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

Presented By

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I am so glade 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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Other Posts:

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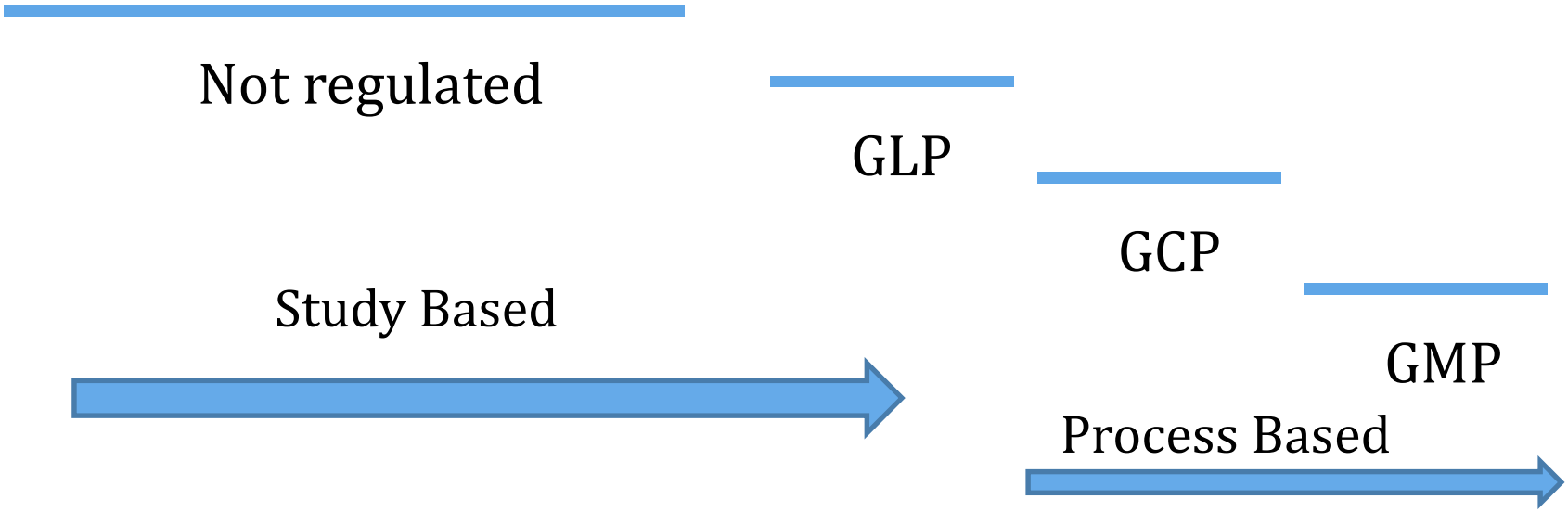
Performance objectives

Highlight

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

Drug development process





Ridley, R., The Process of New Drug Discovery and Development, Second Edition, 2006, World Health Organization

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

Ridley, R., Handbook: good laboratory practice (GLP): quality practices for regulated non clinical research and development, Second edition, 2009, World Health Organization

Classical drug development process 4 well-defined stages

- **Stage I**



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

Ridley, R., Handbook: good laboratory practice (GLP): quality practices for regulated non clinical research and development, Second edition, 2009, World Health Organization

- **Stage II**



- **Non-clinical, not in human.**
- **Safety Testing.**
- **GLP Principles specific for this stage :**

  toxicology.

  mutagenicity.

  safety .

  pharmacology.

  pharmacokinetics.

  bioavailability.

Ridley, R., Handbook: good laboratory practice (GLP): quality practices for regulated non clinical research and development, Second edition, 2009, World Health Organization

- **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).**

Ridley, R., Handbook: good laboratory practice (GLP): quality practices for regulated non clinical research and development, Second edition, 2009, World Health Organization

- **Stage IV**



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

Ridley, R., Handbook: good laboratory practice (GLP): quality practices for regulated non clinical research and development, Second edition, 2009, World Health Organization

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'.

