Short Communication

GOOD LABORATORY PRACTICES (GLP): KEY IN SUCCESS FOR THE DISEASE DIAGNOSTIC FIELD

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INTRODUCTION

Organization of Economic Co-operation and Development (OECD) defined GLP as a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.

GLP is a holistic approach to ensure the consistency, reliability and uniformity of laboratory findings (Carroll, 2016). It includes organizational and personnel management, quality assurance strategies, arrangement of necessary facilities, and test systems for reliable outcomes(WHO, 2009). Moreover, it seeks standard operating procedures (SOP) in different aspects of laboratory management. Quality control assurance and implementations are keys for the success of diagnostic as well as research laboratory. It ensures consistent, reliable and reproducible outcome of the laboratory data and results. GLP procedure is the one which ensures these outcomes. GLP was first introduced by New Zealand and Denmark in 1972, and slowly it has been adopted in several countries across the globe. In 1981, OECD adopted the GLP principles with its international standard. OECD is helping several countries for promulgation and introduction of GLP. GLP is mandatory in the international communities for acceptance of data; once it is accepted by the regulatory bodies of the particular country that follows OECD GLP guidelines (Dybkaer, 1986).

Diagnostic laboratories receive large number of samples, mostly infectious agents, and it is crucial to follow the GLP for quality assurance and safety procedures. The findings from the diagnostic laboratory influences by the quality of specimen received, and laboratory factors, such as proficiency of technical personnel, quality of chemicals and reagents, and quality of result (Macleod et al., 2009). This would determine the outcome of the disease. Under this context, this short communication envisioned to describe the GLP, especially by targeting to the veterinary undergraduates, and graduates, as well as laboratory technicians, working in the diagnostic labs.

Requirements of GLP

Resources

To follow the GLP efficiently, a given laboratory must be equipped with necessary infrastructure and facilities.

Organization

Good organizational structure is key for best performance of assigned task. For effective implementation of GLP by research as well as diagnostic laboratory, it should have clear organizational chart which should reflect the laboratory functions and relationships among the departments as well as units (Gumba et al., 2019).

Personnel

Laboratory must recruit necessary human resource to perform the jobs on time and in GLP-compliant way. It is important to have competent and qualified human resource with defined job description. There should be periodic trainings to update knowledge and skill of the persons working in the lab as well as management. Technical as well as data analysts must have proof of satisfactory training and/or competency with designated laboratory procedure and analysis technique.

Facilities and equipment

Fast and reliable data generation depends upon the laboratory facility and equipment quality. GLP envisage well-structured laboratory facility for receiving good quality samples, sample entry, and storage; processing and conduct experiments and documentation. The facility must have sufficient space to avoid problems of overcrowding, cross contamination, utilities (adequate and stable water and electricity supply). Laboratory equipment must be

functional and there should be provision of periodic maintenance, calibration and validations. These activities must be well documented for precision status of the equipment.

Quality assurance

Quality assurance can be achieved by adopting well-structured organization and responsible technical personnel. Moreover, following GLP principles and guidelines will assure the good quality data. There must be independent monitoring system for effective execution of the ideal laboratory to maintain its quality. Accuracy of data, timely result, quality assurance of technical human resources, and quality of equipment, chemicals & reagents, and validation of test systems are key for quality assurance of the lab. Every lab needs to have internal quality audit system which will give periodic feedback to the laboratory management for quality improvement.

Certification

A good quality lab must be accredited and certified by the regulatory body. Accreditation and certification of laboratory facility, instrumentations, technical personnel and experiments/studies that are carried out according to the GLP guideline is crucial to ensure quality outcome (Bolon, Bradley, Butt, Jensen, & Rao, 2020).

GLP certification

Every country must have GLP certification system. This is complex process, and it needs to pass several steps to get it. The certification body needs to conduct audit of laboratory facility, quality system and data management practices, and fill up the score card which will help to analyze data integrity and quality assurance. The score card would be reviewed and outcome would be discussed with the laboratory management team for further improvement or course correction. Once improved, authority needs to re-score the facility and analyze; if satisfied, certification will be issued. There must be regular re-inspections.

Certification of laboratory facilities

The regulatory body evaluate the A-A of the laboratory. They have well defined Performa to record space, ventilation, storage (different conditions such as room temperature to 196^0C), waste disposal system, SOP, cleaning and sanitation, and sterilization. So, ideal lab needs to arrange necessary facilities, and it should be up to date to get certification from the concerned authority.

Calibration and validation of instrumentations

Data produced by faulty non-calibrated and non-validated instrument may look like valid data, but in real sense it is not. This needs to be addressed by frequent calibration andvalidation by different means. This process is very crucial for analytical laboratories. Detail record of each equipment including serial number, catalog number, manufacturers guidelines need to be well documented and calibrated and validated accordingly.

