STANDARD OPERATING PROCEDURE 25

Auditing of Research Studies in WCTU

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Revision Chronology:	Effective date:	Reason for change:
Version 3.0	16 April 2024	Biennial review: Addition of clearer escalation strategy. Minor clarifications throughout.
Version 2.0	8 April 2022	Biennial review: Change to new format. Change of title. Updates to QA team procedures.
Version 1.5	23 December 2019	Change to new format. Updates to QA team procedures. Addition of new audit types.
Version 1.4	15 July 2016	Minor changes to text. Change to new format.
Version 1.3	9 December 2013	Addition of process to escalate an unsatisfactory response to an audit report and process for triggered audits.
Version 1.2	3 September 2012	Format change. Amended process to inform WCTU which WMS trials require audit.
Version 1.1	12 May 2010	Change WMSCTU to WCTU. Addition of section references for ICH and MRC GCP definition of audit. Amendment to list of report recipients.
Version 1.0	May 2008	

STANDARD OPERATING PROCEDURE 25
Auditing of Research Studies in WCTU

1. Purpose and Scope

This Standard Operating Procedure (SOP) describes the audit procedures for WCTU where they have been delegated to undertake audits on behalf of the sponsoring organisation. This SOP specifically describes the processes for WCTU managed studies, including selection of studies to be audited, which types of audits would be required, the procedures for carrying out different types of audits and reporting audit findings. It also describes the requirements for auditees to respond to audit reports and implement corrective actions.

This SOP is applicable to all staff involved in the conduct of research studies managed by WCTU. For trials and other research studies sponsored by the University of Warwick, that are managed outside of WCTU, plans for auditing will be determined on a study-by-study basis and communicated to researchers by the sponsor's office.

2. Definitions

Audit process	A systematic and independent examination of study-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, sponsors SOPs, GCP and the applicable regulatory requirements. (ICH GCP section 1.6)
Auditee	A person or organisation that is audited.
Auditor	A person authorised to undertake audits to assess compliance.
Trial Master File/ Document audits	A review of trial-specific essential documents or system documentation (e.g., computer system validation package, protocols)
System audits	Looking at the functionality of complete systems (e.g., pharmacovigilance, data management)
Process audits	Looking at the performance of a specific process within systems (e.g., expectedness assessments in safety reporting, data query process)
Vendor audits	Assessment of external service providers (e.g., clinical trial drug supply companies, courier services).

3. Background

Sponsor organisations (institutions that take responsibility for the initiation, management and/or financing of a clinical trial/research study), are legally responsible for auditing research practice and assuring adherence to current legislation and guidelines. As such, it is necessary to audit research for which either the University is the lead sponsor, where a co-sponsorship agreement is in place which delegates audit activities to WCTU, or where WCTU are managing a trial on behalf of an external sponsor, against the standards of the UK Policy Framework for Health & Social Care Research 2017, the Medicines for Human Use (Clinical Trials) Regulations 2004, where applicable, the approved trial documentation, UK laws (e.g. UK GDPR) and against the quality systems of GCP intrinsic to the regulations.

The purpose of an internal audit is to:

- Ensure participants' rights and welfare are being adequately protected
- Assist researchers with compliance to regulatory requirements and University policy
- Assure regulatory compliance, where applicable
- To assess whether staff working on the trial are appropriately trained, are clear about their role and are working to GCP, the protocol and standard operating procedures (SOPs) or other key study documents
- Prepare researchers for potential future external regulatory inspections
- Aid in identifying and correcting problem areas and provide suggestions to improve quality.

4. Procedure

4.1 Responsibilities

QA Manager	• Responsible for ensuring that audits of research studies and randomised clinical trials as described in the 'Definitions' section above are planned and completed in accordance with this SOP. • Provide audit reports to research teams • Escalate outstanding issues to WCTU Governance Committee
Senior Project Manager (SPM)	• Maintain oversight of audit activity on the portfolio • Support prioritisation of audit resolution
Chief Investigators (CI)	• Must permit auditing by the sponsor's representatives and are responsible for ensuring responses to reports of findings are returned, and actions required by the audit are completed within the stipulated timeframe. The CI may delegate completion of actions and/or sending responses to an appropriate team member.
WCTU Governance Committee	• Receive system or process audit reports • Receive serious breach reports from study audits • Oversight of timely completion of audit actions • Follow up on escalated incomplete audit responses
Warwick Sponsorship and Oversight Committee	• Receive copies of audit reports from Warwick sponsored studies

4.2 When?

The WCTU QA Managers will schedule audits as detailed in the annual audit plan. The plan is generated at the beginning of each year using an audit scheduling tool, which considers risk levels and prioritises higher risk studies and processes.

