



# Standard Operating Procedures 1 -13 for Clinical Trials, including Teletrials at Austin Health

## Staff this document applies to:

- All Austin Health All staff and collaborators conducting clinical trials at Austin Health.

## Related Austin Health policies, procedures or guidelines:

[Austin Health Human Research Ethics Committee Terms of Reference](#)

[Consent Policy](#)

[Incident Management Policy](#)

[Management of Blood and Body Fluid & Substance Spills](#)

[Research Policy](#)

[Research Authorship and Outputs Procedure](#)

[Research Misconduct Procedures](#)

[Research Data Management Procedure](#)

[Research Involving Ionising Radiation Procedure](#)

[Research Steering Committee Terms of Reference](#)

[Telehealth Operations Manual](#)

[Telehealth Video Call Policy](#)

[Waste Disposal & Minimisation Policy](#)

## Purpose

To document the Austin Health Standard Operating Procedures (SOPs) for Clinical trials that have been adapted from the [National Standard Operating Procedures for Clinical Trials, including Teletrials](#).

If any Austin Health policies and procedures appears to contradict the information, the policies and procedures take precedence over this set of SOPs.

## Background:

The Austin Health Standard Operating Procedures (SOPs) for Clinical Research have been adapted from the Northern Health Standard Operating Procedures for Clinical Research and [National Standard Operating Procedures for Clinical Trials, including Teletrials](#) that have been developed to assist organisations engaged in conducting clinical trials in Australia to, wherever possible, standardise their procedures for key operations related to clinical trials and teletrials. The SOPs have been developed for the [National Mutual Acceptance \(NMA\) Scheme](#) in Australia and to support a consistent approach to national implementation more broadly which has been endorsed by all states and territories, together with the Therapeutic Goods Administration (TGA) and the National Health and Medical Research Council (NHMRC), through the Clinical Trials Project Reference Group (CTPRG).

The National Standard Operating Procedures for Clinical Trials, including Teletrials, form part of a Teletrials Compendium, developed to support a consistent national approach to implementation of teletrials in Australia, which includes:

- [National Principles for Teletrials in Australia](#), and
- [National Standard Operating Procedures for Clinical Trials, including Teletrials](#).

The documents within the Teletrials Compendium are consistent with minimum standard imposed by the International Council for Harmonisation (ICH) Guideline for Good Clinical Practice E6 (R2), the National Statement on the Ethical Conduct in Human Research 2007 (Updated 2018), and also align with the Clinical Trials Governance Framework which has been designed to support the delivery and integration of high-quality clinical trials service provision into routine hospital care for improved patient outcomes. These National Principles for Teletrials are also consistent

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OPPIC Document ID: GDL-25843 Date of last major update: 19/08/2024 Review Date: 19/08/2027

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with recommendations from the Clinical Oncology Society of Australia's (COSA) Australasian Teletrial Model – A National Guide to Implementation, September 2016.

**Monitoring and compliance review:**

Adherence to the SOPs will be monitored and evaluated through two yearly review by the document owner unless evaluation indicates a review is required, or changes to legislation, practice or strategic direction occur prior to the two yearly review date.

## SOP 1 - Creation, Implementation and Revision of Standard Operating Procedures

### Purpose:

To document the procedure for the adaptation, creation and implementation of new Clinical Research Standard Operating Procedures (SOPs) and review of existing SOPs, based on the National Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia 2020.

### Target Audience:

This SOP applies to any individual delegated the task of writing, reviewing, approving or distributing a clinical research SOP on behalf of Austin Health at the direction of the Discovery & Innovation Unit. This applies in all instances when a need is identified to either create a new SOP or modify an existing one. Authors of SOPs should have experience of the area covered by the SOP and be authorised by the Austin Health Discovery & Innovation Unit to create or modify these. Minor modifications to the SOP not impacting on the substantive content, maybe approved by the Director/Manager of Discovery & Innovation Unit. New SOPs or major modifications to existing SOPs cannot be considered effective until authorised by the Research Steering Committee.

**This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.**

### Initiating the creation of a new SOP or revision of an existing SOP:

All persons engaged in clinical research may:

- Identify the need for a new SOP or a deficiency or an improvement in an existing SOP and suggest appropriate modification.
- Actively invite feedback from users to inform a regular, formal review of the SOP by stakeholders at Austin Health, and to enable a continuous improvement approach.
  - At a minimum, this should be undertaken at least every two years following approval and release of the SOP (including where there may be subsequent revisions to the SOP in future) and will be updated in line with the National Standard Operating Procedures for Clinical Trials, including Teletrials.
- Assess and verify the need for a new or revised SOP.
- Use the approved Austin Health template and assign a document ID number and version date for all new SOPs or to modify an existing SOP.
- Draft the new or modify existing SOP and distribute to relevant stakeholders for review and comment.
- Maintain a record of the review process either on a document tracking review log (including at a minimum the SOP ID, version number, reviewer name, review date, changes and comments noted by reviewer, action by owner, date of action, new version) or electronically by using the tracked changes feature with a file naming paradigm and save files on central drive.
- Incorporate relevant comments and if required redistribute to relevant stakeholders for second review.
- If necessary, repeat the above steps until a final version is ready for approval.
- Update the current version and document approval boxes and/or amend document history box as necessary, ensuring the 'SOP effective date' and 'SOP review by date' is in alignment with the timeframe identified in this SOP.

### ***Approval and Authorisation of the SOP***

Approval processes follow Austin Health's corporate governance for [OPPIC policies and procedures](#). SOPs must be reviewed and signed-off by the Discovery & Innovation Unit Manager or Director, before proceeding to the Research Steering Committee.

Ensure the original signature field and/or amendment history field is completed. File the final approved (in writing) new/amended SOP electronically, and update on the Austin Health OPPIC library and website as applicable.

### ***Training, Implementation, Distribution of the new or revised SOP***

The Discovery & Innovation Unit is responsible for the dissemination and implementation of the SOPs.

All relevant staff members, including research staff, must be notified of the new/updated SOP between the authorisation and the effective date.

Notification of the approved, new or amended SOP will be disseminated via org-wide corporate communications channels and updated on the Austin Health OPPIC and relevant Austin Health training platform/s and websites.

Training is to be recorded as per SOP - 03 Site Staff Qualifications, Training Records and Capability.

### ***Superseded SOPs***

The superseded SOP will be archived per the OPPIC framework.

## SOP 2 - Investigator Responsibilities

### Purpose

To define the Investigator responsibilities associated with undertaking a clinical trial in accordance with International Council for Harmonisation (ICH) [Guideline for Good Clinical Practice E6 \(R2\)](#) ICH-GCP responsibilities for Investigators in clinical trials and teletrials.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and or staff at Austin Health. The responsibilities described in this SOP are additional to, and are to be read in conjunction with, Investigator responsibilities defined in all other National and/or NMA SOPs, individual trial unit SOPs, as well as the Austin Health Research Policy and Research Handbook (pending).

All study personnel involved in the clinical study must operate within their scope of practice.

