



DRAFT WORKING DOCUMENT FOR COMMENTS:

Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products

Main Principles

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DRAFT FOR COMMENTS

SCHEDULE FOR DRAFT WORKING DOCUMENT QAS/26.995

GUIDELINES FOR GOOD CLINICAL PRACTICE (GCP) FOR TRIALS ON PHARMACEUTICAL PRODUCTS

Description of activity	Date
Preparation of a working document.	June 2026
Mailing of the working document to the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations (EAP) inviting comments and posting of the working document on the WHO website for public consultation.	June - August 2026
Consolidation of comments received and review of feedback. Preparation of working document for discussion.	September 2026
Preparation of a working document for discussion and possible adoption by the Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP).	September 2026
Presentation to the sixtieth meeting of the ECSPP.	12 – 16 Oct 2026
Any other follow-up action as required.	TBC

GUIDELINES FOR GOOD CLINICAL PRACTICE (GCP) FOR TRIALS ON PHARMACEUTICAL PRODUCTS

For any further information or request, please send an email to the Norms and Standards for Pharmaceuticals (NSP) Team at WHO, at email nsp@who.int.

Background

The World Health Organization (WHO) first published the Guidelines for good clinical practice (GCP) for trials on pharmaceutical products in 1995, providing the first internationally endorsed framework for the ethical and scientific conduct of clinical trials involving pharmaceutical products. The guideline established foundational standards for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials, with the primary objectives of safeguarding the rights, safety and well-being of trial participants and ensuring the credibility of clinical trial data.

Since the publication of the 1995 WHO GCP guideline, the clinical trial ecosystem has evolved substantially, driven by scientific, technological, ethical and regulatory developments. In parallel, multiple international and WHO instruments relevant to GCP have been issued, including the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guideline for Good Clinical Practice E6, the WHO Handbook for Good Clinical Research Practice, and most recently the WHO guidance for best practices for clinical trials), which highlights systemic challenges and barriers to effective trial conduct and proposes approaches to strengthen national clinical trial ecosystems.

In particular, ICH has undertaken successive revisions of its GCP guideline, culminating in the development of ICH E6 (R3). This revision reflects contemporary scientific thinking and regulatory experience, including a stronger emphasis on risk proportionate approaches, data integrity across the trial lifecycle, and the integration of quality management principles into trial design and oversight. By contrast, the WHO GCP guideline published in 1995 has remained unchanged, creating an increasing divergence between the WHO standard and current global regulatory expectations for clinical trials.

Recognizing this divergence, the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) at its fifty-eight meeting considered the continued relevance and role of

the 1995 WHO GCP guideline. The Committee reaffirmed the continued importance of a WHO issued GCP guideline, particularly for Member States that rely primarily on WHO normative guidance rather than ICH guidelines, and for regulatory systems operating in low and middle income countries (LMICs). At the same time, the Committee acknowledged that the core principles of GCP remain valid, while the implementation context and regulatory expectations have evolved, necessitating an updated approach that adds practical value beyond existing international guidance.

In line with WHO policy on the use of externally developed guidelines, the ECSPP emphasized that WHO may adopt, adapt or incorporate external guidance only where it meets WHO standards for quality, global applicability and inclusive expert representation, and where it can be contextualized to the needs and capacities of Member States across all regions. The Committee noted that while ICH guidelines are scientifically robust and widely influential, not all WHO Member States participate in ICH processes, and direct reference to ICH guidance without WHO contextualization may present challenges for implementation in some settings.

Following extensive discussion, the ECSPP recommended that the WHO GCP guideline be revised using a modular approach, adopting ICH E6 (R3) as the reference standard for GCP principles, while developing WHO specific implementation guidance to facilitate application across diverse regulatory environments. This approach mirrors previous WHO practice in other regulatory domains and is intended to ensure scientific alignment with current international standards, while preserving WHO's mandate to support equitable, feasible and public health oriented implementation of clinical trial requirements globally.

Accordingly, this revision of the WHO Guidelines for good clinical practice for trials on pharmaceutical products replaces the 1995 WHO guideline and establishes an updated WHO GCP framework that is aligned with ICH E6 (R3), reflects current scientific and regulatory thinking. The revised guideline aims to strengthen the quality, integrity and ethical conduct of clinical trials worldwide, while supporting regulatory convergence and facilitating reliance where appropriate, without compromising national regulatory autonomy or public health priorities.

