Conditions and Principles of GCP

Version 1.0

About these conditions and principles

These conditions (UK Clinical Trial Regulation) and principles (ICH-GCP E6 (R3)) describe the expectations for how clinical trials should be designed, conducted, and overseen in the UK. They apply across the entire trial lifecycle and should guide proportionate decision-making.

UK Clinical Trials Regulations – 4 Key Conditions

Condition 1: Compliance with ICH-GCP E6 (R3) (see below)

1. Clinical trials must be conducted in accordance with the principles of good clinical practice set out in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice, as amended from time to time.

Condition 2: Follow the principles of the Declaration of Helsinki

2. Except where it would be a contravention of these Regulations, clinical trials must be conducted in accordance with the principles of the Declaration of Helsinki.

Condition 3: Regard to relevant guidance (e.g., SOPs and policies)

3. The investigator and sponsor must have regard to all relevant guidance with respect to commencing and conducting a clinical trial.

Condition 4: Insurance and Indemnity must in place

4. Provision must be made for insurance or indemnity to cover all liabilities of the investigator and sponsor which may arise in relation to the clinical trial.

ICH-GCP E6 (R3) Principles

The following principles set out the ICH-GCP E6 (R3) expectations that apply to clinical trials and are given legal effect in the UK through the conditions above.

Principle 1: Participant safety comes first

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 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.

Principle 2: Informed consent is fundamental

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).

Principles 3: Independent REC review is required

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.

Principles 4: Trials must be scientifically sound

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.

Principles 5: Trials are run by qualified individuals

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).

Principle 6: Quality is built in by design (QbD)

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.

Principle 7: Oversight is proportionate to risk

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.

Principle 8: Protocols must be clear and feasible

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.

Principle 9: Trials must generate reliable results

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.

Principle 10: Roles, responsibilities and oversight are clear

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.

Principle 11: IMPs should be managed safely and 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.

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