GCP/GMP/GLP

Module 7 Topic 2

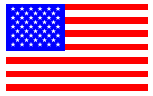
Various regions of the world...

Europe

US

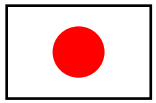
Japan

The ICH steering committee…



USA

European Union



Japan

- Pharmaceutical Research & Manufacturers of America
- European Federation of Pharmaceutical Industry Associates
- Japanese Pharmaceutical Manufacturers Association

THIS LED TO…..

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICH - GCP

- Established - 17th January 1997
- NOW APPLIED GLOBALLY

ICH GCP

Definition

"An international standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials, that provide assurance that the data and reported results are credible and accurate, and 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."

The Principles of GCP as per the ICH

- Clinical trials should be conducted in accordance with the ETHICAL PRINCIPLES that have their origin in the **Declaration of Helsinki**
- A trial should be initiated only if the anticipated benefits justify the risks
- The rights, safety and well-being of the trial subjects **are the most important considerations**
- Trials should be scientifically sound and described in a clear and detailed protocol
- The protocol must have received **prior** approval from the Ethics Committee or IRB

The Principles of GCP as per the ICH

Contd…

- The medical care of patients must always be the responsibility of a **qualified physician**
- Each individual involved in the trial must be qualified by education, training or experience to perform his/her task
- **Freely given** informed consent must be obtained from every subject **prior** to the trial
- All clinical trial information should be recorded in a way that allows its accurate reporting, interpretation and **verification**

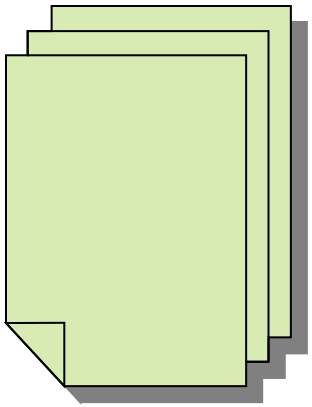
The Principles of GCP as per the ICH

Contd…

- The **confidentiality of the subjects** (patients) should be protected at all times
- All investigational products should be manufactured, handled and stored in accordance with **good manufacturing practices** (GMP)
- All products should be used only in accordance with the **approved protocol**
- Systems that **assure quality** should be implemented at all levels

Documentation

- Key to all successful studies.
- Allows verification of quality and integrity.
- Is a must for GCP compliance:
  - Paper (audit) trail
  - Filing
  - Archiving



As per ICH - GCP:

Documentation includes - 'All records', in any form (including , but not limited to, written, electronic, magnetic and optical records, and scans, x-rays and ECGs) that describe or record of the methods, conduct, and / or results of a trial, the factors affecting a trial and the actions taken

Commandments of Documentation

- If it happens write it down
- Use version numbers and dates
- Establish a good filing system (SOP)
- File so as to retrieve, not retain
- Use Fade free paper
- Retain and archive all data
- Hard copy of computer information
- Ensure controlled access

Standard Operating Procedures

- standardization & uniformity
- instructions & procedures
- clear, concise, practical SOPs
- for documentation, filing and archiving

