Good Clinical Laboratory Practice (GCLP)

An international quality system for laboratories which undertake the analysis of samples from clinical trials

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VERSION 2
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This guideline was originally produced in 2002 with the purpose of providing guidance on the quality system required in laboratories that undertake the analysis of samples from clinical trials.

Since that time, this guidance has been widely adopted internationally by many organisations such as the World Health Organisation (WHO), pharmaceutical companies, research institutions, non-governmental organisations (NGOs), hospitals, contract research organisations (CROs) and academia.

This document is primarily an update of the original GCLP guideline. Many of the changes made are cosmetic, but others are influenced by the authors’ experiences gained in the application of GCLP in many different laboratory settings and trials around the world.

In addition, an increasing number of regulatory audits have included those laboratories involved in the support of clinical trials and, as a result of these audits, the general expectations for laboratories have to some degree been clarified. These expectations have also been reflected within this revision of the GCLP Guideline.

In all cases it is believed that the changes made only clarify the earlier guidance whilst enhancing patient safety and data integrity.
<table>
<thead>
<tr>
<th>CONTENTS</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Preface</td>
<td>1</td>
</tr>
<tr>
<td>2. Scope</td>
<td>2</td>
</tr>
<tr>
<td>3. Introduction</td>
<td>3</td>
</tr>
<tr>
<td>4. Definitions</td>
<td>4</td>
</tr>
<tr>
<td>5. Organisation and Personnel</td>
<td>6</td>
</tr>
<tr>
<td>5.1 Laboratory Management Responsibilities</td>
<td>6</td>
</tr>
<tr>
<td>5.2 Analytical Project Manager Responsibilities</td>
<td>7</td>
</tr>
<tr>
<td>5.3 Laboratory Staff Responsibilities</td>
<td>8</td>
</tr>
<tr>
<td>6. Facilities</td>
<td>9</td>
</tr>
<tr>
<td>6.1 Laboratories</td>
<td>9</td>
</tr>
<tr>
<td>6.2 Archive Facilities</td>
<td>9</td>
</tr>
<tr>
<td>6.3 Waste Disposal</td>
<td>9</td>
</tr>
<tr>
<td>7. Equipment, Materials and Reagents</td>
<td>10</td>
</tr>
<tr>
<td>7.1 Equipment</td>
<td>10</td>
</tr>
<tr>
<td>7.2 Materials and Reagents</td>
<td>10</td>
</tr>
<tr>
<td>8. Standard Operating Procedures (SOPs)</td>
<td>11</td>
</tr>
<tr>
<td>9. Planning of the Work</td>
<td>13</td>
</tr>
<tr>
<td>9.1 Analytical Plan</td>
<td>13</td>
</tr>
<tr>
<td>9.2 Content of the Analytical Plan</td>
<td>13</td>
</tr>
<tr>
<td>10. Sub-Contracting</td>
<td>15</td>
</tr>
<tr>
<td>11. Trial Samples</td>
<td>16</td>
</tr>
<tr>
<td>11.1 Receipt</td>
<td>16</td>
</tr>
<tr>
<td>11.2 Chain of Custody</td>
<td>16</td>
</tr>
<tr>
<td>11.3 Logistics</td>
<td>16</td>
</tr>
<tr>
<td>11.4 Disposal</td>
<td>17</td>
</tr>
<tr>
<td>12. Conduct of the Work</td>
<td>18</td>
</tr>
<tr>
<td>12.1 General</td>
<td>18</td>
</tr>
<tr>
<td>12.2 Additional Work</td>
<td>18</td>
</tr>
<tr>
<td>12.3 Computer Systems</td>
<td>18</td>
</tr>
<tr>
<td>12.4 Method Validation</td>
<td>19</td>
</tr>
<tr>
<td>12.5 Processing Trial Samples</td>
<td>20</td>
</tr>
<tr>
<td>13. Reporting Results</td>
<td>21</td>
</tr>
<tr>
<td>13.1 General</td>
<td>21</td>
</tr>
<tr>
<td>13.2 Analytical Report</td>
<td>21</td>
</tr>
<tr>
<td>13.3 Analytical Results</td>
<td>22</td>
</tr>
<tr>
<td>14. Quality Control (QC)</td>
<td>23</td>
</tr>
<tr>
<td>15. Quality Audit</td>
<td>24</td>
</tr>
<tr>
<td>16.</td>
<td>Retention and Archiving of Records</td>
</tr>
<tr>
<td>-----</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>16.1</td>
<td>Trial Records</td>
</tr>
<tr>
<td>16.2</td>
<td>Laboratory Records</td>
</tr>
<tr>
<td>16.3</td>
<td>Electronic Records</td>
</tr>
<tr>
<td>16.4</td>
<td>Samples and Specimens</td>
</tr>
<tr>
<td>17.</td>
<td>Confidentiality</td>
</tr>
<tr>
<td>18.</td>
<td>Blinding</td>
</tr>
<tr>
<td>19.</td>
<td>Patient Safety</td>
</tr>
</tbody>
</table>
1. PREFACE

