Plymouth Research and Development

NHS University Hospitals Plymouth NHS Trust

Standard Operating Procedure

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Title:	Externally-led audits and regulatory inspection		
Approver		Document No:	QA5
Name:	Chris Rollinson	Version No:	3.0
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1. Purpose

To describe the procedures necessary to prepare, host and participate in an externally-led audit or regulatory inspection at the Trust. Both audits and inspections take place to examine 'systems' and look for good control of processes and opportunities for process improvement. The definition of an audit and inspection can be found in Appendix 1.

2. Scope

This Standard Operating Procedure relates to:

a) hosted studies that may be audited by an independent agency on behalf of the study Sponsor

b) where the Trust is named as Sponsor for Clinical Trials of Investigational Medicinal Products (CTIMPs) and medical devices subject to Good Clinical Practice (GCP) inspection by the Medicines and Healthcare products Regulatory Agency (MHRA)

c) where the Trust is a host site of a CTIMP or device trial, the MHRA may inspect the conduct of the trial by the investigator and the role of the sponsor in overseeing the trial

Although the MHRA is the UK Competent Authority (CA), other CAs i.e. US Food and Drug Administration (FDA) may select a UK site for inspection. The same process detailed in this SOP may be followed.

3. Responsibilities

Trust will be responsible for paying the MHRA inspection fee.

Research Governance Manager will liaise with the MHRA, research staff, supporting services (i.e. IM&T, medical records, Pharmacy) on regulatory inspections and produce an Inspection Dossier.

Assistant Clinical Trials Manager will support the RGM and deputise in their absence.

All research and non-research personnel involved in the audit/ inspection should be available to answer questions and to attend the opening/ closing meeting before the auditor/ inspector leaves the site.

4. Documents needed for this SOP

- MHRA Inspection templates are available here:
    - GCP inspection dossier template
    - GCP inspection dossier clinical trial spreadsheet
    - GCP inspection dossier checklist
    - CAPA guidance for formulating responses to GCP inspection findings

