SOP 28 – Audit Preparation and Process

1.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to outline the investigator's responsibilities in preparing for an audit and to describe the process to be followed. Please note that there may be variations in the process when an external auditor is involved.

1.2 Scope & Responsibilities

This SOP applies to all staff involved in conducting University of Melbourne sponsored investigator-initiated trials (IITs). Sponsor-Investigators/Coordinating Principal Investigators (CPIs), Principal Investigators (PIs), Associate/Sub-Investigator(s), central trial coordinating teams/research coordinators and other staff involved in research duties.

1.3 Procedure

a) Internal Auditor Qualification

Auditors must be independent of studies being audited and qualified by training and experience.

b) Selection Process

When picking projects to audit, will occur dependent on the study type and level of risk the research study poses to the institution, research staff and research participants. Studies may be selected based on the risk factors listed below.

- 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

For internal audits, studies may be selected 'for cause'. An example of a 'for cause' reason for selection are listed below.

- 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

c) Audit Plan

A plan for how the project will be audited will be supplied to the project team. The plan will:

- Define scope and objectives for internal audit
- Provide timelines for internal audit to be conducted
- Identify where and when the internal audit will take place
- Identify requirements to be audited against
- Identify groups and areas to be audited
- List documents and records to be reviewed
- List responsible people whose functions will be audited
- Specify who will receive the final report

The auditee or delegate ensures that the internal auditor will have access to:

- Study files and documents, including electronic versions
- List of participants
- Signed consent form for every participant enrolled in the study
- Participant data files, including medical records*, for the nominated research participants specified in the initial letter
- A member of the research team to answer any questions
- A space for the monitor to sit and review the documents
- Database containing the study data

*If medical records need to be requested from Health Information Services with advanced notice, the researchers must account for this to make sure the correct and complete records are available.

d) Audit Visit

The time commitment for the audit visits will vary depending on the complexity of the study, whether the audit visit is conducted in person or via remote access. The auditee needs to be available to answer questions for at least 30 minutes at the start, during (as required), and 30 minutes at the end of the visit. The process will start with an opening meeting where the Auditor explains the scope and objectives of the audit, and how the audit will be conducted.

Audit activities will include:

- Interviewing researchers and support staff
- Visit to laboratory/pharmacy (site internal audits only, and if applicable)
- Reviewing documents and systems
- Observing activity, e.g. informed consent
- Documenting observations

The documents/systems reviewed during the audit will vary depending on the scope of the audit.

Documents/systems reviewed for University of Melbourne sponsored studies may include (but not be limited to):

- Study/Trial Master File, including:
    - Study approvals/authorisations including ethics, CTN, international regulators (as applicable)
    - Study protocol
    - Reports to HREC, Site Principal Investigators, TGA & international regulatory bodies (If applicable)
    - Training and delegation logs
    - Training of site teams
    - Site Information Files
    - Communication within the central coordinating team and participating sites
    - Manual of Procedures / Study-specific SOPs
    - Data Management Plan, Clinical Monitoring Plan
    - Monitoring Visit Reports
    - Adverse event listing
    - Central non-compliance (serious breaches) log
    - Corrective & Preventive Action Plans (CAPAs)
- Study database and other computerised systems
    - Validation records

Documents/systems reviewed for externally sponsored studies may include (but not be limited to):

- Investigator Site File, including

- Study approval/authorisations including ethics, local governance, CTN (as applicable)
- Communications with Sponsor, Research Ethics & Governance Office, Supporting Departments
- Study protocol
- Training and delegation logs
- Participant source data, including EMR, signed participant informed consent forms
- Case Report Form (CRF) – if electronic CRFs have been used, the internal auditor will need read-only access set up
- Study medication dispensing records, equipment maintenance/calibration records
- Non-compliance (serious breaches) log
- Corrective & Preventive Action Plans (CAPAs)

e) Audit Findings and Report

The internal audit report will include:

- Areas of excellence
- Breaches of the conditions of HREC approval
- Non-compliance with the protocol
- Non-compliance with the Investigators Responsibilities in Research and Informed Consent in Research procedures
- Non-compliance with relevant Standard Operating Procedures

Once the audit has been completed the auditor will complete a draft report, inclusive of non-compliances (and associated grading), and suggested recommendations for improvements.