For this consultation, the GCP guideline comprises three parts to be read together: the Main principles, establishing the foundations of GCP; Annex 1, detailing requirements with supporting appendices; and Annex 2, addressing additional considerations focusing on trials that incorporate decentralised elements, pragmatic elements and/or real-world data.

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1. INTRODUCTION

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. The term “trial conduct” in this document includes processes from planning to reporting, including planning, initiating, performing, recording, oversight, evaluation, analysis and reporting activities as appropriate.

The objective of this GCP Guideline is to provide a unified standard to facilitate the mutual acceptance of clinical trial data for WHO Member States by applicable regulatory authorities.

This guideline builds on key concepts outlined in ICH E8(R1) General Considerations for Clinical Studies. This includes fostering a quality culture and proactively designing quality into clinical trials and drug development planning, identifying factors critical to trial quality, engaging interested parties, as appropriate, and using a proportionate risk-based approach.

Clinical trials vary widely in scale, complexity and cost. Careful evaluation of critical to quality factors involved in each trial and the risks associated with these factors will help ensure efficiency by focusing on activities critical to achieving the trial objectives.

Guideline Scope

This guideline applies to interventional clinical trials of investigational products¹ 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.

The Annexes provide the basis for the appropriate interpretation and application of the principles and should therefore be appropriately considered; however, various approaches to the provisions in the Annexes may be considered provided they are justified and achieve the intended purpose of the application of the principles.

This guideline encourages a risk-based and proportionate approach to the conduct of a clinical trial.

Guideline Structure

¹ For the purpose of this guideline, the term “investigational products” should be considered synonymous with, medicines, vaccines and biological products.

This GCP Guideline is composed of Principles and Annexes that expand on the principles, with specific details for different types of clinical trials. The principles are intended to apply across clinical trial types and settings and to remain relevant as technological and methodological advances occur. The principles outlined in this guideline may be satisfied using differing approaches and should be applied to fit the intended purpose of the clinical trial.

Annex 1, including its Appendices, is intended to provide information on how the Principles can be appropriately applied to clinical trials. Additional annexes may be developed to respond to the needs of interested parties and to address emerging innovations in trial design and conduct. This guideline should be read in conjunction with other WHO and ICH guidelines relevant to the design and conduct of clinical trials, including multiregional trials.

Annex 2, including its considerations, is intended to provide information on how the Principles and Annex 1 can be appropriately applied to clinical trials that incorporate decentralised elements, pragmatic elements and/or real-world data. It is illustrative rather than exhaustive, recognising that trial methodologies will continue to evolve. This Annex should be read in conjunction with the Principles and Annex 1.

2. PRINCIPLES OF GCP

Clinical trials are a fundamental part of clinical research that support the development of new medicines or uses of existing medicines. Well-designed and conducted clinical trials help answer key questions in healthcare and drug development. Their results are essential for evidence-based healthcare decisions. Trials with inadequate design and/or poorly conducted trials may place participant safety at risk, yield inadequate or unreliable results and are unethical. They waste resources and the efforts and time of investigators and participants.

The Principles of GCP are designed to be flexible and applicable to a broad range of clinical trials. This guideline, along with ICH E8(R1), encourages thoughtful consideration and planning to address specific and potentially unique aspects of an individual clinical trial. This includes evaluation of trial characteristics, such as the design elements, the investigational product being evaluated, the medical condition being addressed, the characteristics of the participants, the setting in which the clinical trial is being conducted, and the type of data being collected. Careful consideration of factors relevant to ensuring trial quality is needed for each clinical trial.

The principles are intended to support efficient approaches to trial design and conduct. For example, digital health technologies, such as wearables and sensors, may expand the possible approaches to trial conduct. Such technologies can be incorporated into existing healthcare infrastructures and enable the use of a variety of relevant data sources in clinical trials. This will aid in keeping clinical trial conduct in line with advancing science and technological developments. The use of technology in the conduct of clinical trials should be

adapted to fit the participant characteristics and the particular trial design. This guideline is intended to be media neutral to enable the use of different technologies.

The design and conduct of the clinical trial may be supported by obtaining the perspectives of interested parties, such as patients and their communities, patient advocacy groups and healthcare professionals. Their input can help to reduce unnecessary complexity, improve feasibility and increase the likelihood of meaningful trial outcomes. The use of innovative trial designs and technologies may enable the inclusion of a wider and more diverse population of participants and thereby broaden the applicability of trial outcomes.

