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SOP 710 Good Clinical Practice (GCP) Regulatory Audit or Inspection

For Use in:	Research
By:	All staff
For:	All staff involved in the conduct of research
Division responsible for document:	Research & Development
Key words:	Good Clinical Practice (GCP) Regulatory Audit or Inspection
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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.

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1. Contents

2. Definitions of Terms Used / Glossary

CAPA	Corrective Action, Preventative Action
CI	Chief Investigator
CQC	Care Quality Commission
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
HRA	Health Research Authority
ICH GCP	International Conference on the Harmonisation of Good Clinical Practice
JRGC	Joint Research Governance Committee
MHRA	Medicines and Healthcare Products Regulator Agency
PI	Principal Investigator
R&D	Research and Development
SOP	Standard Operating Procedure

3. Objectives

To describe the procedure relating to the preparation required, prior to, during and after the conduct of a site audit, an inspection by authorised internal, external regulatory body or a Sponsor

4. Scope

ICH GCP E6/SI 2004/1031, SI 2006/1928, Declaration of Helsinki 1996, Data Protection Act 2018, Human Tissues Act 2004, Mental Capacity Act 2005

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5. Purpose

The types of audit and inspection NNUH expect are Regulatory Inspections such as Medicines and Healthcare Products Regulatory Agency (MHRA), Internal Audits and External Sponsor Audit.

Inspections performed by regulatory authorities such as the MHRA, are usually performed for three main reasons:

- To assure integrity of clinical study data
- To assure subject's rights and safety
- To permit sound decisions regarding efficacy and safety

The main objectives of a regulatory inspection are to:

- Determine the compliance of Chief Investigator (CI) with ICH GCP guidelines and regulations
- Assess if monitoring procedures have been satisfactorily implemented by a Sponsor or Contract Research Organisation
- Assess whether data submitted to the regulatory authorities from specific studies are substantiated by appropriate records

The purpose of internal audit is to:

- Verify that participants' rights and welfare are being adequately protected
- Assure regulatory compliance of the Trust as a Sponsor organisation
- Ensure integrity and quality of the clinical study data
- Verify that the audit can assist in identifying training needs and correcting problem areas
- Provide suggestions to improve quality of clinical trials

External Audit / Inspection by Sponsors (Commercial and non-commercial)

- External monitoring of the CI compliance for their studies and the Quality Management System

6. Audit Definitions

GCP site or study inspection

An inspection of an externally sponsored study hosted by NNUH, which involves a medicinal product. The MHRA, acting as the UK Competent Authority undertakes these inspections.

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GCP inspection of the sponsoring organisation

An inspection conducted by the MHRA for studies involving investigational medicinal products or medical devices where the NNUH acts as a sponsoring organisation. The GCP inspection examines the systems used by the organisation to conduct clinical trial research. The inspectors will select a number of clinical trials to examine how the organisation's trial procedures are applied.

Internal Audit

An audit is a systematic and independent examination of trial related activities and documents that determines whether a trial or its related activities were conducted, and the data recorded, analysed and accurately reported according to the protocol, Sponsor's SOPs, GCP and any applicable regulatory requirements. Internal audits will be undertaken as a requirement of Research Governance where NNUH / UEA acts as Sponsor.

In this case the R&D office of NNUH and relevant UEA faculty will undertake the audit, adhering to GCP, see **SOP 003 Research & Development Annual Audit Plan**. NCTU have their own documented annual audit plan.

Auditor / Inspector

To conduct audit within agreed deadlines and to communicate and report findings with clarity and without prejudice.

Auditee / Inspected

To cooperate with the audit / inspection requirements by expeditiously agreeing the timelines, providing staffing and documentary evidence to permit the efficient auditing or inspection of the NNUH sponsored and hosted studies.

The local Principal Investigator (PI) will have responsibility (supported by R&D) for co-ordination of the Site / Study inspection. All the information relating to the particular study at this site has to be made available to the inspectors.

7. Prior to an Audit or Inspection

The Investigator should notify all personnel who need to be aware:

- That there is to be an audit / inspection
- The purpose of the audit / inspection
- When the audit is to take place
- Who should be present, or be available if required

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Personnel to be advised is a follows, but is not restrictive to:

- Trust senior management team
- Departmental director and / or UEA Head of School
- Research Services Manager
- Clinical Research Trials Unit Matron
- R&D Offices of NNUH or UEA
- Research Governance
- Named Archivist
- Sponsor
- Research Ethics Committee
- Co-investigator(s)
- Study coordinator and study administrator
- Research Nurses
- Pharmacy, laboratory and technical departments
- Data Manager and Statistician

Audit by an external auditor / Regulatory Authority of NNUH or UEA as a Sponsoring Organisation:

- The NNUH R&D Office and/or RIN shall lead the preparation and arrangements for the audit developing and agreeing clear timelines with the external party and clearly communicating the requirements to the NNUH and UEA, to individual Investigators and Research teams

In the case of an audit of an externally sponsored study, the investigator and the study team should conduct a thorough review of the following prior to the audit:

- Study Procedures
- Study Protocol
- Case Report forms
- Source Data
- Study Documentation / Trial Master file / Site file
- Patient notes
- Pharmacy and drug records, pharmacy agreements, documentation relating to doses / dispensing
- Signed financial documents/receipts

For audits of CTIMPs or Medical Device Trials

- The R&D Offices of NNUH or UEA shall discuss the review findings with the investigator and study team and shall identify appropriate actions to be taken to ensure that the documents listed above are available and complete.