Weinberg, S., Good Laboratory Practice Regulations Third Edition, 2003, Marcel Dekker, Inc.

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.



Ridely, R., Good laboratory practice training manual for the trainer: a tool for training and promoting good laboratory practice (GLP) concepts in disease endemic countries, Second edition., 2008, World Health Organization

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.

Weinberg, S., Good Laboratory Practice Regulations Third Edition, 2003, Marcel Dekker, Inc.

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.

Ridely, R., Good laboratory practice training manual for the trainer: a tool for training and promoting good laboratory practice (GLP) concepts in disease endemic countries, Second edition., 2008, World Health Organization

Fundamental points of GLP

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).

GLP regs > Protocol > SOPs

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.

Ridely, R., Good laboratory practice training manual for the trainer: a tool for training and promoting good laboratory practice (GLP) concepts in disease endemic countries, Second edition., 2008, World Health Organization

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.

Ridely, R., Good laboratory practice training manual for the trainer: a tool for training and promoting good laboratory practice (GLP) concepts in disease endemic countries, Second edition., 2008, World Health Organization

Now we will go to GCP



Clinical Practice Trials

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

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



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-GCP

International Conference on Harmonisation (ICH)

- 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.

Code of Federal Regulations and ICH Guidelines – www.clinicalresearchresources.com/books/bookstore.html

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.

Code of Federal Regulations and ICH Guidelines – www.clinicalresearchresources.com/books/bookstore.html


PRINCIPLES OF ICH-GCP

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.

Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, April 1996, ICH

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.

Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, April 1996, ICH

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.

Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, April 1996, ICH

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).

Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, April 1996, ICH

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**.

Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, April 1996, ICH

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.

Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, April 1996, ICH

➢Comparison between GLP & GCP

Function	GLP	GCP
Ownership	Facility Management	The Sponsor has the responsibility for the SOP system
Main responsibility for the activity	Study Director	Principal Investigator
Responsibilities for "Production"	Principal Investigator	Pharmacist
Quality	Quality Assurance QA does not approve SOPs QA reviews SOPs for GLP compliance only	Monitor/ Quality Assurance
Archive	Archivist	Archivist

