Role of Good Laboratory Practice (GLP) in Good Clinical Practice (GCP)

Presented By
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Welcome!

I am so glad to be here in this International Conference of GLP, GCP & GMP.

I hope you find a new knowledge of GLP and GCP.
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2. Trainer in Faculty and Leadership Development Center, Cairo University.

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**Other Posts:**

1. Director of Career Center, Faculty of Pharmacy, Cairo University.

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Performance objectives

Highlight

- GLP.
- GCP based on ICH.
- The comparison between GLP & GCP in some aspects.
- The role of GLP to achieve GCP.
Drug development process

Basic Research → Disease Recovery → Drug Recovery → Preclinical Development → Clinical Trials → Manufacturing

- Not regulated
- Study Based
- GLP
- GCP
- GMP
- Process Based

Role of laboratories in medicine

- Research Laboratory
  Discovery & development of new Drugs/therapy
  Fundamental research/mechanisms of diseases
- Medical Testing Laboratory
  Patient care
  Clinical drug trial
- Manufacturing
  Post clinical trials, bulk drugs, cell-based therapy,
  Plasma products, medical device
Role of laboratories in drug development

Stage I
Discovery of active substance

Stage 2
Non-clinical study on SAFETY testing on drugs

Stage 3
Studies in human / Clinical Trials

Stage 4
Post approval Clinical Trials

Manufacturing

Time line approximately 10 yrs

Classical drug development process
4 well-defined stages

- **Stage I**
  - Discovery of potential new drug products.
  - Not covered by a regulatory standard.

- Non-clinical, not in human.
- Safety Testing.
- GLP Principles specific for this stage:
  - toxicology.
  - mutagenicity.
  - safety.
  - pharmacology.
  - pharmacokinetics.
  - bioavailability.

• Stage III

• Clinical Studies, in human.

• GCP is the basis for quality standards, ethical conduct and regulatory compliance (Standard: ISO).

• Phase I (tolerance of test drugs, define human pharmacokinetics) to Phase II (dose-effect relationship) and Phase III (full-scale, often multi-centre clinical efficacy trials in patients).

Stage IV

- Post-approval.
- Drug registered, available on market.
- Any subsequent clinical trials (Phase IV) must comply with GCP (Standard: ISO).

Role of laboratories in clinical trials
-Medical testing laboratories

Pre Study

- Screening.
- Enrolment: inclusion criteria exclusion.

During Study

- Verify effects of drug clinical efficacy.

End of Study

- Monitoring of adverse effects safety.
- Clinical efficacy.
- Data analysis.
- Verification.
Good Laboratory Practice
GLP

• Regulatory Authorities responsible for registering and controlling pharmaceuticals request:
  laboratory to demonstrate data in registration package for a new chemical/drugs has been gathered using ‘good laboratory practice’.

  organization be certified (or accredited) for ‘GLP’.

• Organizations (researchers and medical laboratories) often claimed that they are working under ‘GLP’.

• Clients of laboratories often request that their work be done using ‘good laboratory practice’.

Definition:

- GLP embodies a set of principles that provides a framework within which laboratory studies are planned, performed, monitored, reported and archived.

- **GLP** is Food and Drug Administration (FDA) regulation that believes that implementation of a GLP quality system would avoid a risk-based approach, reduce regulatory burden and encourage science-based technology.

Formal concept of GLP

• GLP is sometimes confused with the standards of laboratory safety like wearing safety goggles.

• GLPs are not guidelines, they have the force of law.

• The term ‘Good Laboratory Practice’ has a SPECIFIC meaning when applied to non-clinical environmental health and safety studies.
The principles of GLP in general

- Concerned with how we organize our laboratories and how we organize our studies.

- Addresses responsibilities for managing people, facilities and equipment for good science.

- Concerned with how we plan, perform and report our experiments and studies.

- Importantly it does not interfere with the ability of scientists to make scientific decision.