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8. Preparation for the Audit / Inspection

The investigator, study team and R&D must make preparations for hosting the Auditors / Inspectors:

- Suitable facilities are booked with appropriate office or a quiet area in which to work, meet people and examine records
- Access to a photocopier is a necessary requirement
- Ensure that all the requested documentation is available
- Note: any missing data or forms should be covered by appropriate signed and dated file notes
- All required study team personnel will be available on the day of the audit / inspection in person
- Details of the study team responsibilities are listed and available in the Trial Master File
- The study team are familiar and confident about their areas of responsibility in order to answer questions by the auditor / inspector

The investigator, study team and R&D must ensure the following are available and current / up-to-date for each Study being audited / inspected:

- A completed Trial Master File. See **SOP 305 Creating and Maintaining the Trial Master File or Investigators Site File**

9. After the inspection

The Auditor / Inspector will, according to their own guidelines inform the necessary persons of the result of the findings. The NNUH R&D office must receive a copy of any findings in order to send the completed report to the Joint Research Governance Committee (JRGC).

10. MHRA Regulatory Inspection

All organisations sponsoring a Clinical Trial of an Investigational Medicinal Product (CTIMPs) or medical devices will be inspected at some point regardless of the risk status of the type of trials conducted.

The majority of MHRA GCP inspections are carried out under the risk-based compliance programme. These can be either systems-based or trial specific. A notification will be received prior to these inspections.

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The MHRA can perform triggered inspections for serious breaches. The Trust may be contacted to arrange an inspection if they suspect the law has been broken. This information might come from:

- A serious breach notification
- A whistle blower
- Other MHRA departments
- The Health Research Authority (HRA) and the Care Quality Commission (CQC)

In rare circumstances, MHRA may give little or no notice of these inspections. The duration of a triggered inspection will take as long as the inspector deems as necessary.

The MHRA inspectors have legal rights

- These include the right to enter any premises involved in clinical trials of investigational medicinal products
- To carry out inspections, take samples, require the production of records and documents, and to take copies of, or copies of entries in records and documents
- Seize and detain substances, articles and documents
- It is a criminal offence to obstruct this process

If you are aware of a serious breach it is better to inform the MHRA as they will help resolve the issue. Do not attempt to cover up potential serious breach.

For sponsor specific MHRA inspection the R&D office will be responsible for co-ordination of the inspection process. All research within the organisation may be inspected.

10.1 MHRA Statutory GCP Inspection Procedure

- Advanced notification will be sent to the organisation via email.
- The organisation **must** submit their Summary of Clinical Trials Systems Dossier within 30 days of notification prior to the inspection dates being set

- Lead Inspector is identified and dialogue opened with the organisation
- Confirmation of Inspection dates provided
- Confirmation of Trials to be Inspected
- Inspection plan finalised

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- Statutory GCP Inspections are normally conducted over **3 to 4** consecutive days by **two inspectors**
- Preparation for the inspection is vital. All data and study teams and supporting departments should be made available for inspection and interview

- Following the sponsor site inspection one or more host sites will be inspected to provide assurance of sponsor oversight of the investigator site
- Host site Inspections are often conducted by **one inspector** usually over **2 to 3** consecutive days

- The Lead Inspector will send a written report of findings once the last site inspection *(if applicable)* has taken place
- Organisation must provide a CAPA – Corrective Action & Preventative Action Plan to address these findings by the date specified by the MHRA
- Once the CAPA plan is accepted, the organisation will receive the MHRA GCP Inspection Statement

11. References and Related Documents

References
ICH GCP E6 / SI 2004/103, SI 2006/1928
Declaration of Helsinki 1996
Human Tissue Act 2004
Data Protection Act 2018
Mental Capacity Act 2005

SOP No.	**SOP Title**
SOP 003	Research & Development Annual Audit Plan
SOP 305	Creating and Maintaining the Trial Master File or Investigators Site File

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12. Approval

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13. Reason for new version and Training Implication

This SOP replaces the previous version number V2

Changes made	
Reason	• New template • Revision in procedure
Training Implication	**Yes**
Actions required	• Review SOP