Where there is evidence of increased risks to a study or process, additional audits may be triggered outside of the annual plan.

Trials, processes, or vendors may also be audited on a voluntary basis (upon request or where there is a suspicion of non-compliance to regulations).

4.3 How?

4.3.1 Notification of Audit

A member of the QA team will notify the relevant personnel when an audit is due, in line with the annual audit plan or where an audit has been triggered due to concerns.

For all audits, the auditees will be informed, and a mutually convenient date agreed.

The audit notification will outline the scope and objectives of the audit, provide a list of the documents or access to databases and electronic files that will be required and state the estimated time the audit is expected to take. The notification will also identify the people who may be required and how findings will be reported back.

4.3.2 Conduct of Audit

- The audit will commence on the agreed date and information will usually be assessed and recorded using template report checklists tailored to the audit type. If on the day of the proposed audit, the auditee or auditor are unavailable, the audit may be postponed until another mutually convenient date can be found.
- Any questions that are identified at the time of the audit may be raised with the auditee or delegate.
- Every attempt will be made to complete the audit within the stipulated timeframe, but where additional time is required, this should be allowed by the auditee.
- Where possible the auditor should arrange to meet with the auditee after completion to summarise the nature of the findings and identify any areas of priority. SPMs should attend this meeting where possible to facilitate conversations around risk and priorities.

4.3.3 Written report of audit findings

- The QA Manager (or delegate) should send the auditee a written report within 28 calendar days identifying any areas of non-compliance and suggested actions to correct the non-compliance or to prevent recurrence.
- The report will include a table of the findings categorised by the grade of the finding detailed below.
- For system or process audits which look across multiple studies, the written report will be provided to the WCTU Governance Committee with recommendations for improvements.
- Findings from system/process audits relevant to a specific study, will be reported to the team concerned.
- For Warwick sponsored studies, information on completed audits will also be provided to the University's Sponsorship and Oversight Committee via WCTU's standard activity report.
- Where an audit has been undertaken by, or on behalf of, an external Sponsor or the organisation co-sponsoring the study, a copy of the report should be forwarded to the relevant sponsors' organisation by the auditor.

Table 1: Categories of audit findings and relevant examples

Serious Breach*:	• Where evidence exists that the safety, wellbeing, rights or confidentiality of trial participants has been (or has significant potential to be) jeopardised. • Where approval of the trial has not been sought or granted from one or more regulatory body (e.g., Ethics committee, MHRA) but the trial has commenced regardless.

	• Where procedures not included on the consent form are being performed or new procedures have been introduced but participants have not been asked to re-consent. • Where significant amendments have been made to the protocol but no new request for approval has been submitted. • Critical checks on data relating to safety and compliance are not being carried out. • Failure to take appropriate steps to protect personal data. • Where reason has been found to cast serious doubt upon the accuracy and/or credibility of trial data.
Violation*:	• Where there has been a significant and unjustified departure from regulations or GCP guidelines e.g., failure to provide participants with a copy of their consent form or Participant Information Sheet (PIS). • Where there have been several minor departures from the regulations or GCP, suggesting a systematic quality assurance failure.
Deviation*:	• Findings which demonstrate that no definite document management systems are in place. • Where there has been a failure by trial staff to inform the relevant authorities of amendments to start/stop dates or study specific documents. • Poor version control. • Data Management Plan does not reflect actual processes.
Observation:	Any minor issues identified during the audit which do not fit the criteria described above. For example, an essential document which is present but has been mis-filed, old versions of documents not marked as 'superseded' etc.

