precluded.
- Storage container (s) should carry identification information, earliest expiration date, and specific storage instructions.

5.2 Characterization

- Each test and reference substance should be appropriately identified (e.g. code, chemical abstract number (CAS), name).
- For each study, the identity, including batch number, purity, composition, concentrations, or other characterizations to appropriately define each batch of the test or reference substances should be known.
- The stability of test and reference substances under conditions of storage should known for all studies.
- The stability of test and reference substances under the test conditions should be known for all studies.

- If the test substance is administered in a vehicle, standard operating procedures should be established for testing the homogeneity and stability of the test substance in that vehicle.
- A sample for analytical purposes from each batch of test substance should be retained for studies in which the test substance is tested longer than four weeks.

6 STANDARD OPERATING PROCEDURES

6.1 General

- A test facility should have written standard operating procedures approved by management that are intended to ensure the quality and integrity of the data generated in the course of the study.
- Each separate laboratory unit should have immediately available standard operating procedures relevant to the activities being performed therein. Published text books, articles and manuals may be used as supplements to these standard operating procedures.

6.2 Application

Standard operating procedures should be available for, but not limited to, the following categories of laboratory activities. The details given under each heading are to be considered as illustrative examples.

- a. Test and reference substance.

Receipt, identification, labeling, handling, sampling and storage.

- b. apparatus and Reagents

Use, maintenance, cleaning, calibration of measuring apparatus and environmental control equipment; preparation of reagents.

c. Record keeping, reporting, storage, and retrieval

Coding of studies, data collection, preparation of reports, indexing system, handling of data, including the use of computerized data systems.

d. Test system (where appropriate)

i. Room preparation and environmental room conditions for the test system.

ii. Procedures for receipt, transfer, proper placement, characterization, identification and care of test system.

iii. Test system preparation, observations, examination before, during and at termination of the study.

iv. Handling of test system individuals found moribund or dead during the study.

v. Collection, identification and handling of specimens including necropsy and histopathology.

e. Quality assurance procedures

Operation of quality assurance personnel in performing and reporting study audits, inspections, and final study report reviews.

f. Health and safety precautions

As required by national and/or international legislation or guidelines.

7. PERFORMANCE OF THE STUDY

7.1 Study Plan (The protocol)

- For each study, a plan should exist in a written form prior to initiation of the study.
- The study plan should be retained as raw data.
- All changes, modifications, or revisions of the study plan, as agreed to by the study director; including justification (s) should be documented, signed and dated by the study director, and maintained with the study plan.

7.2 Content of the study plan

The study plan should contain, but not be limited to the following information:

1. identification of the study, the test and reference substances
 - a. A descriptive title.
 - b. A statement which reveals the nature and purpose of the study.
 - c. Identification of the test substance by code or name (IUPAC; CAS number, etc.)
 - d. The reference substance to be used.
2. information concerning the sponsor and the test facility
 - a. Name and address of the sponsor.
 - b. Name and address of the test facility.
 - c. Name and address of the study director.

3. Dates

- a. The date of agreement to the study plan by signature of the study director, and when appropriate, of the sponsor and/or the test facility management.
- b. The proposed starting and completion dates.

4. issues (where applicable)

- a. The justification for selection of the test system.
- b. Characterization of the test system, such as the species, strain, sub-strain. Source of supply, number, body weight range, sex, age, and other pertinent information.
- c. The method of administration and the reason for its choice.
- d. The dose levels and/or concentrations (s) frequency, duration of administration.
- e. Detailed information on the experimental design, including a description of the chronological procedure of the study, all methods, materials and conditions, type and frequency of analysis, measurements, observations and examination to be performed.

5. Records

A list of records to be retained.

7.3 Conduct of the study

- A unique identification should be given to each study. All items concerning this study should carry this identification.
- The study should be conducted in accordance with the study plan.

