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Base of a Research: Good Clinical Practice in Clinical Trials

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Abstract

This article illustrates the importance of Good Clinical Practice (GCP), defines and outlines the goals of GCP, presents a historical perspective on GCP and Outlines FDA regulations relating to GCP. Ongoing research shows that whether conducting research involving a new drug, a behavioral intervention, or an interview/survey, Good Clinical Practice (GCP) provides investigators and their study teams with the tools to protect human subjects and collect quality data. In this article, the author will define GCP, explain the benefits of following GCP for all types of human research and clinical trial studies, and provide some resources to assist investigators in implementing the tenets of GCP for their own research studies. This article reviews the impact of Good Clinical Practice (GCP) on clinical trials. GCP is likely to follow the International Conference on Harmonization of GCP guidelines in many aspects. GCP will enforce tighter guidelines on ethical aspects of a clinical study. Higher standards will be required in terms of comprehensive documentation for the clinical protocol, record keeping, training, and facilities including computers. Quality assurance and inspections will ensure that these standards are achieved. The additional requirements of GCP are discussed and any advantage to the study subject. GCP aims to ensure that the studies are scientifically authentic and that the clinical properties of the investigational product are properly documented. In this paper, we address the background history and the events that led up to the formation of these guidelines. Today, the GCP are used in clinical trials throughout the globe with the main aim of protecting and preserving human rights.

Keywords: Good Clinical Practice (GCP); ICH-GCP; Quality assurance; Inspections; Clinical trial; Human rights protection

Introduction

GCP is a key requirement for anyone involved in the conduct of clinical research is Good Clinical Practice (GCP) training. GCP is the standard and guidelines to which all research is conducted. GCP is a set of internationally-recognized ethical and scientific quality requirements that must be observed throughout the various stages of a clinical trial. Clinical trial following testing in laboratories and animal studies, the most promising treatments is moved into clinical trials [1]. A clinical trial is sometimes called a clinical study [2]. A clinical trial:

- Is a research study that tests how well an intervention works in a group of people
- Tests for new methods of screening, prevention, diagnosis, or therapy
- Is conducted in phases

During a trial, additional information is learned about an intervention, its risks, and its effectiveness and/or efficacy. Trials can only be conducted if there is an uncertainty about the outcome-trials cannot be conducted if the outcome is already known from a previous study [3,4]. Good Clinical Practice (GCP) is one of the basic sets of rules for hospitals, researchers and pharmaceutical companies engaged in clinical [5].

GCP or Good Clinical Practice refers to an international quality standard provided by the ICH for the purpose of regulating clinical trials that involve human subjects. GCP standards offer assurance as to the effect and safety of compounds developed in clinical trials, human rights protection of trial participants, and also define the roles of clinical research investigators, clinical trial sponsors and clinical research associates.

The fundamental tenet of GCP is that in research on man, the interest of science and society should never take precedence over considerations related to the well being of the study subject [5]. It aims to ensure that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical substances under investigation are properly documented. The guidelines seek to establish two cardinal principles: protection of the rights of human subjects and authenticity of biomedical data generated. It ensures that the studies are implemented and reported in such a manner that there is public assurance that the data are credible, accurate and that the rights, integrity and confidentiality of the subjects are protected.

ICH-GCP

The objective of this ICH GCP Guideline [6] is to provide a unified standard for the European Union (EU), Japan and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions. The International conference on harmonization of technical requirements for registration of pharmaceuticals for human use (ICH) [7,8] is unique in bringing together the regulatory authorities and pharmaceutical industry of Europe, Japan and the US to discuss scientific and technical aspects of drug registration. The guideline was developed with consideration of the current good clinical practices of the European Union, Japan, and the United States, as well as those of Australia, Canada, the Nordic countries and the World Health Organization (WHO). This guideline should be followed when generating clinical trial data that are intended to be submitted to regulatory authorities. The principles established in this guideline may also be applied to other clinical investigations that may have an impact on the safety and well-being of human subjects [9]. The objective of such harmonization is a more economical use of human, animal and material resources, and the elimination of unnecessary delay in the global development and availability of new

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medicines whilst maintaining safeguards on quality, safety and efficacy, and regulatory obligations to protect public health [10-12].

