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Research Governance and Integrity Team Audit SOP

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Version 2.0	19 Jun 2008	Annual review
Version 3.0	08 Feb 2010	Formation of Joint Research Office
Version 4.0	01 Jul 2011	Annual Review
Version 5.0	30 Nov 2012	Annual Review
Version 6.0	18 Feb 2015	Scheduled Review
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Version 8.0	14 Sep 2018	Updated Audit Procedure
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Version 10.0	11 Oct 2021	New template associated with the SOP
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1. PURPOSE

A audit is a process of verifying that a research project meets the ethical and scientific standards for Good Clinical Practice (GCP). A GCP audit can assess the compliance of the investigators, site personnel, sponsors, CROs, monitors, and systems involved in a research project. The main purpose of a GCP audit is to protect the rights, safety, and well-being of the trial participants and to ensure the credibility of the trial data..

[ICH GCP E6 R2 section 5.19.1](#) (Cited 01.12.2023) states “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.”

This SOP describes the audit procedures of the [Imperial College Academic Health Science Centre \(AHSC\)'s](#) Research Governance and Integrity Team (RGIT), acting on behalf of Imperial College and Imperial College Healthcare NHS Trust as Sponsor organisations. This SOP specifically describes the processes for completing and selecting audits that fall under the Department of Health UK policy framework for health and social care research and/or the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments; the procedures for carrying out audits and reporting audit results to Investigators and system owners. At times, systems audit will be conducted where a particular system is selected for audit and a systems owner will be identified as the main contact of the audit. Refer to RGIT Audit working practice document for instruction on how to complete audits. This can be found in Q:\QA\5. Audit Documents

Hosted Studies (whether Imperial are not the sponsor of the study) will not be audited by the RGIT unless in exceptional circumstances however sponsors will be requested to supply copies of any audit reports of hosted studies where a situation of risk to patients' safety, serious non-compliance or data integrity warrant it.

2. INTRODUCTION

As a legal Sponsor organisation (an institution that takes responsibility for initiation, management and/or financing of a clinical trial), Imperial College AHSC's RGIT, representing Imperial College London and Imperial College Healthcare NHS Trust, is responsible for auditing research practice to assess compliance to the study protocol, GCP, SOPs, and all applicable legal & regulatory requirements as a part of a quality management system. As such, it is necessary to audit research for which Imperial College AHSC is the lead Sponsor against the standards of the UK policy framework for health and social care research and the Medicines for Human Use (Clinical Trials) Regulations 2004 where applicable and also against the quality systems of Good Clinical Practice intrinsic to the Regulations.

The purpose of a research audit is to:

- Ensure participant and staff safety
- Ensure participant rights, welfare and well-being are being adequately protected.
- Assess data quality and integrity
- Evaluate trial conduct and ensure researchers' compliance with the protocol, SOPs, GCP and the regulatory requirements and Trust and College policy
- Improve research systems and data quality
- Prepare researchers for external audit processes

- Demonstrate robust research processes to external funders and industry

2.1. Audit Requirement

Under the [UK policy framework for health and social care research 2017](#) and the Medicines for Human Use (Clinical Trials) Regulations 2004, the sponsor is the individual, organisation or partnership that takes on overall responsibility for proportionate, effective arrangements being in place to set up, run and report a research project. The RGIT is responsible for auditing research on behalf of Imperial College AHSC. Studies and systems will be audited:

- As a result of a risk graded assessment (planned/routine audit)
- If there is suspicion/knowledge of significant non-compliance to regulation(s)
(Triggered audit)
- Selection based on agreed audit program

2.2. Role of the Auditor

It is the auditor's primary role to collect evidence of research practice and compare it against the requirements of Good Clinical Practice and Research Governance. The auditor is responsible for documenting observations and conclusions, safeguarding audit documents, records and reports, assessing whether requirements are being met, and developing reports incorporating recommendations for change or adherence. Most audits will consist of two auditors (lead and side auditor). The lead auditor will be responsible for planning, coordinating the whole audit however the side auditor will be required to review relevant study documents and conduct the audit alongside the lead auditor.