### Investigator Responsibilities (CPI/PI/AI)

#### *Before the Research Project Commences*

The Investigator must:

- At all times, fulfil roles and functions as defined in the [National Clinical Trials Governance Framework](#).
- Declare in writing any conflicts of interest, or payments they will receive from other parties with any relationship to the study and notify the Sponsor and Austin Health as per the Austin Health research policies, procedures and guidelines.
- Ensure any payment provided to the participant for undertaking the trial is noted in the Participant Information Sheet and Consent form.
- Demonstrate that adequate participant recruitment is possible.
- Demonstrate adequate staffing levels to ensure success of the study at the site (including any Satellite Site/s).
- Be thoroughly familiar with the appropriate use of the investigational product as described in the protocol, in the current investigational brochure (IB) for medicines or product information for devices and in other information sources provided by the Sponsor.
- Be provided with evidence of HREC approval, Research Governance authorisation, and the registration number of the trial once it is registered on a publicly accessible World Health Organization compliant clinical trials registry, before the first participant is recruited to the study.

#### *During the Course and at the Completion of the Research Project*

The Principal Investigator must:

- At all times, fulfil Roles and Functions as defined in the [National Clinical Trials Governance Framework](#).
- Perform site evaluation of any Satellite Site deemed to be potentially able to recruit participants to the research project. For each trial, infrastructure and training requirements for Satellite Sites are the same for both the Primary and Satellite Sites, and a Satellite Site should have appropriately contracted, qualified and trained Investigator(s) and delegated staff to undertake delegated trial related activities including obtaining informed consent (if required).

- Retain overall responsibility for ensuring the process of consent has been conducted ethically and in accordance with ICH-GCP prior to the participant's entry into the project. This includes where participants provide consent at Satellite Sites under the responsibility of the PI.
  - At their discretion, the PI can delegate the process of conducting informed consent to a suitably qualified Associate Investigator. Suitably qualified means the delegation must be within scope of practice. For example, only a medically qualified doctor may be delegated to conduct the process of informed consent for a drug trial.
  - For teletrials, a detailed Supervision Plan is required, in addition to a Delegation Log required by ICH GCP for all Satellite Sites regardless of experience. The conduct of the trial is detailed under the 'head agreement', (Clinical Trial Research Agreement/Clinical Trial Agreement between the Sponsor and the Principal Investigator's Institution) and a Sub-Contract between the Primary Site and the Satellite Site Institutions (see **Appendix 1: Glossary of Terms**). Trial participants may have trial visits at both the Primary and Satellite Sites, as determined by the Protocol and Supervision Plan.
  - Delegated activities to be performed by a Satellite Site are trial and Satellite Site specific. The Primary Site must consider a Satellite Site's personnel and facilities in developing a Delegation Log and Supervision Plan suitable for a trial. The proposed delegation of duties and Supervision Plan must be agreed with the team and Sponsor at the time of site selection and must be documented before the study is initiated at each Satellite Site.
- Select and initiate the Satellite Site only when a potentially eligible participant population has been identified.
- Ensure all Primary Site and Satellite Site staff are trained on and adhere to these SOPs.
- Ensure study staff, including those at Satellite Sites, are trained in the following as relevant to their role: Protocol, IB, study procedures, Adverse Event (AE)/Serious Adverse Event (SAE) reporting, and that a system for safety reporting duties is in place for all study staff.
- Communicate all Protocol variations and ensure adequate training of all trial personnel in the reason for and implications of the new Protocol. Ensure all personnel are suitably trained to undertake the trial and deliver the trial intervention.
- Ensure that study related documentation files and procedures are established and maintained throughout the study at both the Primary and Satellite Sites (as relevant) in accordance with SOP 07 The Study Master File including procedures for managing the security of information and trial data and a process for managing data security or privacy breaches.
- Ensure study staff, including those at Satellite Sites, have a clear understanding of the process for securely and suitably storing and ensuring accountability for the Investigational Medicinal Product (IMP).
- Sign all trial related documentation during the research project in a timely manner.
- Ensure audit/inspection readiness throughout the study, have oversight of any audit or inspection of their trial at both Primary and Satellite Sites, and ensure any deficiencies identified through audit or inspection are actively managed to ensure continuous improvement.
  - Procedures must be in place to ensure that the Primary Site is made aware of any findings that arise from a Satellite Site audit or inspection.
  - The PI should follow Sponsor requirements to ensure that appropriate Corrective and Preventative Actions (CAPA) have been implemented and findings reported to the health service organisation and HREC.
- Inform relevant staff when recruitment has been completed and mark the Study Master File as closed to recruitment.

- Sign all trial related documentation at the end of the research project such as documents requiring an end date, indicating the research project is completed including but not limited to: Delegation Log, Training Log, Supervision Plan, agreements, progress and final reports, eCRF/CRF, SAE reports, etc.
- Ensure all trial related staff and third-party providers have been informed of the research project closure, results and publication plan.
- Inform the participant's primary care physician (where the participant has consented to do so) of the research project closure, results and, if applicable, the treatment the participant was allocated for notation in the participant's health and medical record.
- Ensure appropriate ongoing care of participants throughout the trial, if a participant withdraws during the trial and/or if a trial is prematurely terminated.
- Record in the participant's health and medical record at the appropriate Institution (which may be a Satellite Site) the treatment the participant was allocated (if applicable).
- Ensure a lay summary of the trial results (usually provided by the Sponsor) is disseminated to participants in accordance with the HREC application/trial Protocol and be prepared to respond to queries from participants in relation to the trial results.
- Document any deviation from the Protocol as per the Sponsor's guide.
- Notify the Sponsor and the Discovery & Innovation Unit if they leave the Institution, in writing with both their new place of employment and contact details and who their proposed replacement is with contact details for recording on all archiving related documentation. Ensure all handover to a new Principal Investigator is completed prior to their last day of employment. This includes transfer of trial documents and data within databases and secure drives.
- Ensure study related documents are archived according to SOP 13 - Site Close Out and Archiving (including at any Satellite Sites as relevant).

## SOP 3 - Site Staff Qualifications Training Records and Capability

### Purpose

The purpose of this Standard Operating Procedure (SOP) is to:

- ensure the appropriate documentation of clinical research site staff qualifications and training records are completed and maintained up to date during the study
- ensure the provision of resources to perform clinical research at all clinical research sites, according to the principles of the ICH GCP (and requirements of the Integrated Addendum to this Guideline published by the TGA), the National Statement, the Australian Code, and the requirements of the National Clinical Trials Governance Framework.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants and staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policy and Research Handbook (pending).