➢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,

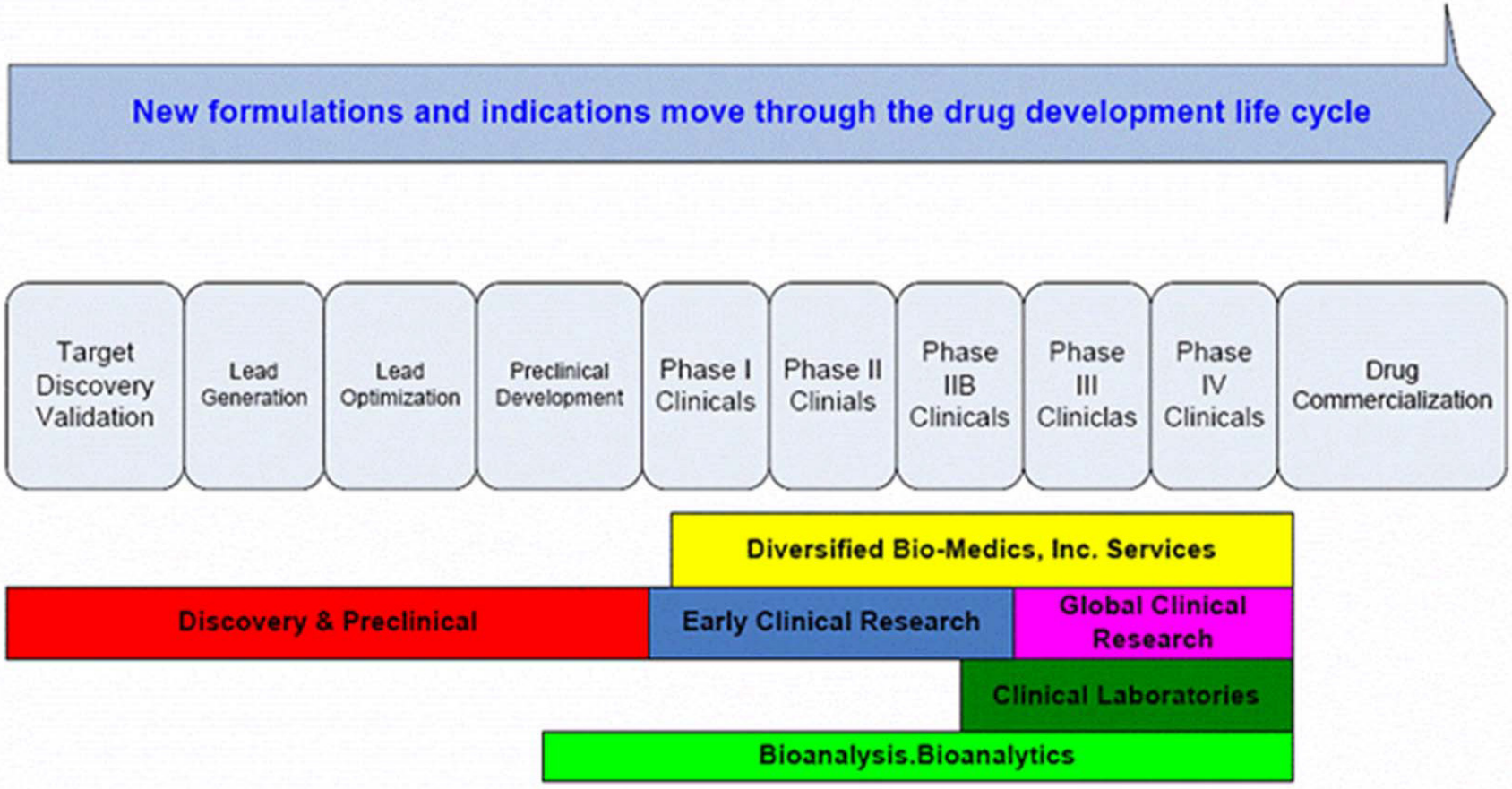
  It will ensure product safety and efficacy under GLP for non-clinical studies and Patient care & clinical studies under GCP and will ensure that the produced results will be valid, reliable, accurate and reproducible.

Applications



Diversified Bio-Medics, Inc.

Drug Development Timeline



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.

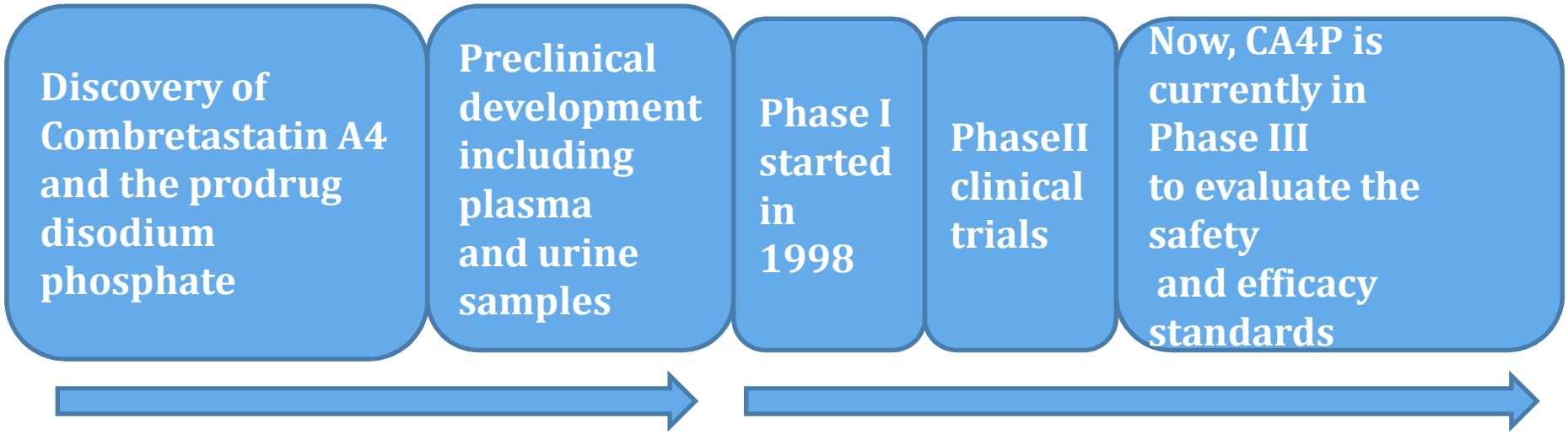
Development of Combretastatin A4 Phosphate (CA4P)