Clinical studies should be carried out according to International Conference on Harmonisation (ICH)/WHO Good Clinical Practice standards [13]. This provides a unified standard for the European Union (EU) [14,15], Japan, and the United States, as well as those of Australia, Canada, the Nordic countries and the World Health Organisation (WHO). Thus, any country that adopts this guideline technically follows this same standard. The purpose is to make recommendations on ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines.

Principles of GCP

1. The rights, safety and well-being of the trial subjects shall prevail over the interests of science and society.
2. Each individual involved in conducting a trial shall be qualified by education, training and experience to perform his tasks.
3. Clinical trials shall be scientifically sound and guided by ethical principles in all their aspects.
4. The necessary procedures to secure the quality of every aspect of the trial shall be complied with.
5. The available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the proposed clinical trial.
6. Clinical trials shall be conducted in accordance with the principles of the Declaration of Helsinki.
7. The protocol shall provide for the definition of inclusion and exclusion of subjects participating in a clinical trial, monitoring and publication policy.
8. The investigator and sponsor shall consider all relevant guidance with respect to commencing and conducting a clinical trial.
9. All clinical information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected.
10. Before the trial is initiated, foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial subject and other present and future patients. A trial should be initiated and continued only if the anticipated benefits justify the risks.
11. The medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor or, when appropriate, of a qualified dentist.
12. A trial shall be initiated only if an ethics committee and the licensing authority comes to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.
13. The rights of each subject to physical and mental integrity, to privacy and to the protection of the data concerning him in accordance with the Data Protection Act 1998 are safeguarded.
14. Provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor which may arise in relation to the clinical trial.

Overview of the Clinical Research Process

Key trial activities include

- Development of the trial protocol
- Development of Standard Operating Procedures (SOPs)
- Development of support systems and tools
- Generation and approval of trial-related documents
- Selection of trial sites and the selection of properly qualified, trained, and experienced investigators and study personnel
- Ethics committee review and approval of the protocol
- Review by regulatory authorities
- Enrollment of subjects into the study: recruitment, eligibility, and informed consent
- The investigational product(s): quality, handling and accounting
- Trial data acquisition: conducting the trial
- Safety management and reporting
- Monitoring the trial
- Managing trial data [16-18]
- Quality assurance of the trial performance and data
- Reporting the trial

Common GCP Issue During Clinical Studies

Informed consent

Correct version

- Length of consent form
- Copy to patients
- Documentation - of contacts, in source files etc.
- Translations
- Ethics committee approval and information to ongoing patients
- Witness

Recruitment and study procedures

Screening procedures before consent

- Incomplete laboratory workup per protocol
- Inclusion/Exclusion exceptions not discussed with medical monitor
- Patient visits outside the protocol allowed window
- Advertisements not approved by sponsor/ethics committees
- Difficulties in enrollment - action from investigator and sponsor

Monitoring

Source data problems

- CRF completion quality
- Study team training issues
- Incomplete essential documentation
- Monitoring frequency issues

Clinical trial supplies

Randomization errors

- Accountability problems
- Improper storage conditions
- Compliance issues
- Blind breaking issues

Safety reporting

Unreported SAEs

- Delayed reporting of SAEs
- Documentation in source files of AEs and SAEs
- SAE reporting to institutional ethics committee
- Additional safety information to ongoing/new patients-consent addenda/amendments.
- Updates to investigators' brochure (Tables 1-4)

Conclusion

Ongoing research shows that whether conducting research involving a new drug, a behavioral intervention, or an interview/survey, Good Clinical Practice (GCP) [19-24] provides investigators and their study teams with the tools to protect human subjects and collect quality data. In this article, the author will define GCP, explain the benefits of following GCP for all types of human research studies, and provide some resources to assist investigators in implementing the tenets of GCP for their own research studies. This article illustrates the importance of Good Clinical Practice (GCP), defined and outlined the goals of GCP, Presented a historical perspective on GCP, Outlined FDA regulations relating to GCP.