The draft report will be reviewed by the auditor and provided to the auditee for review ('fact check') and clarification of any potential issues regarding the non-conformance classifications and recommended actions and opportunities for improvement. This will inform the CAPA plan which outlines actions, accountable persons and due dates for completion of the tasks.

After consultation with the auditee, the report, inclusive of the CAPA will be finalised and provided to the auditee.

NB: If there are any immediate critical findings which may have an impact on participant safety and data integrity of the study, it may be necessary to escalate these issues prior to completion of the audit.

f) Action Completion and Verification

Audits if applicable will consist of a follow-up to verify responses have been applied to the internal audit findings' actionable items and/or that the formal corrective and preventive action (CAPA) plan had been implemented by the research team. The follow-up can be conducted by either:

- email correspondence
- remotely via video link
- on-site

The follow-up process will be as follows:

- The auditee must provide documented evidence to demonstrate that actions are in progress or have been completed.
- The responses will be reviewed by the auditor and 'closed' when evidence is provided for the planned resolution.
- If the items are not resolved, an 'outstanding issues' reminder will be sent to the auditee.

g) Escalation Process and Conflict Resolution

The internal auditor may find items that could have a potentially significant negative impact on the:

- Integrity of the results
- Risks to the research subjects
- Ethical acceptability of the study
- Insurance coverage

The auditor may escalate these items to the relevant committee or require a response from the auditee within a shorter time frame. If the items are not resolved, the HREC may request further steps are taken to address the issues.

It is acceptable for the auditee to propose different resolutions to those items on the auditor's action summary if a sufficient case can be made. Any complaints or discussions about the internal auditing process can be directed to the auditor via the official channels.

If any critical quality or safety issues are identified that are applicable to the clinical research workforce a formal notice will be issued to advise staff of the requirement for improvement.

1.4 References & Useful Links

- ICH Guideline for Good Clinical Practice *https://www.tga.gov.au/resources/publication/corporate-reports/ich-guideline-good-clinical-practice*
- NHMRC: National Statement on Ethical Conduct in Human Research (2007) - Updated 2018 *https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018*
- Australian Clinical Trial Handbook – Guidance on conducting clinical trials in Australia using 'unapproved' therapeutic goods *https://www.tga.gov.au/resources/guidance/australian-clinical-trial-handbook*

1.5 Supporting Templates and Work Instructions

- MCCT SOP 04 - Protocol and Investigational Brochure Requirements
- MCCT SOP 05 - Communication with HREC, RGO, Sponsor and Institution's Insurer
- MCCT SOP 06 - Site Initiation
- MCCT SOP 07 - The Study Master File
- MCCT SOP 08 - Case Report Forms and Source Documents
- MCCT SOP 09 - Participant Informed Consent Process and Documentation
- MCCT SOP 10 - Handling and Shipping of Biological Substances (Cat B) and Dangerous Goods
- MCCT SOP 11 - Management of Investigational Product
- MCCT SOP 12 - Safety Data Monitoring and Reporting Requirements for Clinical Trials
- MCCT SOP 13 - Site Close-Out and Archiving
- MCCT SOP 14 - Data Sharing and Access Procedure for the Release of Data for IITs
- MCCT SOP 15 - Document Management and Version Control
- MCCT SOP 16 - Clinical Trial Registration of Investigator-Initiated Trials
- MCCT SOP 17 - Copying and Certifying Essential Documents
- MCCT SOP 18 - Establishing International Clinical Trials
- MCCT SOP 19 - Regulatory Green Light Approval for Clinical Trial Site Activation
- MCCT SOP 20 - Monitoring Visit Activities for Clinical Trials of Investigational Products
- MCCT SOP 21 - Study Start Up for University of Melbourne Sponsored Clinical Trials