**for definitions, see SOP 31 'Deviations, Violations, Misconduct and Serious Breaches of GCP and/or Trial Protocol'.*

If any findings potentially constitute a serious breach, actions should be taken in line with SOP 31 'Deviations, Violations, Misconduct and Serious Breaches of GCP and/or Trial Protocol'.

4.3.4 Response to written report, follow up and escalation

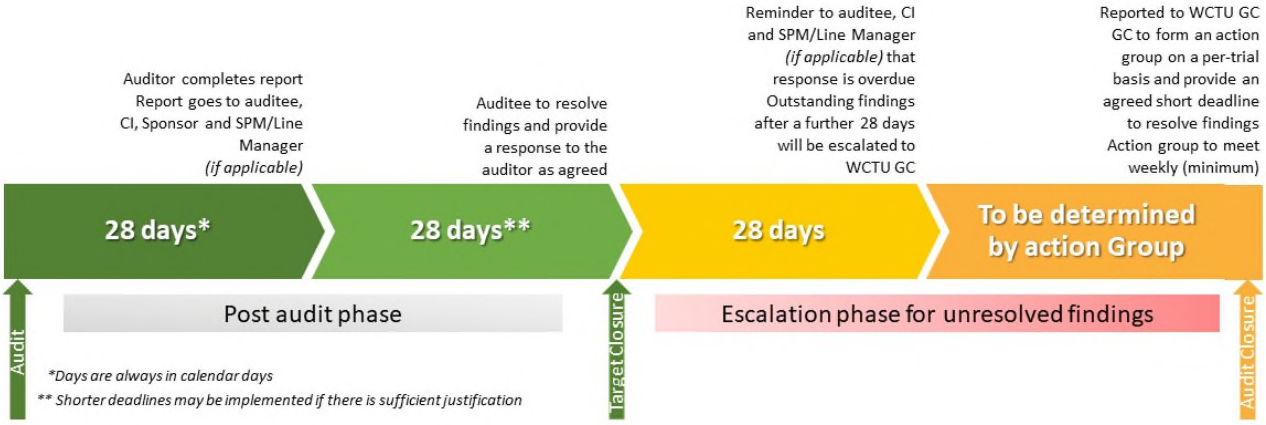
For audits relating to a particular study, it is the task of the auditee to respond to any findings on behalf of the CI. It remains the responsibility of the CI to ensure the required actions are taken to remedy any issues or non-compliances detailed in the report within the timelines indicated.

For system or process audits which look at multiple studies across the portfolio, relevant actions will be assigned to a member of the study team who will coordinate the response on behalf of the CI, who will be responsible for ensuring the required actions are completed.

Oversight of timely completion of audit actions should be provided by the WCTU Governance Committee and, on a per-study basis, oversight of audit status is expected at Trial Management Group Meetings. The expected timelines and escalation for findings that remain unresolved is outlined below.

The audit will be closed by the auditor following receipt of confirmation from the auditee (or delegate) that all required actions have been completed. The auditee may need to provide evidence if requested.

Figure 1: Audit timelines and escalation for unresolved findings



4.3.5 Triggered audits

Where information comes to light regarding any allegations or evidence of systematic non-compliance with a trial/study protocol, the principles of GCP or regulatory requirements, or where a 'trigger' as specified in the study's Monitoring Plan occurs, a triggered or 'for cause' audit will be instigated.

This could be at either WCTU, vendor site, or due to issues identified at a study recruiting site e.g., data anomalies or a higher frequency of errors, protocol violations, persistently late reporting of Serious Adverse Events (SAEs) etc.

The procedure for these audits and subsequent escalation (as necessary) will follow that described above, but with a particular focus on the activity or issue causing concern. A full report will be issued and sent to the auditee and the Principal Investigator (PI) at the site if applicable.

List of abbreviations:

CI	Chief Investigator
GC	Governance Committee
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
ICH	International Conference on Harmonisation
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
PIS	Patient Information Sheet
QA	Quality Assurance
R&IS	Research & Impact Services
SAE	Serious Adverse Event

SOP	Standard Operating Procedure
SPM	Senior Project Manager
WCTU	Warwick Clinical Trials Unit