The regulatory environment within which clinical trials are conducted is continuing to change. Such changes are generally focused upon requiring more rigorous control in order to ensure patient safety and the reliability of data produced.

Whilst the International Committee on Harmonisation (ICH) Good Clinical Practice (GCP) Guideline has now been enshrined into the law of many countries and clearly specifies such requirements as the role of the Ethics Committee, the sponsor and the investigator; when it comes to defining the standards to be applied in the analysis of samples from a clinical trial, it is very vague.

The most applicable references within ICH that indicate the standards required for the analysis of samples are in sections 2.13 ‘Systems with procedures that assure the quality of every aspect of the trial should be implemented’, and in section 8 Essential Documents parts 8.2.12 and 8.3.7.

The analysis of samples collected from healthy volunteers and patients participating in clinical trials forms an essential part of the clinical trials process and provides important data on a range of endpoints. Therefore it is essential that sample collection, analysis and reporting is performed to a standard which will ensure that patient safety is not compromised and that data is reliable, accurate and in compliance with GCP regulations.

Good Clinical Laboratory Practice (GCLP) is intended to provide guidance on the quality system that can be applied internationally by organisations and individuals that undertake analyses of samples from clinical trials. This includes guidance on the facilities, systems and procedures that should be present to assure patient safety as well as the reliability, quality and integrity of the work and results generated during their contribution to a clinical trial.

GCLP is intended to ensure that the requirements of GCP applicable to the analysis of clinical samples are met.
2. **SCOPE**

It is recommended that GCLP be adopted by any organisation that analyses samples generated during the conduct of a clinical trial.

The principles defined in this guideline are intended to be applied equally to the analysis of a blood sample for routine safety screening of volunteers (haematology/biochemistry) as to pharmacokinetics or even the process for the analysis of electrocardiogram (ECG) traces; indeed any sample from a clinical trial that is to be analysed.
3. INTRODUCTION

Good Clinical Practice (GCP)
ICH GCP Guideline is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected; consistent with the principles that have their origin in the Declaration of Helsinki. This ICH GCP Guideline has been implemented into the regulations of many countries.

Good Laboratory Practice (GLP)
GLP is intended to promote the quality and validity of non-clinical test data. It is a managerial concept covering the organisational process and the conditions under which laboratory studies are planned, performed, monitored, recorded and reported (OECD GLP Guideline).

Good Clinical Laboratory Practice (GCLP)
GCLP is applying those standards established under GLP which are relevant to the analyses of samples from a clinical trial, whilst at the same time ensuring that the purpose and objectives of the GCP regulations are satisfied. In so doing, the reliability and integrity of data generated by analytical laboratories can be assured. It is recognised that some organisations and indeed countries, operate proficiency testing and accreditation schemes that laboratories subscribe to. Whilst these provide assurance of the integrity of the analytical process, they may not ensure compliance with GCP.

GCLP is intended to provide a unified guidance that can be applied globally to clinical sample analysis to facilitate patient safety and confidence in the data generated and by so doing, encourage the mutual acceptance of clinical data by regulatory authorities around the world.

It is important to recognise that the guidance outlined in GCLP will be applied across a diverse set of disciplines involved in the analysis of samples from clinical trials. It is therefore important to understand that this guidance should be interpreted and applied to the work of those organisations, with the objective of assuring the quality of every aspect of the work and the safety of the patients involved.
4. **DEFINITIONS**

**Analytical Plan:** a formal authorised document that describes all aspects of the work to be performed by the laboratory.

**Analytical Project Manager:** the individual within the laboratory responsible for the overall conduct of the work defined by the analytical plan.

**Archivist:** the person or organisation responsible for the management of the archive.

**Clinical Protocol:** the clinical trial protocol approved by the sponsor which describes all activities which make up the clinical trial: its objectives, design, methodology, statistical considerations and organisation.

**Computerised System:** a system (consisting of one or more hardware components and associated software) that is involved with the direct or indirect capture of data, processing or manipulation of data, reporting and storage of data, and may be an integral part of automated equipment. Examples include a programmable analytical instrument or a personal computer linked to a Laboratory Information Management System (LIMS).

**Investigator:** the individual responsible for the conduct of the clinical trial, whose role is as defined by ICH GCP.

**Laboratory:** the persons, premises and facilities that are utilised in the analysis of samples from a clinical trial.

**Laboratory Management:** the individual(s) within the laboratory organisation that is responsible for ensuring the facility operates according to GCLP.

**Laboratory Records:** records that confirm and support trial activities and are essential for the reconstruction of the work performed. This may include supporting data such as fridge/freezer temperature records, equipment service, maintenance and calibration records as examples.

**Master Service Agreement:** an overarching contract of general terms and conditions between two parties such as a laboratory and a sponsoring organisation which may be used to underpin work for a number of trials. Study specific terms, conditions, details, roles and responsibilities are then further defined in other documented agreements.

**Quality Audit:** a defined system, including personnel, which is independent of the trial conduct and designed to assure laboratory management of trial and laboratory compliance with GCLP.

**Quality Control (QC):** in process, systematic checking to ensure the quality and accuracy of the work performed and reported, and to eliminate errors.
**Raw Data:** all original records and documentation, or verified copies thereof, which are the result of the original observations and activities during the conduct of the work and are necessary for the reconstruction and evaluation of the reported results. For the purposes of GCLP, ‘source data’ (ICH GCP) and ‘raw data’ are regarded as equivalent.

**Sponsor:** an individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a trial.

**Sample Kit:** the necessary components required to collect clinical trial samples prior to their analysis or evaluation in a laboratory.

**Subject(s):** the healthy volunteer or patient taking part in the trial.

**Trial Samples:** any material from a trial which is to be analysed. This may include, but is not limited to: samples (plasma, serum, urine, faeces, tissues and cells), specimens, data, results, ECG traces or x-ray plates.

**Validation of a Computerised System:** a documented process that demonstrates that a computerised system is suitable for its intended purpose.
5. ORGANISATION AND PERSONNEL

5.1 Laboratory Management Responsibilities

The individual(s) who performs the role of laboratory management should be named.

Laboratory management should ensure that the principles of GCLP as defined in this guideline are complied with in their laboratory, ensuring overall compliance with GCP.

At a minimum it should:

a) Ensure that qualified personnel, appropriate facilities, equipment, and materials are available

b) Maintain a record of the qualifications, training, relevant experience and job description for each individual working within the laboratory and to ensure these records are maintained, current and up to date

c) Ensure that personnel clearly understand the functions they are to perform and where necessary, provide training for these functions. This should include training and competence to perform the techniques required by the clinical protocol, analytical plan or associated analytical methods. Management should provide all staff involved in the analysis or evaluation of clinical trial samples with GCP and GCLP training commensurate with their roles and responsibilities

d) Ensure that Health and Safety precautions within the laboratory are applied according to national regulations

e) Ensure that appropriate Standard Operating Procedures (SOPs) are established and followed and an historical record of all SOPs is maintained

f) Ensure there is a quality audit programme with designated personnel

g) Ensure a programme of QC is operated within the laboratory and where appropriate, membership of external proficiency schemes

h) Ensure an analytical plan exists which defines the analyses to be performed by the laboratory

i) Ensure that any amendments to the analytical plan are agreed and documented
j) Maintain copies of the clinical protocol and analytical plan, including any amendments to these documents

k) Ensure that a sufficient number of personnel are available for the timely and proper conduct of the work

l) Before the work is initiated in the laboratory for each trial, designate an individual with the appropriate qualifications, training, and experience as the analytical project manager. If it is necessary to replace the analytical project manager during a trial, this should be documented

m) Ensure that an individual or organisation is identified as having responsibility for the management of the archives used for the retention of trial and laboratory records

n) Ensure that laboratory records are archived and retained

o) For any work sub-contracted by the laboratory, laboratory management are responsible to the sponsor for its conduct.

