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SCHEDULE L- I
[See Rules 74,78 and 150-E]

GOOD LABORATORY PRACTICES AND REQUIREMENTS OF PREMISES AND EQUIPMENTS

1. General Requirements:

(a) The laboratory or the organization of which it is a part must be an entity that is legally authorized to function and can be held legally responsible.

(b) It is the responsibility of the management to ensure that the laboratory carry out its testing, calibration, validation, and all other technical activities in such a way as to meet Good Laboratory Practices (GLP) requirements.

(c) Laboratory management shall have a qualified individual to be known as quality manager or technical manager for carrying out all technical activities and for the implementation of documented quality system and shall report to the top management directly.

(d) The quality manager shall prepare a schedule for technical audit of the laboratory for GLP compliance by an expert or experts appointed by the top-management other than the in-charge of the laboratory and shall ensure the maintenance of documented quality system as per quality, manual.

2. Premises:

(a) (i) the laboratories shall be designed, constructed and maintained so as to prevent entry of insects and rodents besides cross contamination;

(ii) Interior surface (wall, floor, and ceilings) shall be smooth and free from cracks, and permit easy cleaning and disinfection;

(iii) Adequate provision is made not only for space and equipment for carrying out necessary test but also for utilities like water, power and gas;

(iv) Air ventilations system shall ensure dust free environment.

(b) The laboratories shall be provided with adequate lighting and ventilation and if necessary, air-conditioning to maintain satisfactory temperature and relative humidity that will not adversely affect the testing and storage of drugs or the accuracy of the functioning of the laboratory equipments or instruments.

(c) The drainage system facilities shall be such as to facilitate proper maintenance and prevent water logging in the laboratory.

(d) Tabletops shall be contracted with acid, alkali and solvent resistant material and shall be smooth and free from crevices as far as possible.

(e) All bio-medical laboratory waste shall be destroyed as per the provisions of the Bio-Medical Waste (Management and Handling) Rules, 1996.

(f) Adequate space with proper storage conditions in the laboratory shall be provided for keeping reference and working standards and be maintained by the quality control department. Standard Operating Procedure (SOP) for the maintenance of reference standards and evaluation of Working and Secondary standards shall be prepared by the laboratory.

(g) The air circulation is maintained in the area where sterility test is carried out as per Schedule M.

(h) Bio-burden shall be routinely maintained in the controlled and uncontrolled area (e.g. air locks).

(i) Animal House:

(i) Animal House shall have the approval of the Committee for the Purpose of Control and Supervision Experiments on Animals (CPCSEA).

(ii) Designed in such a way that there is an arrangement to quarantine the new animals procured or purchased and have a 0provision for clean corridor and dirty corridor.

(iii) In case of a diseased animal proper diagnosis shall be done and proper record of treatment shall be maintained.

(iv) Different types of animals shall be housed separately with proper identification.

(v) A Standard Operating Procedure shall be prepared for breeding and care of animals, maintenance, cleaning or sanitation with suitable schedule for cleaning of animal cages, racks, floor and other equipments.

(vi) The animal house shall have proper air-conditioning (temperature and humidity) with proper lighting and be monitored regularly and documented periodically.

3. Personal:

(a) Staff in the laboratory shall possess necessary qualification, proper training and shall have adequate, experience for the assigned duties.

(b) A training record of all the personnel shall be maintained.

(c) Head of the laboratory must be of high professional standing with experience in drug analysis and laboratory management who is responsible for:

(i) ensuring the control and maintenance of documents including the quality system as per the requirements of regulatory authorities which involves all raw data, SOPs documentation exhibits, protocols, training charts, etc.

(ii) Planning and organization the audit of the quality system and initiation as well as follow up action of the corrective actions, if any;

(iii) Investigation of technical complaints;

(iv) Taking final responsibilities for recommending any regulatory action in the event of non-compliance of tested samples.

4. **Equipments:**

(a) The laboratory shall be furnished with all types of equipments as may be necessary for carrying out the different activities within the laboratory.

(b) The analytical instruments shall be housed in the dust-free environment and whenever required, conditions of temperature and humidity shall be maintained and periodic checks on temperature and humidity be made and recorded.

(c) The instruments, instrument bench and surrounding areas shall be kept clean and tidy at all times.

(d) Instruments requiring calibration shall be calibrated at regular intervals and records of such calibration or maintenance be maintained and there shall be written instructions in the form of Standard Operating Procedures for the operation, maintenance and calibration of instruments.