- All data generated during the conduct of 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.
- Any change in the raw data should be made so as not to obscure the previous entry, and should indicate the reason, if necessary, for change and should be identified by date and signed by the individual making the change.
- 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. Corrections should be entered separately by the reason for change. With the data and the identity of the individual making the change.

8. RECORDS AND REPORTS

8.1 Reporting of study results

- A final report should be prepared for the study.
- The use of the international system of units (SI) is recommended.
- The final report should be signed and dated by the study director.
- If reports of principal scientists from co-operating disciplines are included in the final report, they should sign and date them.
- Corrections and additions to a final report should be in the form of an amendment. The amendment should clearly specify the reason for the

corrections or additions and should be signed and dated by the study director and by the principal scientist from each discipline involved.

8.2 Content of the final report

The final report should include, but not be limited to, the following information:

1. Identification of the study, the test and reference substance
 - a. A descriptive title.
 - b. Identification of the test substance by code or name (IUPAC; CAS number, etc.):
 - c. Identification of the reference substance by chemical name.
 - d. Characterization of the test substance including purity, stability and homogeneity.
2. information concerning the test facility
 - a. Name and address.
 - b. Name of the study director.
 - c. Name of other principal personnel having contributed reports to the final report.
3. Dates

Dates on which the study was initiated and completed.
4. statement

A quality assurance statement certifying the dates inspections were made and the dates any findings were reported to management and to the study director.

5. description of materials and test methods

- a. Description of methods and materials used.
- b. Reference to Pharmacopoeia and/or manufacture files.

6. results

- a. A summary of results.
- b. All information and data required in the study plan.
- c. A presentation of the results, including calculations and statistical methods.
- d. An evaluation and discussion of the results and, where appropriate, conclusions.

7. storage

The location where all samples, specimens, raw data, and the final report are to be stored.

8.3 Storage and retention of records and material

8.3.1 Storage and Retrieval

- Archives should be designed and equipped for the accommodation and the secure storage of:
 - The study plans.
 - The raw data.
 - The final reports.
 - The reports of laboratory inspections and study audits performed according to the quality assurance programme.
 - Sample and specimens.

- Material retained in the archives should be indexed so as to facilitate orderly storage and rapid retrieval.
- Only personnel authorized by management should have access to the archives. Movement of material in and out of the archives should be properly recorded.

8.3.2 Retention

- The following should be retained for the period specified by the appropriate authorities.
 - The study plan, raw data, samples, specimens, and the final report of each study.
 - Records of all inspections and audits performed by the quality assurance programme.
 - Summary of qualifications, training, experience and job descriptions of personnel.
 - Records and reports of the maintenance and calibration of equipment.
 - The historical file of standard operating procedures.
- Samples and specimens should be retained only as long as the quality of the preparation permits evaluation.
- If a test facility or an archive contracting facility goes out of business and has no legal successor, the archive should be transferred to the archives of the sponsor(s) of the study(s).

3.7 Apparatus

7. (1) Purpose: To determine whether the laboratory has suitably located, operational apparatus in sufficient quantity and of adequate capacity to meet the requirements of the tests being conducted in the facility and that the materials, reagents and specimens are properly labeled, used and stored.

(2) The inspector should check that-

- Apparatus are clean and in good working order,
- Records have been kept of apparatus operation, maintenance, standardization and calibration, 3.8 Materials, Reagents and Test Items.
- Materials and chemical reagents are properly labeled and stored at appropriate temperatures and that expiry dates are not being ignored. Labels for reagents should indicate their source, identity and concentration and/or other pertinent information.
- Specimens are well identified by test system, study, nature and date of collection,
- Apparatus and materials used do not interfere with the test systems.