### Site Staff Qualifications

The Principal Investigator must:

- Be qualified by education, training and experience, including in skills, competencies and training requirements articulated in the [National Clinical Trials Governance Framework](#), to assume ultimate responsibility for the proper conduct of the research.
- Submit a current *Curriculum Vitae* (CV) to the Discovery and Innovation Unit as part of a clinical trial research governance submission.
- Provide current Australian Health Practitioner Regulation Agency (AHPRA) registration details (sponsors may confirm a registration status from the APRHA website so this information does not need to be maintained in the Investigator Site File).
- Provide evidence of appropriate and current GCP training.
- Provide other relevant documentation requested by the Sponsor, the HREC, and/or the regulatory authority.
- Ensure all investigational site staff, at both Primary and Satellite Sites, or independent third parties, and external service providers have provided appropriate and current evidence that they are qualified by education, training and experience, including in skills, competencies and training requirements articulated in the National Clinical Trials Governance Framework, to assume responsibilities to perform the delegated study-related duties and functions and that they have the legal authority to do so. Delegation should be consistent with the Roles and Responsibilities specified in the National Clinical Trials Governance Framework and recorded in a Study Delegation Log.
- Ensure all investigational site staff, at both Primary and Satellite Sites, independent third parties and/or external service providers, who have been delegated significant responsibilities have a current CV lodged with the research office/ Study Master File (SMF) for sighting by the Sponsor and/or regulatory authority.
- Implement procedures to ensure the delegated study-related duties and functions are carried out safely.
- Implement procedures to ensure integrity of all data generated.

## Site Staff Training Records

The Principal Investigator must:

- Ensure all required staff, including new staff involved during a study, who assist with the clinical trial are informed about and trained on the Protocol, any Investigational Product, and their research-related duties and functions.
- Ensure that for all study specific training provided, there is a record of documents and tools used, including details of who provided the training and when it was provided, by trial specific staff (e.g. on a training record or log).
- Ensure all required training is completed and the training record is kept up to date. A copy must be kept at the Primary Site and/or Satellite Sites (when applicable) and available for review on request by Sponsor, HREC, Discovery and Innovation Unit or external parties such as the TGA, throughout the entire duration of the clinical research trial.

## Capability

The Principal Investigator must:

- When a teletrial is being conducted, the PI, who is always at the Primary Site and never at the Satellite Site, remains responsible for the trial across the cluster.
- Undertake the roles and functions of the Site Principal Investigator specified in the Clinical Trials Governance Framework.
- Demonstrate the potential for recruiting the required number of suitable participants, either from the Primary Site only, or from the Primary Site and associated Satellite Sites, within the specified recruitment period. This may be in the form of de-identified participant recruitment listings or other documented written or printed evidence.
- Have sufficient time to properly conduct and complete the research within the specified period.
- Have an adequate number of qualified staff and adequate facilities for the foreseen duration of the research.
- Ensure that a robust site assessment is undertaken that fully quantifies the capabilities of the Primary Site as well as each Satellite Site to inform the extent to which trial related activities can be delegated to the site. This may include a pre-commencement assessment before a specific trial is proposed so that the process of trial start up is expedited when a suitable trial is identified. For Satellite Sites that have no or limited experience in delivering clinical trials, a staged approach may be undertaken to allow for gradual building of clinical trials capacity and capability (e.g. the Satellite Site is initially involved in less complex trials with greater levels of oversight provided by the Primary Site).
- Maintain a record identifying appropriately qualified persons to whom they have delegated significant research-related duties (on a 'per person' basis) such as a Delegation Log.
  - Staff who as part of routine practice provide ancillary or intermittent care by completing a procedure on a trial patient/participant (i.e. vital signs, electrocardiography (ECG), venepuncture or imaging) generally do not need to sign a Delegation Log (or be listed on a 1572 Form for trials conducted under an Investigational Drug Investigation). However, if a key trial end point is based on reporting from routine care, then this should be clearly reflected in the Delegation Log as in this context, such reporting is considered critical to the trial.
  - Where partnering/service departments (e.g. pharmacy, laboratories, radiology) are involved in trial specific activities (e.g. dispensing Investigational Medicinal Products), the PI may delegate the role of supervising and training departmental staff to a Named Person (e.g. a clinical trial pharmacist). This person would train all staff on any aspects of GCP/the Protocol relevant to their role.

- Where applicable, ensure each Satellite Site maintains its own site Delegation Log separate to the Primary Site. Where the PI has delegated such a task to the Satellite Site Associate Investigator, the Associate Investigator will delegate duties appropriately, sign and date the log and send a copy to the Primary Site, when requested.
  - The process for maintaining the Delegation Log across Primary and Satellite Sites may involve the use of wet signatures, scanned copies and/or e-signatures.
- Develop and complete a Supervision Plan (see related documents) before the commencement of a teletrial, which documents the manner and frequency of supervision to be undertaken between the Primary Site and each Satellite Site, and other study staff, especially Associate Investigators and other team members new to the role. The Supervision Plan must include cover for planned leave.
- Provide oversight, as outlined in the Supervision Plan, to any third party to whom any study related duty or function is outsourced and take responsibility for any study-related duty or function performed and any data generated by the third party.

### GCP Training

In accordance with the National Clinical Trials Governance Framework, it is essential that clinical trial investigators and clinical trial staff with significant delegated trial related responsibilities have access to and undertake training in the principles of GCP as a minimum requirement. Knowledge of GCP should be provided in a way that is proportionate to the individual's role and level of trial activity. A trial risk assessment can be used to inform and justify the level of training; however, the following minimum requirements apply:

#### *Staff with significant Trial related Duties (All Trials):*

- Core trial staff should receive accredited (for example, Australian Clinical Trial Education Centre) GCP training. Refresher GCP training should also be available to trial staff, at appropriate intervals to ensure that staff maintain awareness of current clinical trial standards and legislation.

#### *Ancillary Staff involved in Trials with Novel/Non-Routine Interventions:*

- For staff conducting trial related procedures or involved in the care of trial patients/participants, GCP training may be in an abbreviated format; for example, taking the form of a short departmental trial awareness sessions covering relevant requirements such as:
  - Recording adverse events
  - Documenting activities in source notes
  - Notifying protocol deviations and adverse events to the core trial team
  - Escalating any other issues identified to the core trial team.
- Pharmacy staff involved in general dispensing, under the oversight of a trial pharmacist who may perform training on relevant trial/GCP requirements.

#### *Ancillary Staff involved in Standard Care Trials:*

- Trials involving routine treatment (e.g. comparative effectiveness trials) often involve large numbers of healthcare professionals that are suitably qualified to undertake the trial by virtue of the prior education, training and experience, and work to quality systems outlined in their professional codes of practice.
- Consistent with the Clinical Trials Governance Framework, at a minimum, all trial staff should be made aware of the trial/relevant GCP principles (e.g. at routine meetings, short trial awareness sessions or provision of written materials).
- If there is uncertainty of the training required, this should be referred to the Director of Research for discussion.

Summary of GCP Requirements:

<b>Risk Category</b>	<b>Example of Duties</b>	<b>Training required</b>
Staff with significant Trial related Duties (All Trials)	Principal Investigator Associate Investigators Research Nurses Trial coordinators/managers	GCP training through accredited training program (e.g. Australian Clinical Trial Education Centre)
Ancillary staff involved in Trials with Novel/Non-Routine Interventions	Staff conducting trial-related procedures Staff involved in care of trial participants	Abbreviated GCP training, e.g. short departmental group sessions on key relevant aspects
Ancillary Staff involved in Standard Care Trials	Healthcare professionals involved in routine care of trial participants	Awareness of trial/relevant GCP principles

## SOP 4 - Protocol and Investigational Brochure Requirements

### Purpose

To describe the procedures related to the development of a research Protocol, an Investigational Brochure (IB), and amendments to these documents ensuring compliance to ICH GCP E6 (R2).