Remember…

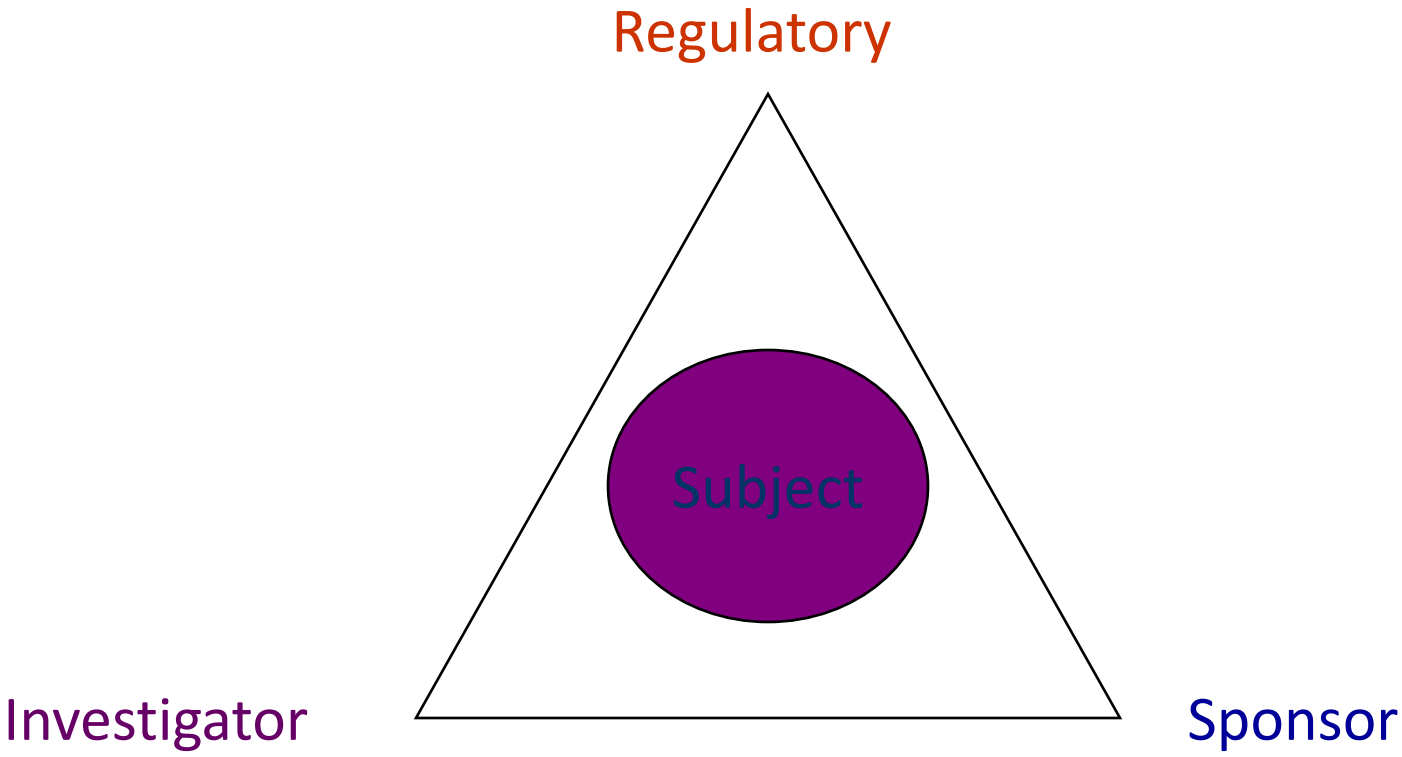
If it is not documented
- it never happened!!!

Remember, **proper documentation** ensures standardization and is the key to all successful studies !

The Tenets of GCP

- Study plan should be well designed by Sponsor
- Every study must follow scientific principles
- IRB must approve study - to ensure protection of rights and safety of subjects
- Informed consent must be freely given
- Sponsor should monitor study for GCP compliance
- Investigator is accountable for all drugs or devices
- Data should complete and accurate
- Records must be kept properly for the time period required
- A Quality Assurance plan must be in place.

Players in clinical research



GCP makes various demands of each

For a GCP-compliant clinical trial...

.....and universally acceptable data...

Each player must be fully aware of his responsibilities as per

Investigator Responsibility

Adequate Resources

- The investigator is responsible for supervising any individual or party to whom the investigator delegates trial-related duties and functions conducted at the trial site
- If the investigator/institution retains the services of any individual or party to perform trial-related duties and function, the investigator/institution should ensure this individual or party is qualified to perform those trial-related duties and function and should implement procedure to ensure the integrity of the trial-related duties and functions performed and any data generated

Investigator Responsibility

Records and Report

Source data should be attributable, legible, contemporaneous, original, accurate and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary(e.g. via an audit trail)

Sponsor Responsibility

Quality Management

- Quality management includes the design of efficient clinical trial protocol and tools and procedure for data collection and Processing, as well as the collection of information that is essential to decision making the methods used to assure and control the quality of the trial should be Proportionate to the risk inherent in the trial and the importance of the information collected. Protocols, case report forms and other operational documents should be clear, concise and consistent

Sponsor Responsibility

The quality management system should use a risk-based approach as described below

Critical process and data identification

- The sponsor should identify those processes and data that are critical to ensure human subject protection and the reliability of trial results

Risk identification

- Risk should be considered at both the system level (e.g. standard operating procedures, computerized systems, personnel) and clinical trial level(e.g. trial design, data collection, informed consent process)

Sponsor Responsibility

Risk Evaluation

The sponsor should evaluate the identified risks, against existing risk control by considering:

- The likelihood of errors occurring
- The extent to which such errors would be detectable
- The impact of such errors on human subject protection and reliability of trial results