SECTION THREE:

INSPECTION AND AUDITS

INSPECTION PROCEDURES

1. Pre-inspection

- **Purpose:** To familiarize the inspector with the facility which is about to be inspected in respect of management structure, physical layout of buildings and range of studies.
- **Prior to conducting a laboratory inspection or study audit,** inspectors should familiarize themselves with the facility which is to be visited. Any existing information on the facility should be reviewed. This may include previous inspection reports, the layout of the facility, organization charts, study reports, protocols and curricula vitae (CVS) of key personnel. Such documents would provide information on:-
 - § The type, size and layout of the facility.
 - § The range of studies likely to be encountered during the inspection.
 - § The management structure of the facility.
- **Inspectors should note,** in particular, any deficiencies from previous laboratory inspections. Where no previous laboratory inspections have been conducted, a pre-inspection visit can be made to obtain relevant information.
- Laboratories should be informed of the date and time of inspector's arrival, the objective of their visit and the length of time they expect to

be on the premises. This will allow the laboratory to ensure that the appropriate personnel and documentation are available. In cases where particular documents or records are to be examined, it may be useful to identify these to the laboratory in advance of the visit so that they will be immediately available during the laboratory inspection.

2. Conduct and Operation of inspection:-

2.1 Starting conference

(1) **Purpose:** To inform the management and staff of the facility of the reason for the laboratory inspection or study audit that is about to take place, and to identify the laboratory areas, study(ies) selected for audit, documents and personnel likely to be involved.

(2) The administrative and practical details of a laboratory inspection or study audit should be discussed with the management of the facility at the start of the visit.

At the starting conference, inspectors, should:-

- Outline the purpose and scope of the visit.
- Describe the documentation which will be required for the laboratory inspection. Such as lists of on-going and completed studies, study plans, standard operating procedures, study reports, etc. access to and, if necessary, arrangements for the copying of relevant documents should be agreed upon at this time.
- Clarify or request information as to the management structure (organization) and personnel of the facility.

- Make an initial determination as to the parts of the facility to be covered during the laboratory inspection.
- Describe the documents and specimens that will be needed for on-going or completed study(ies) selected for study audit.

(3) Before proceeding further with a laboratory inspection, it is advisable for the inspector to establish contact with the laboratory quality assurance unit.

(4) As a general rule, when inspecting a facility, inspectors will find it helpful to be accompanied by a member of the quality assurance unit.

(5) Inspectors may wish to request that a room be set aside for examination of documents and other activities.

2.2 Organization and Personnel

(1) **Purpose:** To determine whether: the laboratory has 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.

(2) The management should be asked to produce certain documents, for example:-

- Floor plans.
- Facility management and scientific organization charts.
- CVs of key personnel involved in the type(s) of studies selected for the study audit.

- List(s) of on-going and completed studies with information on the type of study, initiation/completion dates, test system, route of administration and name of study director.
- Staff training and health surveillance policies, where such policies have been established.
- Staff training records where available.
- An index to the facility's standard operating procedures.
- Specific standard operating procedures related to the studies or procedures being inspected or audited.
- List of the study directors associated with the study(ies) being audited.

(3) The inspector should check, in particular

- Lists of on-going and completed studies to ascertain the level of work being undertaken by the laboratory.
- The identity and qualifications of the study directors, the head of the quality assurance unit and other key personnel.
- Existence of standard operating procedures for the relevant areas of testing.

2.3 Quality assurance programme

(1) Purpose: To determine whether the mechanisms used to assure management that laboratory studies are conducted in accordance with good laboratory practice principles are adequate.

(2) The head of the quality assurance unit should be asked to demonstrate the systems and methods of quality assurance inspection and monitoring of studies, and the system for recording observations made during quality assurance monitoring.

(3) Inspectors should check:-

- The qualifications of the head of quality assurance and of all quality assurance staff.
- That the quality assurance unit functions independently from the staff involved in the studies.
- How the quality assurance unit schedules and conducts inspections, how it monitors identified critical phases in a study, and what resources are available for quality assurance inspections and monitoring activities.
- The extent and depth of quality assurance monitoring during the practical phases of the study.
- The quality assurance procedures for checking the final report to ensure its agreement with the raw data.
- That management receives reports from quality assurance concerning problems likely to affect the quality or integrity of a study.
- The actions taken by quality assurance when deviations are found.
- The quality assurance role, if any, of studies or parts of studies done in contract laboratories.
- The part played, if any, by quality assurance in the review, revision and updating of standard operating procedures.