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants and staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### Protocol Content and Development

- Specific content of a Protocol will vary depending on the research, the level of risk to participants, the phase of the research and study design, and whether a medicinal product, a device, or a therapeutic intervention is being researched. Consequently, the terminology will be different and should be adapted appropriately.
- A range of guidance material may inform and be referred to in development of the Protocol, including but not limited to [Standard Protocol Items: Recommendations for Interventional Trials \(SPIRIT\)](#) and the [Consolidated Standards of Reporting Trials \(CONSORT\)](#).
- However, where the Investigator is responsible for the Protocol development they must ensure the Protocol follows the outline as per [ICH GCP E6 \(R3\)](#) Section 6 Clinical Trial Protocol and Protocol Amendment(s). This Protocol table of contents is not mandated but it is recommended that a trial Protocol should generally include the topics detailed in the section. However, site-specific information may be provided on separate Protocol page(s), or addressed in a separate agreement, and some of the information listed may be contained in other Protocol referenced documents, such as an Investigator's Brochure (IB).
- Where Satellite Sites will be involved in the study, no specific wording will be required in the Protocol, as the following considerations will be addressed in other study-specific documents which may be annexed to the Protocol e.g. the site selection report, ethics application, Supervision Plan, the monitoring manual, laboratory manual, pharmacy manual, safety monitoring manual or a trial specific working guideline. Nevertheless, the following considerations are to be addressed such that Protocol deviations are not created.
  - The process by which participants will be informed about the risks and benefits of participation and their agreement (or otherwise) to participate will be clearly described and documented, including what evidence will be recorded for auditing purposes (i.e. face-to-face, videoconference, via telehealth, skype, phone etc.), as well as exactly who will conduct each aspect of the consenting process, noting that for IMP trials, only medically qualified personal may confirm eligibility, capacity to consent and ask potential participants if they would like to participate.
  - Description of how study procedures will be undertaken, e.g. how visits, assessments, collection of data and medical consultations will be conducted i.e. face-to-face or via telecommunication or a combination of both.
  - Description of storage and handling of Investigational Product, e.g. will the Investigational Product be stored at the Primary Site and shipped to the Satellite Site via appropriate handling and shipping method when a participant is deemed eligible or will Satellite Sites with appropriate facilities store the Investigational Product?
  - Description of storage and handling of laboratory samples at Satellite Sites, if involved and if relevant e.g. frequency of and timelines between transport of samples to Primary Site or direct to a central or local laboratory.
  - Description of the handling of other study related non-IMP materials.

- Description of the roles and responsibilities of Investigators and other staff who will be involved in the study at both the Primary and Satellite Sites.

### **Investigational Brochure Content and Development**

Where the Investigator contributes to the content and development of the IB they must ensure the Investigational Brochure follows the outline as per [ICH GCP E6 \(R3\)](#) Section 7 Investigator's Brochure. The IB should remain up to date via annual revision at a minimum, depending on the type of product and its stage of development.

In some situations, for Investigational Medicinal Products, where a product is registered, and has a well-understood pharmacology, a Product Information document may be substituted for an IB, provided current and comprehensive information about the product under study is available to the Investigators. If a product is registered, but is being trialed for a new indication, or in a different population to the approved indication, an IB must be collated with reference to this new indication/population.

### **Amendment/s to the Protocol and Investigational Brochure**

The Investigator must inform the HREC:

- and obtain acknowledgement of receipt of the updated IB.
- and obtain approval of all amendments to the Protocol including amendments that:
  - Are proposed or undertaken without prior HREC approval to eliminate immediate risks to participants
  - May increase the risks to participants
  - May alter the ethical acceptability of the trial
  - May affect the viability of the trial
  - May impact on the scientific validity of the trial
  - Significantly affect the conduct of the trial (including changes to the Inclusion/Exclusion criteria).
- As soon as possible after any new safety information from other published or unpublished studies is identified that may have an impact on the continued ethical acceptability of the project or may indicate the need for amendments to the research Protocol.
- Notification to the HREC is HREC-specific and the Investigator should be familiar with the terms of reference of their ethics committee. Refer to SOP 05 Communication with HREC, RGO, Sponsor and Institution's Insurer, regarding communication with the HREC.
- The Investigator must comply with any additional conditions placed on the project by the HREC as a result of the Protocol variation.

The Investigator must provide to the Research Governance Officer (RGO) in a timely manner:

- The HREC approval letter for the amendment(s).
- A copy of all HREC approved amended documents.
- A Site Specific Assessment (SSA) Form will need to be completed for both the Satellite Site and the Primary Site.

Where there is an amendment to the Protocol, authorisation from the RGO to continue the project must be obtained from both the Primary and Satellite Sites where a governance aspect has been affected (if required), including Protocol amendments that:

- Are proposed or undertaken without prior HREC approval to eliminate immediate risks to participants. However, that amendment will be implemented prior to governance authorisation.
- May increase the risks to participants.

- Significantly affect the conduct of the trial (including changes to the Inclusion/Exclusion criteria).
- Pose a risk to the Institution.
- Require contract variations or impose additional contractual requirements or obligations by the relevant Institution.
- For a teletrial, if a variation to the Sub-Contract is required, this will need to be negotiated between the Primary and Satellite Sites.

For the avoidance of doubt, where there is an amendment to the Protocol, a variation to the Clinical Trial Sub-Contract between the Primary and Satellite Sites will be needed if the contract variation impacts on the Satellite Site, as determined by the Primary Site.

## SOP 5 - Communication with Discovery & Innovation Unit (which encompasses the HREC & RGO) and Sponsor and Insurer

### Purpose

To describe the procedures relating to communication with the Discovery & Innovation Unit which encompasses the Human Research Ethics Committees (HREC), Research Governance Officer (RGO), Sponsor and Insurer.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and or staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice. This SOP takes into consideration the single ethical review processes. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policy and Research Handbook (pending).

### Communication with Reviewing HREC

When communication regarding key decision points is verbal, the initiating party should follow up verbal communication with written correspondence/e-mail and send to the call recipient. The title of the letter/e-mail should include the subject for discussion followed by a text string which should include the decision topic. Such documentation must be filed in the Study Master File (SMF) and where applicable in the Satellite Site Study File (SSSF).

