University of East Anglia

Our Vision
The best care for every patient

NHS
Norfolk and Norwich University Hospitals
NHS Foundation Trust

SOP 715 Principles of Clinical Research Laboratory Practice

For Use in:	Research
By:	All staff
For:	All staff involved in the conduct of research
Division responsible for document:	Research & Development
Key words:	GCLP, Laboratories, Samples
Name of document author:	Basia Brown
Job title of document author:	Research Governance Coordinator
Name of document author's Line Manager:	Julie Dawson
Job title of author's Line Manager:	Research Services Manager
Supported by:	Julie Dawson NNUH Sarah Ruthven UEA
Assessed and approved by:	Julie Dawson: Research Services Manager NNUH Sarah Ruthven: Research Manager UEA
Date of approval:	2 June 2023
To be reviewed before: This document remains current after this date but will be under review	2 June 2026 (3 years, unless legislation or process changes)
Reference and / or Trust Docs ID No:	15821
Version No:	2
Description of changes:	Update content and format New template

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	Principal Investigator
R&D	Research and Development
SOP	Standard Operating Procedure
TMF	Trial Master File
UEA	University of East Anglia
UKCRC	United Kingdom Clinical Research Collaboration

3. Scope

This SOP applies to Clinical Trials of Investigational Medicinal Products (CTIMPs) sponsored by NNUH.

This SOP also applies to other NNUH sponsored studies where sample analysis is conducted in support of primary or secondary endpoints and objectives or when analysis of samples is critical to the conduct of the trial.

External Sponsors may require use of their own SOPs. 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 to research.

4. Purpose

The aim of this SOP is to define the requirements for the use of laboratory services for analysis and storage of samples in relevant studies sponsored by NNUH, in order to provide quality assurance that the processing of samples 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 Laboratory Practice (GLP)

- A set of standards intended to promote the quality and validity of test data for non-clinical safety studies

Good Clinical Laboratory Practice (GCLP)

- GCLP applies principles established under GLP to the analysis of samples from a clinical trial. At the same time it ensures that the objectives for GCP principles are being carried out.
- 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.

6. Roles and Responsibilities

Analysis Plan / Project Manager (APM)

This is a named individual with responsibility for the conduct of the work defined by the laboratory instructions (such as the Analysis Plan), reporting of the work, and ensuring that the analysis services required are appropriate for the requirements of the study. The APM must be familiar with the requirements of the research, be appropriately trained, including GCP.

The APM should:

- provide input into laboratory instructions for the study.
- ensure that all laboratory work is performed in compliance with the Clinical Trials Regulations, the clinical protocol, and any associated work instruction.
- ensure that the sample management can be undertaken at the local site and / or analytical facility and that analytical staff are trained on study requirements and can adhere to the requirements of the plan.

The APM has the responsibility for assessment of the analytical facility in compliance with GCLP. Please see section 11. Laboratory Self-Assessment Questionnaire for details on assessment process.

- report 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 instructions, then the APM will be responsible for documenting and gaining approvals for these amendments from the Chief Investigator (CI) and Sponsor.
- ensure that all results of analyses are fully documented and recorded
- ensure that after completion of the analyses, the analytical plan, the analytical report and/or analytical results, raw data and supporting documentation are archived and retained.

Chief Investigator/Principal Investigator

- Individual responsible for the conduct of the study.
- Develops the study laboratory instructions in consultation with the APM.

Staff working in laboratories and conducting analysis on samples collected as part of clinical trial must have adequate understanding of GCP. Please see SOP 002 GCP Training for further details on GCP training requirements.

Laboratory / Facility Manager

An individual within an organisation performing the analysis responsible for ensuring that facility operates according to GCLP, that samples are managed in accordance with provided instructions and by an appropriately delegated, trained, and qualified member of the team.

Study Staff

Staff working with study materials should be aware of the guidance and instructions that apply to their work and follow the instructions as specified in the protocol, PIS, laboratory instructions, Standard Operating Procedures and in accordance with documented consent given by the participant.

Sponsor

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

The role of the Sponsor is also to ensure that contractual arrangements are in place to cover the management, finance and indemnity of the laboratory services during the study.