2.4 Facilities

(1) Purpose: To determine whether the laboratory is of suitable size, construction, design and location to meet the demands of the studies being undertaken.

(2) The inspector should check that :-

- The design enables an adequate degree of separation so that, e.g. test substances, animals, diets, etc., of one study cannot be confused with those of another.
- environmental control and monitoring procedures exist and function adequately in critical areas, e.g. animal and other biological test systems rooms, test substance storage areas and laboratory areas,
- The general housekeeping is adequate for the various facilities and that there are, if necessary, pest control procedures.

2.5 Animal House

(1) Purpose: To determine whether the laboratory, if engaged in studies using animals or other biological test systems, has support facilities and conditions for their care, housing and containment, adequate to prevent stress and other problems which could affect the test system and hence the quality of data.

(2) The inspector should check that:-

- There are facilities adequate for the test systems used and for testing needs.
- There are arrangements to quarantine animals being introduced into the facility and that these arrangements are working satisfactorily.

- There are arrangements to isolate animals (or other elements of a test system, if necessary) known to be, or suspected of being, diseased or carriers of disease.
- There is adequate monitoring and record-keeping of health, behaviour or other aspects, as appropriate to the test system.
- The equipment for maintaining the environmental conditions required for each test system is adequate, well maintained and effective.
- Animal cages, racks tanks and other containers, as well as accessory equipment, are kept sufficiently clean.
- Analyses to check environmental conditions and support systems are carried out as required.
- Facilities exist for removal and disposal of animal waste and refuse from the test systems and that these are operated so as to minimize vermin infestation, odours, disease hazards and environmental contamination.
- Storage areas are provided for animal feed or equivalent materials for all test systems; that these areas are not used for the storage of other materials such as test substances, pest control chemicals or disinfectants, and they are separate from areas in which animals are housed or other biological test systems are kept.
- Stored feed and bedding are protected from deterioration by adverse environmental conditions, infestation or contamination.

2.6 Test systems

(1) Purpose: To determine whether adequate procedures exist for the handling and control of the variety of test systems required by the studies undertaken in the facility, e.g. chemical and physical systems, cellular and microbial systems, plants or animals.

(2) Physical and chemical systems.

The inspector should check that:-

- Where required by study plans, the stability of test and reference substances were determined and that the reference substances specified in test plans were used.
- Standard operating procedures exist to cover laboratory activities and that their provisions are observed.
- In automated systems, data generated as graphs, recorder traces or computer print-outs are documented as raw data and archived.

(3) Biological test systems

Taking account of the relevant aspects referred to above relating to care, housing or containment of biological test systems.

The inspector should check that-

- Test systems are as specified in study plans.
- Test systems are adequately identified.
- Animals are adequately and, if necessary and appropriate, uniquely identified throughout the study.

- Housing or containers of test systems are properly identified with all the necessary information.
- There is an adequate separation of studies being conducted on the same animal species (or the same biological test system) but with different substances.
- The biological test system environment is as specified in the study plan or in standard operating procedures for aspects such as temperature or light/dark cycles.
- The recording of the receipt, handling, housing or containment, care and health evaluation is appropriate to the test systems.
- Written records are kept of examination, quarantine, morbidity, behaviour, diagnosis and treatment of animal and plant test systems or other similar aspects as appropriate to each biological test system.
- There are provisions for the appropriate disposal of test systems at the end of tests.

2.7 Test and reference substances

(1) Purpose: To determine whether the laboratory has procedures designed-

- (i)** To ensure that the identity, potency, quantity and composition of test and reference substances are in accordance with their specifications.
- (ii)** To properly receive and store test and reference substances.