According to Van Dongen [4] ultimately it is not difficult for investigators and their study teams to follow GCP – it is simply a question of writing down procedures, documenting what is being done, and preparing for inspection. He goes on to say that there are considerable rewards, not the least of which is the confidence that the data was obtained through a GCP-compliant research study. GCP will enforce tighter guidelines on ethical aspects of a clinical study. Higher standards will be required in terms of comprehensive

1947	Nuremberg Code
1948	Declaration of Human Rights
1960	Pharmacovigilance
1964	Declaration of Helsinki, (last updated 2008)
1965	Institutional Review Board (In the United States, IRBs are governed by Title 45 CFR (Code of Federal Regulations) part 46. These regulations implement provisions of the National Research Act of 1974 defining IRB
1968	WHO convened a Scientific Group on Principles for Clinical Evaluation of Drugs
1974	Belmont Report (USA): created by National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (respect for persons (autonomy), beneficence and justice)
1975	Another WHO Scientific Group was convened to specifically consider all aspects of the evaluation and testing of drugs and to formulate proposals and guidelines for research in the field of drug development
1979	The U.S. Food and Drug Administration (FDA) established regulations for clinical research called "Code for Federal Regulations, title 21, part 50 (protection of human subject)".
1980	International Guidelines for Biomedical Research Involving Human Subjects
1995	WHO's "Guidelines for good clinical practice (GCP) for trials on pharmaceutical products", published in 1995
1996	International Conference on Harmonization (ICH) E6, "Good Clinical Practice: Consolidated Guideline"
1996	ICH-GCP guidelines issued
1997	Universal Declaration on the Human Genome and Human Rights (UNESCO)
1997	International Conference on Harmonization/Good Clinical Practice Guideline
1998	Data Protection Act
2000	Guidelines for Ethics Committees (World Health Organization)
2001	International Standards Organization (ISO), "Clinical investigation of medical devices for human subjects, Part I (General requirements) and Part 2 (Clinical investigation plans) Research Governance Framework (Version 2 2006
2001	EU Clinical Trial Directive: Directive 2001/20/EC
2002	International Ethical Guidelines for Biomedical Research involving Human Subjects (Council for International Organizations of Medical Sciences –CIOMS)
2004	Medicines for Human Use (Clinical Trials) Regulations 2004
2005	Pan American Health Organization (PAHO). Pan American Network on Drug Regulatory Harmonization (PANDRH). "Good Clinical Practices: Document of the Americas"
2005	EU Directive on Good Clinical Practice 2005/28/EC
2006	Human Tissue (Scotland) Act
2006	The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006
2006	The Medicines for Human Use (Clinical Trials) Amendment (No.2) Reg's 2006
2008	International Ethical Guidelines for Epidemiology Studies. CIOMS Geneva, Feb 2008.

Table 1: Historical view of GCP.

Purpose	To harmonize the regulations and guidelines for drug development
Participants	Regulatory agencies/ industries representative from Europe, Japan, US, WHO, Canada, Nordic group and Australia
Goal	To protect the rights, safety and welfare of humans participating in research. To assure the quality, reliability and integrity of data collected. To provide standards and guidelines for the conduct of clinical research. Good Clinical Practice = Ethics + Quality Data.
Process	Developed guidelines applicable for Drugs, Biologics, Medical devices, Approved by ICH members, Adopted by National Regulatory Authorities
Who are responsible for GCP	Sponsors, Clinical Investigators (CIs), Independent Ethics Committees (IECs), Institutional Review Boards (IRBs), Contract Research Organizations (CROs), Research nurses, Clinical Research Coordinators (CRCs), Clinical Research Associates (CRAs), Medical monitors, Data entry personnel etc.

Table 2: Brief introduction of ICH-GCP.

21 CFR 11	Electronic Records & Signatures
21 CFR 50	Protection of Human Subjects
21 CFR 54	Financial Disclosure
21 CFR 56	Institutional Review Boards
(21 CFR Part 312)	Investigational New Drug Application
(21 CFR Part 312.120)	Foreign Clinical Trials not conducted under an IND
(21 CFR Part 314)	Applications for FDA approval to market a new Drug
(21 CFR Part 320)	Bioavailability and Bioequivalence requirements
(21 CFR Part 601)	Applications for FDA Approval of a Biologic License
21 CFR 812	Investigational Device Exemptions
21 CFR 814	Premarket Approval of Medical Devices

Table 3: How does FDA implement GCP?