5. Related documents

- SOP Q3 Audit

6. Acronyms

CA: Competent Authority

CAPA: Corrective and Preventative Actions

CI: Chief Investigator

CRO: Contract Research Organisation

CTIMP: Clinical Trials of Investigational Medicinal Products

CTU: Clinical Trials Unit

FDA: US Food and Drug Administration

GCP: Good Clinical Practice

IGA: Inspection Action Group

MHRA: Medicines and Healthcare products Regulatory Agency

PI: Principal Investigator

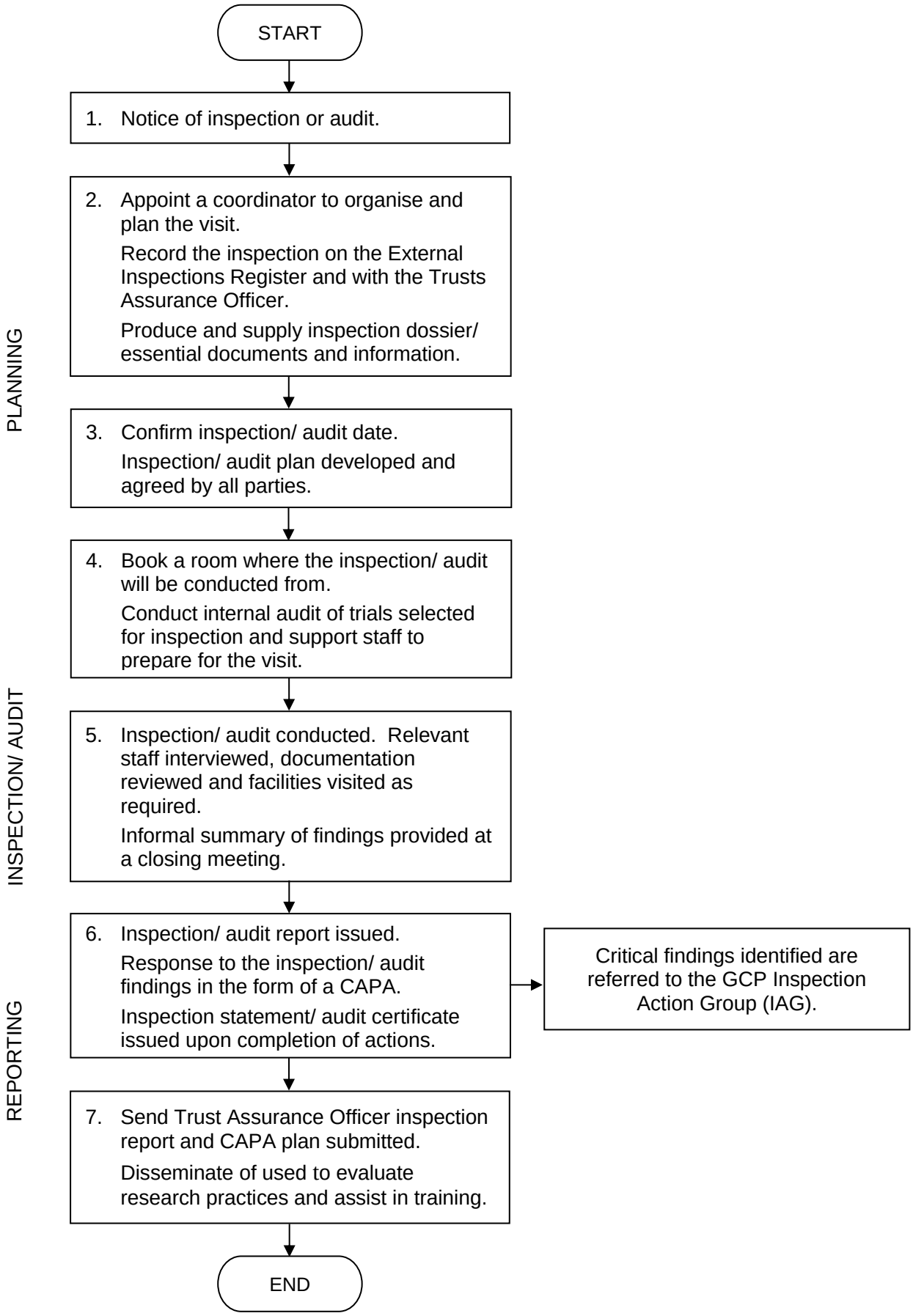
R&D: Research and Development

RMG: Research Governance Manager

SC: Study Coordinator

SOP: Standard Operating Procedure

7. Process map(s)/ flow chart(s)



8. Procedure

Step	Action	Responsibility
1	Advance notice of an audit or inspection received by the Trust: • The Chief Investigator (CI)/ Principal Investigator (PI) and Study Coordinator (SC) will normally be informed of a planned audit for a hosted study. • A regulatory inspection is often notified, usually to the Research and Development (R&D) Operations Director, however, inspectors have a legal right of entry to inspect premises without notification if an inspection is "triggered" i.e. the CA has concerns for patient safety or grounds to suspect improper practices. Notification of the intended audit or inspection should be disseminated to the RGM (or their deputy) and all staff involved in the trial(s), including third parties i.e. Clinical Trials Unit (CTU).	R&D Operations Manager, RGM, CI/PI and SC.
2	Appoint a coordinator to organise and plan the visit. For an audit this will be facilitated by the SC and for an inspection, the RGM or their deputy will be responsible. Record the inspection on the External Inspections Register and with the Trusts Assurance Officer. Produce an inspection dossier and clinical trials spreadsheet to the MHRA within 30 days of the advance notice. The dossier should include: • a list of clinical trials • organisation charts • SOP lists • contact details • overview of facilities • service providers • clinical trials activities For an audit, the SC should supply the auditor with essential documents and information identified as needed in the preparation of the audit.	RGM and SC.
3	Confirmation of inspection or audit date will be supplied including details of the inspection or audit team, duration and practical aspects of the visit. An inspection or audit visit can last three days. Ahead of the visit, a plan will be developed to outline the activities to be covered during the inspection or audit and supplied to the coordinator.	Auditor and inspector.