#### *Prior to study commencement*

The Investigator (CPI/PI/AI) must:

- Choose a NHMRC certified reviewing HREC whose approval is acceptable to the Institution/s where the clinical study is being undertaken (or ensure the responsible HREC chosen by the CPI is likewise acceptable). Currently certified NMA HRECs are documented in jurisdictional policy for public health organisations, and in local Institutional policy for private health organisations.
- Understand the reviewing HREC requirements, submission processes and be aware of their meeting and submission dates to better liaise with Sponsors.
- Be familiar with the relationships between HREC review and approval, governance authorisation and any other processes/approvals that need to be in place (e.g. does the HREC have subcommittees), before any study start up activities can commence. This process and approval flow will be required by Sponsors, auditors and inspectors.
- Submit an ethics application as per the reviewing HREC submission process.
- Include in the relevant section of the ethics application that the trial may be undertaken using telecommunication with Satellite Sites, if applicable, and that the informed consent process and/or some or all study assessments will be undertaken using telecommunication, face to face consultation or a combination of both.
- Submit any other application as per institutional requirements.
- Ensure all documentation and correspondence pertaining to the submission and approval processes is filed in the SMF e.g. correspondence to and from the HREC, RGO or other bodies.
- Ensure the project does not begin at any site until HREC approval and Site Governance Authorisation, including fully executed agreements is in place.

#### *During the study*

The Investigator (CPI/PI/AI) must:

- Comply with all conditions and restrictions applied by the RGO or HREC on the conduct or continuation of the trial.

- Submit all documents/reports/summaries according to the requirements and timelines as stipulated on the respective reviewing HREC approval letter, including but not limited to: Sponsor reports of accumulated safety data outcome analyses; proposed changes to the Protocol; major or Serious Breaches; annual progress reports; and unforeseen events that might affect continued ethical acceptability of the trial.
- Comply with the reporting requirements outlined in SOP 12 Safety Data Monitoring and Reporting Requirements for Clinical Trials, and central HREC and Local Governance Safety Reporting Requirements noting that individual reports of Adverse Events, Serious Adverse Events, Suspected Unexpected Serious Adverse Reactions, Unanticipated Serious Adverse Device Events and six-monthly line listings should NOT be submitted to the reviewing HREC unless otherwise advised.
- Note that although all deviations must to be reported to the trial Sponsor, only the sub-set of deviations that have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the clinical trial must be reported to the HREC. These deviations (also known as ‘Serious Breaches’) should also be reported by the Principal Investigator (PI) to their Institution, as they may impact on medico-legal risk, the responsible conduct of research, or adherence to contractual obligations.
- Immediately notify the reviewing HREC of any notification received from a participant in a trial that they intend to initiate a claim for compensation against either the Sponsor and/or the Institution.
- File all documentation in the SMF/SSSF.

#### *At the end of the study*

The Investigator (CPI/PI/AI) must:

- Submit a trial termination/closeout report according to the requirements and timelines as required by the respective reviewing HREC. This may be stipulated in the approval letter and/or on their website.
- File all documentation in the SMF/SSSF.

#### **Communication with the Research Governance Office**

For the purpose of this SOP, the Clinical Trial Research Agreement (CTRA), other contracts, such as service level agreements, other site-specific trial related documentation and the Site-Specific Assessment (SSA) Form constitute a research governance application for the Primary Site. Similarly, for the Satellite Site, a site-specific assessment/research governance application consists of the Sub-Contract, the SSA Form and other site specific, trial related documentation. This application must be submitted in parallel to the HREC submission.

In most cases, the final document to be provided to the RGO is the HREC approval. This has the advantage of enabling an RGO review in parallel to the HREC review and allows a timelier RGO authorisation which may lead to expedited study start up. It is important to note, that HREC approval must be obtained and submitted to the RGO, prior to the final RGO authorisation being granted.

#### *Prior to study commencement*

The Investigator (CPI/PI/AI) must:

- Submit the Clinical Trial Research Agreement (CTRA), HREC approval, the SSA Form, evidence of any relevant GCP training, and any other required documentation to the RGO.
- Ensure all documentation and correspondence pertaining to the submission and approval processes is filed in the SMF.
- Ensure each Satellite Site in the cluster (whether in a different Hospital and Health Service (HHS) to the PI or the same HHS) completes a Clinical Trial Sub-Contract and a SSA Form and submits to their RGO.
- Facilitate resolution of RGO queries promptly.

- Await site specific RGO authorisation before any study related activity can occur at that site.
- Ensure the Satellite Site files all documentation in the SSSF.

#### *During the trial*

The Investigator (CPI/PI/AI) must:

- Submit all governance related documents/reports/summaries to the relevant RGO according to the requirements and timelines as stipulated by the respective RGO including but not limited to:
  - changes to the CTRA/Sub-Contract
  - changes to the budget
  - any change that might affect continued financial acceptability of the trial
  - Any change that may increase Institutional risk.
- Serious Breaches (those deviations that may have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the clinical trial) should be reported by the PI to their Institution, as they may impact on medico-legal risk, the responsible conduct of research, or adherence to contractual obligations.
- Immediately notify the RGO of any notification received from a participant in a trial that they intend to initiate a claim against either the Sponsor and/or the Institution.
- Ensure all training and accreditation remains current.
- Ensure the Satellite Site files all documentation in the SSSF.

#### *At the end of the trial*

The Investigator (CPI/PI/AI) must:

- Notify the RGO the trial has terminated/closed and submit a Final Report.
- Communicate research findings to participants when possible.
- File all documentation in the SMF/SSSF. Poor compliance with the Protocol or Good Clinical Practice (GCP) can lead to data being rejected by regulatory authorities, can compromise participant safety and can nullify a trials insurance/indemnity. ICH GCP requires that the PI (or delegate) document and explain any deviation from the Protocol and requires that noncompliance with the Protocol, SOPs, GCP, and/or applicable regulatory requirement(s) lead to prompt action to secure compliance.

### **Communication with the Sponsor**

The Investigator (CPI/PI/AI) must:

- Comply with the reporting requirements outlined in SOP 12 Safety Data Monitoring and Reporting Requirements for Clinical Trials and should consult and adhere to existing guidance for safety monitoring and reporting published by NHMRC and the TGA (see References).
- Notify the Sponsor within 24 hours of any Serious Adverse Events (SAE) involving trial participants under the care of the Investigator and where relevant notify the PI in parallel.
- Notify the Sponsor promptly regarding any changes significantly affecting the conduct of the trial, and/or increasing the risk to participants and where relevant notify the CPI/PI/AI. Communication must be followed up with written report/email and filed in the SMF/SSSF.
- Notify the Sponsor of any protocol deviation or breach (which may include significant deviation from the Protocol) and where relevant notify the CPI/PI/AI.
- Be available to meet with the Sponsor to discuss study progress, issues and safety.
- Provide the Sponsor with copies of all correspondence from the reviewing HREC and/ or RGO.

- Immediately notify the Sponsor of any notification received from a trial participant that they intend to initiate a claim for compensation against either the Sponsor and/or the Institution.

#### **Communication with Institution's Insurer**

If you becomes aware that a trial participant intends to make a claim for compensation against the Institution or Sponsor for injuries arising as a result of participating in a clinical trial undertaken at the Institution or any of the Satellite Sites under supervision by the Institution please promptly notify the details to Austin Health Legal who are authorised by Executive to communicate with our Insurer, and will ensure prompt notification in writing.

