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Good Clinical Practice (GCP) and Its Importance

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ABSTRACT

Good clinical practice (GCP) plays most important role in the clinical trials. There are some guidelines which have to be followed by the investigator, organisation and sponsor of the trial. In this review we tried to summarise the GCP.

Keywords: Good clinical practice, GCP-ICH

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INTRODUCTION

A standard for clinical studies which encompasses the design, conduct, monitoring, termination, audit, analyses, reporting and documentation of the studies and which ensures that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical Product (diagnostic, therapeutic or prophylactic) under investigation are properly documented.

Good Clinical Practice is a standard for designing, conducting, performing, monitoring, auditing, recording, analyzing, and reporting clinical trials. Provides assurance that data and reported results are credible and accurate and that the rights and confidentiality of subjects are protected.

Main objectives of the GCP is - To avoid research misconduct and fraud as this is a growing public and professional concern nowadays; Compliance with this standard provides public assurance that the rights, safety and wellbeing of trial subject are protected, consistent with the principles that have their origin in the Declaration of Helsinki; To assure that the clinical trial data are credible; To provide a unified standard for different countries to facilitate the mutual acceptance of clinical data by the regulatory authorities.

The International Conference on Harmonization (ICH) Guidelines:
-Provide a unified standard to facilitate the mutual acceptance of the clinical data by the regulatory authorities in jurisdictions
-The ICH Guidelines are an effort to define GCP and to create and provide a unified standard for designing, conducting, recording and reporting trials that involve the participation of human subjects
-GCP is an international ethical and scientific quality standard for designing, conducting, and recording trials that involve human subjects – Safety, Quality and Efficacy.

PRINCIPLES OF GCP-ICH

The principles are based on those of the International Conference on Harmonization (ICH) of technical requirements of registration of pharmaceuticals for human use. They are as following:

1. 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. Before a trial is initiated, foreseeable risk and inconvenience 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. The rights, safety and well-being of the trial subjects are the most important considerations and should prevail over interest of science and society.

4. The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
5. Clinical trials should be scientifically sound, and described in a clear, detailed protocol.
6. A trial should be conducted in compliance with the protocol.
7. The medical care given to and medical decision made on behalf of subject should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
8. Each individual involved in conducting a trial should be qualified by education training and experience to perform his or her respective task(s).
9. Freely given informed consent should be obtained from every subject prior to clinical trial participation.
10. All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
11. 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. 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. System with procedures that assure the quality of every aspect of the trial should be implemented.

HISTORY OF GOOD CLINICAL PRACTICE

Prior to an actual set of guidelines to follow for good clinical practice, clinical studies were dangerous and could result in serious disease, or possibly death.
The Nuremburg Code of 1947 - Experiments performed in germany during WWII opened the eyes of the world for guidance for clinical testing on humans. The code did set ethical guidelines, but it lacked legislation to back it up.

Declaration of Helsinki - In 1964, the World Medical Association established recommendations guiding medical doctors in biomedical research involving human subjects. These guidelines influenced national legislation, but there was no set standard between nations.

Mission of the GCP Program

The Good Clinical Practice Program is the focal point within FDA regarding issues in human research trials regulated by FDA. The Good Clinical Practice Program: Coordinates FDA policies; Contributes to leadership and direction through participation in FDA's Human Subject Protection/Bioresearch Monitoring Council; Coordinates FDA's Bioresearch Monitoring program with respect to clinical trials, working together with FDA's Office of Regulatory Affairs (ORA); Contributes to international Good Clinical Practice harmonization activities.

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RESPONSIBILITIES

An IRB/IEC should safeguard the rights, safety, and well-being of all trial. Special attention should be paid to trials that may include vulnerable subjects. The IRB/IEC should obtain the following document: Trial protocol(s) / amendment(s), written informed consent form(s), subject recruitment procedures, written information to be provided to subjects, investigator's brochure (IB), available safety information, information about payments and compensation available to subjects, the investigator's current curriculum vitae etc. The IRB/IEC should review a proposed clinical trial within a reasonable time. The IRB/IEC should conduct continuing review of each ongoing trial at intervals appropriate to the degree of risk to human subjects, but at least once per year. Adequately addresses relevant ethical concerns and meets applicable regulatory requirements for such trials. The IRB/IEC should review both the amount and method and of payment to assure that neither presents problems of coercion or undue influence on the trial subjects. Payments to a subject should be prorated and not wholly contingent on completion of the trial by the subject.