5.2 Analytical Project Manager Responsibilities

The analytical project manager has the responsibility for the overall conduct and reporting of the analyses being performed by the laboratory.

These responsibilities should include, but not be limited to, the following functions:

a) Agree to the analytical plan by dated signature prior to initiation of the work

b) Ensure that procedures specified in the analytical plan are followed, and that authorisation for any modification is obtained and documented together with the reasons for change

c) Ensure that all results of the analyses are fully documented and accurately reported

d) Sign and date the analytical report, if issued, to indicate acceptance of responsibility for the validity of the results

e) When analytical results are issued, the analytical project manager should ensure that these results are only issued under the dated signature of an authorised signatory

f) Ensure that after completion of the analyses, the analytical plan, the analytical report and/or analytical results, raw data and any supporting study documentation are archived and retained
Prior to the initiation of analytical work, lines of communication should be established and documented between the sponsor, or their representative, and the analytical project manager.

5.3 Laboratory Staff Responsibilities

All laboratory staff involved in the conduct of a trial should be aware of GCLP, those parts of GCP that apply to their work and be fully aware of the function they are to perform.

All staff are responsible for recording raw data promptly, accurately and in compliance with GCLP and are responsible for the quality of their data.

All staff are responsible for following the instructions given in the clinical protocol, analytical plans and SOPs.
6. FACILITIES

6.1 Laboratories

The laboratory should be of suitable size, construction and location to meet the requirements of the trial and minimise any disturbances that might interfere with the validity of the trial or its results.

The laboratory should have appropriately designed facilities of sufficient size for the type of work being performed and provide an adequate degree of separation and security to assure the integrity of samples at all times.

Suitable space should be available for the preparation of sample kits in order to ensure accurate preparation of such materials.

There should be appropriate storage areas as needed for samples and supplies. Storage areas should be separated as appropriate to prevent contamination or mix up and to protect the integrity of samples or materials.

6.2 Archive Facilities

Appropriate space should be provided for the safe and secure archive storage of data, reports, samples and specimens.

These facilities should be suitable to accommodate the types of material that will be archived and to protect contents from untimely deterioration.

Archive facilities must be secure to prevent unauthorised access to the retained materials.

If suitable facilities cannot be provided for the storage of trial records, alternative arrangements should be made. This could include the use of third-party contract archive facilities.

6.3 Waste Disposal

The handling and disposal of waste generated during the performance of a trial should be carried out in a manner that is consistent with local regulatory requirements.
7. **EQUIPMENT, MATERIALS AND REAGENTS**

7.1 **Equipment**

Equipment used in the analysis of trial samples and operation of the laboratory should be suitably located and of appropriate design and adequate capacity.

Equipment used should be periodically inspected, cleaned, maintained and calibrated as appropriate. Records of maintenance and any unscheduled maintenance or calibration should be retained.

Calibration and maintenance frequency will be determined by laboratory management and should be designed to ensure that all equipment remains fit for purpose.

An equipment service schedule should be maintained that lists all relevant items of equipment and the schedule of planned service and calibration activities.

Any item of equipment that is out of service for any reason should be clearly identified as such and removed from use.

Equipment users should be suitably qualified and trained in the operation of the equipment.

In all cases, equipment used should be demonstrably fit for purpose.

7.2 **Materials and Reagents**

Materials used in the analysis of trial samples should be demonstrably fit for purpose and appropriately stored.

Reagents should be suitably labelled and indicate the identity, concentration, specific storage instructions and stability. Stability information may include the preparation date and earliest expiration date.
8. STANDARD OPERATING PROCEDURES (SOPS)

A laboratory should have documented SOPs approved by laboratory management that are intended to ensure the quality and integrity of the work performed and the data generated.

SOPs should be periodically reviewed to ensure they remain current and up to date.

A list of current SOPs which includes the version number should be maintained up to date.

Staff within the laboratory should have SOPs relevant to the activities being performed therein immediately available. Published textbooks, articles and manuals may be used as supplements to these SOPs provided that these are also retained.