Sponsor Responsibility

Risk Control

- Risk reduction activities may be incorporated in protocol design and implementation, monitoring plans, agreement between parties defining roles and responsibilities, systematic safeguards to ensure adherence to standard operating procedure and training in processes and procedures
- Detection of deviation from the predefined quality tolerance limits should trigger an evaluation to determine if action is needed

Sponsor Responsibility

Risk Communication

- The sponsor should communicate quality management activities to those who are involved in or affected by such activities, to facilitate risk review and continual improvement during clinical trial execution

Sponsor Responsibility

Risk Review

- Review risk control measures to ascertain whether the implemented quality management activities remain effective and relevant, taking into account emerging knowledge and experience

Risk Reporting

- The quality management approach implemented in the trial and summarize important deviation from the predefined quality tolerance limits and remedial action taken in the clinical study report
  (ICH E3. 9.6 Data Quality Assurance)

Trial Management, Data Handling, and Record Keeping

- The sponsor should base their approach to validation of such system on a risk assessment that takes into consideration the intended use of the system and the potential of the system to affect human subject protection and reliability of trial results

Trial Management, Data Handling, and Record Keeping (Contd)

- The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionally testing, data collection and handling system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning. The responsibilities of the sponsor, investigator, and other parties with respect to the use of these computerized system should be clear, and the users should be provided with training in their use

Monitoring (Contd)

- On-site monitoring is performed at the sites at which the clinical trial is being conducted Centralized monitoring is a remote evaluation of accumulating data, performed in a timely manner, supported by appropriately qualified and trained persons(e.g. data managers, biostatisticians)
- Centralized monitoring processes provide additional monitoring capabilities that can complement and reduce the extent and/or frequency of on-site monitoring and help distinguish between reliable data and potentially unreliable data

Monitoring

- The flexibility in the extent and nature of monitoring described in this section is intended to permit varied approach that improve the effectiveness and efficiency of monitoring
- The sponsor may choose on-site monitoring, a combination of on-site and centralized monitoring, or, where justified, centralized monitoring

Review, that may include statistical analyses, of accumulating data from centralized monitoring can be used to:

- Identify missing data, inconsistent data, data outliers, unexpected lack of variability
- Examine data trends such as the range, consistency ,and variability of data within and across sites.
- Evaluate for systematic or significant errors in data collection and reporting at a site or across sites; or potential data manipulation or data integrity problems.
- Analyze site characteristics and performance metrics.
- Select sites and/or processes for targeted on-site monitoring.

GMP
Good Manufacturing Practices

GMP

Definition:

WHO defines Good Manufacturing Practices (GMP) as “that part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.”

Why GMP is important

- A poor quality medicine may contain toxic substances that have been unintentionally added
- A medicine that contains little or none of the claimed ingredient will not have the intended therapeutic effect

Ten Principles of GMP

- Design and construct the facilities and equipments properly
- Follow written procedures and Instructions
- Document work
- Validate work
- Monitor facilities and equipment
- Write step by step operating procedures and work on instructions
- Design ,develop and demonstrate job competence
- Protect against contamination
- Control components and product related processes
- Conduct planned and periodic audits

List of important documents in GMP

- Policies
- SOP (Standard Operating Procedure)
- Specifications
- MFR (Master Formula Record)
- BMR (Batch Manufacturing Record)
- Manuals
- Master plans/ files
- Validation protocols
- Forms and Formats
- Records

What are cGMPs?

- cGMP refers to the Current Good Manufacturing Practice regulations enforced by the US Food and Drug Administration (FDA)
- cGMP provide for systems that assure proper design, monitoring and control of manufacturing processes and facilities
- Adherence to the cGMP regulations assures the identity, strength, quality and purity of drug products by requiring that manufacturers of medications adequately control manufacturing operations

GLP
Good Laboratory Practices

Objectives of GLP

- GLP (Good Laboratory Practice) was first introduced in NewZealand.
- GLP makes sure that the data submitted are a true reflection of the results that are obtained during the study
- GLP also makes sure that not to indulge in any fraud activity by labs
- Promotes international acceptance of tests

Principles

- Test Facility Organization and Personnel
- Quality Assurance Programme
- Facilities
- Apparatus, Material, and Reagents
- Test Systems
- Test and Reference Items
- Performance of the Study
- Reporting of Study Results
- Storage and Retention of Records and Materials