#### ***Communication with Solicitor, Sponsor and CPI/PI/AI***

If the Investigator is notified or becomes aware that a trial participant intends to make a claim against the Institution or Sponsor for injuries arising because of participating in a clinical trial undertaken at the Institution or any of the Satellite Sites under supervision by the Institution, the Investigator must promptly notify the following in writing that such an action is intended:

- the Institution's authority
- the CPI/PI/AI as relevant
- the Sponsor.

The Sponsor, or the Institution acting as Sponsor, will generally be responsible for reporting to their respective solicitors.

## SOP 6 - Site Initiation

### Purpose

To describe the procedures related to site initiation of a clinical trial at all sites.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and or staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice. This SOP takes into consideration the single ethical review processes. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### Site Initiation

#### *Prior to initiation of the study*

The Investigator must:

- Reach a mutual agreement with the Sponsor a scheduled date, time and location for the Study Initiation Visit at the participating site to ensure the site is prepared to commence the study. In the case of a teletrial, this may be at the Primary Site only, or could include (remotely) the Satellite Site/s as determined by the study complexity by the Sponsor/PI.
- Review all study related documentation and be familiar with the Investigational Product and Protocol.
- Ensure that all relevant staff involved with the study, (Associate Investigator, Pharmacist, Clinical Research Coordinator and others as appropriate including trial related staff at a Satellite Site), have been advised of the meeting and are able to attend either in person or via videoconference.
- Be in possession of all required approvals and authorisations to conduct the research project.
- For teletrials, ensure a Supervision Plan (see related documents) is in place, that documents the manner and frequency of supervision to be undertaken with other trial staff, especially those new to the role, and, where relevant, trial related staff at a Satellite Site. A Supervision Plan is to be created by the Primary Site for each Satellite Site.
- Not initiate a Satellite Site under the Teletrials Model until such time as a potentially eligible participant population is identified.

#### *During the initiation Visit*

The Investigator must ensure the following are available and/or addressed:

- Study Master File (SMF) containing all required essential documents and review arrangements for organising and maintaining study files (Satellite Site Study File in the case of the PI initiating a Satellite Site).
- A list of all study personnel attending the initiation meeting on an attendance log/Training Log with full name, signature, date and the method attended i.e. in person or via videoconference.
- Original, signed and dated curriculum vitae of all study personnel involved in the study at the site and any Satellite Sites for which the Investigator has responsibility.
- Other documents such as financial disclosures, statement of investigator, delegation log, training Logs, medical licenses and other essential documents as per Sponsor requirements.
- A contact list with names and contact details of all study personnel from all sites including Satellite Sites, Sponsor and independent third-party service providers is available.
- Timeline for shipment, delivery and receipt of Investigational Product, participant

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recruitment strategies, and other study related supplies to site.

- A laboratory manual, where applicable, clearly defining sample handling instructions and processes, shipping procedures, documentation handling, contact list of all laboratories involved and any other laboratory activity to be undertaken during the trial.
- A pharmacy manual clearly defining any activity linked to the handling or the Investigational Medicinal Product (IMP)/Investigational Medicinal Device (IMD).
- Any specialised equipment required will be available throughout the period of the trial, e.g. centrifuge, freezer, etc.
- The Case Report Form (CRF), completion guidelines and that they are accessible by all sites.
- Training in all aspects required by the Protocol is recorded on the Training Log.
- Archiving of study records at the end of the study.
- Subsequent training for staff not in attendance at the Initiation Visit. Such initiation training can be conducted remotely where feasible. It is critical however, that this training is undertaken and documented before they commence activities in the study.
- Trial Monitoring Plan.
- Supervision Plan for the satellite sites, if the trial is a teletrial.
- For each teletrial, the above steps must be repeated for each Satellite Site to be established under the Primary Site.

*At the conclusion of the initiation visit*

The Investigator must:

- File the Sponsor's initiation visit report/letter and all other essential documents in the SMF.
- Ensure that the staff at the Satellite Site files all communication and documentation in the SSSF.

## SOP 7 - The Study Master File or Investigator Site File

### Purpose

ICH GCP defines Essential Documents as 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.

The purpose of this SOP is to describe the procedures related to the maintenance of the Study Master File (SMF) or Investigator Site File (ISF) held at all clinical research sites/units, according to [ICH GCP E6 \(R3\)](#) Section 8 to ensure it is current at all times for the duration of the clinical study.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and or staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice. This SOP takes into consideration the single ethical review processes. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### The Study Master File – Principal Investigator Responsibilities

The Principal Investigator must:

- Ensure an SMF/ISF is created, if not provided by the Sponsor, prior to study commencement and ensure that it contains at a minimum the Essential Documents listed in Appendix 8 Study Master File Index Example of the [National Standard Operating Procedures for Clinical Trials, including Teletrials, 2020](#).
- The SMF/ISF is stored at the Primary Site (Satellite Site Study File in the case of the PI initiating a Satellite Site).
- Where the Teletrial Model is implemented, have control of all Essential Documents and records generated by the Investigator/Institution/Satellite Site before, during, and after the trial.
- Establish the maintenance rules of the SMF and relationship between the Primary Site Study Master File (SMF) and Satellite Site Study File (SSSF). When establishing the maintenance rules, it will be important to ensure that key documents from the SSSF are present in the SMF/ISF and vice-versa after the close out of the study but prior to archiving, so that a full record of all study activities under the control of the Principal Investigator (PI) is contained in the SMF.
- As the SMF/ISF contains identifiable data and proprietary information, it should also be stored securely with restricted access to authorised staff.
- Establish prior to the commencement of the trial and maintain a current record of the location of all Essential Documents including Source Documents and where relevant, study related Essential Documents from the Satellite Site. The storage system used during the study and for archiving (irrespective of the type of media used) should provide for document identification and location, version history, searchability and retrieval for the length of the archiving retention time.
- File Essential Documents in a timely manner.
- Ensure Satellite Sites also maintain SSSF and file study related Essential Documents in a timely manner, with focus on version control.

- Maintain a current contact list of all study personnel including staff at all Satellite Site/s within the Cluster involved in the clinical trial, clearly identifying the Primary Site, the Satellite Site and any external service provider.
- Ensure study documentation is kept and archived as specified in SOP 13 Site Close-Out and Archiving.
- Ensure regular monitoring and auditing of site files to source documents is undertaken by the Sponsor, as per Trial Monitoring Plan.