The analytical methods to be followed should also be documented and formally approved by laboratory management. Such documents may be issued as SOPs but can equally be standalone documents, provided that the control, approval and retention processes are equivalent.

SOPs should be available for, but not be limited to, the following types of activities: the details given under each heading are to be considered as illustrative examples.

a) Materials and reagents
   Supply, preparation, labelling, handling, shipment and storage

b) Equipment operation, maintenance, servicing, cleaning and calibration of equipment and computerised systems

c) Preparation of sample kits

d) Procedures for receipt, storage, identification, chain of custody and care of trial samples

e) Procedures linked to patient safety and confidentiality such as expedited reporting of results, unblinding and blinding of samples and procedures for dealing with the receipt of unexpected, unscheduled or poorly labelled samples

f) Procedures for the analysis of trial samples and the conditions and criteria under which any repeat assays are performed
g) Record keeping, reporting, storage and retrieval
   Coding of trials, data collection, preparation of reports, indexing systems and handling of data, including the use of computerised data systems

h) The retention of trial and laboratory records, and the operation of the archive

i) QC procedures
   The QC procedures operated by the laboratory to ensure the quality and accuracy of results

j) Quality audit procedures
   Operation of the quality audit programme in performing and reporting trial audits, inspections and analytical report reviews

k) Contracts and agreements.
9. PLANNING OF THE WORK

9.1 Analytical Plan

For each trial the laboratory is involved in, a written analytical plan should be produced by the laboratory prior to initiation of the work.

The analytical plan should describe the work to be performed by the laboratory and be available to the staff involved in that work.

This plan should be an exact reflection of the requirements detailed in the clinical protocol and only include work that is covered by the informed consent given by the trial subjects.

This plan should be agreed by the dated signature of the analytical project manager and sponsor.

The analytical plan may be a controlled document or form part of the contractual agreement with the sponsor, or be contained within the clinical protocol.

The analytical plan should be retained as part of the laboratory records for the trial.

All changes, modifications or revisions to the agreed analytical plan should be documented, including justification[s], and be agreed by the dated signature of the analytical project manager and sponsor. Copies of all such amendments should be maintained with the original analytical plan.

9.2 Content of the Analytical Plan

The analytical plan should be sufficiently detailed to provide clear instruction to those undertaking the work as to what is required and contain, but not be limited, to the following information where applicable:

Identification of the work:

a) Descriptive title

b) A statement that indicates the nature and purpose of the work

c) A unique identifier that will link the work within the analytical plan to the clinical protocol, whilst retaining the chain of custody and identity of all trial samples.
Information concerning the sponsor and the laboratory:

d) Name, address and contact details of the sponsor and any representatives

e) Name, address and contact details of the investigator(s)

f) Name and address of the laboratory

g) Name and contact details of the analytical project manager.

Dates:

h) The date of agreement to the analytical plan by signature of the analytical project manager and the sponsor

i) The proposed starting and completion dates for the laboratory work.

Analytical Process:

j) The methods to be used during the analysis of trial samples. Reference to published analytical methods may also be made. This should include detailed information on the analytical design, methods, materials and conditions, type and frequency of analysis, measurements, observations and examinations to be performed

k) The preparation and shipment by the laboratory of any materials such as sample kits to be used in the collection of trial samples must be covered. This could be contained in the analytical plan or in a separate document for logistics

l) The type and number of trial samples to be received by the laboratory

m) The method and condition under which trial samples are transported from one location to another

n) For ‘blinded’ or ‘coded’ trials, the conditions of blinding and the unblinding procedure should be followed.

Records:

o) A list of the records to be retained and their archive location on completion of the work

p) Method of reporting results.

Quality Audit:

q) The quality audits to be performed to assure the quality and integrity of the data generated, and the accuracy of reported results.
10. SUB-CONTRACTING

No analytical or other study related work should be sub-contracted by the laboratory without the prior approval of the sponsor.

When work is sub-contracted by the laboratory, laboratory management is responsible to the sponsor for the conduct of this sub-contracted work.

To maintain GCLP for all the work, prior to placement of any sub-contracted work, assurance should be obtained to confirm the sub-contractor will work in accordance with GCP, GCLP and any trial requirements.