3. PROCEDURE

3.1. Auditor Qualification

Auditors must be suitably qualified by education, training, and experience. Auditors training must be documents as per RGIT_SOP_025 Quality Control (QC) and Quality Assurance (QA) and RGIT_SOP_024 Training.

3.2. Selection Process

3.2.1 Types of audits

It is a regulatory requirement for sponsors to conduct regular planned audits of CTIMP studies within their portfolio. An annual audit program should cover a selection of RGIT sponsored CTIMP and non-CTIMP NHS studies and systems. The exact number of audits will vary across each annual audit program, see RGIT audit working practice document.

CTIMPs and non-CTIMPs will be risk assessed for audit selection using the sponsorship risk assessment (see 3.2.2). Studies can also be selected or targeted based on emerging issues. These are known as triggered audits. The criteria for triggered audits are listed below but not limited to:

- Serious Breach
- Regulator directed
- Whistle blowing
- Lack of correct study approvals in place
- Temporary Halt
- Inadequate data entry
- SAE misreporting
- Critical finding at monitoring visit
- System non-compliance

- Multiple protocol deviations that lead to subject safety or data integrity of a study

The ultimate decision to conduct the triggered audit will be on a case by case basis and the above would be discussed at the RGIT audit meeting (scheduled approximately every other month) or senior management team (SMT) meeting if required.

3.2.2 Sampling Frame

Audits of sponsored studies/sites will follow a risk-based approach. During the sponsorship process studies will be risk assessed according to RGIT_SOP_009. A risk score will be calculated for each study and inserted in the sponsor database.

A sponsor report will be run to establish the sample of studies to be selected for audit based on their status and risks. The sample will consist of approved studies and it will usually exclude studies in set-up, archived. The following are risk factors which affect the risk score of the study which impacts on the choice of studies selected for audit in the audit program.

Example risk factors for study/programme selection
<ul style="list-style-type: none"> • Study population (e.g. size, vulnerable subjects, new indications) • Product characteristics (e.g. new products or with specific risks) • Therapeutic area • Duration of study • Applicability of regulations (e.g. international vs non-international) • Importance of study to future marketing submission (e.g. study phase, pivotal or supporting study) • Level of experience of research/clinical team • Confidence in service providers • Number and nature of outsourcing activities and associated interfaces for responsibility • Level of complexity of study and training requirements (e.g. e-system usage/medical device requirements) • Regional distribution of sites

3.3. Audit Plan

An audit plan will be developed by the RGIT auditor and sent to the researcher/system owner or delegated individual involved prior to beginning the audit.

The plan should:

- Define scope and objectives for audit
- Provide timelines for audit conduct
- Identify where and when the audit will take place
- Identify requirements to be audited against
- Identify groups and areas to be audited
- List documents and records to be studied
- List responsible people whose functions will be audited
- Clarify who will get the final report and when it will be ready

Audit Method

There are two type of audit methods.

1. On site audit

2. Remote audit

On-site auditing is where the auditor performs the auditing procedures at the location of the auditee.

Remote auditing is where the auditor conducts the audit without being physically present at the auditee location. Methods of conducting a remote audit include video conferencing (Zoom, Skype, file sharing, and via telephone.

Please note, for routine audits, onsite audits should be conducted unless a remote audit is agreed with the SMT and/or QA team.

It is understood that there are additional risks to privacy of participants when remote monitoring/auditing is undertaken. Therefore, all members of the RGIT who undertake monitoring and auditing using remote EHR access are required to read and sign the [RGIT_TEMP_071](#) as per the RGIT SOP 049 ICHT Remote Monitoring.

3.4. Audit Conduct

The process will start with an opening meeting whereby the auditor explaining the scope and objectives of the audit, and how it will be carried out. Examples of audit techniques include:

- Interviewing researchers
- Reading documents
- Reviewing manuals
- Studying records
- Reading reports
- Analysing data
- Observing activity
- Examining conditions
- Confirming interview evidence
- Documenting observations

Refer to the RGIT audit working practice document (RGIT_WPD_001) for full details in planning, coordinating and conducting the audit process.

3.5. Audit Findings

[ICH GCP E6 R2 - 5.19.3](#) "The observations and findings of the auditor(s) should be documented."

ICH GCP E6 R2 - 5.20.1 "Noncompliance with the protocol, SOPs, GCP, and/or applicable regulatory requirement(s) by an investigator/institution, or by member(s) of the sponsor's staff should lead to prompt action by the sponsor to secure compliance. If noncompliance that significantly affects or has the potential to significantly affect human subject protection or reliability of trial results is discovered, the sponsor should perform a root cause analysis and implement appropriate corrective and preventive actions."

Audit conclusion. The audit should close with a meeting This allows for sharing of positive experiences and procedures as well as discussion for areas improvements are recommended.

Once the practical audit has been completed the auditor will develop a summary and make preliminary recommendations to assist with research conduct and:

The auditor will:

- List any gaps in compliance with any supporting evidence
- Cross-reference with regulatory requirements

If there are any critical findings which may have an impact on subject safety and data integrity of the study, it may be necessary to request these issues escalate prior to practical completion of the audit. Refer to section 3.10 for escalation process.

3.6. Final Audit Report and Dissemination

The lead and side auditor will review the gathered information and compile a final report within one month. Once the final report is complete it will be disseminated to the study CI/auditee/system owner or delegated individual, and stored as per the RGIT audit working practice document. If there are any issues prior to this, the auditor should liaise with the Research Governance and QA manager or Quality Assurance Facilitator.

3.7. Action Completion

It is the Chief Investigator/auditee/system owner's responsibility to ensure action is taken to correct any identified gaps/findings in regulation compliance. If any advice or assistance is required, the auditor will be able to help with this. The Chief Investigator/auditee/system owner is expected to respond to the audit report within **1 month** of receipt of the audit report and corrective actions and preventative actions (CAPA) made within a timely manner. A shorter timeline may be requested by the auditor if there are critical findings identified at the audit.

3.8. CAPA verification

Every audit will consist of a follow up to verify that the CAPA's had been implemented. The follow up can be conducted in 2 ways:

- Remotely
- On-site

The purpose of this follow up is to ensure that the agreed CAPA for audit findings have been implemented by the team. It is the responsibility of the auditor and/or the RGIT management to decide what type of follow-up is appropriate/required. The lead auditor which conducted the initial audit will conduct the CAPA verification checks except in cases of mitigating circumstances. The auditor must ensure that all actions requested are in progress or have been completed by the study CI/auditee/system owner or delegated individual.

Remote follow-up

Remote follow-up should be conducted in situations where it is possible to review the required CAPAs and other required changes through documentation sent to the RGIT. It is possible for the auditor to complete this follow-up remotely from the RGIT office.