Reagents/materials certification

In research and diagnostic laboratories, reagents, chemicals and materials need to be purchased from the reliable company. Several low quality manufacturers are mushrooming specially in the third world countries. Products from those companies need to be discouraged. All reagents, chemicals, solutions must be well labeled. They should be clear labeled with expiry date, date of open, composition of chemicals and reagents.

Sampling and sample tracking

Research/diagnostic laboratories receive diverse type of samples for processing. Sample collection (type of sample) packaging and preservation (leak-proof packaging), different type of preservative depending upon the type of sample); means of transportation need to be well documented and mentioned in the sample Performa. Once received, samples need to be coded before processing. This must maintain the connection between data generated in the lab and original source of sample.

Safe laboratory practices

Big laboratories should be established away from the pubic area. Lab building itself should be designed in such a way that there should be one door system right from sample receipt and final result dispatch. Every laboratory must be well ventilated and equipped with waste disposal mechanism. There should be separate disposal system for biodegradable, environment friendly waste materials, chemicals, reagents and damaged equipment. Disposal of microorganisms and tissues is critical and they should be treated separately. Disposal pit should be well structured and leaked proof to avoid underground water contamination by chemicals and infectious agents(Wade, Pai, Eisenberg, & Colford, 2003).

Each and every person working in the lab should follow the safety first rule. Safe laboratory practices include personal, workplace and environmental safety issues. Every lab should figure out the safety issues of each experiment and should formulate the safety rules, regulations and procedure for them. Person working in the laboratory must use protective equipment, such as caps, gown, shoes, gloves, and glasses in special cases. Laboratory management should formulate the safety contract and signed by every personnel working in the laboratory. Safety contract should clearly state the general guidelines including general cleaning procedures, prohibited activities, such as eating in the lab, replacement of used equipment, reagents, follow SOP of every experiment, and equipment used. Similarly, safety issues of chemicals, such as smell, touch, taste as well as use of safety hood should be clearly instructed in the safety contract. Safety measures during minor to major accidents, such as broken glasses, fire, short circuits and spillover of chemicals should also be mentioned in the guideline and must be followed by everybody working in the lab.

Biological Safety Level (BSL)

BSL is a series of protection measures taken in the laboratories dealing with different categories of living organisms. There may be primary and secondary contaminations in the biological laboratories (Weidmann, Silman, Butaye, & Elschner, 2014). Primary contaminations and protection against them deals with the protection of people working in the lab and immediate laboratory environment from infectious agents while secondary contamination deals with the protection of environment external to the working laboratory. Based on nature of organism, BSL is divided into four distinct categories which are summarized in Table (1) (WHO, 2004).

Table 1. WHO Biosafety levels

Biosafety level	**BSL-1**	**BSL-2**	**BSL-3**	**BSL-4**
Description	well defined organisms, no contamination, rarely cause any disease	Contaminant, moderate risk, diseases of different severity	High contaminant, aerosol transmission, serious/potentially lethal disease	Maximum contaminant, high risk agents, life-threatening disease
Organism	*E. coli*	Influenza, HIV, Lyme disease, Hepatitis A, B, and C viruses, pathogenic strains of E. coli &*Staphylococcus, Salmonella, Plasmodium falciparum & Toxoplasma gondii.*	T*uberculosis*, SARS corona virus, MERS corona virus,	Ebola, Nipah virus
Pathogen type	minimum hazard to personnel & environment	Associated with human disease and pose moderate hazards to personnel and the environment	Indigenous/exotic agents with potential aerosol transmission, causes serious or potentially lethal disease	Dangerous & exotic agents that pose a high risk of aerosol transmitted laboratory infection and life-threatening disease.
Autoclave requirement	None	None	Yes	Yes

Documentations

Proper documentation helps for effective management of laboratory. Every activities conducted in the lab must be recorded manually as well as electronically. Use of equipment, type of samples, cleaning and disinfection, and procedure adopted after completion of experiment need to be documented which would ensure safety issues of the equipment as well as laboratory environment. These records may be required during legal challenges due to concern of decisions based on the original results. These records must be stored at least for five years. In some of the countries it is necessary to keep them until ten years.

Laboratory book

Lab book is the asset of every diagnostic and research laboratory. Everything right from sample collection to result need to be recorded on it. There must be page number of lab book and none of the pages are allowed to be removed. Source of sample, sample registry, standard operating procedures, test procedures, specification of chemicals and reagents used, certificate of analysis with relevant test protocols, calibration, validation and training records must be written with date and signed by the laboratory in charge. Lab book must not take out of the laboratory and keep safe.

Manual

Routine protocols should be documented in the form of laboratory manual and everybody should follow it. The protocol should include proper sampling technique for different kind of specimens and their transport. It should also state the criterion for acceptance and rejection of samples based on sample collection and transportation tools used. Detailed procedure for sample processing, storage and retrieval should be clearly stated in the laboratory manual.

