Whitehall Training

GCLP — Good Clinical Laboratory Practice

The basics of GCLP and how it differs from GCP (Good Clinical Practice) and GLP (Good Laboratory Practice).

GCLP is a set of standards for labs performing analysis or evaluation of clinical trial samples. It exists because, the laws and regulations that apply to clinical trials contain little specific guidance for clinical laboratories.

Why not use GCP?

GCP is primarily about patient safety, rights and well-being. The internationally recognised GCP guideline (ICH E6) describes the responsibilities and expectations of all participants in the conduct of clinical trials. As well as patient safety, it covers monitoring, reporting and archiving and many more aspects. However, it barely references the activities performed in clinical laboratories.

Why not use GLP?

GLP has been around since the 1970s but, although it provides very prescriptive guidance, in most countries it should only be applied to the non-clinical safety testing of pharmaceuticals, cosmetics, pesticides, industrial chemicals etc.

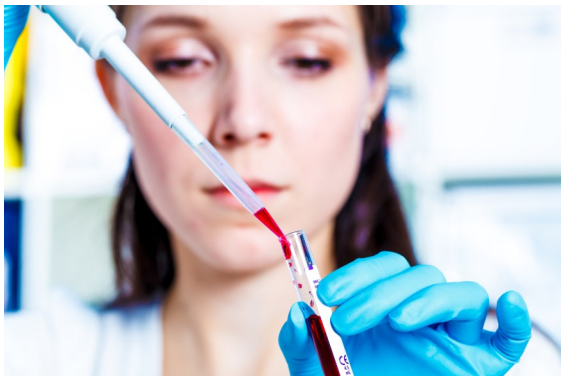
The law

In 2012, the EMA has published GCLP guidance — **http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/05/WC500127124.pdf** Since then, this has become used as a reference in many other countries worldwide.

What does GCLP cover?

GCLP rules cover a wide range of areas relating to the operation of clinical testing labs —

1 — Facilities, Organisation & Personnel



Labs need to be large enough for adequate separation of different activities. For instance, there should be suitable accommodation for samples, reagents and paperwork.

Consider providing specified areas for the receipt, tracking and storage of samples. Sample handling arrangements must help maintain sample integrity and prevent cross-contamination. Bear in mind that activities can be separated either physically or through time.

Other aspects to think about are provisions for waste disposal, and decontamination of equipment etc. Also the facilities need to be secure with controlled access.

Before starting any analytical work, the roles and responsibilities of the staff need to be precisely defined. This should cover the people working in — laboratory management, scientific analysis, quality assurance, reporting, and archiving.

All staff must have the right training for their role and this should be well documented. The lab should maintain an updated record of past experience, qualifications etc.

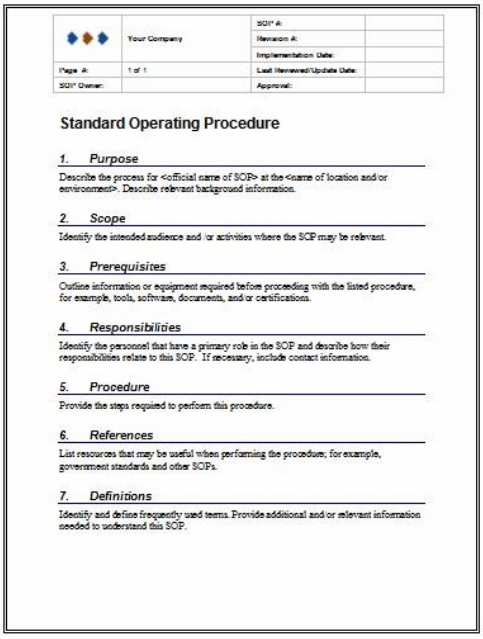
2 — Contracts & Agreements

Contracts and agreements must be in place before any work starts. The sponsor and the lab should agree over exactly what work is to be performed, the type of data to be generated and the timelines. The agreement normally requires a legally binding contract, unless the lab is part of the sponsor organisation. In this case, an SLA or other internal document may be sufficient.

Contracts and agreements must not conflict with the clinical protocol, and this must be checked when any new study is planned. Contracts must comply with local legislation and ethical requirements too. Where multiple studies are undertaken by one lab, a master service level agreement may enough.

The lab's quality system must include a written process in place for drafting, agreement, review & revision of contracts.

3 — SOPs & Instructions



Your Company

Standard Operating Procedure

1. Purpose

Describe the process for <official name of SOP> at the <name of location and/or environment>. Describe relevant background information.