### The Study Master File – Contents

- All essential documents should be provided to the site in electronic format.
- Study related Essential and Source Documents generated for/by the Primary Site, will be filed in the SMF/ISF. SMF/ISFs can be maintained either in paper, hybrid or electronic formats. Access to electronic SMF/ISF will be via a secure user name and password.
- The SMF/ISF should be prefaced with an index of contents as well as indicate the location(s) of all Essential/Source Documents.
- Certified copies of study related Essential and Source Documents generated for/by the Satellite Site, the identity of which will be established prior to the commencement of the trial, will be sent to the Primary Site and filed in the SMF/ISF, on request by either, the Sponsor, monitor or Primary Site staff as per rules established prior to the commencement of the trial and documented in the Supervision Plan.
- Where financial documentation, such as the Clinical Trial Agreement and Sub-Contract, invoicing and remittances etc. may be filed in a separate location to the SMF/ISF, the location is to be recorded on the SMF/ISF index. A copy may be filed in the SMF/ISF if requested by the Sponsor.
- A copy of ethics and governance documentation, such as the HREA or SSA, safety reports, project or annual reports etc. will be filed in the SMF/ISF, the location is to be recorded on the SMF/ISF index.
- Clinical trial units may engage the services of an external provider to facilitate the administrative processes of ethics and governance submission on behalf of the principal investigator, as per institutional guidelines. Quality assurance of these documents will be the responsibility of the unit to ensure ICH GCP compliance.
- All study team members are required to provide an abbreviated curriculum vitae (CV) in line with SOP 03 Site Staff Qualifications, Training Records and Capability, which should detail clinical experience and relevant training (see relevant documents). CVs will be provided every two years unless a change in information has occurred. CV signatures may be wet ink or electronic and copies will be filed into the SMF/ISF.
- All study team members will provide approved ICH GCP training certificates, which will be filed in the SMF/ISF.
- If required, the sponsor will provide the principal investigator with a complete statement of investigator (Form FDA 1572, US Department of Health and Human Services). Signatures may be wet ink or electronic and copies will be filed into the SMF/ISF.
- If required, financial disclosure forms (FDF) will be collected from investigators. Signatures may be wet ink or electronic and copies will be filed into the SMF/ISF.
- Wet ink signed or copies of other essential documents including (but not limited to) delegation logs, training logs, and patient logs will be filed in the SMF/ISF.
- Investigational Product handling documentation e.g. shipping, receipt, Interactive Voice Response System (IVRS), Interactive Web Response System (IWRS), codes, randomisation list and accountability and destruction documents etc. may be kept in a separate file e.g. at the site pharmacy. In this case the location is to be recorded on the SMF/ISF index. However, the records must be made available to Sponsors, monitors, auditors and regulatory agencies at

any time. The Investigational Product documentation will be archived with the SMF/ISF after completion of the study.

- Sample handling procedures are to be clearly documented if performed, as per the laboratory manual and in compliance with the SOP 10 Handling and Shipping of Biological Substances (Category B) and Dangerous Goods. Sample management records at both Primary and Satellite Site/s including the storage, processing and transportation of samples between Satellite and Primary Sites are filed in the SMF/SSSF as agreed.
- Essential clinical trial correspondence including (but not limited to) correspondence with ethics and governance committees, data safety management boards, regulatory authorities, and relevant sponsor communications will be filed in the SMF/ISF.
- Other study related materials handling documentation are filed in the SMF/ISF as agreed.

### **The Satellite Site Study File - contents**

The content of the Satellite Site Study File (SSSF) can be decided with the study team and the Sponsor. The SSSF may be a sub-set of the SMF/ISF and should be prefaced with an index of contents as well as indicate the location(s) of all Essential/Source Documents.

The Satellite Site Study File should contain:

- All the relevant site-specific Essential Documentation pertinent to the activities that have been and that are to be performed at the Satellite Site.
- All Source Documents generated at the Satellite Site (or indicate the location of all Source Documents for example the EMR at the Satellite Site).
- Relevant HREC approval and governance authorisation documentation.
- Sub-Contract with the Clinical Trial Agreement in annexure.
- Study specific Supervision Plan.
- Satellite Site Delegation Log, Training Records, and Site-Specific Assessment form.
- Investigational Product shipping, receipt and accountability documents.
- Details of the processing, storage of samples at both Sites and transportation between Satellite and Primary Sites and related documentation (if performed).
- Files notes indicating if the original document is found in another location e.g. pharmacy folder with the pharmacy, a document will be found in the SMF.
- Other study related materials handling documentation are filed in the SSSF as agreed.

## SOP 8 - Case Report Forms and Source Documents

### Purpose

To describe the procedures related to the completion of electronic and paper-based Case Report Forms (CRF), and maintenance of Source Documents.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and or staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### Completion of Case Report Forms

Where electronic medical records (EMR) are used, a validation system is required with an inbuilt correction and audit trail feature. In the case where there is no inbuilt validated audit trail, printed records of the changes and corrections (e.g. data queries) must be retained.

The Principal Investigator must:

- Ensure the accuracy, completeness, legibility, (including any changes or corrections) and timeliness of Source Data and data recording adheres to the Protocol, monitoring plan requirements and the Supervision Plan.
- Ensure that any party delegated to perform data entry or signing for data completeness is recorded on the Delegation Log and is trained to perform those trial related duties and functions.
- Ensure that changes to the paper Source Document do not obscure the original entry, are traceable (signed and dated) and explained (i.e. an audit trail should be maintained).

### Source Documents

The Investigator must:

- Maintain adequate Source Documents and trial records including all key observations on each of the trial participants.
- Store all trial related documents in a Study Master File/Satellite Site Study File as required by the applicable regulatory requirement, Sponsor and Protocol and take measures to prevent accidental or premature destruction of these documents.
- Ensure, for both paper and electronic documents, all changes, corrections and amendments are tracked, and version dates and numbers, are updated to reflect the changed data and to maintain the integrity of the data. An explanation of the changes is noted in a record of change.
- Ensure all staff are aware that, upon request, direct access to all trial related records is given to the monitor, auditor, HREC, RGO or regulatory authority, to enable Source Data verification, Sponsor audits or regulatory inspection. Direct access is stipulated in the CTRA and outlined to the participant via the PICF.
- Ensure direct access is provided in accordance with the Austin Health Research Policy.
- Access to the participant's trial related information should be limited to authorised users. Where access (e.g. for trial monitors, auditors and inspectors) cannot be limited to trial participants, certified paper copies of trial-related information should be printed. Ensure that for telehealth and/or telecommunication consultations, the call is documented in the participant's health and medical record at each site as documented in the Supervision Plan, which will detail where the original and certified copies are stored. The written record will include a summary of the Protocol number, consultation; follow up instructions and that the visit was conducted via telehealth.

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- For paper records, ensure that the agreed approach to Source Documents in the Supervision Plan is followed. This could include requiring a certified copy of any key Essential Documentation generated at the Satellite Site to be sent to the Primary Site for filing in the SMF/ISF e.g. SAE reports, to allow remote monitoring by the Sponsor and for auditing and inspection purposes. These can be sent via email or post.
- Where EMR are in use, access to the patient's/participant's trial related information must be limited to authorised users only. The Investigator must ensure appropriate controls are in place to allow access to the patient's/participant's EMR for the purpose of monitoring the study and that access is provided. Authorised users should include CRAs, auditors and regulatory inspectors, subject to those users meeting local access requirements.
- For teletrials, providing access to the Satellite Site EMR from the Primary Site (for PI oversight and study monitoring) is to be encouraged to increase the efficiency of study conduct under the Teletrial Model.