GLP standards

- GLP standards include:

  - International Organization for Standardization (ISO)

  - The Organization for Economic Co-operation and Development (OECD) Principles of Good Laboratory Practice which:

    Define and describe a quality system concerned with the organizational processes and conditions under which a non-clinical health and environmental safety study is conducted.

OECD afforded fundamental points of GLP which applied in whatever industry targeted, stresses the importance of the following main points.

- **Resources**: Organization, personnel, facilities, equipments.
- **Rules**: Protocols, concept of Study Director, Standard Operating Procedures (SOP).
  
  \[
  \text{GLP regs > Protocol > SOPs}
  \]

  \[
  \text{GLP regs supercede the protocol and the SOPs}
  \]

- **Characterization**: Test items, test systems.
- **Documentation**: Raw data, final report, archives.
- **Quality Assurance**: Independence from study conduct.

GLP in the OECD principles

- ‘A quality system concerned with the organizational process and the conditions under which non-clinical health and environmental studies are planned, performed, monitored, recorded, archived and reported.’

- It does not concern with the technical validity of the studies.

Now we will go to GCP
Clinical Practice Trials

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Phase IV</th>
<th>Phase V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Checking for safety</td>
<td>Checking for efficacy</td>
<td>Checking effectiveness</td>
<td>Test long term safety</td>
<td>Translational research</td>
</tr>
<tr>
<td>10-20 healthy volunteers</td>
<td>~ 200 samples</td>
<td>~ 1000s samples</td>
<td>Real patients</td>
<td>Research on data collected</td>
</tr>
<tr>
<td>Unexpected side effects may occurs</td>
<td>How good is the intervention</td>
<td>Looking for rare side effect</td>
<td>Involve untested group of people</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If not good, normally detect here</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cone, Ms., *Guidelines for good clinical practice (GCP) for trials on pharmaceutical products*, 1995, WHO
Prior to an actual set of guidelines to follow for GCP, clinical studies were dangerous and could result in serious disease, or possibly death.

So, the formation of the International Conference on Harmonization (ICH) led to the creation of the Consolidated Guidance on GCP.
Good Clinical Practice (GCP)

- A standard for designing, conducting, recording and reporting of studies involving human subjects.

- Public assurance that the **rights, safety and well-being** of trial subjects are protected.
Good Clinical Practice

- Designing
- Conducting
- Reporting
- Clinical Trials or Studies
- Analysis
- Monitoring
- Recording
Under GCP, FDA requires that people be informed:

- The study involves research of an unproven drug, the purpose of the research.
- The duration that the participant will be expected to participate in the study.
- The nature and the transparency in the study.
- Possible risks/benefits to the participant.
- Participation is voluntary and that participants can quit the study at any time without penalty or loss of benefits to which they are otherwise entitled.
ICH was initiated on April 1990, in a meeting hosted by European Federation of Pharmaceutical Industries Associations (EFPIA).

In 1997 – ICH GCP became law in some countries.

GCP also, is protected through existing ICH-GCP Guidelines with co-sponsors (voting right); European Commission, European Federation of Pharmaceutical Industries Associations (EFPIA), Japanese Ministry of Health, Labour and Welfare (JMHLW), Japan Pharmaceutical Manufacturers Association (JPMA), Pharmaceutical Research and Manufacturers of America (PhRMA) and FDA.
Aims of ICH

- Unify registration requirements for new products
- Reduce medicinal product development costs: more economical use of animal, human and material resources.
- Accelerate medicinal product licensing times: avoid repeat testing in different regions.
- Increases patent protection times through reducing delay in licensing times.
PRINCIPLES OF ICH-GCP
1. **Conduct trials according to GCP**

Clinical trials should be conducted in accordance with the **ethical** principles that have their origin in the *Declaration of Helsinki*, and that are consistent with GCP and the applicable regulatory requirement(s).

2. **Weigh risks vs. benefits**

Before a trial is initiated, foreseeable *risks and inconveniences* should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
3. To exceed subjects wellbeing over the science

The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.

4. Have adequate information to justify trial

The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
5. Write a sound protocol
Clinical trials should be scientifically sound, and described in a clear, detailed protocol.

