Whitehall Training

ICH GCP
Good Clinical Practice

What is GCP?

Good Clinical Practice (GCP) is based on 13 principles to help minimise the risk of participating in a clinical trial and to ensure that participants understand exactly what is involved…

1) Clinical trials should be conducted in accordance with specific ethical principles
2) Risks should be weighed against anticipated benefits for the trial participant and society. A trial should only take place if the anticipated benefits justify the risks
3) The rights, safety, and well-being of the trial subjects must prevail over interests of science and society
4) Non-clinical and clinical information on an investigational product (IMP) 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 must follow the protocol that has been pre-approved by an ethics committee, or similar body
7) The medical care given to subjects should always be the responsibility of a qualified physician/dentist
8) Each individual involved in a trial should be qualified by education, training and experience
9) Freely given informed consent should be obtained from every subject before clinical trial participation
10) All clinical trial information should be recorded, handled, and stored so it can be accurately reported, interpreted and verified, whether paper or electronic
11) Any records that could identify subjects should be kept confidential to protect their privacy
12) Manufacture, handling, and storage of investigational products should be in accordance with applicable good manufacturing practice (GMP) and trial protocol
13) There must be systems in place that assure the quality of every aspect of the trial.

Competent Authorities & Ethics Committees

In GCP, the governing regulatory authority is known as a "Competent Authority" and it plays a key role in clinical trials.

The CA reviews safety, efficacy and quality data about the IMP and gives an opinion regarding its use in the proposed clinical trial. When the trial is underway, it has responsibility for maintaining its opinion through collecting and reviewing Serious Adverse Event (SAE) data and safety reports.

The ethics committee (EC) has different names depending on the country in which the trial is being held — for example, in the US they are called IRBs, in Canada, they are called REBs and in Australia, they are known as HRECs. They may be organised differently, but they all fulfil the same basic purpose.

ECs are present to safeguard the rights, safety, and well-being of all trial subjects. In particular, they pay special attention to trials that may include vulnerable subjects.

They provide an opinion on the trial before it begins — approving, suggesting modification, rejecting, or terminating a trial);

To achieve this, the committee needs to review all aspects of the trial including the risks, investigators qualification, the protocol, information given to subjects and payment made to subjects.

They also need to review the trial at least annually.

The Informed Consent Form (ICF)...

The ICF is the primary method used to explain the details of the trial to participants. It must be written in clear, non-medical language such that the participants will understand. It will be reviewed by the EC before the trial to check that it contains details such as…

- That the trial involves research and what it hopes to achieve
- The reasonably foreseeable risks or inconveniences to the subject
- Any alternative procedures or courses of treatment that may be available to the subject
- The compensation and/or treatment available to the subject in the event of trial-related injury
- The anticipated expenses and/or payment, if any, to the subject for participating in the trial
- That the subject's participation in the trial is voluntary and that they may refuse to participate or withdraw from the trial, at any time, without penalty or loss of any benefits
- That the monitors, the auditors, EC & CA will be granted direct access to the subject's original medical records for verification of clinical trial procedures.
- The persons to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury
- The foreseeable circumstances under which the subject's participation in the trial may be terminated
- The expected duration of the subject's participation in the trial
- The approximate number of subjects involved in the trial.

The Investigator

The Investigator is pivotal to clinical trials and plays a key role in maintaining GCP. They do this in partnership with the sponsor of the trial.

Broadly speaking, the investigator has responsibility for site- and subject-related matters and the sponsor has responsibility for the overall conduct of the trial.

Investigators are responsible for…

- Maintaining qualifications of trial staff
- Providing adequate resources
- Medical care of trial subjects
- Communication with EC
- Safety reporting
- Complying with the trial protocol
- Managing IMP at site
- Randomization procedures and unblinding
- Informed consent of trial subjects
- Keeping records and reports
- Issuing progress reports
- Providing final report(s)

The Sponsor

The sponsor of a trial is an individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial. Commonly sponsors are pharmaceutical companies or governmental research organisations like the National Institute for Health Research (NIHR) or the US FDA.

