SOP 715 Principles of Clinical Research Laboratory Practice

For Use in:	Research & Development
By:	All staff
For:	All staff involved in the conduct of research
Division responsible for document:	Research & Development
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SOP 715, Principles of Clinical Research Laboratory Practice

This Standard Operating Procedure (SOP) is available on the Research & Development pages on the NNUH website

Copies printed from the website are only valid on the day of printing.

1. Contents

2. Definitions of Terms Used / Glossary

AP	Analysis Plan
APM	Analysis Plan Manager
CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCLP	Good Clinical Laboratory Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
ICH	International Conference for Harmonisation
ISF	Investigator Site File
LAP	Laboratory Analysis Plan
MHRA	Medicines and Healthcare products Regulatory Agency
NNUH	Norfolk and Norwich University Hospital
JRGC	Joint Research Governance Committee
PI	Principle Investigator
R&D	Research and Development
SOP	Standard Operating Procedure
UKCRC	United Kingdom Clinical Research Collaboration
TMF	Trial Master File
UEA	University of East Anglia

3. Scope

This SOP applies to Clinical Trials of Investigational Medicinal Products (CTIMPs) sponsored by NNUH. External Sponsors may require use of their own SOPs; this will be specified in site agreements. It is the responsibility of the local PI to ensure that study specific SOPs can be operated without conflict with this SOP and in accordance with all organisational polices related

4. Introduction

The aim of this SOP is to define the requirements for the use of laboratory services for analysis and storage of samples in CTIMPs sponsored by NNUH, in order to provide quality assurance that the processing authorise of samples in CTIMPs meets the standards of Good Clinical Practice (GCP).

5. Definitions

Good Clinical Practice (GCP)

- GCP is the international ethical, scientific and practical standard to which all clinical research is conducted.
- It is important that everyone involved in research is trained or appropriately experienced to perform the specific tasks they are being asked to undertake. Laboratories which undertake analysis of samples for CTIMPs may be subject to regulatory inspection from the MHRA.

Good Clinical Laboratory Practice (GCLP)

- GCLP is a guidance tool for the analysis of clinical trial samples which incorporates the legal requirements of GCP. The principles of GCLP should be interpreted and applied by any laboratory that analyses samples generated during the conduct of clinical trials – in particular primary or secondary endpoints. Unlike GCP, GCLP is not recognised as a standard by the MHRA.

Good Laboratory Practice (GLP)

- GLP is a quality system concerned with the organisational process and the conditions under which **non-clinical** health and environmental safety studies are planned, performed, monitored, recorded, archived and reported. Laboratories involved in clinical trials (human samples) must adhere to the GCP standard.

6. Roles and Responsibility

Analysis Plan Manager (APM)

This is a named individual with responsibility for the conduct and reporting of the work within the laboratory, ensuring that the analysis services required are appropriate for the requirements of the study. The APM should ensure that all laboratory work is performed in compliance with the Clinical Trials Regulations, the clinical protocol and any associated work instruction. The APM must be familiar with the requirements of the research, be appropriately trained, including GCP and be able to ensure that the laboratory analysis plan can be undertaken at the local site and that analytical staff can adhere to the requirements of the plan.

The named individual(s) is responsible for reporting the results of the analysis or evaluation and any deviations from the work instruction or clinical protocol to the Sponsor or the Sponsor's representative.

If any serious breaches of GCP are identified they must be reported to the Sponsor or their representative immediately. In some circumstances it may be necessary for laboratory personnel to report serious breaches directly to the MHRA. The laboratory should maintain documented procedures to describe the actions that would be taken in the event of a serious breach.

If any amendments are made to the laboratory analysis plan then the APM will be responsible for documenting and signing off these amendments and notifying the Chief Investigator (CI) and Sponsor.

The APM has the responsibility for the completion of the UKCRC Self-Assessment Questionnaire, if it has been deemed a requirement.

