University of Hertfordshire

QUALITY ASSURANCE AUDIT AND INSPECTION

Clinical Trials Support Network (CTSN)

Standard Operating Procedure for the Audit and Inspection of UH sponsored/co-sponsored Clinical Trials

SOP Number: SOP-23-02	**Effective Date:** 10/08/22
Version Number: 2.0	**Review Date:** 3 years (or as required)

1. BACKGROUND

This is a University of Hertfordshire (UH) Standard Operating Procedure (SOP). SOPs are required to assist Researchers in conducting research in accordance with the principles of Good Clinical Practice (GCP) and relevant regulations and guidance.

Quality Assurance (QA) refers to all actions in place to ensure that clinical trials are performed to meet the requirements of Good Clinical Practice (GCP). Quality Control (QC) is a system put in place by QA and refers to the set of operational techniques and activities undertaken to verify that the requirements for quality of the trial related activities have been fulfilled. QA and QC activities involve auditing against the trial protocol and SOPs.

An audit is*:*
"A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor's Standard Operating Procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirements." (ICH GCP 1.6)

An audit is a formal planned process and can take place prior to, during or after the participant recruitment phase.

The purpose of auditing is to:

- Ensure participant and staff safety.
- Assist researchers with compliance to regulatory requirements and University of Hertfordshire policy.
- Improve research systems and data quality.
- Prepare researchers for external audit processes.
- Demonstrate robust research processes to external funders and industry.

Throughout the audit, general information exchange between the auditor and the person(s)/institution being audited is acceptable and essentially is used as an evaluation tool. Any results obtained from an audit should be used to train staff and improve upon the quality of research conducted.

An inspection is:
"The act by a Competent Authority of conducting an official review of documents, facilities, records, quality assurance arrangements and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor and/or Contract Research Organisation's (CRO's) facilities or at other establishments that the Competent Authority sees fit to inspect". (ICH 1.29)

An inspection is a formal process that has legal implications if non-compliance with the regulations is found. It is therefore imperative that all trial related documentation is maintained and continually updated in readiness for an inspection.

Where there are potential conflicts between different collaborating organisations' SOPs, project level working instructions should be developed, to determine precedence.

The types of audits and inspection the CTSN expect are Internal Audits, External Sponsor Audits and Regulatory Inspections (e.g., MHRA).

Internal Audits are often undertaken prior to an external inspection and is undertaken as a requirement of Research Governance where UH/CTSN acts as host. Internal Audits are conducted to verify that:

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

All organisations sponsoring CTIMPS, or medical devices will be inspected at some point regardless of the risk status of the type of trials conducted. External Audits/Inspection by Sponsors are conducted of the CI compliance for their studies and the QMS.

Inspections are performed by regulatory authorities e.g., MHRA for the following purpose:

- To assure integrity of clinical study data.
- To assure participant rights and safety.
- To permit sound decisions regarding efficacy and safety.

2. PURPOSE

The aim of this Standard Operating Procedure (SOP) is to describe to research staff the process for preparing for an audit or inspection either by the sponsor/co-sponsor, CTSN or by the Competent Authority (CA) for clinical trials that fall under the UK Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) and the European Clinical Trials Directive (EUCTD). The SOP will cover the processes necessary to prepare, host and participate in a regulatory inspection by the Competent Authority.

Both audits and inspections take place to examine 'systems' and look for good control of processes and opportunities for process improvement.

3. APPLICABLE TO

This applies to all staff involved in clinical research sponsored/co-sponsored by UH, including, but not limited to: Chief Investigators, Principal Investigators, Research Fellows, Consultants, Statisticians, Clinical Trial Pharmacists, Research Managers, Research Nurses, Clinical Trial Practitioners, Allied Health Professionals, Trial co-ordinators/Managers, Clinical Studies Officers, Data Managers and Research Assistants.

4. RESPONSIBILITIES

4.1 The Sponsor:

- Is responsible for auditing research practice and assuring adherence to current legislation and guidelines.

4.2 The Auditor:

- On behalf of the CTSN, is responsible for performing routine audits of the organisation's clinical trials to ensure they are conducted in compliance with UK clinical trials regulation, protocol and SOPs.
- Must be qualified by training and experience to conduct audits properly.
- Must be independent to the research team/research systems.

4.3 Auditee/Inspected

- To cooperate with the audit/inspection requirements by agreeing to timelines, providing staffing and documentary evidence to permit the efficient auditing or inspection of the UH sponsored and hosted studies.
- The local PI will have responsibility for coordination of the Site / Study inspection. All the information relating to the particular study at this site has to be made available to the inspectors.

4.4 Personnel

- The Chief/Principal Investigator, research personnel, and personnel from other departments involved in the audit/inspection such as pharmacy, laboratory should be available to answer questions and to attend the final meeting before the auditor/Inspector leaves the site.

5. PROCEDURE

Please notify the CTSN (uhclinicaltrialsupportnetwork@herts.ac.uk) of any planned audits.