(e) Equipments records shall be maintained and such records shall contain the following:

(i) name of equipment or machine or apparatus;

(ii) Manufacturer's name, model number and type of identification;

(iii) Serial number;

(iv) Date on which equipment was received in laboratory;

(v) Current location;

(vi) Condition when received (e.g. new, used, re-conditioned);

(vii) Copy of the manufacturer's operating instructions;

(vi) frequency of calibration;

(vii) frequency of maintenance;

(viii) log Book (day to day entry including status of the equipment);

(ix) staff responsible for monitoring the calibration and maintenance stairs of the equipment;

(x) calibrating records;

(xi) list of authorized users or operators, if any;

(xii) history of any damage, malfunction, modification or up gradation, repair and calibration;

(xiii) List of spares and accessories, if any.

(f) A progress register for non-functional equipments and action for procurement of spares and accessories, monitoring thereof, shall be maintained.

(g) A Standard Operating Procedure for preventive maintenance of machine or equipment or apparatus shall be prepared by the laboratory.

(h) Other equipments such as burette, pipettes, volumetric flasks, weight boxes, thermometers, etc., shall be thoroughly checked for accuracy of calibration before acceptance of use.

(i) Maintained procedure in the form of Standard Operating Procedures must be prepared and regular servicing must be performed by the maintenance engineer or specialist.

(j) Equipments, instruments giving anomalous results or defective must be labeled as 'out-of-order' till they are repaired and after instrument is repaired it should be calibrated before use.

(k) The maintenance of equipments for services like electricity, gas, water, steam, and compressed gas shall be handled by competent person.

(l) Autoclaves must meet the requirements described for operations, safety and validation procedures, and the validation carried out by the laboratory shall be recorded.

(m) Fume Cupboards.

Work involving the evolution of harmful and obnoxious vapors shall be carried out in a fume cupboard. The exhaust system of the fume cupboard shall be checked frequently to ensure that it is in order. There should be a water drainage system inside the fume cupboard and shall be checked frequently to ensure that there is no water logging and it is in order.

5. Chemicals and Reagents:

(a) The storage and handling of chemicals and reagents shall be done in a manner considering the physicochemical properties of these substances and the hazards involved in their use.

(b) All reagents and solutions in the laboratory shall be properly identified with a label.

(c) A standardization register shall be maintained by the laboratory along with its raw data and Standard Operating Procedure for preparation and standardization on stock solutions, standard solutions, and volumetric solutions must be prepared for the guidance of staff.

(d) Containers of stock solutions and of standard solutions shall bear the following details:

(i) name of analytical chemist who prepared the solution;

(ii) Date of preparation;

(iii) Each volumetric solution shall have 'use before date' depending upon the stability of the solution; and

(iv) Standardization records.

(e) The transfer of hazardous chemicals and reagents from one container to another container shall be carried out with suitable equipment by taking the care of safety and no make-shift or hazardous methods must be resorted to.

6. Good house keeping and safety:

(a) General and specific written down instructions for safety shall be circulated to each staff member and the instructions be revised periodically as appropriate (e.g., poster displays, audio-visual material and by seminars/conferences).

(b) Standard Operating Procedure for safety, house-keeping and loss prevention shall be prepared in accordance with

the various rules, and regulations of the Government of India include the following requirements, namely:-

(i) Safety data sheets must be made available to staff before testing is carried out;

(ii) Drinking, eating and smoking shall not be permitted in the laboratories; food for human consumption shall not be kept in working or storage area; food meant for test animals shall be handled by the workers under the guidance of a veterinary doctor or qualified person. In the animal house, the facilities for collection and disposal of animal waste or safe sanitary storage of waste before removal from testing be provided;

(iii) Staff must wear laboratory coats or other protective clothing including gloves and face masks and eye protection wherever required;

(iv) the laboratories shall have adequate first aid kit and fire fighting equipments located at the right places and the staff must be familiar and trained with the use of fire fighting equipment including fire extinguishers, fire blankets and gas masks;

(v) Operators carrying out sterility tests shall wear sterilized garments including headgear, face masks and shoes;

(vi) The staff must be educated in the first aid techniques, emergency care and use of antidotes; and

(vii) Safety rules in handling cylinders of compressed gases must be observed and staff must be familiar with relevant colors identification codes;

(c) Protective Precautions to be taken in Laboratories:

(i) water showered shall be installed at appropriate places in the laboratory;

(ii) Rubber suction bulbs must be used on manual pipettes and siphons;

(iii) warnings, precautions, and written instructions must be given for work with violent, uncontrollable or dangerous reactions (e.g. mixing water and acids, biological such as infectious agents, etc.);

(iv) Appropriate facilities for the collection, storage, and disposal of wastes shall be made available;

(v) Staff must be aware of methods for safe disposal of corrosive or dangerous products by neutralization or deactivation and of the need for complete disposal of mercury and its salts;

(vi) Staff must also be aware about the safety precautions to be adopted while handling potassium cyanide and cyanogens bromide;

(vii) A Standard Operating Procedure for handling, collection, disposal of chemical and biological wastes be prepared.