Chief Investigator/Principal Investigator

Lead on the development of the study laboratory analysis plan in consultation with the APM. For multisite trials the CI may delegate responsibility to the Principal Investigator (PI) on any given site.

Sponsor

The Sponsor is responsible for ensuring that the Laboratory and staff are appropriately trained and equipped to meet study and regulatory requirements.

Contractual arrangements are in place to cover the management, finance and indemnity of the laboratory services during the study.

The laboratory analysis plan is referenced in the contract, and included as a schedule, if appropriate. Ensure that a copy of the laboratory analysis plan is held in the Sponsor files.

Trial Monitor/Trial Auditor

The Research Trial Monitor/Trial Auditor will be responsible for the monitoring / audit of the laboratory services provided to the study, on behalf of the Sponsor. Monitoring reports written by the Trial Monitor on these services will be included in regular monitoring reports to the Sponsor. Audit reports written by the Trial Auditor will also be sent to the Joint Research Governance Committee.

7. Laboratory Services

These are the services provided for the processing, analysis and reporting of samples relating to CTIMPs. They may involve NHS or Norwich Research Park laboratories or elsewhere, or other off-site laboratory services. This also includes the use of fridges and freezers to store samples, as well as sub-contracted services, when one laboratory may subcontract services out to another provider; however sub-contracting can only take place where Sponsor approval has been given for this.

The designation does not include laboratory activities undertaken for routine clinical care and diagnosis.

8. Sample Storage and Accountability

All biological samples obtained for research use must be stored and be traceable (chain of custody) through a complete audit trail according to the Human Tissue Act and individual trial protocols. A system for recording all research samples stored in the laboratory for a study should be in place, and this can be in the form of a study specific tracking log.

A system for recording the storage conditions must be in place to ensure that storage conditions are kept within defined limits and meet protocol requirements using either a temperature log or an automated system.

9. Transfer of Samples

It is essential that the chain of custody of samples is documented and includes the location of samples, who is moving the samples, when they are moved and where the samples have been moved to.

A suggested Research Sample Transfer Form is available in Appendix 1.

10. Laboratory Analysis Plan (LAP)

A LAP should be prepared before the study starts, with details of the analyses and methods to be used in the study. This is to be set up by the CI/PI and analysis plan manager (APM) (see roles and responsibilities) prior to the start of the study. It ensures that all staff, facilities, documents, resources, equipment and reagents will be available and fit for purpose at the start of the study. It is agreed and signed by the CI, Sponsor and APM and a copy is to be held in the Trial Master File (TMF). It may also form part of, or be referenced within, the study protocol and/or a Laboratory Agreement. The plan will include the following:

- Study title
- Nature and purpose of the study
- IRAS/REC/Eudract reference
- Confirmation of Trust capacity and capability
- Names of CI/PI and Analysis Plan Manager (within the appropriate laboratory)
- Name and location of laboratory services to be used
- Number of participants, number of visits, tests per visit
- Type of samples to be analysed
- Type and detail of tests to be undertaken (analytical methods and validation)
- Confirmation that informed consent for tissue samples is in place
- Sample collection, storage conditions and transport (if required), duration and location of sample storage (chain of custody)
- Disposal of sample details (safe handling of samples)
- Duration of study
- Method of reporting and details of who receives the reports
- Location of result storage and duration of time results should be stored for
- Details of specific analytical methods to be used and validation processes
- Reference to any specific laboratory SOPs relevant to the processing of the samples, including maintenance and monitoring of equipment, eg fridges and freezers.
- Reference to the version of the study protocol used to define the requirements
- Details of staff requirements
- Details of laboratory accreditation certificates
- Storage and retention of records Date and version of plan

11. Laboratory Self-Assessment Questionnaire

In addition to the LAP, it may be a requirement for laboratories undertaking sample analysis to complete the *UKCRC Self-Assessment Questionnaire for assessing regulatory compliance in laboratories that perform the storage and analysis or evaluation of research samples*.