Clinical trials should be designed to protect the rights, safety and well-being of participants and assure the reliability of results. Quality by design should be implemented to identify the factors (i.e., data and processes) that are critical to ensuring trial quality and the risks that threaten the integrity of those factors and ultimately the reliability of the trial results. Clinical trial processes and risk mitigation strategies implemented to support the conduct of the trial should be proportionate to the importance of the data being collected and the risks to trial participant safety and the reliability of trial results. Trial designs should be operationally feasible and avoid unnecessary complexity.

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. These principles are applicable to trials involving human participants. 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.

- 1.1. The rights, safety and well-being of the participants are the most important considerations and should prevail over interests of science and society.
- 1.2. The safety of the participants should be reviewed in a timely manner as new safety information becomes available, which could have an impact on participant safety, their willingness to continue in the trial or the conduct of the trial.
- 1.3. Foreseeable risks and inconveniences should be weighed against the anticipated benefits for the individual participants and society. A trial should be initiated and continued only if the anticipated benefits justify the known and anticipated risks.
- 1.4. When designing a clinical trial, the scientific goal and purpose should be carefully considered

so as not to unnecessarily exclude particular participant populations. The participant selection process should be representative of the population groups that the investigational product is intended to benefit, once authorised, to allow for generalising the results across the broader population. Certain trials (e.g., early phase, proof of concept trials, bioequivalence studies) may not require such a heterogeneous population.

1.5. A qualified physician or, when appropriate, a qualified dentist (or other qualified healthcare professionals in accordance with local regulatory requirements) should have the overall responsibility for the trial-related medical care given to and medical decisions made on behalf of participants; however, the practical interactions and the delivery of medical care and decisions can be carried out by appropriately qualified healthcare professionals in accordance with applicable regulatory requirements.

1.6. The confidentiality of information that could identify participants should be protected in accordance with applicable privacy and data protection requirements.

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.

2.1. Freely given informed consent should be obtained and documented from every participant prior to clinical trial participation. For potential participants unable to provide informed consent, their legally acceptable representatives, acting in the participants' best interest, should provide consent prior to clinical trial participation. These potential participants should be informed about the trial in a manner that facilitates their understanding. In the event that a minor is a participant, assent should be collected from that minor, as appropriate, and in accordance with local regulatory requirements (see ICH E11(R1) Clinical Investigation of Medicinal Products in the Pediatric Population).

2.2. The process and information provided should be designed to achieve the primary objective of enabling potential trial participants to evaluate the benefits, risks and burden of participating in the trial and to make an informed decision on whether or not to participate in the trial. The information provided during the informed consent process should be clear and concise so as to be understandable by potential participants or legally acceptable representatives.

2.3. The informed consent process should take into consideration relevant aspects of the trial, such as the characteristics of the participants, the trial design, the anticipated benefits and risks of

medical intervention(s), the setting and context in which the trial will be conducted (e.g., trials in emergency situations), and the potential use of technology to inform participants (or their legally acceptable representatives) and obtain informed consent.

- 2.4. In emergency situations, where consent cannot be obtained prior to trial participation, consent should be obtained from the participant or their legally acceptable representative as soon as possible in accordance with applicable regulatory requirements and the processes approved by the institutional review board/independent ethics committee (IRB/IEC).

3. Clinical trials should be subject to an independent review by an IRB/IEC.

- 3.1. A trial should be conducted in compliance with the protocol that received prior IRB/IEC approval/favourable opinion.

- 3.2. Periodic review of the trial by the IRB/IEC should also be conducted in accordance with applicable regulatory requirements.

4. Clinical trials should be scientifically sound for their intended purpose and based on adequate and current scientific knowledge and approaches.

- 4.1. The available nonclinical and clinical information on an investigational product(s) should be adequate to support the proposed clinical trial.

- 4.2. Clinical trials should be scientifically sound and reflect the state of knowledge and experience with the investigational product(s), including, if applicable, the condition to be treated, diagnosed or prevented; the current understanding of the underlying biological mechanism (of both the condition and the investigational product); and the population for which the investigational product is intended.

- 4.3. There should be periodic review of current scientific knowledge and approaches to determine whether modifications to the trial are needed, since new or unanticipated information may arise once the trial has begun.

5. Clinical trials should be designed and conducted by qualified individuals.

- 5.1. Individuals with different expertise and training may be needed across all phases of a clinical trial, such as physicians, nurses, pharmacists, scientists, ethicists, technology experts, trial coordinators, monitors, auditors and biostatisticians. Individuals involved in a trial should be qualified by education, training and experience to perform their respective task(s).