2. Scope

Identify the intended audience and /or activities where the SOP may be relevant.

3. Prerequisites

Outline information or equipment required before proceeding with the listed procedure, for example, tools, software, documents, and/or certifications.

4. Responsibilities

Identify the personnel that have a primary role in the SOP and describe how their responsibilities relate to this SOP. If necessary, include contact information.

5. Procedure

Provide the steps required to perform this procedure.

6. References

List resources that may be useful when performing the procedure, for example, government standards and other SOPs.

7. Definitions

Identify and define frequently used terms. Provide additional and/or relevant information needed to understand this SOP.

Written procedures underpin the lab's quality system, helping protect the quality and integrity of the data being generated. They should be easy to understand, and can be split into smaller chunks if one overall SOP for any procedure becomes too unwieldy. There must be a procedure in place to control the generation, authorisation, review, amendment and withdrawal of such instructional documents, i.e. the "SOP on SOPs".

All SOPs need to be regularly reviewed and kept where they can be accessed by the staff who need them. There should be SOPs covering a wide range of aspects of the lab work, including —

- sample and reference material handling – receipt, storage and processing
- clinical kit preparation
- analysis or evaluation of clinical trial samples – methods and their control
- patient safety and confidentiality
- data collection and retention – trial- and non-trial-specific data and records
- quality control (QC) activities.

4 — Planning the Work

Ideally, the lab should receive the full clinical trial protocol but, if this isn't possible, they should be given the sections of the protocol that are relevant to the work they will be doing. It is critical that the lab remains up to date with the current version of the protocol and receives amendments as they are approved.

The clinical protocol does not normally include detailed lab parameters, so an analytical plan or work instruction should be drawn up prior to any work starting. This should include detail such as the exact methodology to be employed, sample shipment and preparation criteria, reporting routes and timeframes, quality assurance activities, etc.

Ideally the sponsor will agree the analytical plan to confirm it does not exceed or contradict the clinical protocol.

5 — Carrying Out the Work

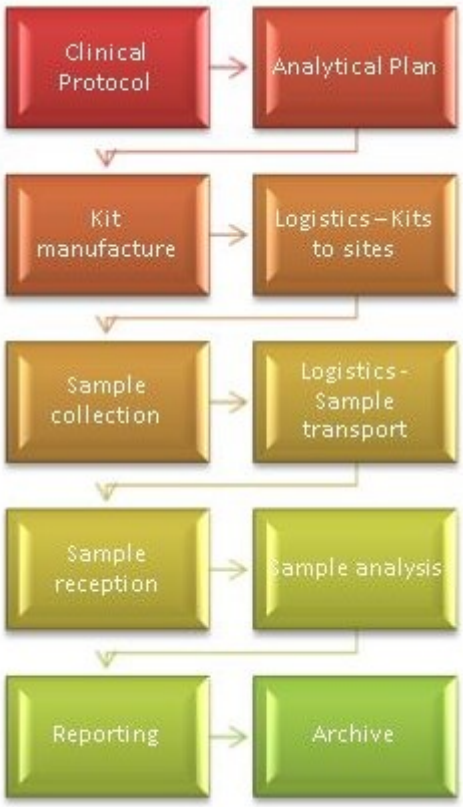
All activities on a study should be driven by written policies and procedures, in order to be able to confirm years into the future that the analysis has been conducted in a way that assures its quality. Any deviations from the trial protocol or lab SOPs need to be documented, investigated and their impact assessed.

The activities undertaken should be documented not only through SOPs and plans but also through records captured at the time of the activity.

Many of these activities are not analytical, but they are all important for the process to function properly.

Some labs prepare kits containing all the sampling materials required for subjects on a study. The kit contents, the shipment details and the numbers of kits must be agreed in writing with the sponsor.

Kit preparation needs to be carefully controlled, with clear separation of activities and environmental monitoring to ensure the kits remain fit for use.



Security & integrity…

Once samples are taken, they need to be clearly labelled and securely transported to the lab — regardless of the distances involved. Depending on the sample, this could involve temperature control and monitoring throughout. The lab needs a formal booking process and should only analyse samples that have been formally identified.

Protecting confidentiality…

GCP grants every subject on a clinical trial the right to privacy and confidentiality. This means that no subject identifiers should be received in an off-site laboratory. However, mistakes can be made and so occasionally samples will come through with information on them that can identify the subject.

The lab needs a process that defines how to deal with samples and other information that could compromise the subject's right to privacy. The information will need to be masked in a way that does not obliterate other information that may be needed to identify the sample during the analytical process.