If it has been deemed necessary (e.g. Laboratory is new to Sponsor, laboratory's first involvement with a CTIMP) for the laboratory to complete the self-assessment questionnaire it should be done so at the earliest opportunity (including pre-funding where possible) to ensure full costing and awareness of the requirements for MHRA compliance.

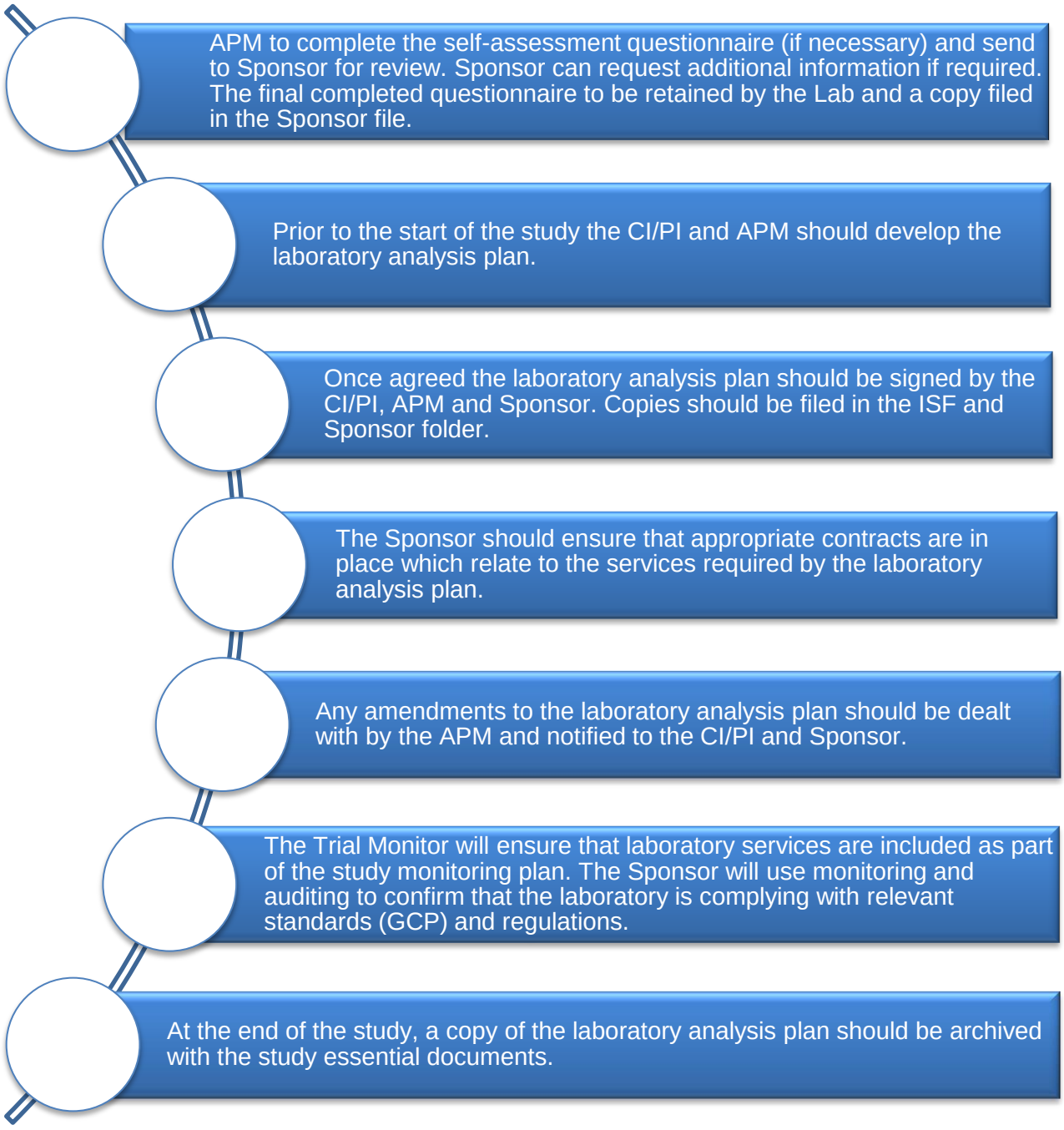
The APM has the responsibility for the completion of the UKCRC Self-Assessment Questionnaire.