Standard operating procedure (SOP)

SOPs of each equipment and protocol are key for adopting GLP guideline. Major steps of experiments conducted in the lab must follow the GLP and protocol must be approved by concerned authority before start. Any changes in the experiments/study design must be amended by the authority/regulatory body. All routine procedures and protocols must be described in the SOPs which will be the part of documentation system of the lab (Hallin & Wichman, 2007). Certain techniques must be standardize by the lab itself which will ensure the comparison of results among studies and these standardized tolls must be written in SOPs.

Reference standard

Standardization of protocol and comparison of outcome with standard reference value will give guideline for data analysis. Depending on the nature of the experiment, reference values of each experimental outcome should be either taken from universal value or set locally/regionally/nationally. This will give guideline for result analysis and interpretation.

Data management

Data are the outcome of any scientific experiment. Raw data are the primary information of any study and they need to be protected will be important for reconstruction of the experiments and traceability of the outcome. Research data would be analyzed statistically and diagnostics would be performed directly. Whatever the use, outcome and interpretations of the study must be true and accurately reflection of raw data (Esch et al., 2010). The outcome of the study and its interpretation must be included in the report, and reflection of GLP principles and their elements should be well considered in the report (Kendall et al., 2016). Data saving is important to archive in future. Data and methodology could be reconstructed several years later. So, data saving for extended time without any loss and deterioration that would allow fast excess need to be arranged in the lab. Data must be saved electronically as well as physically, e.g. in the lab manual.

Legal issues

Every lab needs to follow the GLP principles and guidelines (Jena & Chavan, 2017). If any of the labs is not following it, lab would be disqualified, and data generated from such laboratory will not have any legality.

REFERENCES

Bolon, B., Bradley, A., Butt, M. T., Jensen, K., & Rao, D. B. (2020). International Regulatory Guiding Documents and Best Practice Recommendations on Peripheral Nervous System (PNS) Histopathologic Evaluation in Good Laboratory Practice (GLP)-Compliant Animal Toxicity Studies. *Toxicologic Pathology*, *48*(1), 78–86. https://doi.org/10.1177/0192623319861364

Carroll, E. E. (2016). Going GLP: Conducting Toxicology Studies in Compliance with Good Laboratory Practices. *U.S. Army Medical Department Journal*, *3*(16), 64–69.

Dybkaer, R. (1986). Elements of good practice in decentralized clinical laboratories. *Upsala Journal of Medical Sciences*. https://doi.org/10.3109/03009738609178516

Esch, P. M., Moor, C., Schmid, B., Albertini, S., Hassler, S., Donzé, G., & Saxer, H. P. (2010). Good laboratory practice (GLP) - Guidelines for the development and validation of spreadsheets. *Quality Assurance Journal*. https://doi.org/10.1002/qaj.466

Gumba, H., Waichungo, J., Lowe, B., Mwanzu, A., Musyimi, R., Thitiri, J., … Kariuki, S. (2019). Implementing a quality management system using good clinical laboratory practice guidelines at KEMRI-CMR to support medical research. *Wellcome Open Research*, *3*, 137. https://doi.org/10.12688/wellcomeopenres.14860.2

Hallin, P., & Wichman, A. (2007). Chapter 16. Standard Operating Procedures for Good Laboratory Practice Work. In *Good Clinical, Laboratory and Manufacturing Practices*. https://doi.org/10.1039/9781847557728-00223

Jena, G. B., & Chavan, S. (2017, October). Implementation of Good Laboratory Practices (GLP) in basic scientific research: Translating the concept beyond regulatory compliance. *Regulatory Toxicology and Pharmacology*. Academic Press Inc. https://doi.org/10.1016/j.yrtph.2017.07.010

Kendall, G., Bai, R., Błazewicz, J., De Causmaecker, P., Gendreau, M., John, R., … Yee, A. (2016). Good Laboratory Practice for optimization research. *Journal of the Operational Research Society*. https://doi.org/10.1057/jors.2015.77

Macleod, M. R., Fisher, M., O'Collins, V., Sena, E. S., Dirnagl, U., Bath, P. M. W., … Howells, D. W. (2009). Good laboratory practice: preventing introduction of bias at the bench. *Stroke; a Journal of Cerebral Circulation*. https://doi.org/10.1161/STROKEAHA.108.525386

Wade, T. J., Pai, N., Eisenberg, J. N. S., & Colford, J. M. (2003). Do U.S. Environmental Protection Agency water quality guidelines for recreational waters prevent gastrointestinal illness? A systematic review and meta-analysis. *Environmental Health Perspectives*, *111*(8), 1102–1109. https://doi.org/10.1289/ehp.6241

Weidmann, M., Silman, N., Butaye, P., & Elschner, M. C. (2014). *Working in biosafety level 3 and 4 laboratories : a practical introduction*. Jena: Wiley-VCH Verlag GmbH & Co.

WHO. (2004). Laboratory biosafety manual Third edition World Health Organization. *World Health Organization*, 1–178.

WHO. (2009). Handbook Good L Aboratory P Ractice, 1–328.