(2) The inspector should check that:-

- There are standard operating procedures for recording the receipt, and for the handling, sampling, usage and storage of test and reference substances.
- Test and reference substances containers are properly labeled.
- Storage conditions are appropriate to preserve the concentration, purity and stability of the test and reference substances.
- There are standard operating procedures for the determination of identity, purity, composition, stability, and for the prevention of contamination of, test and reference substances, where applicable.
- There are procedures for the determination of the homogeneity and stability of mixtures containing test and reference substances, where applicable.
- Containers holding mixtures (or dilutions) of the test and reference substances are labeled and that records are kept of the homogeneity and stability of their contents, where applicable.
- When the test is of longer than four weeks duration, samples from each batch of test and reference substances have been taken for analytical purposes and that they have been retained for an appropriate time.
- Procedures for mixing substances are designed to prevent errors in identification or cross-contamination.

2.8 Apparatus

(1) **Purpose:** To determine whether the laboratory has suitably located, operational apparatus in sufficient quantity and of adequate capacity to meet the requirements of the tests being conducted in the facility and that the materials, reagents and specimens are properly labeled, used and stored.

(2) The inspector should check that:-

- Apparatus are clean and in good working order.
- Records have been kept of apparatus operation, maintenance, standardization and calibration.

2.9 Materials, Reagents and Test Items.

- Materials and chemical reagents are properly labeled and stored at appropriate temperatures and that expiry dates are not being ignored. Labels for reagents should indicate their source, identity and concentration and/or other pertinent information.
- Specimens are well identified by test system, study, nature and date of collection.
- Apparatus and materials used do not interfere with the test systems.

2.10 Standard operating procedures

(1) **Purpose:** To determine whether the laboratory has written standard operating procedures relating to all the important aspects of the laboratory's operation, considering that one of the most important management techniques for controlling

laboratory operations is the use of written standard operating procedures. These relate directly to the routine elements of test conducted by the laboratory.

(2) The inspector should check that:-

- Each laboratory area has immediately available relevant, authorized copies of standard operating procedures.
- Any amendments or changes to standard operating procedures have been authorized and dated.
- Historical files of standard operating procedures are maintained.
- standard operating procedures are available for, but not necessarily limited to, the following activities-
 - Receipt, identification, labeling, handling, sampling, usage and storage of test and reference substances.
 - Maintenance, cleaning and calibration of measuring apparatus and environmental control equipment.
 - Preparation of reagents and dosing formulations.
 - Record-keeping, reporting, storage and retrieval of records and reports.
 - Preparation and environmental control of areas containing the test systems.
 - Receipt, transfer, location, characterization, identification and care of test systems.

- Handling of the test systems before, during and at the termination of the study.
- Disposal of test systems.
- Use of pest control and cleaning agents.
- Quality assurance programme operations.

2.11 Performance of the study

(1) To verify that written study plans exist and that the plans and the conduct of the study are in accordance with good laboratory practice principles.

(2) The inspectors should check that:-

- The study plan was signed by the study director.
- Any amendments to the study plan were signed and dated.
- The date of the agreement to the study plan by the sponsor was recorded (where applicable).
- Measurements, observations and examinations were recorded directly, promptly, accurately and legibly and were signed (or initialed) and dated.
- Any changes in the raw data, including data stored in computers, did not obscure previous entries, included the reason for the change and were signed and dated.
- Computer-generated or stored data have been identified and that the procedures to protect them against unauthorized amendments or loss are adequate.

- the computer software used within the study is reliable, accurate, and can be validated,
- Any unforeseen events recorded in the raw data have been investigated and evaluated.
- The results presented in the reports of the study (interim or final) are consistent and complete and that they correctly reflect the raw data.

2.12 Reporting of Study Results

(1) Purpose: To determine whether final reports are prepared in accordance with good laboratory practice principles.

(2) When a final report is available, the inspector should check that:-

- It is signed and dated by the study director and, where appropriate, by other principal scientists.
- The study director has signed a statement indicating acceptance of responsibility for the validity of the study and confirming that the study was conducted in accordance with good laboratory practice principles.
- A quality assurance statement is included in the report and that it is signed and dated.
- Any amendments were made by the responsible personnel.
- It lists the archive location all samples, specimens and raw data.