The Self-Assessment Questionnaire along with the supporting documentation can be found at the following link: https://www.ukcrc-ctu.org.uk/page/Guidance and by scrolling down to the heading: *UKCRC Registered CTUs Network publishes Guidance on QA oversight of laboratories.*

The final completed version of the laboratory self-assessment questionnaire should be retained by the laboratory and presented during a study set up should it be requested. A copy should be filed in the Sponsor file.

The Laboratory Self-Assessment Questionnaire is NOT study specific and will only have to be completed once, unless future changes require updates.

12. Procedure for laboratory involvement in an NNUH Sponsored Clinical Trial



13. References

UK Policy Framework for Health and Social Care Research. (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/)

EU Clinical Trials Directive 2001/20/EC into UK law (Statutory Instrument 2004 No.1031: The Medicines for Human Use (Clinical Trials) Regulations 2004 as amended)

MHRA (2009) GOOD CLINICAL PRACTICE *Guidance on the maintenance of regulatory compliance in laboratories that perform the analysis or evaluation of clinical trial samples.* Issue 1.

European Directive 2001/20/EC

European Directive 2005/28/EC

The Medicines for Human Use (Clinical Trials) Regulations 2004, Statutory Instrument 2004 No.1031.

The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006, Statutory Instrument 2006 No.1928.

The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006, Statutory Instrument 2006 No.2984.

The Medicines for Human Use (Clinical Trials) Amendment Regulations 2008, Statutory Instrument 2008 No.941.

The Medicines for Human Use (Miscellaneous Amendments) Regulations 2009, Statutory Instrument 2009 No.1164.

Human Tissue Act 2004

MHRA Good Laboratory Practice: http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodLaboratoryPractice/index.htm

WHO / TDR Handbook: good laboratory practice (GLP): quality practices for regulated non-clinical research and development - 2nd ed: https://www.who.int/tdr/publications/documents/glp-handbook.pdf

WHO /TDR Handbook: Good Clinical Laboratory Practice (GCLP): https://www.who.int/tdr/publications/documents/gclp-web.pdf

UKCRC Laboratory Guidance documents: https://www.ukcrc-ctu.org.uk/page/Guidance

UKCRC: Self-Assessment Questionnaire for assessing regulatory compliance in laboratories that perform the storage and analysis or evaluation of research samples.

14. Appendix 1: Research Sample Transfer Form (Suggested Template)

Study Title……

APM / Laboratory Study Contact ……

Chief Investigator ……

List of samples to be removed from Laboratory

Reason for removal of samples: ……..

Have the samples been anonymized (check study protocol) Yes / No

Details of Person retrieving the samples:

Name: Signature: Date:

Sample Destination: ……..

Method of Transportation (check study protocol) ……..

……

Authorisation for removal (i.e. Lab manager)

Name: Signature: Date:

Will the specimen/isolate be returned for disposal? Yes/No

If yes, details of retrieval and contact for retrieval of samples ……

……

Receipt of Samples at new location

Name: Signature: Date:

Please sign and email back to (*enter study laboratory contact name and email address*)

15. Approval

Author:	**Francesca Dockerty**
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Signature:	*Francesca Dockerty*
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Role:	**Research Services Manager**
Signature:	*Julie Dawson*
Date:	*27/08/2019*
Approved & Authorised UEA:	**Sarah Ruthven**
Role:	**Research Manager**
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Date:	*27/08/2019*

16. Reason for Update and Training Implication

This replaces SOP 715 V1.4

Update	Reason	Training Implication	Action
SOP format, Addition of definitions, review from NNUN and UEA laboratory staff.	To ensure SOP is current and user friendly	Yes	Review SOP and update training matrix