The agreement for sub-contracted work (contract/service level agreement and/or analytical plan) should clearly specify the role and responsibilities, the detail of the analyses to be performed and the retention of trial data.
11. TRIAL SAMPLES

11.1 Receipt

Procedures for the receipt, handling, storage, retrieval and management of trial samples should be designed to prevent mix-ups and maintain their integrity. Trial samples should be adequately identified at all times.

Samples should be transported in such a way that their integrity and viability remains unaffected.

Trial samples should be checked on receipt to confirm their identification. Records of identity, source, date of arrival and condition on arrival should be maintained.

11.2 Chain of Custody

Facilities and procedures should be designed and operated to maintain trial sample identification and traceability at all times.

Records should be maintained to allow the reconstruction of the chain of custody of trial samples received, and to allow the retrospective evaluation of the conditions under which samples are stored.

Trial sample storage areas should be monitored where controlled conditions are required to maintain the integrity of the samples. Records to confirm the storage conditions attained should be maintained and retained. Contingency plans should be in place that cover the actions to be taken in the event of the malfunction of equipment or facilities that could impact on the storage of samples. Such plans should ensure the integrity of the stored samples.

11.3 Logistics

When a laboratory prepares sample kits or materials used for the collection of trial samples, the systems used for the preparation, distribution, sample collection and return of such materials to the laboratory must be documented and the systems and procedures used should be validated.

Details of the logistics required on a given trial should be documented in the analytical plan or similar document approved by the sponsor and analytical project manager.
The type of material required, the type and design of the package, the timing and means of distribution both from the laboratory to the Investigator site and return, the checks performed and storage requirements should be detailed in the above document.

The processes involved in these logistics should be subject to QC procedures to confirm conformance of practice with defined requirements.

11.4 Disposal

Records of disposal of any retained samples should be maintained and retained.
12. CONDUCT OF THE WORK

12.1 General

The work should be conducted in accordance with the clinical protocol and the analytical plan.

All analysis or evaluation of trial samples must be performed in accordance with the clinical protocol and thereby patient informed consent. Consequently, a check should be made to ensure that the analytical plan does not conflict with or exceed the requirements detailed in the clinical trial protocol.

The analytical method used should be selected to ensure it is suitable and will provide reliable results. Such methods should be validated to ensure results generated are accurate and reproducible.

Samples should be uniquely identified at every stage of the analysis.

Samples should be analysed within the defined timeframe as determined at the time of method validation. Workflows in the laboratory should be such that a sample could not be overlooked and therefore not analysed in the correct timeframe.

All data generated during the conduct of the laboratory work should be recorded directly, promptly, accurately and legibly. These data should be signed or initialled and dated by the individual responsible for the collection of the data.

Any change in the data should be made so as not to obscure the previous entry, and should indicate the reason for the change and should be identified by date and signed or initialled by the individual making the change.

12.2 Additional Work

Any additional work to that agreed in the analytical plan should be sanctioned by the sponsor and not compromise informed consent, unless there are urgent patient safety implications.

12.3 Computer Systems

Computerised systems should meet the general requirements for equipment as described in this booklet. Due to the nature of computerised systems and their key role in the operation of the laboratory, further requirements apply to their use. In all cases, computer systems should be appropriately validated and maintained, and be demonstrably fit for purpose.
When a computer system is used to capture raw data, a definition of what constitutes the raw data should be documented. This is usually documented within the SOP for that system.

Computerised systems used to receive, capture, process or report data should be acquired, developed, tested, released, used, maintained and retired according to established guidelines or laws.


Procedures should exist which address the security and operation of the computer systems. This should include the maintenance of a data audit trail, which include the date/time and individual responsible for the collection of the data, system change control procedures, maintenance and system security procedures that ensure the integrity of trial data.

Access to computer systems should be restricted to authorised personnel.

If data is retained electronically, means should exist to ensure the data held can always be retrieved.

12.4 Method Validation

The selection of instrument platforms and analytical methodologies should take into account current regulatory standards/guidelines and sponsor expectations, where appropriate.

Such guidance includes, but is not limited to: FDA Guidance for Industry on Bioanalytical validation (CDER 2001); Best Practices for Chromatography and Ligand Binding Assays (AAPS 2007); EMA guideline on the Validation of Bioanalytical Methods.

