Update of Good Clinical Practice Standards ICH E6 (R3)
2025

CEIm Sant Pau

Good Clinical Practice (GCP) is 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 assure that the rights, safety and well-being of trial participants are protected; that the conduct is consistent with the principles that have their origin in the Declaration of Helsinki; and that the clinical trial results are reliable.

Principles of Good Clinical Practice:

The overarching principles provide a flexible framework for clinical trial conduct. They are structured to provide guidance throughout the life cycle of the clinical trial. The principles are interdependent and should be considered in their totality to assure ethical trial conduct and reliable results.

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 applicable regulatory requirement(s). Clinical trials should be designed and conducted in ways that ensure the rights, safety and well-being of participants.
2. Informed consent is an integral feature of the ethical conduct of a trial. Clinical trial participation should be voluntary and based on a consent process that ensures participants (or their legally acceptable representatives, where applicable) are well-informed.
3. Clinical trials should be subject to an independent review by an IRB/IEC.
4. Clinical trials should be scientifically sound for their intended purpose and based on adequate and current scientific knowledge and approaches.
5. Clinical trials should be designed and conducted by qualified individuals.
6. Quality should be built into the scientific and operational design and conduct of clinical trials.
7. Clinical trial processes, measures and approaches should be implemented in a way that is proportionate to the risks to participants and to the importance of the data collected and that avoids unnecessary burden on participants and investigators.
8. Clinical trials should be described in a clear, concise, scientifically sound and operationally feasible protocol.
9. Clinical trials should generate reliable results.
10. Roles and responsibilities in clinical trials should be clear and documented appropriately.
11. Investigational products used in a clinical trial should be manufactured in accordance with applicable Good Manufacturing Practice (GMP) standards and be managed in accordance with the product specifications and the trial protocol.

Main changes and new features:

General Aspects

- Principle-based approach: A more flexible framework is adopted, applicable to different types of studies (including pragmatic, low-intervention trials, and those with innovative designs).
- Emphasis on proportionality: The application of requirements should be proportional to the risk of the study and the complexity of the interventions.
- Orientation toward quality by design: Prioritizing from the outset those aspects that most impact participant safety and the credibility of the data.

This approach seeks to ensure that clinical trials are more dynamic, agile, and adaptable to the specific needs of each study, without compromising participant safety or data integrity.

Scope of Application

- Extension to various types of clinical research: This is not limited to classic drug trials, but can be applied to studies with devices, non-pharmacological interventions, and real-world settings.
- Recognition of tests with decentralised elements.

Reinforced Key Principles

- Ethics: primacy of the well-being of the participant and respect for human rights, with special attention to vulnerable populations.
- Informed and continuous participation: consent is conceived as a dynamic process, not a single act. It highlights the importance of participants being well informed and fully understanding the risks and benefits of the trial and enabling innovative forms of consent (electronic, remote).
- Transparency and public trust: transparency is encouraged in the registration of clinical trials and the reporting of results. This includes the obligation to register trials in public and open access databases, as well as the publication of results in an objective and non-promotional manner.

Organization and Responsibilities

- Sponsor
  - The sponsor's responsibility includes the implementation of risk-proportionate strategies to ensure the rights, safety and well-being of trial participants and the reliability of trial results throughout the entire clinical trial life cycle.
  - Obligation of supervision and quality assurance regardless of outsourcing.
  - Adoption of risk-based monitoring strategies as standard.

- Researcher:
  - Greater responsibility for electronic data management and security of participants in studies with decentralized elements.
  - Duty to guarantee the integrity and reliability of electronic data by meeting key criteria of being attributable, legible, contemporaneous, original, accurate, complete, secure and reliable.
  - Reinforcement of the role of the researcher in the supervision of tasks delegated to the team: they must document competencies, training and responsibilities.
  - Reinforcement of the duty of prompt and transparent communication to the ethics committee of critical deviations and relevant findings.

Roles and responsibilities in clinical trials should be clear and adequately documented.

Test Design and Conduct

- The design and conduct of the clinical trial can be supported by the perspectives of different stakeholders, such as patients and their communities, patient associations and healthcare professionals. Their input can

help reduce unnecessary complexity, improve feasibility, and increase the likelihood of meaningful trial outcomes.

- The use of innovative trial designs and technologies can enable the inclusion of a wider and more diverse population of participants and thus expand the applicability of trial results.
- The use of technology in conducting clinical trials should be tailored to the characteristics of the participants and the particular design of the trial.
- Quality by design must be implemented to identify the factors (i.e., data and processes) that are critical to ensuring trial quality, as well as the risks that threaten the integrity of those factors and, ultimately, the reliability of trial results.
- The risk mitigation processes and strategies applied in the conduct of the trial should be commensurate with the importance of the data collected and the risks to the safety of the participants and the reliability of the test results.
- Clinical trial designs must be operationally feasible and avoid unnecessary complexity.

Data Management and Documentation

- A section dedicated to data governance is included.
- This section provides guidance to responsible parties (i.e. investigators and sponsors) on the proper management of data integrity, traceability and security, thereby enabling the accurate reporting, verification and interpretation of information related to clinical trials.
- Focus on data integrity: attributable, readable, contemporary, original, accurate, complete, secure, and reliable.
- Documented procedures should be established to ensure the appropriate use of computerised systems in clinical trials for essential activities related to data collection, processing and management.

Safety

- More dynamic security reports, adapted to the type of study and data source.
- Reinforcement in the continuous evaluation of the benefit-risk balance.

In summary, ICH E6 R3 PCBs represent an evolution towards:

- Incorporation of relevant principles in technological advances and the design of clinical trials.
- Facilitating an increasingly digital ecosystem.
- Emphasis on reflective processes throughout the conception, design, execution and analysis of clinical trials.
- Risk-based approach (protection of participants) and proportionality.

Important note for all staff involved in clinical research:
The ICH E6(R3) guide on Good Clinical Practice has entered into force on July 23, 2025 and it is mandatory to have an updated certificate when submitting a study to the CEIm.
You have available the free online course, organized by The Global Health Network Training Centre. It can be completed in approximately 45-60 minutes and a certificate is issued if a minimum of 80% is obtained in the final assessment.
You can do it at the following link:
ICH E6 Good Clinical Practice Standards (R2)