1.6 Glossary

Adverse Event	Any untoward medical occurrence in a patient or clinical trial participant administered a medicinal product or other intervention. It does not necessarily have a causal relationship with this treatment.
Adverse Reaction (AR)	Any untoward and unintended response to an investigational medicinal product related to any dose administered.
Auditee	The person or organisation that is under examination by the internal audit. The auditee must allow the internal auditor access to all information and documentation requested during the process and provide reliable information.
Auditor	The person responsible for facilitating the audit process from planning to reporting.
Case Report Form (CRF)	Data collection tool used to record all the protocol required information to be reported to the sponsor on each research/trial participant. The CRF may be paper or electronic.
Clinical Monitoring Plan (CMP)	In accordance with the Integrated Addendum to ICH E6 (R1) Guideline for Good Clinical Practice E6 (R2) Section 5.18.7 (that was formerly adopted by the TGA with annotations on 8 February 2018), the Sponsor should develop a monitoring plan that is tailored to the specific human subject protection and data integrity risks of the trial. This plan must describe the monitoring strategy, the monitoring responsibilities of all the parties involved, the various monitoring methods to be used, and the rationale for their use.
Clinical Trial	Clinical trials can involve investigating new or existing medicines, medical devices and other medical or non-medical interventions. For example, a clinical trial could involve new drugs, medical devices, biologicals, vaccines, surgical and other medical treatments and procedures. Psycho-therapeutic and behavioural therapies help service changes, preventative care strategies and educational interventions are also examples of clinical trials. Researchers might also conduct clinical trials to evaluate diagnostic or screening tests and new ways to detect and treat disease.
Clinical Trial Notification (CTN)	One of two schemes used by the Therapeutic Goods Administration (TGA) to authorise the supply of unapproved therapeutic goods, including medicines, medical devices, and biologicals, to participants participating in clinical trials in Australia. The CTN scheme is appropriate for trials where the reviewing ethics committee has enough scientific and technical expertise to review the proposed use of the unapproved therapeutic good(s). Most investigator-initiated trials would be in this category.
Essential Documents	Documents which individually and collectively permit evaluation of the conduct of a study 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 (GCP) and with all applicable regulatory requirements. Filing essential documents at the Sponsor site and participating trial sites also assists with the successful management of the trial.
Good Clinical Practice (GCP)	A standard for the design, conduct, performance, monitoring, auditing, recording, analyse, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.
Human Research Ethics	A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines. The National Statement requires that all research proposals involving

