Module 1: Introduction to good clinical practices applied to research

Introduction

 Estimated reading time: 10 minutes

This module introduces the updated Good Clinical Practice (GCP) Course, based on the ICH GCP E6(R3) Guideline, and the WHO Guidance for best practices for clinical trials. It highlights the importance of these guidelines in clinical research, emphasizing their role in safeguarding participant welfare and ensuring the reliability of generated data.

Additionally, this module outlines the key stages of the research process, aligned with international recommendations to promote research that adheres to ethical and methodological standards.

Learning Objectives

By the end of this module you will be able to:

- Understand the concept of Good clinical practice
- Recognize the relevance of the ICH GCP E6(R3) and WHO guideline in clinical research
- Identify the key steps in the research process
- Understand the importance of ethics in the context of GCP and its practical application in clinical research

Good Clinical Practice

Good Clinical Practice (GCP) is an internationally recognized ethical, quality and scientific standard[2, 3] for the design, conduct, and reporting of clinical studies involving human participants. Its primary objective is to ensure the protection of participants' rights, safety, and well-being, while also guaranteeing the reliability and credibility of study data and results.

The principles of GCP are established in key international regulatory frameworks[2, 3] taking as a reference the ICH GCP E6(R3) Guideline of the International Council for Harmonisation (ICH)[1]. The GCP sets a quality and ethical standard for conducting Clinical Trials reinforcing compliance with fundamental ethical principles, such as those outlined in the Declaration of Helsinki

> The **ICH GCP E6(R3)** define Good Clinical Practice as "*an international, ethical, scientific, and quality standard for the conduct of trials that involve human participants. Clinical trials conducted in accordance with this standard will help to ensure that the rights, safety, and well-being of Trial Participants are protected; that the conduct is consistent with the principles that originate in the Declaration of Helsinki; and that the clinical trial results are reliable*[1]."

Additionally, the World Health Organization (WHO) Guidance for Best Practices for Clinical Trials (GCT)[4] aligns with the principles of ICH GCP E6(R3) and complements it by providing a broader global perspective. This is particularly relevant for research conducted in diverse regulatory environments and low-resource regions, where adapting to local contexts is essential. The WHO GCT emphasizes inclusivity, accessibility, and the harmonisation of ethical research practices worldwide.

Both guidelines are governed by the Declaration of Helsinki[5] and the ethical standards established by the Council for International Organizations of Medical Sciences (CIOMS)[6].

Declaration of Helsinki: Developed by the World Medical Association (WMA), the Declaration of Helsinki serves as a global ethical framework for conducting research involving human participants, ensuring that participant welfare takes precedence over scientific and commercial interests.

ICH GCP E6(R3) applies to interventional clinical trials of Investigational Products[1] that are intended to be submitted to Regulatory Authorities The **Principles of GCP in this guideline may also be applicable** to other interventional clinical trials of investigational products that are not intended to support marketing authorisation applications in accordance with local requirements.

This course explores the fundamental principles of Good Clinical Practice as outlined in the ICH E6(R3) guideline and the WHO Guidance for Best Practice for Clinical Trials.

Principles of Good Clinical Practice and their Reflection of the Ethics of the Belmont Report

The Belmont Report establishes the ethical basis for research involving human subjects, providing guidelines for treating participants with dignity, ensuring their well-being, and promoting fairness in their selection[7]. The GCP principles operationalise these ethical ideals into specific standards. The ICH GCP E6(R3)[1] and WHO GCT[2] further emphasises the need for all Clinical Trials to comply with universal ethical standards.

Clinical Research Pillars

Before proceeding, let's take a moment to recall the ethical pillars of all research: respect for people, beneficence/non-maleficence, and justice [5-7].

+ Respect for people

+ Beneficence

+ Justice

If you would like to delve deeper into research ethics, you can access the WHO Research Ethics Online Training (V2) for free.

Stages of the Clinical Research Process

In all clinical research, the application of ethical principles, guidelines and recommendations are essential at each stage of the process, ensuring both the protection of participants and the scientific integrity of the study[8-10]. The 4 basic and general stages of the clinical research process are briefly reviewed below.

Stages

Although ICH E6(R3) *primarily applies* to interventional Clinical Trials, its principles may be

applicable to other types of research, particularly in areas related to ethics, participant protection, and data integrity and reliability.

Planning of the Study and Ethics Approval

This initial stage involves the **preparation of documents** that reflect that the ethical requirements applied to human subjects' research are ensured in the **planning of the study**. ICH GCP E6(R3) promotes a proactive risk-based approach, where study planning should identify critical-to-quality factors from the start.

ICH_GCP_E6_R3_Planning

The studies' documents will be rigorously evaluated by the local ethics committees and regulators for approval of the study. The Protocol is the primary document, but other documents are also required for submission to the ethics committee, as will be detailed in modules 4 to 7.

The protocol is the core document that defines the study's objective, methodology, and procedures. It must be clear, operationally feasible, and designed to ensure both scientific rigor and ethical integrity, aligning with Good Clinical Practice principles to safeguard participant rights, safety, and data reliability.

All documents pertaining to a study proposal must be submitted for review and approval by a local Institutional Review Board (IRB) when available and an Independent Ethics Committee (IEC).

Evaluation of the documents by Ethics committees and institutional review boards ensure that the study meets standards of protection and respect for participants. As defined in the ICH GCP E6(R3), from this point forward in the course, the acronym IRB/IEC will be used to refer to them.

Important: A study **should NOT be initiated** without prior approval from the ethics committee and Regulatory Authorities of the jurisdiction in which the research will be conducted.

Initiation of the Study (Setup)

The study setup follows a structured process that encompasses all phases, from identifying study sites to enrolling the first participant.

