Fundamentals of GCP And GCLP Quality Assurance and How to Apply Them..

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Objectives

- Understand different regulations governing laboratory operations.
- Understand the Uniqueness of GCLP to GCP provisions
- Practical applications of GCLP regulations
- Understand the “Professional” Meaning and Usage of the Different Regulations.
Highlights:

- Definitions
- Importance of the different Regulations
- GCP Quality Assurance
- Case Studies
- The Requirements
- Conclusions.
Definitions – GCP

- Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.

- Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki (ICH GCP Guideline).
Good Laboratory Practice (GLP) is a managerial concept covering the organizational process and the conditions under which laboratory studies are planned, performed, monitored, recorded and reported.

It is intended to promote the quality and validity of test data.

(OECD GLP Guideline).
Definition—GCLP

- International regulations intended for use by Medical laboratories handling samples meant for clinical research/trial.
- Embraces both the research and clinical aspect of GLP
- Compliance with this regulations shows that GCP requirements have been met.
Bio analytical Measurements

- Lab based analysis

- Analysis is performed using human samples, but data generated will generally not be reported to physicians for use in diagnosis and/or treatment of subjects. Eg. PK/PD studies; Immunogenicity studies, Biomarker studies.
Why these regulations

- Assures the acceptability of research data generated across various labs—reproducibility, validity & credibility of data.
- Improves EBM practice, Translational research,
- Facilitates NDA and the approval.
- Saves cost for Sponsors, CRO etc
- Improves patients care and QoL

Can you suggest more??
What is GCP Quality Assurance??

Definition

- All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).
GCP– Quality Requirement

- Systems with procedures that assure the quality of every aspect of the trial should be implemented.
Fundamental Basis of Quality in clinical trial

- **Pre-clinical Testing including toxicology**
- **PHASES I, II, III & IV Human studies**
- **Study design, conduct, recording & reporting**

GOOD CLINICAL PRACTICE (GCP) Regulations

GOOD LABORATORY PRACTICE (GLP) Regulations

SCOPE OF GLP and GCLP

- **Good Clinical Practice**: Good Laboratory Practice. This regulation is for laboratories that handle pre-clinical studies required for full clinical trial. It is required for regulatory application, submission and approval.

- **Good Clinical Laboratory Practice**: is a regulation applicable to clinical laboratories that handle samples for clinical trial purposes. It is also required for regulatory approvals.
## Regulatory Standards for CT Quality Assurance

<table>
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<tr>
<th>Applicable Laboratory Practice</th>
<th>Laboratory Category</th>
<th>Industry Applicable International Standards</th>
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<tr>
<td>GCLP</td>
<td>Medical Laboratories</td>
<td>CLIA, CAP, ISO15189, WHO/AFRO Guideline</td>
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<tr>
<td>GLP</td>
<td>Non-Medical Laboratories</td>
<td>21–CFR: GLP for non-clinical lab studies, OECD–principles of GLP and compliance monitoring</td>
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GCP Quality Concerns
GCP: Area of Quality Concern

- Protocol Development
- IRB/IEC Review Process (membership, documentations)
- Subject selection/Recruitment (adhering to inclusion and exclusion criteria)
- Measurable End Points.
- Missing Data
- Statistical Issues.
- Informed Consent Document/Process
- Laboratory (GCLP, ISO 15189, TQM, QA, QC)
- Data Collection (SD, CRF, EDC, Data Quality)
- EHR, LIMS, PACS
Monitoring Visits (Pre, during trial and close-out)
Drug (GMP, GLP)
Final Reporting
DMC
Case study: A routine laboratory that handles clinical samples for routine patient management did well in EQA programme, but failed GCLP audit.

Is this possible????

Why???????
EQA Programme only focuses on the analytical processes of the laboratory and does NOT necessarily assess GCLP compliance which is a comprehensive QMS for clinical labs handling CT samples.
A CRO outsourced clinical samples to one of the ISO certified clinical laboratories during a clinical trial of a hypertensive drug. The samples were analyzed and results used to fill an IND application. Six months later and in the process to review the data supplied by the CRO, the regulatory agency went to the lab for an audit in order to ascertain the submissions made by the CRO. The Auditors requested to see the samples submitted, but could not because the samples have been discarded by the laboratory for lack of space in the deep freezer. Based on this finding, the regulatory agency refused the approval of the hypertensive drug for lack of evidence.

Can the actions of this lab be justified?? Please share.
By GCP regulation and by inference GCLP guideline, laboratories that handle samples for clinical trial are expected to keep and preserve such samples for at least 2 years even after the close out of the clinical research and the approval of the drug.

The Rule:
Case study III

A GCLP clinical laboratory was recently audited by NAFDAC to assess for compliance with the guideline. The Auditors found the following:

- The laboratory staff have not undergone any re-training for the last one year
- There was no evidence of revalidation of reagents
- There was no evidence of calibration of balances, thermometers, centrifuges for the last one year
- Rough sheets containing laboratory data were found in the dust bin.

What could be wrong with this Lab??
Case Study IV

- A change was effected on a laboratory data in the Case Report Form (CRF), but was not reflected in the Source Document (SD). This raises some doubt on falsification of laboratory data and also caused serious embarrassment to the institution and her laboratory staff.

- What can you call this?
GLP AND GCLP Requirements

- Organisation and Personal
  - Well established lab structure
  - Organogram
  - The right people to drive the structure
  - Training and retraining and regular competency assessment.
  - All training records should be properly kept.
  - JD of all staff
  - CVs of all staff
  - An evidence to proof that each staff has read and understood his applicable JD.
Requirements Cont’d

- Facilities
- Equipment, materials and reagents
- Standard Operating Procedures (SOPs)
- Planning, conduct and reporting
- Quality Control and Quality audits
- Retention of study records and reports
GCLP Concerns

- Organization
- Processes, procedures
- Resources
- Responsibilities
- Equipment

Staff, SOPs, validation instruments, Quality Manual

Organogram
Budget
Systems
Environment

Lab activities, Pre-analytical & Post activities
EQA

Expressed in writing by top Management.
Mission & vision.
Value Statement
Conclusion

- Achieving the best available evidence for the treatment of diseases and translating research findings to clinical benefits, quality and well thought research is highly essential.

- Such studies should be conducted with the utmost quality that is required.

- This implies that all the required regulations stipulated for the conduct of clinical research should be applied; and where they do not exist, efforts should be made achieve same.
If we must attract clinical research to our region, abiding by these regulations cannot be compromised.

It is our collective responsibility to develop the system which will ensure that the required standards are implemented.