Storage…

The lab needs to have sufficient capacity for storing samples in the correct conditions. There should be back up capacity in case a fridge or freezer breaks down.

The storage facilities should be monitored to ensure that the samples are fit for purpose.

There should be clear procedures in place to cover what should be done if these storage conditions fall outside acceptable limits.

Analysis…

All analysis work should to be performed using appropriately validated methods. The only exception would be where the method is being validated as one of the objectives of the clinical trial.

Guidance is internationally available on method validation, e.g. from the EMA, FDA and Japan's MHLW. The main objective of validation is to ensure the method is robust, reliable and reproducible, i.e. not dependent on only one technician being able to make it work, or needing to be routinely run multiple times before the results look acceptable.

Data should be recorded directly, promptly, accurately and legibly. Any changes should made so as to leave the original entry legible and the reasons for the change should be recorded and justified. Where electronic data is concerned, it is best to maintain an electronic data trail, and therefore important that systems are designed and implemented with this requirement in mind.

No additional work should be performed on samples beyond that specified in the protocol. Because the protocol is the basis for subject consent, work outside the protocol would be breach the subjects' consent.

Patient safety is of the utmost importance, and sometimes an unscheduled analysis or evaluation may be required for urgent clinical reasons. There should be documented procedures for these situations.

The results of laboratory analyses should be authorised by a suitably qualified member of lab staff, and should be issued in a timely manner as laid out in the analytical plan.

Reporting…

Whatever the style used, reports must be complete and accurate, and QC checks can help.

Ideally trial reports should include a reference stating that the analysis was performed in compliance with the relevant national and international regulations and guidance.

6 — Quality Control

Quality control checks should be an integral part of the activities of the lab. They should be defined in the laboratory SOPs and methods. A vast number of QC steps could potentially be taken, but the overarching requirement is that they should minimise the risk of mistakes. For this reason it may be appropriate to take a risk-based approach when decided on type and frequency of checks.

QC checks are most effective when performed by a second person (or automatically, such as on an analyser), so technicians are not checking themselves.

7 — Quality Assurance & Audit

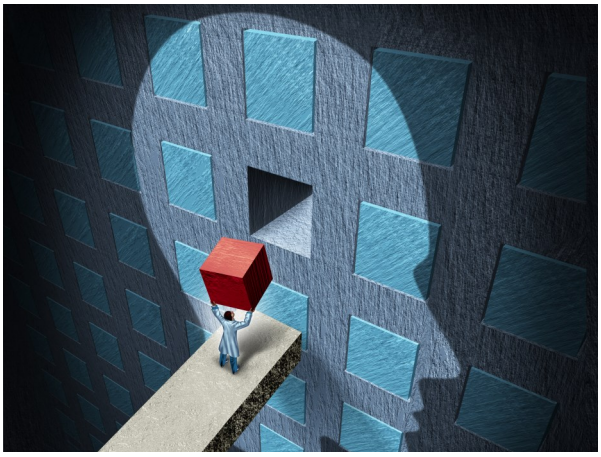
Independent QA should be in place to ensure data integrity and to safeguard subjects' rights under GCP. Routine QA activities should be documented in SOPs or policies, and it is good practice to maintain audit schedules. Key aspects for QA will be compliance with the applicable legislation and with internal SOPs and policies.

Assurance should cover compliance with things like — GCP, the clinical protocol, policies and SOPs, and archiving of data.

QA audits should be done by someone independent of the work that is being reviewed. Additionally, those individuals involved in the QA should be appropriately qualified and experienced.

Audit results should be recorded, and reported to lab management, who should ensure appropriate responses are made, and corrective actions taken, in a timely manner.

8 — Archiving & Data Retention



The facilities for archiving should be secure, and designed to accommodate the type of material needing to be stored. The aim is to keep the material secure, intact and safe from deterioration or interference. The confidentiality of the subjects on the trial also needs to be maintained.

For electronic data, the lab will need to ensure that the data remains usable over a timeframe of many years. Because technology develops so quickly, something that was readable a few years ago may not be now.

It is imperative that those responsible for IT in the GCLP laboratory understand the long-term record retention requirements of the regulated environment.

The archive must only be accessible to authorised individuals. A designated staff member will be responsible for the archive, and it is accepted good practice that they are not involved with the generation of the data or supporting records that they hold.

If materials are removed from the archive there must be a process in place to ensure they are returned in a timely manner, and to check that the returned material is complete and intact. This is only possible if there is a good record of what has gone into archive in the first place, of course.

Whitehall Training

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

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