Sheffield Teaching Hospitals NHS
NHS Foundation Trust

Research Department

STANDARD OPERATING PROCEDURE

For Cause Audit (Internal)

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Approved by	*Research Manager*

Standard Operating Procedure: STH Research Department
For Cause Audit

This Standard Operating Procedure (SOP) has been produced in accordance with ICH-GCP, the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent Amendments and the Department of Health Research Governance Framework (2005). The SOP outlines the processes involved when the STH Research Department undertakes an internal *for cause* audit of a research project and should be read in conjunction with the Research Department's SOPs for Misconduct and Fraud and, Non Compliance and Management of Serious Breaches of GCP or the Trial Protocol.

Background

As a host organisation and Sponsor of clinical research, STH is obliged to exercise an independent audit function to ensure that the research undertaken in STH is conducted in accordance with ICH-GCP and all applicable Regulations.

Routine audits are conducted by the STH Research Department from time to time to meet with the requirements of the Department of Health Research Governance Framework. However, it may also be necessary to conduct a *for cause* audit where non-compliance with ICH-GCP or applicable Regulations is suspected. For cause audits may be conducted at the request of the Medical Director, Director of R&D or Clinical Research Office (CRO) Director.

Definition

According to ICH-GCP, 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 SOPs, GCP and the applicable regulatory requirements"

Purpose

A *'for cause'* audit is conducted following a critical incident. The following are examples of when a *for cause* audit may be conducted:

- When there is reason to believe that a trial is not being conducted in accordance with the Regulations or accordance with the approved study protocol.
- At the request of a senior member of staff as part of an official STH investigation, for example as part of an investigation into misconduct and/or fraud.
- Following occurrence of a Serious Adverse Event (SAE) or other clinical incident when it is thought patient safety may be at risk as a result of the trial.

A *for cause* audit may be requested for any research project based at STH whether involving human subjects recruited via STH or their data or tissue.

Process

A *for cause* audit is an in depth examination of the components of a research project including but not limited to all records and documents, observations and processes. The audit may involve interviews with the principal investigator, co-investigators and collaborators.

The following may be inspected during a *for cause* audit:

- **Essential documentation**
  See ICH-GCP section 8 for list of essential documentation
- **Processes**
  For example the process of taking informed consent, reporting SAEs, tissue sample processing
- **Equipment**
  equipment used in a study may be inspected for maintenance and calibration; this includes freezers, medical equipment and computing equipment used for data storage
- **Personnel**

The qualification/experience of research staff may be examined through scrutiny of CVs, training records and conduct of interviews with the auditors

Procedures

Preparing for the Audit

1. Medical Director, Director of R&D, CRO Director requests a *for cause* audit in response to a critical incident and informs the Research Manager and QA Lead.
2. The Research Manager liaises with the QA Lead and/or Director of R&D to determine the scope and format of the audit and the need for formal interviews with any relevant parties.
3. The Research Manager or QA Lead identifies personnel to undertake the audit. The audit team will usually be the Researcher Co-ordinator in whose Directorate the audit is taking place accompanied by the QA Lead or another Research Department Coordinator.
4. The R&D Coordinator records the intention to undertake a *for cause* audit of a study on the Research Department Database.
5. The Director of R&D or Research Manager notifies the principal investigator in writing of the decision to undertake a *for cause* audit of a research project, copying in the Director of R&D, CRO Director, Medical Director and Clinical Director of the relevant Directorate.
6. The Research Department may request that the Investigator Site File is forwarded to the Research Department pending the audit.
7. The R&D Coordinator arranges a date for the audit and sends a letter to the PI detailing the arrangements for the audit, the purpose of the audit,and the format of the audit
   7.1. The letter confirms the documentation that the PI will need to make available for review. This will include the Investigator Site File and completed case report forms and may include the patient medical notes. If patient notes are to be examined the R&D Coordinator will request that medical notes for all patients recruited to the study are made available for the audit unless a very large number of patients has been recruited in which case a decision on what proportion of subjects' medical notes should be made available will be made on a case by case basis. In this case, where possible, the R&D Coordinator should specify (by study ID number) which subject notes should be made available for review
   7.2. The letter requests that the PI ensures:
      7.2.1. A suitable meeting room is booked for the duration of the audit
      7.2.2. All key personnel working on the study are notified that an audit is to take place
      7.2.3. Where requested that the PI and other key personnel will be available to discuss aspects of the research with the auditors. Separate interviews may be arranged where interviews are requested but cannot be scheduled to coincide with the audit.
      7.2.4. The Investigator Site File (including, if applicable, Case Reports Forms) and, where applicable, patient medical notes or other source data are made available to the auditors
      7.2.5. All relevant support departments involved in the study (for example Pharmacy, Laboratory Medicine, Medical Imaging) are notified of the audit
8. The Research Co-ordinator prepares for the audit following the procedure described in SOP B131.