7. Maintenance, calibration, and validation of equipments:

(a) All equipments, instruments and other devices used in the laboratory shall use appropriate methods and procedures for all tests or calibrations and they shall be regularly calibrated and validated. The frequency of calibration may differ from instrument to instrument.

(b) The original equipment manufacturer's recommendations along with the experience of the laboratory staff and the use of equipment per day may also be considered while fixing the frequency of calibration.

(c) For most of the equipments and instruments, Standard Operating Procedures for calibration and calibration schedule be prepared by the laboratory and a logbook shall also be prepared by each laboratory of proper documentation of calibration results.

8. Reference materials:

(a) Reference material are necessary for the testing and, or calibration, validation or verification of a sample or of equipment, instruments or other devices and all such materials shall be traceable to agency authorized by Government of India or any other International body.

(b) The laboratory shall prepare working standard by comparing with the reference standards and shall be routinely checked for their purity by selecting parameters such as identity, loss on drying or on water, impurity and assay, etc.

(c) Whenever, any new reference material is received by the laboratory, a code number shall be assigned and this code number shall be quoted on the laboratory note book and analytical work sheet. The working standard shall also be provided with identification code.

(d) A register pertaining to reference and working materials must be maintained by the laboratory. The followings details may be mentioned in the register:

(i) Source of supply;

(ii) Code number of the reference material;
(iii) Date of receipt;
(iv) Batch number or identification number of the supplying agency;
(v) Details like assay value, water content or any other information provided;
(vi) Storage condition of the material; and
(vii) Date of expiry, if any and date of manufacturing if possible.

(e) All working standards shall be checked at appropriate intervals or before use to ensure that it has not deteriorated or decomposed during storage. These observations be recorded in a register. All the reference and working storage between 2-8^{0}C shall be stored in a refrigerator. Wherever recommended the material may not be allowed to be frozen.

9. Microbiological Cultures:

(a) Standard Operating Procedure for maintenance of microbial culture and sub-culture must be prepared by the laboratories.

(b) If the culture have become non-viable or mutant, proper procedure shall be followed to destroy these cultures by autoclaving under an authorized personnel for biological testing. Preferably not more than five passages may be prepared.

(c) All activities be carried out in an aseptic area by authorized person.

(d) The laboratories shall perform standard biochemical tests on the sub-culture as given in literature to ensure their viability.

10. **Quality system:**

The quality system shall be designed to ensure the following objectives:-

(a) The measurements and calibrations shall fully conform to the compendia requirements and the methods demonstrably based on validation protocols are followed.

(b) It shall be effective in providing necessary assurance the activities or processes or techniques or practices comply with planned arrangements.

(c) It helps in early detection and correction of non-conformities.

(d) Remedial action on the observations by internal and external audits are taken appropriately and

(e) It shall have a documented quality policy for the organization.

11. **Internal quality system audits:**

(a) Internal audits are done to assure the integrity of the analysis and such audits shall be conducted periodically with a predetermined schedule and procedure with appropriate checklist, to verify that the operations continue to comply with the requirements of quality system and requirements of regulatory authorities. Internal quality audits shall be carried out by trained and qualified personnel who are independent of the activity to be audited.

(b) The periodicity of quality audit shall be fixed by the Head of the laboratory so that each activity is audited at least once in a year.

(c) Head of the laboratory will be responsible for initiation of the corrective action arising from audits and verification of corrective action arising form audits and verification of corrective action.

(d) Whenever any non-compliance or any diversion is noticed by the team in implementing quality policy or quality system, protocols, the same will be attended by the Quality Manager. The problem will be analyzed and necessary actions will be taken with proper documentation.

(e) The Quality Manager shall maintain all the records of the analysis being conducted which includes test system, the type of analysis, date on which analysis is done, etc. and quality Manager shall also maintain copies of all analysis is done, etc. and quality Manager shall also maintain copies of all protocols pertaining to different activities being cheeked by the audit team.

12. **Management review:**

Quality system reviews shall be conducted by the top management at least once in every twelve months and the agenda of review shall generally cover the following:-

(i) Report or input of internal audits;

(ii) Matter arising from previous reviews;

(iii) Report of external audits, if any;

(iv) Surveillance report, if any;

(v) Result of proficiency testing;

(vi) Complaints or feedback received from users of laboratory services;
(vii) Details of in-house quality control checks;
(viii) Need of amendment of the quality system and documentation;
(ix) Induction training of new staff; and
(x) Any other requirements of the laboratory.