Each analytical method used in the analysis of trial samples should be appropriately documented, validated, controlled and approved with acceptance criteria defined. Changes to a method should be controlled and validated, resulting in the issue of a further version of the method.

Records to demonstrate the validity and suitability of such methods within the trial laboratory should be retained.

Analytical platforms/methods should not be changed during the course of a trial without prior consultation and agreement with the sponsor. Such changes must be controlled, documented and appropriately authorised, and may result in the need for further method and equipment validation.
12.5 Processing Trial Samples

Trial samples should be analysed and reported within a timeframe consistent with patient safety issues, clinical protocol, the analytical plan, SOP and any contractual requirements.

Repeat Analysis

The laboratory should have documented procedures governing rules for repeat analysis.

It is not acceptable to selectively report data. Consequently, the rationale for performing repeat analysis and the reason for the selection of the data to be reported should be documented.

Safety

Laboratory procedures should take account of local legislation and standard practice in addressing the safe handling of hazardous substances and trial materials.

Deviations

The impact of any deviations from the analytical plan or the laboratory’s SOPs or documented policies should be assessed and documented. Where there is potential for a deviation to impact on the integrity or reliability of trial data, patient confidentiality, patient consent or patient safety; appropriate procedures should be implemented to ensure the issue is reported to the sponsor or their representative immediately.
13. REPORTING RESULTS

13.1 General

It is acceptable to report analytical results in a number of different ways.

The analytical plan should indicate the type of reporting mechanism to be followed and the time scale for issue. Regardless of how data is reported, it must be complete and accurately reflect the raw data.

Examples of typical reporting mechanisms include:

Analytical Reports: a formal report which may be issued on completion of the work detailed in the analytical plan

Analytical Results: a document(s) containing just the results, which is usually issued rapidly on completion of sample analysis on a given day for a given subject

The decision as to the type of report produced should be agreed between the sponsor and analytical project manager and when appropriate, the investigator.

Issue of Reports

All reports should be subject to a QC review to ensure the accuracy and validity of the information produced.

Copies of the reports should be provided to the sponsor and investigator, as appropriate.

A copy of all reports issued should be retained by the laboratory.

13.2 Analytical Report

The analytical report should be signed and dated by the analytical project manager to indicate acceptance of responsibility for the validity of the data reported.

Content of the Analytical Report

An analytical report should contain, but not necessarily be limited to, the following:

a) Identification of the analytical work by a descriptive title and identification number

b) The clinical trial number

c) Name and address of the sponsor

d) Name and address of laboratory that performed the work and any laboratory
conducting sub-contracted work

e) Name of the analytical project manager

f) The start and completion dates of the laboratory work

g) Identification of any quality audit activities

h) Description of methods and materials used including data manipulation techniques and any statistical methods used

i) Presentation of the results

j) All information and data required by the analytical plan

k) The location(s) where the analytical plan, any specimens required to be retained, data and the final analytical report are to be archived.

Corrections or additions to a final analytical report once issued should be in the form of an amendment. Amendments should clearly specify the reasons for corrections or additions and should be authorised by the dated signature of the analytical project manager.

13.3 Analytical Results

Analytical results should be appropriately and accurately reported. Such results should include, but not necessarily be limited to, the following:

a) Identification of the analytical work by its unique identification/trial number

b) Identity of the sponsor

c) Identity of the laboratory that performed the analysis, including any sub-contracted assays

d) The investigator to whom the results are directed

e) Presentation of the results.

The analytical results should be issued under the dated signature of an authorised signatory.

Analytical results may be reissued when corrections or additions are required. In such circumstances the amended document must clearly indicate that the results have been amended, and the reason for any such change.
14. QUALITY CONTROL (QC)

The laboratory should operate appropriate QC procedures to ensure the quality and accuracy of all aspects of the work performed and reported.

QC procedures may apply, but are not limited, to the following aspects of the work:

a) Within analytical batch acceptance criteria
b) External proficiency scheme results
c) Production of analytical plans and consistency with clinical protocol
d) Acceptability of materials and reagent supplied
e) Secondary tube labelling or aliquoting
f) Sample kit preparation
g) Sample receipt, handling and storage
h) Results/reports reflect raw data accurately.

Documenting and trending of QC sample results to indicate drift in the analytical performance should be maintained. Defined acceptance criteria should be established and documented.