During the Audit

9. The following personnel should, wherever possible, be available during the conduct of the audit to answer any queries the auditors may have:
   9.1. Local Principal investigator
   9.2. Study co-investigators
   9.3. Research Nurse/Study Site Coordinator
   9.4. Support Department personnel (eg. Pharmacy)
10. The auditors explain to the investigator or the available members of the research team the purpose and plan for the audit
11. The auditors review the essential documentation following the procedure described in SOP B131.
    11.1. Essential documentation that may be inspected during the audit includes but is not limited to:
       11.1.1. Investigator Site File
       11.1.2. Case Report Forms (CRFs)
       11.1.3. Patient Medical Notes

11.1.4. Pharmacy and Drug Records *(Where the trial involves an IMP);* for all IMP studies the auditors will visit Pharmacy. All essential pharmacy documentation should be made available for review. This includes:
- 11.1.4.1. drug accountability record
- 11.1.4.2. drug administration log
- 11.1.4.3. patient compliance record
- 11.1.4.4. drug storage record
- 11.1.4.5. drug shipment record
- 11.1.4.6. code break procedures
- 11.1.4.7. delegation log

12. The Research Department auditors may visit other relevant support departments as necessary.
13. The Research Department auditors meet with the PI and/or other member(s) of the research team at the end of the audit if appropriate to discuss preliminary findings and to explain the next stages of the audit process

Post Audit

14. The Research Department auditors prepare an audit report and summary following the audit. The audit report will be prepared as described in SOP B131. The summary report covers
    - 14.1. The purpose of the audit
    - 14.2. Key findings from the audit
    - 14.3. Actions for the Principal investigator/research team
    - 14.4. Other recommendations
15. The Research Department auditors circulate the final report and summary to the QA Lead, Research Manager, CRO Director and Director of R&D who review the findings and the recommendations and actions and amend accordingly. The summary report is reported up to the Medical Director. The summary report is forwarded to University Personnel as necessary.
16. The auditors send the PI a copy of the finalised audit report and summary. Action is undertaken in line with the Research Department SOP on Non Compliance and Management of Serious Breaches. Should the investigator have any issues with the content of the report they can contact the Research Department to discuss the outcome of the audit.
17. The Research Department may request a meeting with the PI to discuss the audit findings and recommendations if appropriate. The meeting involves the Research Department auditors, QA Lead, Research Manager and/or Director of R&D or Medical Director as appropriate.
18. The PI carries out the actions and recommendations requested in the audit report and completes the Investigator Actions and Comments column against each finding to confirm the action taken. The PI returns the completed audit report to the Research Department auditors.
19. The Research Department auditors review the response received from the investigator and if necessary a follow-up visit is arranged depending on the severity of the findings of the initial audit and the quality of the investigators remedial action plan.
20. The Research Co-ordinator files a copy of the audit report and investigator response in the R&D master file.
21. The Research Co-ordinator updates the Research Department Database with the outcome of the audit.

Associated Documents

#	Document	Research Department Network Location	Website	Database	Who
1	Audit and Monitoring template	S:\General\!_Working Drafts\Research Governance\Monitoring documents	No	N/A	EW/AL