5.1. Internal Audits

5.1.1 Prior to an internal 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.

5.1.2 Preparation for the internal audit or inspection

The investigator, study team, Sponsor and CTSN 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 requested documentation is available.
- Any missing data or forms should be covered by appropriate signed and dated file notes.
- All required study team personnel should 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.

5.1.3 After the internal audit or inspection

The Auditor/Inspector will, according to their own guidelines inform the necessary persons of the result of the findings.

The CTSN (uhclinicaltrialsupportnetwork@herts.ac.uk) must receive a copy of any findings in order to send the completed report.

5.2. External Sponsor Audits

Audit by an external auditor/Regulatory Authority or external Sponsor of UH as a Sponsoring Organisation:

- The CTSN shall lead the preparation and arrangements for the audit.
- Developing and agreeing clear timelines with the external party and clearly communicating the requirements to UH, to individual Investigators and Research teams.

5.2.1 Prior to an external audit

In the case of an audit of an individual 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 (see ICH guidance),
- Study Documentation / Trial Master file / Site file,
- Patient's notes,
- Pharmacy and drug records, pharmacy agreements, documentation relating to doses / dispensing,
- Signed financial documents/receipts,

5.2.2. Preparation for an external audit

It is important that:

- Documents are up to date, reviewed and staff familiar with location and content.
- There is a clear Audit trail.
- Relevant documents bear dates and version numbers.
- A Tracking log is kept if documents are updated (evidence of distribution and receipt).
- Patient hospital notes should include up to date annotations, copy of consent form, General Practitioner (GP) letters, laboratory results, X-ray results etc. related to participation in the clinical trial.
- There are Pharmacy/drug accountability records.

5.3. MHRA Regulatory Inspection

5.3.1 Prior to an MHRA Regulatory Inspection

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. Payment for the audit will be arranged by the Sponsor. For co-sponsored trials the fee will be split equally between the sponsors.

A regulatory inspection is often notified, however there are exemptions if the Competent Authority has concerns for patient safety or grounds to suspect that improper practices are accruing at a site. Under these circumstances, the MHRA can perform triggered inspections for serious breaches. The Sponsor 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 necessary.

5.3.2. Preparation for Regulatory Audit or Inspection

- All data, 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.

5.3.3. After the Regulatory Audit or Inspection

- The Lead Inspector will send a written report of findings once the last site inspection (if applicable) has taken place.
- Organisation must provide a Corrective Action & Preventative Action Plan (CAPA) to address these findings by the data specified by the MHRA.

- Once the CAPA plan is accepted, the organisation will receive the MHRA GCP Inspection Statement.

6. RELATED DOCUMENTS

- ICH Harmonised Tripartite guideline for Good Clinical Practice (1996)
- gSOP-06 TMF/Site File
- gSOP-28 Management of Source Data
- gSOP-41 CRF Completion

7. APPENDICS

- Appendix 1 – Definitions

8. VERSION HISTORY/REVISIONS

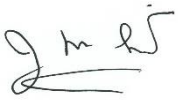
Version Number	Effective Date	Reason for Change
2.0	**10/08/22**	Three-year review

9. AUTHORSHIP & APPROVAL

Author Megan Smith

Signature  **Date 25/07/22**

Pro Vice-Chancellor (Research & Enterprise) Approval
Professor J M Senior

Signature  **Date 08/08/22**

10. AGREEMENT

Please detach and retain in your training files

I have read and understood the contents and requirements of this SOP (gSOP-23-02) and accept to follow by UH policies in implementing it.

Recipient

Signature: ……..…...……..…….……Date:.....…….……..

Name & Position: ……..……..

Appendix 1 – DEFINITIONS

Case Record Form (CRF) - a printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject".

Chief Investigator (CI) - A Registered Physician, Dentist, Pharmacist or Registered Nurse who has overall responsibility for the conduct of the trial.

Clinical Trial - A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or control) to evaluate the effects of those interventions on health outcomes.

Clinical Trial of Investigational Medicinal Product (CTIMP)
A study that looks at the safety or efficacy of a medicine/food stuff/placebo in humans as defined by the Medicines for Human Use Regulations (2004).

Good Clinical Practice (GCP) - as defined in the Regulations.

International Conference on Harmonisation (ICH) – Produced a series of guidelines in 1996, E6 being the guideline on Good Clinical Practice, otherwise known as (ICH-GCP).

Investigational Medicinal Products (IMP) - means a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial. This includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -

- used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,
- used for an indication not included in the summary of product characteristics under the authorisation for that product, or
- used to gain further information about the form of that product as authorised under the authorisation

Principal Investigator (PI) - A Registered Physician, Dentist, Pharmacist or Registered Nurse who has responsibility for the conduct of the trial at a host site.

The Medicines & Healthcare products Regulatory Agency (MHRA) - UK Competent Authority responsible for regulation of clinical trials.

The Regulations - Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.