


STANDARD OPERATING PROCEDURE

SOP 715

Principles of Clinical Research Laboratory Practice

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1 ABBREVIATIONS

AP	Analysis Plan
APM	Analysis Plan Manager
CRTU	Clinical Research and Trials Unit
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCLP	Good Clinical Laboratory Practice
GCP	Good Clinical Practice
ICH	International Conference for Harmonisation
MHRA	Medicines and Healthcare products Regulatory Agency
NNUH	Norfolk and Norwich University Hospital
RGC	Research Governance Committee
SOP	Standard Operating Procedure
UEA	University of East Anglia

2 INTRODUCTION

The aim of this SOP is to describe the process for all health care research activities within the UEA and NNUH. It aims specifically to define the requirements for the use of laboratory services for analysis of samples in CTIMPs sponsored by NNUH or UEA, in order to provide quality assurance that the processing of samples in CTIMPs meets the standards of Good Clinical Laboratory Practice (GCLP). The transposition of the 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) provides provision for the inspection of clinical laboratories. In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) has responsibility for monitoring clinical laboratories for compliance with the Clinical Trials Regulations.

3 SCOPE

This SOP applies to all healthcare research Sponsored by NNUH or UEA which falls within the scope of the Research Governance Framework (2nd edition 2005). Where additional legislation applies - for example the Medicines for Human Use (Clinical Trials) Regulations 2004 (and amendments) or the Medical Devices Regulations 2002 - required procedures will be indicated. External Sponsors may require use of their own SOPs and 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 policies related to research

4 DEFINITIONS

Good Clinical Laboratory Practice (GCLP)

GCLP is a quality standard for the analysis of clinical trial samples and which incorporates the legal requirements of GCP. The principles of GCLP should be

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interpreted and applied to any laboratory that analyses samples generated during the conduct of clinical trials. Laboratories which undertake analysis of samples for CTIMPs may be subject to regulatory inspection from the MHRA.

Laboratory Services

These are the services provided for the processing, analysis and reporting of samples relating to CTIMPs. They may involve NHS or university laboratories in Norwich or elsewhere, or other off-site laboratory services. Also included are subcontracted services, when one laboratory may subcontract services out to another provider, and the use of fridges and freezers to store samples. The designation does not include laboratory activities undertaken for routine clinical care and diagnosis.

Use of Fridges and Freezers

All biological samples obtained for research use must be stored and be traceable through a complete audit trail according to the Human Tissue Act and individual trial protocols.

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

When samples are removed from the fridge or freezer the date and destination must be entered onto the tracking log following the practice of the laboratory providing the fridge or freezer.

Laboratory Analysis Plan (AP)

A detail of the analyses to be used in the study. This is to be set up by the CI/PI and analysis plan manager (APM) 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 and APM and a copy is to be held in the TMF. It may also form part of, or be referenced within, the study protocol and/or a Laboratory Agreement.

Further details on the content of an analysis plan are available in Appendix 1.

Analysis Plan Manager (APM)

The analysis or evaluation of clinical trials should be overseen by an Analysis Plan Manager. 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. He or she must be familiar with the requirements of the research and be able to ensure that the analysis plan can be

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undertaken at the local site and that analytic 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 GCLP 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 analysis plan then the APM will be responsible for documenting and signing off these amendments and notifying the CI and Sponsor.

5 RESPONSIBILITY

CI/PI

For the development of an analysis plan, in consultation with the APM. For multisite trials the CI may delegate responsibility to the PI on any given site.

APM

The APM will be responsible for ensuring that the laboratory services and analytical staff are appropriate for the study and adhere to the principles of good clinical practice for laboratories. They should have authority, or delegated authority, to ensure that the laboratory services provided are fit for purpose. This will include maintenance and servicing of equipment, test validation and staff training. Records of these must be available for audit and monitoring purposes.

The APM will be responsible for oversight of any amendments to the analysis plan, ensuring that changes are documented, signed and that the CI is notified of these changes, and then that they are correctly implemented.

Sponsor

The Sponsor will be responsible for ensuring that appropriate contractual arrangements are in place to cover the management, finance and indemnity of the laboratory services during the study. These may be covered by standard contracts, service level agreements or material transfer agreements, and the analysis plan should be referenced in these documents and included as an appendix if appropriate. Details of relevant financial arrangements for the provision of laboratory services should also be included in the appropriate contracts.

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The Sponsor will be responsible for ensuring that a copy of the analysis plan is held in the Sponsor files.

Trial Monitor/Trial Auditor

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

6 PROCEDURE

- 6.1 Prior to the start of the study the CI/PI and APM should develop the analysis plan.
- 6.2 When the analysis plan is agreed it should be allocated a version number and signed by the APM and CI/PI with a copy sent to the Sponsor.
- 6.3 The CI/PI will retain a copy in the TMF.
- 6.4 The Sponsor will retain a copy in the Sponsor files.
- 6.5 The Sponsor should ensure that appropriate contracts are in place which relate to the services required by the analysis plan.
- 6.6 The Sponsor should ensure that appropriate indemnity is in place if laboratory services are contracted externally.
- 6.7 Any amendments to the analysis plan should be dealt with by the APM and notified to the CI/PI and Sponsor.
- 6.8 The Trust Research Trial Monitor will ensure that laboratory services are included in routine monitoring visits as part of the study monitoring plan.
- 6.9 At the end of the study, a copy of the analysis plan should be archived with the study essential documents.

7 REFERENCES

MHRA Good Clinical Laboratory Practice:

<http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodLaboratoryPractice/index.htm>

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

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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

8 LIST OF APPENDICES

Appendix 1: Analysis Plan Details

Appendix 2: Change Control, Revision and Review Sheet

Appendix 1: Analysis Plan Details

The plan will include the following:

- Study title
- Study R&D/ethical/ Eudract reference
- Date of Trust approval of the study.
- 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
- Confirmation that informed consent for tissue samples is in place
- Sample collection and storage conditions
- Duration and location of sample storage
- Disposal of sample details
- 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
- Date and version of plan.

A reference to the working location of the analysis plan should be should be stored in the Trial Master File. At the end of the study the analysis plan must be archived as an essential trial document.

Appendix 2: Change Control, Revision and Review Sheet

CHANGE CONTROL, REVISION AND REVIEW SHEET: SOP715		
Version No	Change Date	Reason for Change
1.1	01/01/2014	Minor typing corrections and requirements for monitoring and audit reports from laboratory services to go to Joint Research Governance Committee. Combining of SOP change and review sheets.
1.2	21/01/2014	Addition of principles of fridge or freezer use and associated monitoring systems.
Reviewer: NC	Designation: Lead Research Nurse	Signature and Date: Noreen Cushen 20th January 2014
1.2	13.11.2015	No changes made
Reviewer: Sue Kerry	Designation: Chief Biomedical Scientist	Signature and Date: 13 th November 2015
Reviewer:	Designation:	Signature and Date: