# Research Governance and Integrity Team Audit SOP

| | |
|---|---|
| SOP Reference: RGIT_SOP_018 | |
| Version Number: 10.0 | |
| Effective Date: 11 Oct 2021 | Review by: 19 Oct 2023 |
| Author: Cheuk Fung Wong, Research Governance and Quality Assurance Manager | |
| Approved by: Ruth Nicholson, Head of Research Governance and Integrity | Date: Ruth Nicholson Digitally signed by Ruth Nicholson Date: 2021.10.11 09:06:53 +01'00' |

| Version | Date | Reason for Change |
|---|---|---|
| Version 1.0 | 31 May 2007 | Annual review |
| 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 |
| Version 7.0 | 10 Aug 2017 | Scheduled Review |
| Version 8.0 | 14 Sep 2018 | Updated Audit Procedure |
| Version 9.0 | 19 Oct 2020 | Scheduled Review. Templates removed and administrative changes to SOP. JRCO name change to RGIT. |
| Version 10.0 | 11 Oct 2021 | New template associated with the SOP |

**Table of Contents**

## 1. PURPOSE

ICH GCP E6 R2 section 5.19.1 “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 selecting those studies and systems for audit 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 further details on system audits and system owner.

Hosted Studies 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.

This guidance is to assist auditees in understanding the audit process; so that they are prepared should they be selected for audit.

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 audit)
- If there is suspicion/knowledge of significant non-compliance to regulation(s) (Triggered audit)

A written report on study progression does not constitute audit and should be submitted for every study in addition to audit requirements. For a detailed description on the risk assessment process please refer to RGIT_SOP_009, this SOP which can be found on the SOP, Associated Documents & Templates page..

### 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 be generated on a risked based approached which may cover a selection of RGIT sponsored studies and systems. This includes CTIMPs, non-CTIMPS, internal sponsor files, vendors and systems within the unit. The exact number of studies/systems/vendors selected for audit 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 monthly audit meeting 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 Documas database.
A Documas 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 and those that have recently been audited or inspected. 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** |
|---|
| • Study population (e.g. size, vulnerable subjects, new indications)<br>• Product characteristics (e.g. new products or with specific risks)<br>• Therapeutic area<br>• Duration of study<br>• Applicability of regulations (e.g. international vs non-international)<br>• Importance of study to future marketing submission (e.g. study phase, pivotal or supporting study)<br>• Level of experience of research/clinical team<br>• Confidence in service providers<br>• Number and nature of outsourcing activities and associated interfaces for responsibility<br>• Level of complexity of study and training requirements (e.g. e-system usage/medical device requirements)<br>• 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

### 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.”

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 requests escalate these issues prior to practical completion of the audit. Refer to section 3.10 for escalation process.

**Grading of findings**

Audit findings are graded using the following criteria:

| | |
|---|---|
| **Critical:** | A finding defined as one with the capacity to directly undermine the integrity of the entire study. It’s a weakness of, or non-compliance with, one or more processes indicating a systematic quality assurance failures which, if not resolved, **will cause harm** to patients or data integrity and/or organisation reputation that requires the **immediate** notification and attention of senior management and clear timelines for resolution. |

| | |
|---|---|
| | For example findings:<br>▪ Where evidence exists that the safety, wellbeing, rights or confidentiality of study subjects has been (or has had significant potential to be) jeopardised.<br>▪ Where reason has been found to cast serious doubt upon the accuracy and/or credibility of study data.<br>▪ Where approval for the study has not been sought from one or more regulatory agency/body or granted from one or more regulatory agency/body (e.g. Ethics committee, MHRA) but the study has commenced regardless. Where significant procedures not covered/included on the consent form are being performed or where new procedures have been introduced into the study protocol but where participants who had consented prior to their introduction have not been asked to re-consent.<br>▪ Where following study approval, significant amendments have been made to the study protocol or documentation but no new request for approval has been submitted.<br>▪ Where inappropriate, insufficient or untimely corrective action has taken place regarding previously reported major findings<br>**A combination of multiple "major" audit findings may result in a "critical" systemic audit finding even though each of the findings is not "critical".** |
| **Major:** | A finding defined as one that compromises the integrity of a certain component(s) of the study. Weakness of, or non-compliance with, a control process indicating a systematic quality assurance failures which, if not resolved, **has the potential to cause harm** to patients or data integrity and/or organisation reputation that requires the **timely** notification and further investigation by senior management and clear timelines for resolution.<br><br>For example:<br>▪ Where there has been failure to comply with the regulatory requirements e.g. failure to assess and report SAEs and/or SUSARs accurately and to the correct bodies.<br>▪ Where there has been a significant unjustified departure from GCP e.g. failure to provide participants with a copy of their consent form or Participant Information Sheet.<br>**A combination of multiple "minor" audit findings may result in a "major" systemic audit finding, even though each of the finding are not "major** |
| **Minor/ Other:** | Any other findings, defined as those 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.<br><br>For example:<br>▪ Which demonstrate that no definite document management/organisation processes are in place at site. |

### 3.6. Final Audit Report and Dissemination

Over the following weeks from the initial audit, 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/ system owner or delegated individual, the relevant NHS Trust R&D office, and stored in the Imperial College AHSC Research Governance and Integrity Team. 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/system owner's responsibility to ensure action is taken to correct any identified gaps in regulation compliance. If any advice or assistance is required, the auditor will be able to help with this. The Chief Investigator/system owner is expected to respond to the audit report within **1 month** 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 via a follow up audit

The purpose of this follow up is to ensure that the agreed corrective and preventative actions for audit findings have been implemented by the team. It is the responsibility of the auditor and 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/ system owner or delegated individual.

**Remote follow-up**

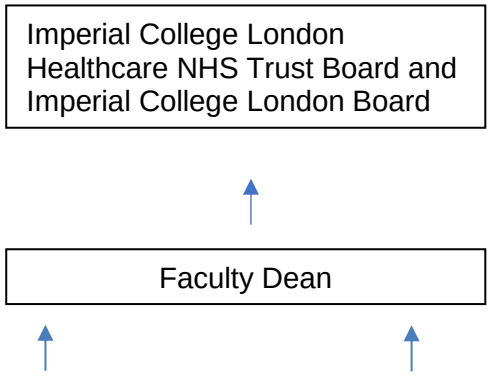
Remote follow-up audits should be conducted in situations where it is possible to review the required CAPAs and other required changes through documentation sent to the RGIT. It is possible for the auditor to complete this follow-up remotely from the RGIT office.

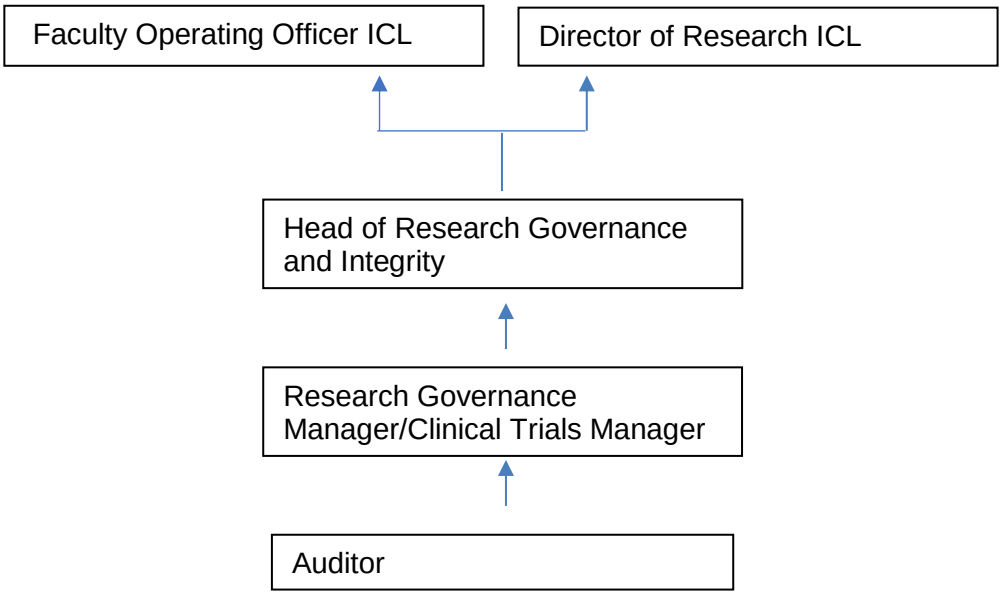
**On-site follow-up**

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

### 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 7May2020)

GCP auditing course – Principles and Practice by RQA (cited on 7May2020)

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

RGIT_SOP_009/Sponsorship and Indemnity

## 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 RGIT Audits – RGIT_WPD_001**
**Appendix 2 Remote Access, Monitor & Auditor Declaration form – RGIT_TEMP_071**