Where appropriate, the laboratory should subscribe to membership of appropriate external accreditation/performance/proficiency schemes. Such schemes can provide useful indicators as to the competency of the laboratory to accurately perform such work.
15. QUALITY AUDIT

Independent auditing of the laboratory should be conducted to assure patient safety, patient confidentiality, data integrity and compliance with GCP. This includes confirmation that the clinical protocol, analytical plan, SOPs and this guideline are being complied with.

Facilities, systems, equipment, analytical procedures, QC procedures, data recording, personnel records, reports and archive process should be audited at intervals following a prearranged programme.

Audits should be conducted by a competent person(s) designated by laboratory management. This person(s) should be independent of the work being audited. Independent audits by external experts may also be utilised.

All audit results should be recorded. Reports of the audits should contain all the observations made during the audit.

Analytical project managers and laboratory management should respond to these audit reports in a timely manner indicating any corrective actions.

Any corrective actions indicated should be tracked to ensure appropriate implementation.
16. RETENTION AND ARCHIVING OF RECORDS

A laboratory will generate two types of records during the conduct of a trial: trial records and laboratory records. Both types of records need to be retained and are required for the reconstruction of the work.

16.1 Trial Records

The sponsor is responsible for ensuring such records are retained for as long as they are required by regulatory authorities to support the performance and results of the trial.

A laboratory may be required by the sponsor to retain these records on their behalf. This shall be defined in the analytical plan along with the duration of retention.

The types of records to be retained should include, but not necessarily be limited to, the following:

- The clinical protocol, analytical methods used and analytical plan
- Procedural and processing data
- Raw data
- The issued results/report.

16.2 Laboratory Records

Laboratory management is responsible for ensuring the records required to support the compliance status of the laboratory are retained.

The type of laboratory records to be retained include, but are not limited to, the following:

- Records of the qualifications, training, experience and job descriptions of personnel
- Reports of the maintenance, calibration and validation of equipment
- The historical file of SOP including the index, plus any operating manuals used as part of the SOP
- The records of all QC tests and results performed to confirm the accuracy of the work performed including the records of any results from proficiency schemes
- Records of temperature storage for samples
- Records of all audits performed by the quality audit function.
If a laboratory does not have appropriate facilities for the storage of such materials in the manner defined, the use of commercial contract archive facilities should be used.

If a laboratory goes out of business and has no legal successor, the archive material should be transferred to a suitable archive designated by the sponsor of the trial.

Controls should be in place to ensure that any retrieval or loan from the archive is authorised by laboratory management and that the material is returned promptly after use and intact.

16.3 Electronic Records

If any records, be they trial or laboratory, are to be retained and archived electronically then they should be retained in such a way as to ensure they remain retrievable and in human-readable format.

16.4 Samples and Specimens

Samples and specimens should be retained as required by GCP, the clinical protocol and analytical plan, but only as long as the quality of the sample permits evaluation.

Trial samples should be retained in such a way as to ensure their integrity.

Samples may be retained for further analysis outside of the original aims of the trial, provided this is defined in the clinical protocol and approved by the Ethics Committee.

Retention of such samples should be performed in such a manner as to afford meaningful evaluation.
17. CONFIDENTIALITY

Procedures for the handling of trial samples, collection of data and reporting of results should be designed to maintain subject confidentiality within the requirements of GCP, Declaration of Helsinki and the clinical protocol.

Procedures should assure that a sponsor’s proprietary information is not disclosed to anyone other than authorised individual(s).
18. **BLINDING**

The laboratory should be aware of any blinding and unblinding conditions that apply to a trial and take care not to inadvertently unblind a trial.

Particular care should be taken in reporting results to ensure unblinding does not occur.

The sponsor should be informed of any event, either accidental or arising as a result of an investigation, which may compromise study blinding.

19. **PATIENT SAFETY**

The safety of trial subjects takes precedence over any other aspect of the trial. Consequently, prior to the initiation of laboratory work, lines of communication should be established with the sponsor to ensure that any issues that may impact on patient safety are reported without delay. This may include, but is not limited to, the reporting of unexpected or out of range results and significant deviations from GCP, the clinical protocol or analytical plan.

The need to expedite the reporting of results should always be considered and discussed with the sponsor prior to the initiation of a new trial involving the laboratory.