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Audit of Research Systems

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Version	Date	Reason for Change
1.0	10th Nov 2016	Addition of external audits

1.0 Purpose

This SOP describes the procedure for carrying out internal and external audits of research systems within BSUH. This SOP specifically describes the processes for selecting topics to be audited, the procedures for carrying out audits and reporting audit findings. It also describes the requirements for auditees to respond to audit reports and implement corrective actions where applicable.

2.0 Introduction

In compliance with the 13th principle of International Conference on Harmonisation-Good Clinical Practice (ICH-GCP), BSUH has implemented a system of Quality

Assurance (QA). As part of the implementation of this QA system, audits are performed.

This SOP does not cover monitoring of clinical trials.

Abbreviations and Definitions:

Term	Description
Audit	A systematic, independent and documented process for obtaining audit evidence (records, statements of fact or other information which are relevant and verifiable) and evaluating it objectively to determine the extent to which the audit criteria (set of policies, procedures or requirements used as a reference) are fulfilled. For clinical trials: 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), GCP and the applicable regulatory requirement(s).
Auditor	For the purpose of this SOP: the person responsible for setting up and executing the audit plan. This role may be taken on by a Quality Assurance (QA) Manager or other independent staff member.
Audit Plan	An audit plan describes the aims and objectives of the audit, the scope, resources required, audit methodology, audit sites and timing of the audit. The audit plan also describes how the audit will be reported.
Audit Programme	A description of the specific audit(s) planned for a specific time frame, which is agreed upon by the relevant oversight committee.
Audit Report	A written evaluation by the auditor of the results of the audit.
Corrective and preventive action (CAPA) plan	A plan produced by the auditee detailing the actions to be taken following an audit to correct the issues found and to prevent the issues from reoccurring.
GXP	Refers to Good Clinical Practice (GCP), Good Laboratory Practice (GLP) and/or Good Manufacturing Practice (GMP).

3.0 Responsibilities

Research Governance and Quality Assurance Committee (RGQAC)

- Review and approval of audit programme
- Review of audit plans
- Review of audit reports and CAPAs

Quality Assurance (QA) Manager

- Producing and managing the delivery of the audit programme
- Assigning an auditor to each audit
- Reviewing audit plans
- Reviewing audit reports as applicable
- Ensuring that the findings are reported and escalated in compliance with R&D processes

Auditor

- Providing input in the audit programme where requested
- Developing audit plans
- Performing audits
- Writing audit reports
- Reviewing the auditees' responses to the audit report to ensure that the appropriate CAPA plans have been put in place
- Maintaining relevant documentation of the audit process

Auditee

- Providing evidence of compliance to the regulations, standards and/or guidelines selected to be audited against upon request
- Supporting the practical logistics of an audit
- Writing a response report to any audit findings requiring a response, incorporating a robust CAPA plan

Head of R&D

- To act as facilitator, if the appropriate CAPA cannot be agreed between the auditor and auditee.

All BSUH staff and those delegated to work on BSUH sponsored trials are required to cooperate with the audit programme.

4.0 Procedure

4.1 Audit Programme

The Quality Assurance (QA) Manager will prepare and circulate the audit programme for the forthcoming year to relevant staff annually. Topics to be audited will be identified via risk-based strategies, considering the findings of previous monitoring visits, audits and/or inspections, legislation changes, SOP updates and as a result of other issues that have been identified in the previous year.

The annual audit programme will be signed off by the Research Governance & Quality Assurance Committee (RGQAC) annually. The audit programme may be periodically amended if audits are triggered due to non-compliance and/or safety issues that are tabled at the RGQAC.

The outcome audit programme will be reported to the RGQAC annually at the end of the audit programme period.

4.2 Audits of Clinical Trials

The audit programme for clinical trials (including Clinical Trials of Investigative Medicinal Products) will include the auditing of the following topics against applicable regulations and international standards and is scheduled on a rolling basis:

- Data management (including statistics)
- IMP management (for CTIMPs)
- IT system management
- Pharmacovigilance
- Quality management systems
- Sample management
- Serious Breach reporting
- Training
- Trial quality management

4.3 Audit Plans

An audit plan will be written prior to each audit. This plan will define the objectives, scope, auditees, resources required, methodology, timelines for generating the audit report, and the key stakeholders who should receive the audit report.