The laboratory instructions should be referenced in the contract with the analytical facility, and included as a schedule, if appropriate. Ensure that a copy of the laboratory instructions 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. Please see SOP 330 Monitoring of CTIMP and Medical Devices and SOP 003 Audit Plan for further details.

7. Laboratory Services

These are the services provided for the storage, processing, analysis, and reporting of samples for the purpose of assessing protocol endpoint(s). They may involve NHS, Norwich Research Park laboratories, 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.

Samples managed by the local hospital clinical laboratory as per routine clinical care and diagnosis, are outside of scope of this SOP. However, reference ranges and Clinical Pathology Accreditation (or equivalent) certificates will be filed in the Investigator Site File.

7a. Contracting

NNUH as a Sponsor need to have an assurance that a provider of laboratory services has sufficient expertise, facilities, and training to meet study and regulatory requirements.

SOP 700 Vendor selection, approval, and oversight as well as laboratory assessment (see section 13) should be followed in the process of selection of external laboratory services.

The APM is responsible for completing laboratory assessment and vendor risk assessment and providing them to the Sponsor for review.

Where samples are to be sent to an external organisation (including Laboratories within Norwich Research Park) for storage or analysis, a contract must be in place prior to any sample shipment.

No analytical or other study related work should be subcontracted without the prior approval of the sponsor.

8. Sample Storage and Accountability

All samples obtained for research use must be stored and be traceable (chain of custody) through a complete audit trail from collection to disposal. 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. Please see Appendix 1 as an example of a Sample Tracking Log. The Sample Tracking Log must be retained in the Investigator Site File.

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 records from an automated system. Record of storage conditions should be filed in the Investigator Site File.

9. Transfer of Samples

Details of shipment conditions and packing materials should be described as part of the laboratory instructions.

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 2.

When using courier services, the transfer of samples needs to be tracked and a confirmation of receipt of correct samples must be provided by receiving laboratory.

Details of all shipments and receipts must be retained in the Investigator Site File.

10. Sample management

Instructions and processes for key activities relating to the management of samples may be detailed in the protocol or separate laboratory manual, work instruction, analytical protocol, or analytical plan. If a document other than the protocol is utilised it must be written in accordance with the protocol (and any subsequent amendments), and be approved by the Analytical Plan Manager and Sponsor.

The agreed sample management document must be in place prior to any sample management being undertaken for a study.

Study samples must be collected and processed in accordance with the approved protocol, laboratory instructions, PIS, contractual arrangements and in accordance with documented consent given by the participant.

A copy of instructions should be held in the Trial Master File (TMF) and be referenced in the agreement with laboratory services. The plan of work will include, but is not limited to the following:

- Study title
- Nature and purpose of the study
- IRAS number / REC
- Name and address of Sponsor
- Names of CI/PI and Analysis Plan Manager
- Name and location of laboratory services to be used and name of Laboratory Manager
- Details of specific analytical methods to be used and validation processes (analytical design, methods, materials, conditions, type and frequency of analysis, measurements, observations and examinations. Details of validation methods)
- Sample collection, storage conditions and transport (if required), duration and location of sample storage and how samples will be traced
- Preparation and shipment of materials

- The methods and conditions under which trial materials must be transported
- Disposal of sample details
- Duration of study – the proposed start and completion dates of work
- Method of reporting and details of who receives the reports including quality audits to be performed to assure the quality and integrity of the data generated and the accuracy of reporting.
- A list of records to be retained and their location on completion of work
- Reference to any specific laboratory SOPs relevant to the processing of the samples, including maintenance, monitoring and calibration of equipment eg fridges and freezers
- Reference to the version of the study protocol used to define the requirements
- Details of staff training requirements
- Details of laboratory accreditation certificates
- Storage and retention of records. Dave and version of plan, signatures of Sponsor, APM and CI

11. Sample disposal or long-term storage

At the end of the study all remaining samples will be disposed of or transferred for long term storage, in an appropriate HTA licensed area, in accordance with the trial protocol, ethical approval and each participant's consent status.

Samples must be either disposed of or transferred to long term storage within twelve (12) months of the End of Study notification or the time specified in the ethics application.

If consent has been given for storage for future research or biobanking, relevant samples must be transferred to suitable storage within HTA licensed premises. Consent forms must be retained for the duration of sample storage.

Sample disposal must be documented and retained by the laboratory.