Committee (HREC)	human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.
Informed Consent	A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate, Informed consent is documented by means of a written, signed and dated informed consent form.
Investigator	A person responsible for the conduct of the clinical trial at a trial site. There are four types of Investigator roles used to describe Investigators with different levels of responsibility for the conduct of clinical trials. These are described below. • Sub-Investigator Any individual member of the clinical trial team designated and supervised by the Principal Investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). May also be referred to as Associate Investigator. • Coordinating Principal Investigator (CPI) If a study is conducted at more than one study site, the Principal Investigator taking the additional responsibility for coordination of the study across all sites in a region is known as the Coordinating Principal Investigator (CPI). This role applies to externally sponsored studies where the Sponsor may be a collaborative research group, commercial Sponsor or an institution. The Principal Investigator at each site will retain responsibility for the conduct of the study at their site. • Principal Investigator The PI is the person responsible, individually or as a leader of the clinical trial team at a site, for the conduct of a clinical trial at that site. As such, the PI supports a culture of responsible clinical trial conduct in their health service organisation in their field of practice and, is responsible for adequately supervising his or her clinical trial team. The PI must conduct the clinical trial in accordance with the approved clinical trial protocol and ensure adequate clinical cover is provided for the trial and ensure compliance with the trial protocol. • Sponsor-Investigator An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a participant. The term does not include any person other than an individual (eg, it does not include a corporation or an agency). The obligations of a sponsor investigator include both those of a sponsor and those of an investigator.
Investigator-Initiated Trials (IITs)	A clinical trial which is initiated and organised by an Investigator i.e. an individual rather than a collaborative group, company, or organisation. In these cases, the Investigator will take on the role of the trial sponsor and will then be responsible for the extensive GCP and regulatory requirements associated with both the management and conduct of the trial.
Investigational Medicinal Product (IMP)	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Investigational Medical Device (IMD)	A device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.
Monitor	A person appointed by the Sponsor to undertake the role of monitoring for the trial. Monitors should be appropriately trained and should have the scientific and/or clinical knowledge needed to monitor the trial adequately.
Participant	A participant is a person that is the subject of the research.
Participant Information and Consent Form (PICF)	The PICF provides information about research and its requirements so that the prospective participant can decide if they wish to take part in the research. In general, this includes the purpose, methods, demands, risks, and benefits of the research. It must provide information to participants in a concise format that they are likely to understand. It must be participant centred.
Protocol	A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial.
Protocol Deviation	A protocol deviation is any breach, divergence or departure from the requirements of GCP or the clinical trial protocol.
Research	"Includes at least investigation undertaken to gain knowledge and understanding or to train researchers" (National Statement on Ethical Conduct in Human Research 2007 [Updated 2018]). For the purpose of this guidance, research includes any research that requires submission to and approval from an HREC and/or research governance office. This may include (but is not limited to) observational research, clinical trials, quality assurance projects and laboratory research.
Serious Breach	A breach of Good Clinical Practice or the protocol that is likely to affect to a significant degree: a) The safety or rights of a trial participant, or b) The reliability and robustness of the data generated in the clinical trial. Note: this guidance's definition of serious breach differs from the definition in the Australian Code for the Responsible Conduct of Research and is about deviations from the requirements of Good Clinical Practice or the clinical trials protocol.
Sponsor	An individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study.
Study Team	Refers to the extended group of people involved in a research study. This includes the investigator team and any additional members of staff who are involved in the set-up or conduct of the study e.g. research nurse, research assistants.
Suspected Breach	A report that is judged by the reporter as a possible serious breach but has yet to be formally confirmed as a serious breach by the Sponsor.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	This is a serious adverse event: • Where there is at least a reasonable possibility of a causal relationship between an intervention and an adverse event (in other words the relationship of the SAE to the trial drug/device/other intervention cannot be ruled out) and • That is unexpected, meaning that the nature or severity of the reaction is not consistent with the known scientific information (e.g. Investigator's Brochure for an unapproved investigational product or product information document or similar for an approved, marketed product).
Trial Coordinator	A Trial Coordinator has a significant role in the management of the clinical trial at the Sponsor level and provides leadership in clinical trial activities to ensure that the trial is completed within budget, on time and of the highest quality. A Trial Coordinator is responsible for managing the planning, implementation, and tracking of the clinical monitoring process, administration, and start-up of the clinical trial at the participating site and maintaining an overview of the conduct of

	the trial at sites. Some common roles and responsibilities performed by the Trial Coordinator include: • Participate in protocol development, CRF design and clinical study report writing • Guide in the creation and development of important study documents and manuals • Conduct feasibility assessments • Develop study budgets • Oversee participant recruitment • Oversee overall trial conduct • Ensure compliance of site-staff with the trials Standard Operating Procedures • Ensures compliance to all regulatory requirements both at a local and international level • Ensures compliance to all data protection requirements both at a local and international level • Ensures compliance to all safety reporting requirements both at a local and international level • Conduct team meetings and site-staff training programs • Overall responsibility of the trial • Supervise in-house clinical trial staff
Unexpected Adverse Reaction (UAR)	An adverse reaction, the nature or severity of which is not consistent with the Reference Safety Information (RSI).
Urgent Safety Measure (USM)	A measure required to be taken to eliminate an immediate hazard to a participant's health or safety.
Quality Assurance (QA)	Covers all policies and systematic activities implemented within a quality system. QA ensures that data are recorded, analysed, and recoded in accordance with the protocol and GCP. The use of GCP guidelines ensures ethical and scientific quality standards for the design, conduct, recording, and reporting of HREC approved clinical trials that involve research participants.

1.7 Revision Chronology

Document History			
Version	**Effective Date**	**Summary of Changes**	**Author**
1.0	29 May 2026	Initial Version	Renata Phyland