Two decades ago, combretastatins (CA1-4), as natural antimitotic agents, were isolated from the bark of the South African tree *Combretum caffrum.*

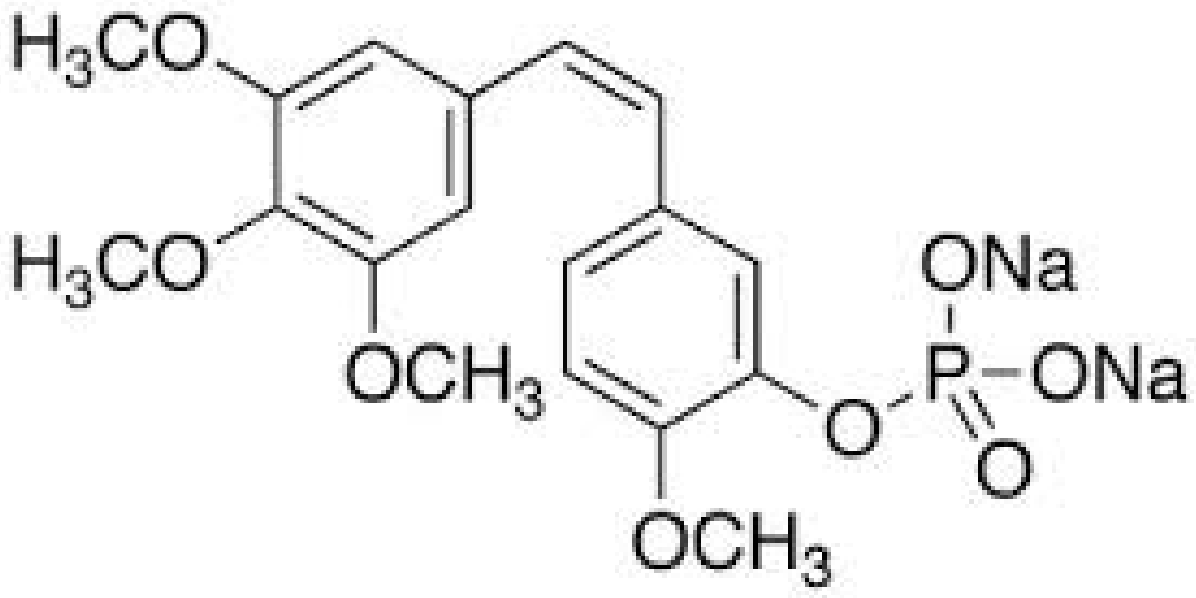


Pettit, G.; Singh, S.; Boyd, M.; Hamel, E.; Pettit, R.; Schmidt, J. and Hogan, F.; J. Med. Chem., **38**, 1666 (1995).

An Example Of A Drug Development Life Cycle



X., Wang, et al, Journal of Chromatography B, 877 (2009) 3813–3821
H., Yang, et al, Bioorganic & Medicinal Chemistry 20 (2012) 903–909



CA4P

This many people working for a year to make this much drug!



Conclusion

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!