2.13 Storage and Retention of Records

(1) Purpose: To determine whether the facility has generated adequate records and reports and whether adequate provision has been made for the safe storage and retention of records and materials.

(2) The inspector should check:-

- The archive facilities for the storage of study plans, raw data, final reports, samples and specimens.
- the procedures for retrieval of archived materials.
- The procedures whereby access to the archives is limited to authorized personnel and records are kept of personnel given access to raw data, slides, etc.
- That an inventory is maintained of material removed from, and returned to, the archives.
- That records and materials are retained for the required or appropriate period of time and are protected from loss or damage by fire, adverse environmental conditions, etc.

SECTION IV:

GLP GUIDELINES - CHECKLIST

1.0 Premises	Yes	No
1.1. Is size, construction, designed and equipment of the Lab. Suitable for the conduct of tests?	£	£
1.2. Is the space for writing, recording and storage of samples and documents sufficient?	£	£
1.3. Are chemical, pharmacological and microbiological Labs. Well separated and away from Administrative area?	£	£
1.4. Are the sensitive instrument placed in separate room with proper arrangements to avoid vibration, electrical interference and humidity, etc?	£	£
1.5. Is the construction material easily cleanable?	£	£
1.6. Are the heating, ventilation and air-conditioning systems adequate to provide optimum environmental conditions for the employees and Lab. Animals?	£	£
1.7. Is there a provision for safe storage of the waste awaiting disposal?	£	£
1.8. Does the quality manual exist in the Lab. And address the internal organization of the laboratory?	£	£
1.9. Does the quality manual address the safety regulations?	£	£
1.10. Is there safety education programmer?	£	£
1.11. Does the laboratory comply with fire regulations and electricity regulations?	£	£
1.12. Are fume cupboards available and checked regularly for their function?	£	£
1.13. Are there proper containers and arrangements for the storage of flammable chemicals?	£	£
1.14. Is there an emergency power supply to maintain essential services?	£	£

2.0 Personnel	Yes	No
2.1. Is the supervision of laboratory tests done by scientists?	£	£
2.2. Is the education, training and experience of the person conducting or supervising the test proper?	£	£
2.3. Is the summary of biodata and job description of each individual engaged in the conduct or supervision of the tests available in the Lab. Record?	£	£
2.4. Is sufficient number of personnel available in the Lab. For the timely and proper conduct of the tests according to the specifications and protocol?	£	£
2.5. Are the personnel reporting about their health status to their supervisors to maintain the record?	£	£
2.6. Are the personnel engaged in the Labs. Wearing clothing appropriate for their duties?	£	£
2.7. Is cloth changing facility available to prevent any microbiological and chemical contaminations?	£	£
2.8. Is there regular and proper education and training programmers for the personnel to keep them up-dated in their fields?	£	£
2.9. Are the training programmes involving within the Lab. Senior staff?	£	£
2.10. Is there provision for the staff to visit and attend outside training facilities?	£	£

2.11. Is there a staff library and meeting room?	£	£
2.12. Is there a direct outside telephone for emergency use?	£	£
2.13. Is mouth pipetting prohibited?	£	£
2.14. Are gas cylinders handled according to regulations?	£	£

3.0 Equipment	Yes	No
3.1. Are the equipments used in the generation, measurement and assessment of data appropriately designed and have the capacity to perform the tests required as per specifications?	£	£
3.2. Are the equipment and instruments checked, serviced and calibrated periodically by an organization / assigned individual?	£	£
3.3. Is service record properly maintained for all equipment indicating the next date of service or calibration?	£	£
3.4. Are written operating instructions available for all instruments and is staff trained on new instruments when received?	£	£
3.5. Are defective equipment withdrawn from use until the fault has been rectified?	£	£
3.6. Is electrical equipment properly connected, Earthed and checked regularly?	£	£

