

Good Clinical Practice (GCP) Training

GCP training should:

- Be provided to all study personnel engaged in a clinical trial of a drug, device, biologic and/or behavioral intervention as defined by the National Institutes of Health.
- Meet the minimum criteria* for International Conference on Harmonisation (ICH) GCP training including: GCP Overview, the Principles of ICH GCP and Investigator responsibilities. (see below)
 - Be accepted as “common currency” by industry sponsors so as to eliminate redundant training requests
 - Contribute to fulfilling Food and Drug Administration expectations for study personnel training
- Research personnel should take GCP training at a minimum of every three years, in line with the current clinical research training organizations and industry expectations

The agreed upon minimum criteria* for International Conference on Harmonisation (ICH) training in Good Clinical Practice (GCP) should include the following:

- I. GCP Overview
- II. Principles of ICH GCP
- III. Consequent investigator and/or study coordinator responsibilities

Regardless of the approach chosen, GCP training should include an overview of Good Clinical Practice and the 13 ICH GCP Principles outlined in the 1996 document: Harmonised Tripartite Guideline for Good Clinical Practice E6(R1):

http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

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 the applicable regulatory requirements.
2. Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
3. The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
4. The available non-clinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
5. Clinical trials should be scientifically sound and described in a clear, detailed protocol.
6. A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favorable opinion.
7. The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
8. Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective tasks.
9. Freely given informed consent should be obtained from every subject prior to clinical trial participation.
 - All clinical trial information should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification.
10. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements.
11. Investigational products should be manufactured, handled and stored in accordance with applicable good manufacturing practice. They should be used in accordance with the approved protocol.
12. Systems with procedures that assure the quality of every aspect of the trial should be implemented.

In addition, the training should emphasize the following investigator responsibilities:

(1) Investigator Qualifications and Agreements

- Investigator qualification (education, training, experience)
- Demonstrate evidence of adequate training (provide up-to-date CV)
- Awareness of and compliance with GCP and regulatory requirements
- Investigational product familiarity
- Allow for monitoring/auditing/inspection to enable sponsor/regulatory oversight
- Introduce definitions of monitoring (1.38), audit (1.6) and inspection (1.29)
- Use of qualified support staff
- Document delegation of duties to appropriately qualified persons

(2) Adequate Resources

- Potential to recruit suitable subjects
- Sufficient time to conduct trial
- Sufficient qualified staff and adequate facilities to conduct trial
- Staff are adequately informed about protocol, Investigational Product (IP) and tasks related to the protocol

(3) Medical Care of Trial Subjects

- Qualified physician or dentist who is an investigator or sub-investigator should be responsible for all trial related medical decisions
- During and following the trial, the investigator/institution should ensure appropriate medical care for adverse events (AEs) and clinically significant lab deviations related to trial and inform subjects if medical care is needed for intercurrent illness.
- Inform primary (family) physician of subject's participation in trial (after obtaining permission from the subject)
- Physician to make a reasonable effort to ascertain the reasons for subject's premature withdrawal from the trial

(4) Communication with IRB/IEC

- Definition of IRB (1.31) and IEC (1.27)
- Before trial begins, obtain written, dated approval/favorable opinion for protocol and all documents provided to subjects (e.g., informed consent form (ICF), advertisements)
- Provide a copy of Investigator's Brochure/updated IB
- Before and during the trial, provide all documents required by IRB/IEC for review and appropriate approval/favorable opinion

(5) Compliance with Protocol

- Conduct trial according to approved protocol, GCP and applicable regulatory requirements (e.g., sufficient documentation to support subject meeting inclusion/exclusion criteria)
- Document the acceptance to follow protocol in a protocol signature page or contract
- Protocol deviation process: no deviations or changes prior to sponsor and IRB/IEC approval
 - Exception: Deviation necessary to eliminate immediate hazard to trial subject
- Deviations need to be documented and rationale submitted to sponsor, IRB/IEC and regulatory authorities

(6) Investigational Products

- Responsibility for IP (refer to 1.33) accountability and delegation of activities and supervision of an appropriately qualified person
- Documentation of delivery, inventory, dispensation, usage, disposal or return and reconciliation of all IP and other study medication
- Stored per requirements
- IP usage per protocol
- Explanation of correct use of IP to subjects and periodic check for understanding/compliance

(7) Randomization Procedures and Unblinding

- Follow the trial's randomization procedures
- Blinded trials: Promptly document and report to sponsor any premature unblinding

(8) Informed Consent of Trial Subjects

- Definition of Informed Consent
- Explain the informed consent process and informed consent form (ICF): IRB/IEC written approval in advance of use for written consent and other written information to be provided to subjects
 - Subject to be fully informed of all pertinent aspects of the trial prior to participation
 - The informed consent discussion and form needs to include all relevant explanations. Refer or link to ICH 4.8.10.
 - Language used in oral and written information (ICF) should be understandable to subject or legal representative and impartial witness (where applicable)
 - Subject should have ample time to review the ICF and to ask any questions and receive answers before decision is made
 - Subject should not be unduly influenced to participate
 - ICF should be obtained/signed prior to a subject's participation in a trial (before any study procedures are performed)
 - Subject should be aware that withdrawal is possible at any time
 - Subject should not be asked to waive legal rights or release investigator or sponsor from liability for negligence
 - Written informed consent form must be updated/approved when new information is available that may be relevant to subject's consent
- Informed consent of special population:
 - Refer to or add definition of Vulnerable Subjects: When a subject (e.g., minor, incapacitated) can only be enrolled with the consent of the legal representative, the subject must be informed to the level of their understanding, provide assent (where this is feasible) and personally sign and date the consent form.
 - In emergency situations where the subject and legal representative are unable to consent, enrollment requires protective measures to be described in protocol or other IRB/IEC approved documents; subject or legal representative should be informed as soon as possible and consent to continue and other consent as appropriate.
 - If the subject/legal representative is unable to read, an impartial witness must be present during the consent discussion and sign and date the consent form.
- Informed Consent documentation: The ICF should be signed and personally dated by the subject and/or the legal representative and by the person who conducted the consent.
 - A signed and dated copy of the ICF should be given to the subject or the legal representative (including any other written information provided to the subject).
 - The Informed Consent process should be documented in the medical record/source file (as well as documentation regarding communication of new information).

(9) Records and Reports

- Definition of Source Documents: The actual documents (originals) GCP glossary (brief)
- Refer to or add definition of Source Data
- Definition of Essential Documents
- The need to maintain and retain essential documents
- Case report forms and all required reports (written or electronic)
 - Accuracy, legibility, completeness of data
 - Data to be consistent with source data
- Corrections are dated and initialed, do not obscure original entry and are explained if necessary (applies to written and electronic changes/updates). Retain records of changes and corrections.
- Financial aspects documented in an agreement between sponsor and investigator/institution
- Direct access to all trial-related documents by the monitor, the auditor, the IRB/IEC or regulatory authority

(10) Progress Reporting/Final Reports

- Investigator submits written summaries of progress to IRB/IEC at least annually or as required
- Provide written reports to sponsor and IRB/IEC (and institution where required) of any significant changes affecting the study or increased risk to subjects
- Upon completion of trial, provide sponsor with all required reports
- Final report with a summary of trials and outcomes submitted to IRB/IEC and regulatory authorities as required

(11) Safety Reporting

- Adverse Event (AE) definition
- Refer to or add definition of Adverse Drug Reaction (ADR) (1.1) and Unexpected ADR (1.60)
- AE Reporting: All adverse events (AE) and/or laboratory abnormalities should be reported to the sponsor within the time period defined in protocol.
- Definition of a SAE
- All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting
 - Prompt follow-up by detailed written reports
 - Subjects should be identified by unique code numbers
 - Report unexpected serious drug reactions according to regulatory and IRB/IEC requirements
 - Sponsor and IRB/IEC may need additional information for reported deaths (e.g., autopsy report)

(12) Premature Termination or Suspension of Trial

- Responsibility to promptly inform the trial subjects and ensure appropriate therapy and follow-up. Inform regulatory authorities when required.
- Responsibility for communication of study termination or suspension of study to sponsor,
- IRB/IEC and institution as applicable, including a detailed written explanation

Finally, in the event an investigator is also serving as Sponsor of the clinical trial, additional responsibilities are expected as outlined in Section 5 (pages 20-30) of the Harmonised Tripartite Guideline for Good Clinical Practice E6(R1).*

*Minimum Criteria for ICH E6 GCP Investigator Site Personnel Training 3 (Excerpt from TransCelerate BioPharma Operating Principles) Version 1.1: February 7, 2013 © 2013 TransCelerate BioPharma Inc. All rights reserved.