INFORMED CONSENT

Investigators should ensure that they obtain approval for the written consent form to be used in the study from the ethics committee prior to the trial starting. Consent forms and information sheets should be revised when important new information becomes available that may be relevant to participant's consent. Revised consent forms should first be approved by the ethics committee before being used. Neither the investigator nor the trial staff should coerce or unduly influence an individual to participate or to continue in a trial. The investigator or the person designated by the investigator should fully inform the participant or the participants's legal representative of all the pertinent aspects of the trial including the written information provided to participants. The language used in the oral and written information about the trial should be non-technical as practical and should be understandable to the participants and the participant's legal representative (where applicable). Before consent is obtained, the investigator should provide participants with ample time and opportunity to inquire about details of the trial and decide whether or not to participate. Prior to participant's recruitment to the trial, the written informed consent form should be signed and dated by the participant or by the participant's legal representative. If a participant is unable to read, or the representative unable to read, an impartial witness should be present during the entire consent discussion and oral consent may be given. The witness confirms that the study information was understood and that informed consent was given freely. Both the informed consent discussion and the written information sheet should include explanations about what the trial involves, the purpose of the trial, the trial treatment and whether randomisation occurs as well as details of foreseeable risks or inconveniences.

PARTICIPATING PARTIES

- IRB/Ethics Committee
- Investigators

- Sponsor
- Regulatory Authorities

ROLES & RESPONSIBILITIES

To safeguard study subjects' rights & welfare by:

- Evaluation/disposition of study proposal
- Evaluation of proposed subject consent materials
- Evaluation of emergency use consent methodology
- Evaluation of investigator qualifications
- Ongoing review of study progress (at least yearly)
- Evaluation of proposed subject compensation plans

COMPOSITION & OPERATIONS

Membership has qualifications & experience to evaluate science, medical aspects & ethics of proposed study:

≥ 5 members
≥ 1 member whose primary interest in nonscientific
≥ 1 member independent of institution or study site
- Written SOPs & records
- Decisions rendered at announced meetings with quorum in attendance
- Only members participating in review should vote
- Investigator may provide info on study, but should not be involved in review or vote
- Nonmembers with expertise in special areas may be invited to assist with review (but cannot vote)

PROCEDURES

- Document group membership & qualifications
- Schedule meetings & notify members
- Conduct initial & ongoing review of studies
- Determine ongoing review frequency
- Provide expedited review of minor study changes, in accordance with regulatory requirements
- Specify that no subject should be enrolled in study prior to IRB/EC approval
- Specify that no deviations from protocol should be initiated without prior IRB/EC approval
– Emergency situations require immediate notification of IRB/EC after the fact
- Specify that Investigator should promptly report:
– Protocol deviations
– Changes increasing subject risk or study procedures

– Serious and unexpected adverse events
• Notify Investigator promptly of:
– Study-related decisions
– Reason for decisions
– Procedures for appeal of decisions

REQUIRED RECORDS

• Relevant records maintained ≥ 3 yr after study completion
• Records available for review by regulatory authorities

WHAT IS REVIEWED

• Investigator Brochure or Report of Prior Investigations
• Study protocol & amendments
• Investigator qualifications
• Informed consent documents, including subject recruiting tools
• Other written information provided to subjects
• Subject compensation plans
• Adverse events

INVESTIGATOR ROLES & RESPONSIBILITIES

• Qualified to conduct study
• Have adequate resources to conduct study
• Provide medical care to study subjects
• Regular communication with IRB/EC reviewing study
• Compliance with study protocol
• Maintenance of investigational product accountability
• Compliance with study randomization & unmasking procedures
• Provide informed consent to study subjects