4. Cleanliness	Yes	No
4.1. Are the Lab premises and equipment kept clean in accordance with written cleaning schedules?	£	£
4.2. Are personnel wearing clean protective clothing appropriate to the duties assigned?	£	£
4.3. Is the disposal of waste material done with care?	£	£

5.0. Standards, Reagents and Controls	Yes	No
5.1. Are all the reference standards obtained from a qualified source?	£	£
5.2. Is the expiration date and other details properly given / labeled?	£	£
5.3. Is the certificate of analysis obtained with each standard?	£	£
5.4. Are the reference standards properly stored and handled?	£	£
5.5. Are reagents made by a competent person according to the given procedure?	£	£
5.6. Are the prepared reagents properly labeled indicating concentration, standardization factor, shelf-life and storage conditions?	£	£
5.7. Are the prepared reagents duly signed and dated?	£	£
5.8. Are the expiration dates for standards and reagents validated?	£	£
5.9. Is the quality (purity, grade) of water used in a test specified?	£	£
5.10. If a “treatment system” is used to prepare water for laboratory use, does a written procedure exist for monitoring that system?	£	£

6.0. Sampling	Yes	No
6.1. Is there appropriate storage arrangement for the received samples, calibrators and strains, etc, and log book of samples' kept up dated?	£	£
6.2. Is the storage of samples before and after testing specified?	£	£
6.3. Is the sampling of the drug / material batches done according to recommended quality control sampling procedures?	£	£
6.4. Is the method of sampling properly referred?	£	£
6.5. Are the cleaning / storage protocol followed?	£	£
6.6. Is the sample container labeled indicating its contents, batch / lot no., date of sampling and reference to the bulk container from where taken?	£	£
6.7. Are the sampling equipment cleaned after each use and stored separately from other Lab. equipment?	£	£
6.8. Is proper care taken to avoid any contamination or deterioration of the sampled material or the resealed container?	£	£

7.0. Product Specifications	Yes	No
7.1. Are the specifications always approved by the person responsible for quality control, defining fire nature and quality of each finished product?	£	£
7.2. Is each specification such as: Product's name; Description of package & details; Sampling instructions; tests & Limits with methods in detail; Safety precautions; Storage conditions; Frequency of re-examination of stored product; indicated and provided?	£	£
7.3. Are the procedures for laboratory tests provided in detail?	£	£
7.4. Does a protocol exist that states what changes would cause a revalidation to occur?	£	£

8.0. Record of Analysis	Yes	No
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8.1. Is the record of receipt and testing of products containing the following??	£	£
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- I. Product / material name and code.
- II. Date of receipt and sampling.
- III. Source of product / material.
- IV. Date of testing.
- V. Batch / lot number.
- VI. Indication of tests performed.
- VII. Reference of the method use.
- VIII. Results [regarding release / rejection / status].
- IX. Decision.
- X. Signature of the analyst & decision maker.

8.2. Are the analysts keeping basic records such as tests, calculations, charts and readings?	£	£
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8.3. Is the instrument used identified with the raw data?	£	£
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8.4. Is there a way to track a final report to the original raw data?	£	£
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8.5. If a retest is performed, is its reason mentioned?	£	£
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9.0. Testing Procedures	Yes	No
9.1. Is the testing Lab. Having standard testing procedures to ensure quality, integrity and the validity of file data generated by such methods?	£	£
9.2. Is written procedures manual available as basic GLP requirement?	£	£
9.3. Are the samples tested according the relevant specifications? Are results verified before acceptance or rejections?	£	£
9.4. Is there any specific protocol to deal with doubtful / failed samples?	£	£

10.0. Documentation **Yes** **No**

10.1. To avoid risk of errors. Is proper documentation maintained as prime necessity of quality assurance? £ £

10.2. Are the documents prepared to address the following: £ £

(a) Title, nature and purpose of document is superseded document mentioned if any?

(b) Is the document arranged in way that any required change can be made easily?

(c) Is document self-explanatory and easy to use?