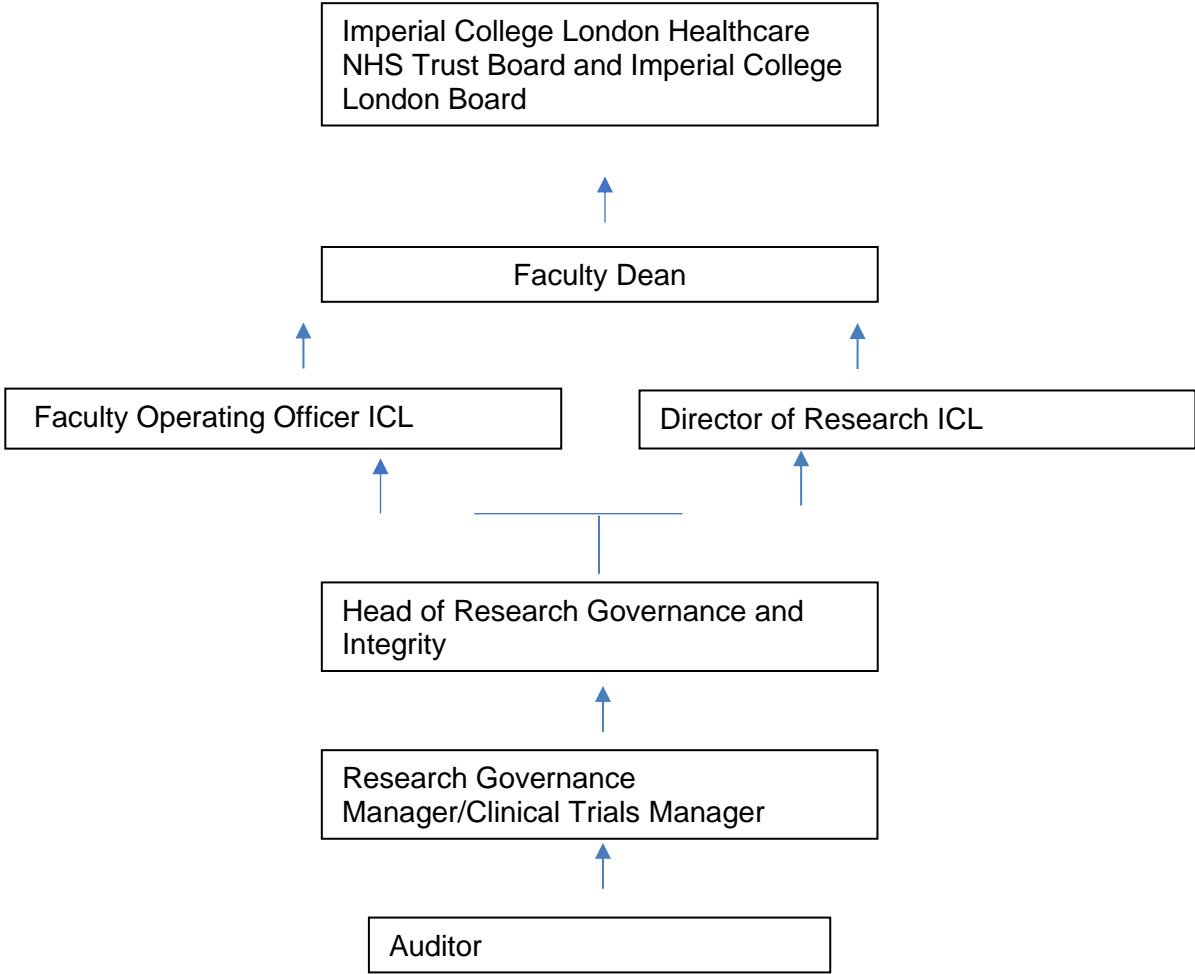
On-site follow-up

On-site follow-up should be conducted in situations where the auditor is required to attend the office/site of the study CI/auditee/system owner or delegated individual to review and verify the required CAPAs and/or other required changes.



3.9. Escalation Process and Conflict Resolution

In the face of any dispute the reports and findings/grading will be reviewed in accordance with the Research Governance and Integrity Team (RGIT) escalation policy. The below diagram provides the escalation route:



4. REFERENCES

UK policy framework for health and social care research 2017

UK Clinical Trials (Medicines for Human Use) Regulations 2004;

ICH GCP E6 R2 (2017)

[MHRA website on GCP for clinical trials](#) (cited on 10 April 2023)

NHS R&D Forum. Distinguishing different types of Monitoring and Audit, November 2008

RGIT_SOP_009 Sponsorship and Insurance Approval

RGIT_SOP_024 Training

RGIT_SOP_025 Quality Control (QC) and Quality Assurance (QA)

RGIT SOP 049 ICHT Remote Monitoring

5. APPENDICES

The following Appendices list the following Templates associated to this SOP which can be found on the SOP which can be found on the [SOP, Associated Documents & Templates page](#).

Appendix 1 to RGIT Audit working practice document