13. **Standard operating Procedures:**

(a) Standard Operating procedures are written procedures for different activities being conducted in a laboratory and shall include the following characteristics:
(i) they shall be written in a chronological order listing different steps leading to an analysis of drugs or calibration of an instrument;
(ii) testing laboratories shall have Standard Operative Procedure manuals and have its periodic review;
(iii) it shall be user friendly documents and shall include designation of the person responsible for intended activity.

(b) Standard Operating Procedures in addition to those recommended under various activities shall also be prepared to the minimum in respect of the following:-
(i) sample handling and accountability;
(ii) receipt identification, storage, mixing and method sampling of the test and control articles;
(iii) record keeping, reporting, storage and retrieval of data;
(iv) coding of different studies, handling of data including use of computerized data system;
(v) operation of technical audit personnel in performing and reporting audits, inspections and final report reviews;
(vi) routine inspection of cleaning, maintenance, testing, calibration and standardization of instruments;
(vii) action to be taken in respect of equipment failure;
(viii) analytical data methods;
(ix) health and safety protection;
(x) data handling and storage retrieval;
(xi) health and safety protection;
(xii) animal room preparations;
(xiii) animal care;

(xiv) storage and maintenance of microbial cultures;
(xv) maintenance of sterility room (i.e. constant maintenance and monitoring of Aseptic condition of sterility room);
(xiv) Use and storage of reference standards;
(xv) Procurement of stores and equipment;
(xvi) Monitoring of testing of samples;
(xvii) Method of retention of unexpended samples, their location, maintenance and disposal;
(xviii) Document control;
(xix) Redressal of technical complaints;
(xx) House-keeping;
(xxi) Corrective and preventive action;
(xxii) Working procedure (test methods);
(xxiii) Calibration manual; and
(xxiv) Training manual.

14. **Protocols and specifications archive:**

(a) Every laboratory shall have a specification archive and current versions of all necessary specifications shall be kept as per the requirements of the Act and the rules made there under and the National Pharmacopoeia (Indian Pharmacopoeia).

(b) All updates and corrections must be noted in the master volumes of Pharmacopoeias to prevent the use of absolute section; supplement and addendum shall also made available in the laboratory.

(c) The specification archive shall contain the following:

(i) list of all the pharmacopoeias;

(ii) a file on patent and proprietary medicines (non-pharmacopeial) test methods to specifications prepared and validated by the manufacturer or by the laboratory itself. The test methods shall be submitted to the concerned Drug Control Authority. The validated test methods developed by the manufacturer or the laboratory shall stand to the requirements of compendial parameter in regard to its precision, Accuracy, reproducibility, specificity, linearity, and ruggedness etc.

15. **Raw data:**

(a) Raw data refers to the laboratory work sheet, note books or analysis sheet, records, memorandum, notes or extract copies thereof so that may be the results of general observations and other activities and such raw data shall include hand written notes, photographs, software, drawing, computer printouts, spectral charts, dictated observations or recorded data from automated equipments. The raw data also includes record on receipt of animals, result of environmental monitoring, calibration, records of equipments, integrator output form analytical equipment, including equipments, integrator output form analytical equipment, including work-sheet used to read a note, information form Light Emitting Diode (LED) display of any equipment.

(b) A single line shall strike through the date being changed; the correct information shall be recorded along with the old data and the reason of change. The analyst making the change shall be identified at the time of data output. The original entry must be saved and the system shall have audit trail for all data.

(c) Data integrity and security shall be maintained and the data shall not be accessible to any unauthorized person.

16. **Storage and archival:**

(a) The residual sample shall be retained in proper storage condition for a period of one year after the final report.

(b)The laboratory must establish and maintain procedures for the identification collection, indexing, retrieval, storage, maintenance, and disposal of all quality documents.

(c) All the raw data, documentation, Standard Operative procedures, protocols, and final reports are to be retained and there shall be archives of orderly storage and expeditious retrieval of all raw data, documentation, protocols, interim and final report. The archive shall provide a suitable environment that will prevent modification, damage, or deterioration and/or loss.

(d) The condition under which the original documents are stored must ensure their security and confidentiality.

(e) Paper documents shall not be kept for long periods under high humidity and raw data in the form of tape and discs are to be preserved with care.

(f) In case of storage of only optical disc, for life of disc shall be longer than the storage time.

(g) Raw data on thermal paper might fade away with time; therefore, a photocopy of the thermal paper shall be retained in the archive.

(h) Time for which records are retained shall be prescribed in the documents.