ICH_GCP_E6_R3_Initiation

The formal start of a research is considered from the moment the Protocol receives ethical and regulatory approval, which includes authorisation from the IRB/IEC and the competent Regulatory Authorities for each jurisdiction where the study will be conducted. Before participant recruitment can commence, it is essential to take practical measures to ensure that local site teams are adequately prepared to conduct the study at the highest quality standards.

This involves study-specific training to familiarise the team with the protocol's requirements and their assigned responsibilities, as well as broader preparatory steps, such as this course, which provides a foundational understanding of the quality standards applicable to all clinical studies.

As will be detailed in Module 5: Principles applied in the initiation of the study, training should be conducted on a regular basis to contribute to study implementation, maximising the quality and safety of clinical research.

The formal start of a clinical study is considered from the moment the protocol receives ethical and regulatory approval, while the start of recruitment is the first step of interaction with participants, seeking their enrolment in the study according to the previously approved selection criteria.

Study conduct; recruitment data collection and Risk Management

ICH_GCP_E6_R3_Conduct

Conduct of the study is the stage where the research team carries out all the activities described in the Protocol, such as recruitment of participants, data collection, safety Monitoring, and Adverse Events assessment, ensuring adherence to the ethical principles of respect for persons, beneficence, and justice, as will be detailed in Module 6: The principles applied in the Conduct of the Study focused on Risk Management.

An essential part of implementation is the conduction of the risk management plan. This plan includes preventive and responsive measures to identify, assess and mitigate risks, such as adverse events and protocol Compliance issues.

Conclusion, Closure and Post Study

ICH_GCP_E6_R3_Closure

This phase encompasses the final procedures necessary to terminate a study in accordance with ethical and scientific guidelines.

Termination occurs when the interventions specified in the Protocol, the collection, consolidation, analysis of data and interpretation of results are completed. The balance of risks and benefits must be reassessed, especially if new findings about the safety or effectiveness of the intervention emerge.

Study closure is a process involving a number of administrative and ethical activities. IRB/IEC, Regulatory Authorities and funding organizations are notified of study completion, and a final report is provided that includes the results and any significant deviations from the protocol. Closure also involves archiving all essential study documents in accordance with standardised procedures and local legislation, ensuring their accessibility for future Audit or review.

Study completion is the end of the active phase of implementation while closure is the formal administrative step that ensures the documented completion of the study in compliance with ethical and regulatory standards.

After formal closure, the post-study phase focuses on communicating the results to participants and the scientific community, following ethical principles of transparency and fairness. In addition, ethical guidelines highlight the importance of continuity of care for participants after the closure of the Clinical Trials, which may involve additional follow-up and the provision of free or accessible medication as part of an ethical commitment to the health and well-being of those who have contributed to the research. These final procedures will be discussed in Module 7: Principles applied in the Conclusion, Closing and post-trial.

Practical Application of Good Clinical Practices in Different Contexts

In some regions and countries, such as Europe[3] and the USA[2], the requirements of ICH GCP E6(R3) guidelines are embedded in their legislation. However, even though this requirement is limited to specific studies, such as Clinical Trials with investigational medicinal products, many other stakeholders (e.g. funding agencies, IRBs, scientific publishers) request that all studies are conducted according to GCP principles to ensure a similar 'standard'[2, 3].

It is important for investigators in low-and middle-income countries to clearly demonstrate that they are adopting the principles of GCP and are therefore working to this same standard. This ensures that the participants are protected, and the results are just as reliable as the results from research conducted in any other GCP compliant study across the globe[10, 11].

Summary and Key Points to Remember

Good Clinical Practice is a significant step towards promoting more inclusive, ethical and adaptive clinical research, especially in resource-limited settings. By integrating fundamental ethical principles and defining key steps in the research process, they provide a framework to ensure that studies are conducted according to standards of safety, ethics and scientific rigor. This approach not only optimises the quality of research but also reinforces the commitment to protecting the rights and well-being of participants, ensuring that clinical research effectively responds to the needs of diverse populations and contexts.

Key points to remember:

- Good Clinical Practices are international standards for participant protection and data integrity in clinical research
- The ICH GCP E6(R3) emphasises a central role of the participant and justice and equity in Clinical Trial
- The WHO GCT is a global framework for conducting ethical and scientifically sound clinical trials
- Ethical principles and good clinical practices are cross-cutting and must be adhered to at all stages of research, from design, conduct, reporting of results and study closure
- Although Good Clinical Practice (GCP) was originally designed for interventional clinical trials, its principles can and should be applied to non-interventional studies as well, particularly regarding ethical review (IRB/IEC oversight), Informed Consent processes, data integrity, participant protection and Confidentiality

Knowledge Check

Case Scenario: Dr. Reyes is designing a clinical study to evaluate a new topical treatment for eczema in children. She prepares a comprehensive protocol including risk mitigation strategies, informed consent and assent forms, and materials for recruiting parents. Before beginning the study, she submits all documents to the local IRB/IEC for review. The ethics committee identifies that the assent form for children is too technical and recommends simplifying the language. Dr. Reyes revises and resubmits it for final approval before starting recruitment.

1. **What is the main ethical reason for obtaining IRB/IEC approval before starting a study?**

- To accelerate publication
- To collect more data
- To ensure participant protection and study ethics
- To complete trial registration faster

2. **Why did the IRB/IEC recommend changes to the assent form for children?**

   - The form was missing graphics
   - The language was not appropriate for the age of the participants
   - The form lacked a QR code
   - The sponsor hadn’t signed it

3. **What core ethical principle from the Belmont Report is best reflected in the committee’s request to revise the assent form?**

   - Justice
   - Respect for persons
   - Beneficence
   - Scientific integrity

Submit

Module 2

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