INVESTIGATOR RESPONSIBILITIES

• Appropriate Qualifications
• Training & experience demonstrated via: Medical license, CV, Specialized study training, GCP training.
• If study responsibilities delegated, need a list of qualified persons to whom responsibilities are delegated
• Adequate Resources
• Suitable staff & good methods for keeping them apprised
• Suitable facilities
• Appropriate patient population
– Access to disease or condition

– Volume of patients with disease or condition

• Medical Care: Make medical decisions regarding patient treatment, Adequate care for study-related adverse events, Diligence in ascertaining reason(s) for subject withdrawals from study

IRB/EC COMMUNICATIONS

• IRB/EC approval prior to study initiation
• IRB/EC kept apprised of events & progress during study
• Conduct study in accordance with protocol
• May not deviate from protocol without Sponsor/IRB approval
• Document deviations from protocol

➢ Investigational Product Accountability

• Maintain accountability at study site
• Document product receipt & disposition
• Maintain product in a secure area
• Use product only in accordance with protocol
• Disallow use of product by anyone not registered with study

➢ Randomization Procedures & Unmasking

• Follow study randomization procedures
• Unmask only in accordance with protocol
• Document noncompliance or premature unmasking

➢ Subject Informed Consent

• Comply with regulatory requirements
• Update consent documents as necessary
• Inform subject that study involves “investigational” product
• May not coerce subject to participate
• May not waive subject’s legal rights
• Keep subject informed of new information regarding study
• Provide informed consent in understandable language
• Give subject the chance to ask questions
• If subject can’t read, need impartial witness
• If subject is “disadvantaged”, need legally authorized witness
• Get subject consent in writing prior to initiation of study procedures
• Give subject a copy of signed consent document

SPONSOR ROLES & RESPONSIBILITIES

• Study quality assurance
• Appropriately qualified medical personnel to advise on study
• Utilization of qualified personnel in study design & operations
• Study management, data handling & record keeping
• Investigator selection & training
• Definition/allocation of study responsibilities

- Facilitation of communications between Investigators
- Study compensation (investigators and/or subjects) & financing
- Regulatory authority notification/submission
- Confirmation of IRB/EC review/approval
- Investigational product information
- Investigational product manufacturing, packaging, labeling & coding
- Investigational product supply & handling
- Record access
- Ongoing safety evaluation & reporting
- Serious/unanticipated adverse event reporting
- Study monitoring
- Study noncompliance procedures
- Study termination or suspension notification
- Study reports
- Sponsor may transfer responsibilities to CRO
  - Transfer must be documented in writing
  - Sponsor still has ultimate responsibility for study quality and data integrity

INVESTIGATOR BROCHURE

A compilation of clinical & non-clinical data on the product that is relevant to the product's study in humans necessary for Investigator & IRB/EC review to assess the risks/benefits associated with study.

CONCLUSION

Good clinical practices are important for the clinical studies. By this study it is clear that good clinical practices are necessary not only for the investigators but all the participants like organization, participant and sponsor of the study. GCP can provide better results for better life.

REFERENCES

[1] ICH Harmonised Triparartite Guideline. Guideline for good clinical practice. www.inch.org.
[2] Trivedi JK. Good Clinical Practice. Ind J Psychiatry 1999; 41(1):1-4.
[3] Sweatman J. Clin Pharmacol 2003; 55: 1-5.
[4] Wallnofer AE, Cohen AF. Br J Clin Pharmac 1993; 35: 449-450.
[5] Guidelines for Good Clinical Practice (GCP) for trial on pharmaceutical products. WHO Technical Report Series, No. 850, 1995; Annex3. www.apps.who.int
[6] Morice A. Br J Clin Pharmac 1999; 32:529-530.
[7] Good Clinical Practice Resource Guide, Division of Microbiology and infectious disease, may 2011.
[8] A Guide to ICH Good Clinical Practice (GCP), Published by the R&D Office The Hillingdon Hospital, Updated June 2006.

[9] Medicines & Healthcare products Agency (MHRA) www.mhra.gov.uk.
[10] ICH Harmonised Tripartite Guideline for GCP, Institute of Clinical Research, 1996.