Whether an individual or an organisation, the sponsor maintains the lion's share of responsibility for a trial and is ultimately held to account if things go wrong.

Sponsor responsibilities include…

- Quality Management systems, QA & QC
- Trial design, management, data handling & records
- Investigator Selection & providing medical expertise
- Financing, inc. compensation to participants
- Notification/Submission to CA
- Information, manufacture, labelling, coding & supply of IMP
- Safety information & Adverse Drug Reaction Reporting
- Monitoring & audit

The Monitor

Monitors are appropriately trained individuals who are hired by sponsors to monitor the trial properly. They must be thoroughly familiar with the IMP, protocol, and the ICF. They should also be trained in the sponsor's SOPs, GCP and local regulations.

The sponsor determines the extent and manner of monitoring. As a general rule, trial sites should be visited before, during and after the clinical phase. Not all data needs to be verified, a properly instituted statistical sample may be acceptable.

If the study uses centralized monitoring, the outcome of any centralized monitoring should also be reported in the Monitoring Report produced by the monitor.

The monitor is the main line of communication between the investigator and the sponsor.

What the monitor does at a monitoring visit depends very much on the stage of the trial, for example...

	Before clinical phase	During clinical phase	After clinical phase	Throughout the trial
Checking investigator qualifications	Yes	Yes		
Checking facilities are suitable	Yes			
Checking that IMP has been stored in the right conditions		Yes		
Checking that IMP has been disposed of properly		Yes	Yes	
Checking that participants have given written consent		Yes		
Checking that source documents are accurate & up-to-date		Yes	Yes	
Checking that essential documents are properly filed & maintained				Yes
Checking that all adverse events are reported		Yes	Yes	
Communicating any deviations from the protocol, SOPs, GCP, & regulatory requirements to the investigator & taking appropriate action to prevent recurrence				Yes
Ensuring the Investigator has a current Investigator's Brochure (IB)	Yes	Yes		
Checking that EC and CA approvals are in place	Yes	Yes		
Checking that the Investigator is following the protocol & any amendments		Yes		
Checking that the Investigator only recruits suitable subjects		Yes		
Checking that receipt, use and return of IMP is controlled & documented				Yes

Documentation

There are several documents that are key to the GCP process. We have already mentioned the Protocol and the Informed Consent Form, but others include…

The Investigator Brochure...

The Investigator Brochure is a key document specified by ICH GCP. The IB is the handbook for an IMP. It should contain all of the background safety and efficacy data (including pre-clinical data) that will allow an investigator or other clinician to make an informed judgement regarding the risk balance of a trial.

It is core to GCP that trials are not undertaken until foreseeable risks and inconveniences are weighed against anticipated benefits and the benefit justifies risk.

The Case Report Form...

The Case Report Form (CRF) is used by the sponsor to collect data from each trial participant. The CRF may be paper or electronic and will vary between trials, as it is specifically designed to capture the information required to support the hypothesis being tested with the trial. The CRF should also contain details of any Adverse Events.

Part of the Monitor's role is to audit CRFs to ensure they are complete and accurate.

The Trial Master File...

The Trial Master File (TMF) is the collection of documents that must be maintained to comply with regulatory requirements. There should only be one TMF for any trial, though parts may be the responsibility of the sponsor and some may be the responsibility of the Investigator. The part of the TMF that falls under the Investigator, may be referred to as the "**Investigator Site File**" or **ISF**.

Whitehall Training

This is the end of Whitehall Training's short **ICH GCP** — **Good Clinical Practice** course.

Expanded online versions of this training, complete with exam and certificate, are available from the Whitehall Training website – **https://www.whitehalltraining.com/all-good-clinical-practice-gcp-training-courses-online**