A completed sample tracking log must be maintained in the Investigator Site File.

12. Analytical Report

An analytical report should be provided to the Sponsor and contain, but not be limited to, the following:

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

b) IRAS number

c) Name and address of the Sponsor.

d) Name and address of the Investigator(s).

e) Name and address of any trial facilities and any investigator sites involved, including identity of any Investigators.

f) Name and address of the Analytical Project Manager.

g) The start and completion dates of the laboratory work.

h) A Quality Audit Certificate (if applicable).

i) Description of methods and materials used to include data manipulation techniques and any statistical methods used.

j) Presentation of the results.

k) All information and data required by the analytical plan.

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

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

Please refer the SOP 335 Research project closure for timelines on submitting final study report.

13. 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.

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

	APM to complete the self-assessment questionnaire and (if necessary) vendor assessment (see SOP 700 vendor selection) and send to Sponsor for review. Sponsor can request additional information if required. The final completed questionnaire to be retained by the Lab and a copy filed in the Sponsor file.
	Prior to the start of the study the CI/PI and APM should develop the detailed instruction relating to sample management as well as relevant tracking logs and provide them for Sponsor approval.
	Once agreed the laboratory instructions should be signed the CI/PI, APM and Sponsor. Copies should be filed in the ISF and Sponsor file.
	The Sponsor should ensure that appropriate contracts are in place which relate to the services required by the laboratory service and transport of samples.
	Study samples will be collected and processed in accordance with the approved study documents: protocol, PIS, laboratory instructions, contractual arrangements and in accordance with documented consent given by the participant.
	Any amendments to the laboratory instructions should be dealt with by the APM and notified to the CI/PI and Sponsor.
	For CTIMPs the Trial Monitor will ensure that laboratory services are included as part of the study monitoring plan. The Sponsor will use monitoring and auditing to confirm that the laboratory is complying with relevant standards (GCP) and regulations.

15. References and Related Documents

References
ICH GCP E6 / SI 2004/1041
UK Policy Framework for Health and Social Care Research.
The Medicines for Human Use (Clinical Trials) Regulations 2004
MHRA (2012) GOOD CLINICAL PRACTICE Guide. Chapter 13 – Clinical Trial Samples – analysis and evaluation
Human Tissue Authority. Code of Practice and Standards. Code E: Research
MHRA Good Laboratory Practice: Good laboratory practice - MHRA Inspectorate (blog.gov.uk)
Good Clinical Laboratory Practice (GCLP) - GOV.UK (www.gov.uk)
UKCRC Laboratory Guidance documents: https://ukcrc-ctu.org.uk/guidance-for-ctus/
UKCRC: Self-Assessment Questionnaire for assessing regulatory compliance in laboratories that perform the storage and analysis or evaluation of research samples. https://ukcrc-ctu.org.uk/guidance-for-ctus/

Related Documents	
SOP No.	**SOP Title**
SOP 002	GCP Training
SOP 003	Audit Plan
SOP 330	Monitoring of CTIMP and Medical Devices
SOP 335	Research project closure
SOP 700	Vendor selection

16. Approval

Author	Basia Brown
Role	Research Governance Coordinator
Approved & Authorised NNUH	Julie Dawson
Role	Research Services Manager
Signature	DocuSigned by: Julie Dawson 4CBAB366CF354A2...
Date	02 June 2023 | 12:11 BST
Approved & Authorised UEA	Sarah Ruthven
Role	Research Manager
Signature	DocuSigned by: Sarah Ruthven 6EB42B4E497249C...
Date	02 June 2023 | 2:50 BST

17. Reason for new version and Training Implication

This SOP replaces the previous version number V1.5

Changes made	What changes have been made to the contents of the document
Reason	• New layout • Revision in procedure • Change in legislation
Training Implication	**Yes**
Actions required	• Additional training may be required

Appendix 1. Sample Tracking log

Study Title			
Investigator			
IRAS no		**Site name:**	

Participant ID	Specimen ID	Specimen type	Date & time collected	Sample storage location (including location in the fridge)	Staff Initials	Sample removed		Reason for removal			
								Transfer			Disposal
						Date	Staff initials	Date Shipped / transferred	Receiving Laboratory	Date received	Date of disposal

Appendix 2: 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: