Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording, and reporting clinical trials that involve human subjects. Developed by the International Conference on Harmonisation (ICH) to be a unified standard for the European Union (EU), United States, and Japan, it ensures that the rights, safety and well-being of trial subjects are protected, consistent with principles set forth by the Declaration of Helsinki, and that the clinical trial data are credible. It is important to adhere to the GCP guidelines when participating in clinical trials because they provide a framework for ethical conduct, and will help to ensure that the data you collect is accurate and complete. Though individual countries, states, and institutions may have additional standards and requirements, following the ICH’s GCP Guidelines is vital, as they facilitate drug approval across borders and allow medical products to be more rapidly supplied around the world to patients in need. This chapter outlines good clinical practice procedures based on the GCP Guidelines.

Principles of GCP and the Roles of the Parties Involved

Before a clinical trial can be performed, adequate clinical and nonclinical data must be available to support the trial, and it must be demonstrated that the potential benefits outweigh the risks. For a clinical trial to be conducted appropriately, all people involved, including sponsors, monitors, institutional review boards (IRBs)/research ethics committees (RECs), and investigators, must follow the GCP Guidelines.

There are 13 General Principles of ICH GCP:

1. Clinical trials must 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 requirement(s).

2. Before a trial is initiated, foreseeable risks and inconveniences must 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 must prevail over interests of science and society.

4. The available clinical and nonclinical information on an investigational product must be adequate to support the proposed clinical trial.

5. Clinical trials must be scientifically sound and described in a clear, detailed protocol.

6. A trial must be conducted in compliance with the protocol that has received prior IRB/REC approval/favorable opinion.

7. The medical care given to, and medical decisions made on behalf of, subjects is the responsibility of a qualified physician or healthcare professional.

8. Each individual involved in conducting a trial must be qualified by education, training, and experience to perform his or her respective task(s).

9. Freely given informed consent must be obtained from every subject prior to clinical trial participation.
10. All clinical trial information must be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification.

11. The confidentiality of records that can identify subjects must be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s) and standard(s) of medical practice.

12. Investigational products must be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.

13. Systems with procedures that assure the quality of every aspect of the trial should be implemented.

**Sponsor Responsibilities:** The GCP Guidelines state that the trial sponsor’s responsibility is to set forth clear protocols for the trial design. The protocol must be scientifically sound, of high quality and supported by previous clinical and nonclinical information. This insures that the maximum benefit is reached. Sponsors must implement and maintain quality assurance and quality control systems throughout each stage of the trial to ensure that the trial is conducted in compliance with the protocol and that data are correctly recorded. A contract research organization (CRO) may be contracted by the sponsor to assume some or all of the sponsor’s trial-related duties. The CRO would be responsible for quality assurance and control, but the ultimate responsibility remains with the sponsor.

The trial sponsor must assign investigators who have the proper education, training, or experience necessary to conduct the trial and who are familiar with the investigational product. The sponsor must enlist qualified professionals, such as biostatisticians, clinical pharmacologists or physicians as appropriate, to supervise the conduct of the trial, handle data, conduct statistical analyses and prepare trial reports. The sponsor must also set guidelines for financial compensation for all trial staff and subjects.

The responsibilities of the sponsor also include following Good Manufacturing Practice (GMP), storing and supplying the investigational product properly, and conducting ongoing safety evaluations of the investigational product. The GCP Guidelines require that the sponsor report any adverse events, both serious and unexpected, to all concerned parties - including regulatory authorities.

According to the GCP Guidelines, the sponsor may establish an Independent Data Monitoring Committee (IDMC) to assess the progress of the trial, monitor the safety and efficacy data at specific intervals, and recommend whether the trial should be continued, modified, or terminated.

The sponsor should appoint an appropriately trained or experienced monitor to oversee the trial. The main purpose of the monitor is to ensure that the rights and well-being of subjects are protected; to ensure the reported data are accurate, complete, and verifiable; and to verify that the trial is being conducted in compliance with the protocol and GCP Guidelines.

Finally, the sponsor is responsible for designing a plan for data management including documentation, data handling, and record keeping. The sponsor must maintain all trial-related documentation.

**Investigator Responsibilities:** An investigator is responsible for all aspects of a clinical trial conducted at his or her trial site. The GCP Guidelines state that the assigned investigator must be able to conduct the trial in a timely manner, find an appropriate number of subjects, and delegate necessary tasks to adequately trained staff. The investigator must have an adequate number of qualified staff as
available for the foreseeable duration of the trial and who are properly informed about the protocol, investigational product, and their trial-related duties and responsibilities. The investigator must maintain a list of appropriately qualified persons to whom he or she has delegated trial-related duties. Without adequate staff, the completion of the trial may be delayed and the benefit of conducting the trial will not be maximized. The investigator must ensure that a qualified physician (or dentist when appropriate) provides proper medical treatment to all trial subjects for trial-related problems during the course of the study and arranges for referral for non-trial related problems during the trial as well ongoing care at the completion of the trial.

The investigator is responsible for assuring that no research-related procedures take place prior to approval of the protocol by an IRB/REC. The GCP Guidelines also require that any deviations or changes to the protocol (which are rare), any changes that increase risk to subjects or significantly affect the conduct of the trial, all adverse drug reactions, or new information that may have an impact on the safety (serious/life-threatening unanticipated events) of the subjects or the conduct of the trial be immediately reported to the IRB/REC. In addition, all serious adverse events (SAE) should be immediately reported to the study sponsor, followed by a detailed, written report. An SAE or serious adverse drug reaction (serious ADR) is defined as any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

The investigator must obtain freely given informed consent from the trial subjects or the subjects’ representatives, and must inform participants of all possible risks of the trial. No research-related procedures may take place prior to obtaining this consent.

The investigator is responsible for the accountability of the investigational products at the trial site, but this responsibility may be delegated to an appropriate pharmacist or other qualified individual.

The GCP Guidelines require that the investigator allow monitoring and auditing by both the trial sponsor and the regulatory authorities to ensure proper compliance with the protocol and GCP Guidelines.

**Institutional Review Board Responsibilities:** The composition and roles of IRBs/RECs are discussed in another chapter. The GCP Guidelines require that an IRB/REC review every proposed clinical study to safeguard the rights, safety, and well-being of all trial subjects. The IRB/REC is responsible for reviewing all protocols and for giving an approval/favorable opinion before the trial can be conducted. The IRB/REC should continuously conduct reviews to ensure the safety of trial subjects. These reviews should be conducted at intervals appropriate to the degree of risk to human subjects, but a minimum of once a year is required. If there are any reported protocol deviations, any changes, or adverse events, the IRB/REC must make a decision concerning the future of the trial and relay this decision in writing, including the reasons for the decision, and the procedure for appealing this decision, to the trial’s investigator.

The GCP Guidelines state that the IRB/REC must retain all relevant trial-related records for a period of at least 3 years after trial completion and make them available at the request of the regulatory authorities.

**Conclusions**

The GCP Guidelines are an important element in the process of drug development. By following these principles, all parties ensure that the clinical trial is conducted in a manner that supports the rights
and well-being of human subjects and allows for new medicines to be most efficiently tested and approved for general use.

**Resources**