6. Receive IRB/IEC approval
A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.
7. Use qualified physicians
   The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.

8. Use qualified & trained support staff
   Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).
9. Obtain informed consent
Freely given informed consent should be obtained from every subject prior to clinical trial participation.

10. Record information appropriately
All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification.
11. Protect data

The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

12. Handle investigational products appropriately

Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.

13. Ensure Quality

Systems with procedures that assure the quality of every aspect of the trial should be implemented.
## Comparison between GLP & GCP

<table>
<thead>
<tr>
<th>Function</th>
<th>GLP</th>
<th>GCP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ownership</td>
<td>Facility Management</td>
<td>The Sponsor has the responsibility for the SOP system</td>
</tr>
<tr>
<td>Main responsibility for the activity</td>
<td>Study Director</td>
<td>Principal Investigator</td>
</tr>
<tr>
<td>Responsibilities for “Production”</td>
<td>Principal Investigator</td>
<td>Pharmacist</td>
</tr>
<tr>
<td>Quality</td>
<td>Quality Assurance QA does not approve SOPs QA reviews SOPs for GLP compliance only</td>
<td>Monitor/ Quality Assurance</td>
</tr>
<tr>
<td>Archive</td>
<td>Archivist</td>
<td>Archivist</td>
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</table>
The role of GLP in GCP

• Role of laboratories in Clinical Trials including medical testing laboratories must meet the needs of all patients and the clinical personnel responsible for the care of those patients.

• Such services include arrangements for requisition, patient preparation, patient identification, collection of samples, transportation, storage, processing and examination of clinical samples together with subsequent validation interpretation reporting and advice, in addition to safety and ethics in medical laboratory work.
• If research in Laboratory practice concern with quality, reliability and integrity of studies, reporting of verifiable conclusions and the traceability of data and for non-clinical safety studies,

It will ensure product safety and efficacy under GLP for non-clinical studies and Patient care & clinical studies under GCP and will ensure that the produced results will be valid, reliable, accurate and reproducible.
Applications
Drug Development Timeline

New formulations and indications move through the drug development life cycle

- Target Discovery Validation
- Lead Generation
- Lead Optimization
- Preclinical Development
- Phase I Clinicals
- Phase II Clinicals
- Phase IIB Clinicals
- Phase III Clinicals
- Phase IV Clinicals
- Drug Commercialization

Diversified Bio-Medics, Inc. Services

- Discovery & Preclinical
- Early Clinical Research
- Global Clinical Research
- Clinical Laboratories
- Bioanalysis.Bioanalytics
Diversified Bio-Medics, Inc., a development stage company 2003 at USA, focuses on providing bio-manufacturing and laboratory services to biotechnology and biopharmaceutical industries to provide manufacturing material for clinical trials, as well as manufacturing services including validation, license application, & packaging. It also plans to develop and manufacture drugs, such as monoclonal antibodies, enzymes, interferon, .....................etc.
Two decades ago, combretastatins (CA1-4), as natural antimitotic agents, were isolated from the bark of the South African tree *Combretum caffrum*. 

Discovery of Combretastatin A4 and the prodrug disodium phosphate

Preclinical development including plasma and urine samples

Phase I started in 1998

Phase II clinical trials

Now, CA4P is currently in Phase III to evaluate the safety and efficacy standards

Discovery & Preclinical GLP

Early Clinical Research GCP

CA4P
This many people working for a year to make this much drug!
Indeed, applying GLP built on understanding the needs of pharmaceutical industry and laboratories have an important role in clinical trials to achieve GCP.
Recommendations

• Should be started with GLP with accurate laboratory practice.
• Calibrate equipment to standard form, therefore giving right measurements.
• Correct/accurate accounts of the actual lab study.
• Adequate test systems.
• Provide assurance of the safety of the newly developed compounds.
• Focus on the protection of human rights in clinical trials.
• Provide standards on how clinical trials should be conducted.
• Define the roles and responsibilities of clinical sponsors, clinical research investigators, Clinical Research Associates, and monitors.
Thank You!