Step	Action	Responsibility
4	Book a meeting room for the auditors or inspectors for the duration of their visit in which to conduct staff interviews and review documents. Conduct an internal audit of the trial(s) selected for regulatory inspection, as described in SOP Q3 Audit. Support staff to prepare for the visit but at a minimum all staff should: • refresh knowledge of current regulations and standards • have awareness of own responsibilities and/ or delegated duties within the trial • ensure training record(s), CVs and job descriptions are up to date • check essential documents (refer to Appendix 1) including electronic documents are up to date, correctly filed and are readily accessible or easily retrievable	RGM, SC and all staff involved in the audit/ inspection.
5	During the visit, the inspection or audit team will hold an opening meeting, interview sessions with staff, review documents (including the Trial Master File (TMF) for Trust sponsored studies) and may visit facilities such as data management units, archives, pharmacy and laboratories. Supply the inspector or auditor with any additional documentation on request. Findings identified during the visit will be summarised by the inspector or auditor at a closing meeting, giving staff opportunity to correct any misunderstandings.	RGM and all staff involved in the audit/ inspection.
6	Deficiencies found will be detailed in a written report and graded at 3 levels - critical, major and other as defined in Appendix 1. Critical inspection findings are referred to the GCP Inspection Action Group (IAG) who decides on the actions to be taken. Response to the findings must be supplied to the auditor or inspector, along with a Corrective and Preventative Action (CAPA) plan. It may be necessary to supply periodic reports on the progress of proposed CAPAs. Acceptability of the response will be assessed by the audit or inspection team. Further information may be requested. Upon resolution of the findings a closing email will be sent, along with an inspection statement or audit certificate.	Auditor, inspector, RGM, and SC.

Step	Action	Responsibility
7	Notify the Trust Assurance Officer with the initial inspection report and subsequent CAPA plan submitted. Dissemination of audit or inspection findings should be used to evaluate research practices and assist in staff training.	RGM.

9. Changes from last revision

SOP template change and merge of SOP T1 Researcher Audit Guidance with QA5.

Appendix 1: Definitions

Audit	The purpose of a sponsor's audit, which is independent of and separate from routine monitoring or quality control functions, should be to evaluate trial conduct and compliance with the protocol, SOPs, GCP, and the applicable regulatory requirements. E6(R2) 5.19.1
Essential Documents	Essential Documents are those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements. E6(R2) 8.1
Graded Findings: Critical	a) Where evidence exists that significant and unjustified departure(s) from applicable legislative requirements has occurred with evidence that: • the rights, safety or well-being of trial subjects either has been or has significant potential to be jeopardised, and/or • the clinical trial data are unreliable and/or • there are a number of Major non-compliances (defined in (d) and (e)) across areas of responsibility, indicating a systematic quality assurance failure, and/or b) Where inappropriate, insufficient or untimely corrective action has taken place regarding previously reported Major non-compliances (defined in (d) and (e)) c) Where provision of the TMF does not comply with Regulation 31A 1-3, as the TMF is not readily available or accessible, or the TMF is incomplete to such an extent that it cannot form the basis of inspection and therefore impedes or obstructs inspectors carrying out their duties in verifying compliance with the Regulations
Major	d) A non-critical finding where evidence exists that a significant and unjustified departure from applicable legislative requirements has occurred that may not have developed into a critical issue, but may have the potential to do so unless addressed, and/or e) Where evidence exists that a number of departures from applicable legislative requirements and/or established GCP guidelines have occurred within a single area of responsibility, indicating a systematic quality assurance failure.
Other	f) Where evidence exists that a departure from applicable legislative requirements and/or established GCP guidelines and/or procedural requirement and/or good clinical practice has occurred, but it is neither Critical nor Major.
Inspection	The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organisation's (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies). E6(R2) 1.29