The audit plan will be provided to the auditee at least 30 days before the planned audit date. The audit plan must be reviewed by the QA Manager or delegate prior to being sent to the auditee. Where the QA Manager writes the audit plan it is recommended to have the audit plan reviewed by another suitably qualified individual.

4.4 Performing the Audit

The auditor is responsible for carrying out the audit according to the agreed audit plan using document review and interviews. Prior to the audit, the auditee may be requested to provide documentation to allow to auditor to prepare for the audit.

At the audit visit, the auditor will escalate significant issues to applicable staff where required. It is recommended that the auditor meets with the auditee(s) to discuss the findings of the audit visit and CAPA preparation where required.

4.4.1 Categorisation of non-conformances

Non-conformances are categorised as:

Critical Findings

Where evidence exists that significant and unjustified departures from applicable legislative requirements has occurred with evidence that

- The safety, wellbeing or confidentiality of trials subjects either have been or have significant potential to be jeopardised and or
- The clinical trial data are unreliable and/or
- There are a number of major non-compliances across areas of responsibility, indicating a systematic quality assurance failure and/or
- Where inappropriate insufficient or untimely corrective action has taken place regarding previously reported major non-compliance

Major Findings

- A non-critical finding where evidence exists that a significant and unjustified departure from applicable legislative requirements has occurred that may have not developed into a critical issue, but may have the potential to do so unless addressed and/or
- Where evidence exists that a number of departures from applicable legislative requirements and/or established GxP guidelines have occurred within a single area of responsibility, indicating a systematic quality assurance failure

For both Major and Critical findings, Corrective and Preventive Actions (CAPA) are required.

Minor Findings

Where evidence exists that a departure from the following has occurred but it is neither critical nor major:

- Applicable legislative requirements and/or

- Established GxP guidelines
- Procedural requirements

In summary, minor findings are not systematic and do not jeopardise the safety if subjects or the integrity of the data. For all minor findings, corrective actions are required but preventive actions are optional.

4.5 Writing the audit report and Corrective and Preventative Actions CAPAs

The auditor will ensure that the auditee is informed of the timeframes surrounding the generation of the audit report.
The audit report will be reviewed by the QA Manager or delegate. Where the QA Manager has completed the audit, it is recommended that the audit report is reviewed by another suitably qualified individual. The auditor will ensure that the report is sent to the auditee within 10 working days. If non-conformances are identified, the auditor will list each finding and request that for each a CAPA plan is prepared by the auditee within 30 days of receipt of the report and the report returned to the auditor.

CAPAs will be tracked using the CAPA register. This will be reviewed on a regular basis by the QA Manager to ensure that CAPA reports have been received for all findings and the reports closed.

4.6 Closing the Audit

Once the auditee has returned the audit report with completed CAPA plans, the auditor will review and if satisfied, confirm acceptance of the CAPAs. The report will also be reviewed by the RGQAC.

Once the report is fully signed the audit report will be filed in the R&D Audit file, and the audit will be considered as closed.

4.7 Audit Certificate

Where a specific trial(s) has been audited, the auditor will prepare an audit certificate. This certificate should be filed in the Trial Master File. The audit certificate will contain the following information:

- Trial name
- Auditee name
- Name(s) and job title of the auditor
- Date of issuing the audit certificate
- Contents of the audit (e.g., subjects and date of the audit, and date of issuing the audit report)

4.8 Re-Audit

If necessary, a re-audit may be recommended by RGQAC to determine if the CAPA plans have been effective.

If the CAPA plans have not been effective, outstanding issues will be escalated to RGQAC for further action.

5.0 Training

This is a 'read and understand' SOP. To evidence that you have read and understood this SOP, please complete your SOP Training Matrix.

Please note that the R&D department discourages the retention of hard copies of SOPs and can only guarantee that the most up-to-date version is on the Trust website.

6.0 Cross Reference SOPs

SOP/RD/005 Monitoring of Research Projects

7.0 References

Section 5.19 of ICH Harmonised Tripartite Guideline For Good Clinical Practice E6

The Global Guideline for GCP Audit http://ichgcp.net/the-global-guideline-for-gcp-audit