(d) Are the filling instructions clear?

(e) Are the headings and the space for entries adequate?

(f) Are the reproduced documents clear and legible?

10.3. Are the documents containing only necessary and not superfluous data? £ £

10.4. Are the corrections in the documents in a way that the original entry is not lost? £ £

10.5. Are the documents kept up to date and any amendment is formally signed by the authorized person?

If any permanent amendment is made, are the new documents prepared to replace it on priority?

10.6. Are the out-dated or superseded documents removed from active use, and a copy retained for reference?

11.0. Precautions in the Microbiology Laboratory Yes No

- | | | | |
|--------|--|---|---|
| 11.1. | Are laboratory coats worn and protective gears like gloves, mask, and cap used when necessary? | £ | £ |
| 11.2. | Is eating, drinking and smoking prohibited in the Lab? | £ | £ |
| 11.3. | Are adequate preventive measures for any spilled cultures, cuts and abrasions reported and recorded? | £ | £ |
| 11.4. | Are the inculcating wire loops, needles etc. flamed red before and after use and preventive measures to stop formation of aerosols from living cultures, made? | £ | £ |
| 11.5. | Are articles and containers coming in contact with living cultures sterilized before putting into washings? | £ | £ |
| 11.6. | Are all solid disposable items (i.e. cotton plug, agar gel, cultured Petri dishes) incinerated? | £ | £ |
| 11.7. | Are used pipettes placed in pipette jars containing disinfectant solution? | £ | £ |
| 11.8. | Are hands thoroughly washed with proper disinfectant solution before leaving the microbiology Lab? | £ | £ |
| 11.9. | Are all aseptic techniques, transfers and other unit operations performed inside a laminar flow unit? | £ | £ |
| 11.10. | Is the location of first aid cabinets, eye irrigation bottles and fire extinguishes known by all laboratory workers? | £ | £ |

- | | | | |
|--------|--|---|---|
| 11.11. | Is there a separate room for the preparation of culture media?
Have sterilizer cycles been validated for media preparation? | £ | £ |
| 11.12. | Is there an environmental monitoring program for the area
where testing is performed? | £ | £ |
| 11.13. | Are standard tests and controls used to validate media,
methods and test environment properly referred? | £ | £ |
| 11.14. | Is the sterility testing performed in proper test area? | £ | £ |
| 11.15. | Is it referred that the test was performed manually or by a
system totally automated? | £ | £ |
| 11.16. | Are there written procedures for environmental testing and
action level response? | £ | £ |
| 11.17. | Is the testing environment proper where bacterial endotoxins
testing is performed? | £ | £ |
| 11.18. | Is the testing method used to depyrogenate testing supplies
referred? | £ | £ |
| 11.19. | Is the depyrogenation certification given / checked with the
supplies? | £ | £ |
| 11.20. | Are the cell lines and standard strains of organisms
maintained? | £ | £ |

12.0. Laboratory Animal Facilities and care	Yes	No
12.1. Are the laboratory animals used in biological tests maintained under optimum conditions of health, in separate premises with sufficient room and space (to assure proper separation of species and quarantine)?	£	£
12.2. Are there appropriate facilities for collection and disposal of all animals waste or refuse?	£	£
12.3. Is the cleaning of animal rooms / and cage trays done daily according to a written schedule?	£	£
12.4. Are the storage areas for feed and bedding and equipment separate and protected from infestation and contamination?	£	£
12.5. Are the new animals, when received, kept separate for health observations for one week?	£	£
12.6. Are animal cages, racks and accessory equipment cleaned and sanitized at appropriate intervals?	£	£
12.7. Is the bedding material used absorbent and free animals dry between changes?	£	£
12.8. Is the health care programme as per acceptable veterinary practice routinely followed?	£	£
12.9. Are the animals cared for by experienced personnel and all basic protocols observed by all workers?	£	£

12.10. Is the time interval appropriate between testing on the same £ £
animals?

12.11. Are the thermometers often calibrated? £ £

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