6. Quality should be built into the scientific and operational design and conduct of clinical trials.

6.1. Quality of a clinical trial is considered in this guideline as fitness for purpose.

6.2. Factors critical to the quality of the trial should be identified prospectively. These factors are attributes of a trial that are fundamental to the protection of participants, the reliability and interpretability of the trial results and the decisions made based on those trial results. Quality by design involves focusing on critical to quality factors of the trial in order to maximise the likelihood of the trial meeting its objectives.

6.3. Strategies should be implemented to avoid, detect, address and prevent recurrence of serious noncompliance with GCP, the trial protocol and applicable regulatory requirements.

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.

7.1. Trial processes should be proportionate to the risks inherent in the trial and the importance of the information collected. Risks in this context include risks to the rights, safety and well-being of trial participants as well as risks to the reliability of the trial results.

7.2. The focus should be on the risks associated with trial participation. For clinical trials involving patients, the focus should be on risks that go beyond those associated with usual medical care. The risks relating to investigational products that have a marketing authorisation when used in the clinical trial context may differ from the usual care of patients and should be taken into consideration.

7.3. Risks to critical to quality factors should be managed proactively and adjusted when new or unanticipated issues arise once the trial has begun.

7.4. Trial processes should be operationally feasible and avoid unnecessary complexity, procedures and data collection. Trial processes should support the key trial objectives. The sponsor should not place unnecessary burden on participants and investigators.

8. Clinical trials should be described in a clear, concise, scientifically sound and operationally feasible protocol.

8.1. A well-designed trial protocol is fundamental to the protection of participants and for the generation of reliable results.

8.2. The scientific objectives of any trial should be clear and explicitly stated in the protocol.

8.3. The clinical trial protocol as well as the plans or documents for the protocol execution (e.g., statistical analysis plan, data management plan, monitoring plan) should be clear, concise and operationally feasible.

9. Clinical trials should generate reliable results.

9.1. The quality and amount of the information generated in a clinical trial should be fit for purpose and sufficient to provide confidence in the trial's results and support good decision making.

9.2. Systems and processes that aid in data capture, management and analyses, as well as those that help ensure the quality of the information generated from the trial, should be fit for purpose, should capture the data required by the protocol and should be implemented in a way that is proportionate to the risks to participants and the importance of acquired data.

9.3. Computerised systems used in clinical trials should be fit for purpose (e.g., through risk-based validation, if appropriate), and factors critical to their quality should be addressed in their design or adaptation for clinical trial purposes to ensure the integrity of relevant trial data.

9.4. Clinical trials should incorporate efficient and robust processes for managing records (including data) to help ensure that record integrity and traceability are maintained and that personal information is protected, thereby allowing the accurate reporting, interpretation and verification of the relevant clinical trial- related information.

9.5. Essential records should be retained securely by sponsors and investigators for the required period in accordance with applicable regulatory requirements. These essential records should be available to regulatory authorities, monitors, auditors and IRBs/IECs (as appropriate) upon request to enable appropriate evaluation of the trial conduct in order to ensure the reliability of trial results.

9.6. The transparency of clinical trials includes timely registration on publicly accessible and recognised databases and the public posting of clinical trial results. Communicating trial results to participants should be considered. Such communication should be objective and non-promotional.

10. Roles and responsibilities in clinical trials should be clear and documented appropriately.

10.1. The sponsor may transfer or the investigator may delegate their tasks, duties or

functions (hereafter referred to as activities), but they retain overall responsibility for their respective activities.

10.2. Agreements should clearly define the roles, activities and responsibilities for the clinical trial and be documented appropriately. Where activities have been transferred or delegated to service providers, the responsibility for the conduct of the trial, including quality and integrity of the trial data, resides with the sponsor or investigator, respectively.

10.3. The sponsor or investigator should maintain appropriate oversight of the aforementioned activities.

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.

11.1. Investigational products used in a clinical trial should be manufactured in accordance with applicable GMP standards.

11.2. Measures should be in place to ensure that the investigational product provided to trial participants retains its quality.

11.3. Investigational products should be used in accordance with the protocol and relevant trial documents.

11.4. Manufacturing, handling and labelling of investigational products should be undertaken in a manner that aligns with treatment assignment and maintains blinding, where applicable.

11.5. Investigational product labelling should follow applicable regulatory requirements.

11.6. Appropriate processes should be implemented for the handling, shipping, storage, dispensing, returning and destroying or alternatively disposing of the investigational product.