Clinical Trial: Following testing in laboratories and animal studies, the most promising treatments is moved into clinical trials. A clinical trial is sometimes called a clinical study. A clinical trial: • Is a research study that tests how well an intervention works in a group of people • Tests for new methods of screening, prevention, diagnosis, or therapy • Is conducted in phases During a trial, information is learned about an intervention, its risks, and its effectiveness. Trials can only be conducted if there is an uncertainty about the outcome	
Type of Clinical Trial	**Description**
Treatment	Test new treatments, new combinations, new approaches to surgery or radiation therapy, or clinical management strategies
Prevention	Look for better ways to prevent a disease in people who have never had the disease. In the case of diseases other than HIV/AIDS, to prevent the disease from returning. Better approaches may include medicines, vaccines, and/or lifestyle changes
Diagnostic	Determine better tests or procedures for diagnosing a particular disease or condition
Screening	Test the best way to detect certain diseases or health conditions
Quality of Life (or Supportive Care	Explore and measure ways to improve the comfort and quality of life of people with a chronic illness

Table 4: Some types of clinical trials.

documentation for the clinical protocol, record keeping, training, and facilities including computers. The additional requirements of GCP are discussed and any advantage to the study subject. GCP aims to ensure that the studies are scientifically authentic and that the clinical properties of the investigational product are properly documented. In this paper, we address the background history and the events that led up to the formation of these guidelines. Today, the GCP are used in clinical trials throughout the globe with the main aim of protecting and preserving human rights. Quality assurance and inspections will ensure that these standards are achieved. This article reviews the impact of Good Clinical Practice (GCP) on clinical trials.

References

1. Bhandari M, Busse JW, Jackowski D, Montori VM, Schunemann H, et al. (2004) Association between industry funding and statistically significant pro-industry findings in medical and surgical randomized trials. CMAJ 170: 477-480.
2. Gad SC (2009) Clinical Trials Handbook. John Wiley and Sons.
3. Meinert CL, Tonascia S (1986) Clinical trials: design, conduct, and analysis. Oxford University Press, USA.
4. Van Dongen AJ (2001) Good Clinical Practice, a transparent way of life. A review. Comput Med Imaging Graph 25: 213-216.
5. Vijayananthan A, Nawawi O (2008) The importance of Good Clinical Practice guidelines and its role in clinical trials. Biomed Imaging Interv J 4: e5.
6. Food Drug Administration (FDA) (1997) International conference on harmonization, good clinical practice: consolidated guidelines. Federal Register 62: 25692–25709.
7. EMEA (2000) Clinical Investigation of Medicinal Products in the Pediatric Population.
8. EMEA (2002) ICH Topic E 6 (R1): Guideline for Good Clinical Practice.
9. Otte A, Maier-Lenz H, Dierckx RA (2005) Good Clinical Practice: Historical background and key aspects. Nucl Med Commun 26: 563-574.
10. Smith A (2009) Still relevant after all these years? Should ICH GCP be Reviewed and Revised?
11. Vadivale M (1999) ICH-GCP Guidelines for Clinical Trials. Berita MMA..
12. Ministry of Health Malaysia (2004) Malaysian Guidelines for Good Clinical Practice. (2ndedn), Ministry of Health Malaysia.
13. ICH (1997) ICH M3 Maintenance of the ICH Guideline on Non-Clinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals.
14. European Parliament (2001) Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. Official Journal of the European Communities 121: 34-44.
15. European Medicines Agency (2002) ICH Harmonized Tripartite Guideline

E6: Note for Guidance on Good Clinical Practice (PMP/ICH/135/95). London: European Medicines Agency.

16. Office of Human Subjects Research (1949) The Nuremberg Code.
17. http://www.ushmm.org/research/doctors/Nuremberg_Code.htm
18. http://www.wma.net/e/policy/b3.htm
19. Imperial College Clinical Research Governance Office (2007) Good Clinical Practice.
20. ICH (1996) ICH harmonised tripartite guideline guideline for good clinical practice E6(R1), International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.
21. World Medical Association (WMA) (2000) Declaration of Helsinki, 52nd WMA General Assembly. Edinburgh, Scotland.
22. (1997) Good Clinical Practice: Consolidated Guidelines. International Conference on Harmonisation.
23. EMEA (1998) ICH E9: Statistical Principles for Clinical Trials.
24. EMEA (2001) ICH E10: Choice of Control Group and Related Issues in Clinical Trials.