## SOP 9 - Participant Informed Consent Process and Documentation

### Purpose

To describe procedures and documentation management relevant to the initial and ongoing informed consent process, including consenting via telehealth. The objective is to conduct the process of voluntary, informed consent through ongoing communication and information exchange between a patient/participant and a clinician about the best interests of each participant. The provision of sufficient and ongoing information to make an informed decision is understood as “informed consent” and this term will be applied in this context in this SOP.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and or staff. All study personnel involved in the clinical study must operate within their scope of practice. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### Informed Consent Process

In obtaining and documenting Informed Consent, all persons involved in the research must comply with Austin Health’s Consent and Telehealth Policies, meet the literacy guidelines [National Statement](#) Chapter 2.2, the [National Clinical Trials Governance Framework](#) (including the Roles and Functions of Identified Positions) and applicable regulatory requirements, and adhere to [ICH GCP R3](#) and to the ethical principles that have their origin in the [Declaration of Helsinki](#).

### Establishing the Informed Consent Process

- The Principal Investigator (PI) for any research project retains overall responsibility for ensuring the process of consent has been conducted ethically and in accordance with ICH-GCP prior to the participant’s entry into the project. This includes where participants provide consent at Satellite Sites under the responsibility of the PI. However, at their discretion, the PI can delegate the process of conducting informed consent to a suitably qualified Associate Investigator as described in SOP 02 Investigator Responsibilities, and SOP 03 Site Staff Qualifications, Training Records and Capability, and the [National Clinical Trials Governance Framework](#). Suitably qualified means the delegation must be within scope of practice. For example, only a medically qualified doctor may be delegated to conduct the process of informed consent for a drug trial. Delegation of all activities must be recorded in a Delegation Log or similar. The PI remains responsible for any delegated activity.
- Participant Information Statement & Consent Forms must meet a health literacy level of 3 or less on the hemingway scale.
- The Investigator must ensure that they have the relevant Research Governance approval, inclusive of approval by an appropriate HREC, for all written information and any other media used to provide information to potential participants, before these forms, information or other materials may be used to recruit or form part of the informed consent process for any participant.
- When changes have been made to approved Participant Information resources the Investigator must have the relevant HREC's written approval and authorisation from the local RGO, before these may be used as part of the informed consent process for any participant.

### Process for Obtaining Informed Consent

- If a participant expresses interest in participating in a research study, the PI or delegate must ensure that the potential participant has a copy of the current version of the HREC approved Participant Information and other approved media. This can be provided in person, by telehealth or by telephone and email or web link.
- Potential participants, or their legally acceptable representative, should be given adequate time to read any information or to watch any approved media and to discuss with any family

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and friends and/or their family doctor, prior to agreeing to participate. The PI or delegate may also offer the potential participant the opportunity to bring a friend or family to any meeting with the PI/delegate.

- Whilst delegates such as Study Coordinators/Nurses or other appropriately qualified persons may initiate the process of recruitment and informed consent, and provide guidance around the written information and media, capacity to consent, answering all medical questions, and later part of consent process including signing of the consent form must only be conducted by Medical and Dental qualified persons working within their scope of practice and appropriate to oversee the use of an unregistered medicine.
- The PI or delegate must assess the potential participant's understanding of what they are agreeing to, that they are aware of the purpose of the study, what will be involved and any risks that may exist. The participants must demonstrate that they fully understand the implications of decisions that may be made within the course of the research. This is capacity to consent.
- After all questions are satisfactorily answered, potential participants who wish to participate in the research will provide a record of their agreement either through physically signing a paper copy of the consent form or electronically signing a consent form using an approved format that accurately documents the time, date and authenticity of their signature. The PI/delegate will countersign and date that the consent process has occurred. Ideally this will be done contemporaneously; however, under special circumstances related to the nature of the study the HREC may approve this signature to occur later with appropriate documentation.
- Witnesses are not a requirement in Australia unless they are providing a signature on behalf of a person who cannot sign themselves or are attesting to a translation of the Participant Information provided (see also ICH GCP Section 4.8.9). If a witness is required, the witness should sign and personally date the witness section of the consent forms.
- Once all parties have signed the Informed Consent documentation, the participant will receive a copy, and all other written information and media provided to the participant that were used as part of the consent process. A copy of the signed consent documentation must be placed in the participant's medical record to indicate that person is participating in research as part of their medical care.
- Participants may withdraw their consent at any time without giving a reason.

**Process for confirming consent where new information arises/re-consent:**

- This process applies to the necessity to obtain and document a participant's expressed willingness to remain in a study. This may arise if changes/amendments are made to the Protocol after the trial has started. The PI or delegate must contact the HREC to obtain ethical approval for these changes and to discuss the need, or immediacy of need, to inform existing participants.
- The PI will ensure that all currently enrolled participants are re-contacted in a timely manner with the relevant new information as approved by an HREC. Unless there is a significant safety concern HRECs will not usually require that patients/participants be recontacted immediately. There are potential implications for blinding of any studies and care must be taken when developing the process for recontact. If approved by the HREC, continued consent may be obtained verbally and recorded in the participant's medical records and Source Documents.
- Where there is an amendment to the PICF, this should be signed by the participant as confirmation of their willingness to continue in the trial. This must be recorded and kept in the medical records and the ISF.

## Additional Considerations

[The National Statement on Ethical Conduct in Human Research](#) states that when conducting the process of consent with a patient, the "...information must be presented in ways suitable to each participant." (section 2.2B). This is further clarified by describing how information regarding the trial must take into account "the need for accurate and reliable translation (written and/or oral) into a participant's first language or dialect." (section 5.2.16).

When a patient with additional considerations is identified as a potential clinical trial participant, adaption to the method of information giving or tools used in the informed consent process may be required, as detailed in section 4: ethical considerations specific to participants and section 5.2.17 of the [National Statement](#).

This may include:

- Non-English-Speaking Clinical Trial Participants - translation of documents when necessary and possible or use of an independent interpreter through Austin Health.
- Visually impaired: use of a family member or friend to read documents to the patient, or braille translation via computer application.
- Hearing impaired: use of an Auslan interpreter.
- Physically impaired: use of a family member or friend to scribe on the patient's behalf (if they are unable to do it themselves).
- Unable to read: use of a family member or friend to read documents to the patient, use of impartial witness.
- Young Person (under the age of 18): use of a legal guardian.
- Clinical Trial Participant with Cognitive Impairment, Intellectual Disabilities or Mental Illness, the informed consent process should be sought from:
  - That person if he or she has the capacity to consent, or from the person's guardian or any person or organisation authorised by law.
  - Where the impairment, disability or illness is temporary or episodic, an attempt should be made to seek consent at a time when the condition does not interfere with the person's capacity to give consent. In such circumstances, consent should be witnessed by a person who:
    - Has the capacity to understand the merits, risks and procedures of the research or is independent of the study team (impartial witness).
    - Where possible, a person who knows the clinical trial participant and is familiar with his/her condition.
- Clinical Trial Participants Highly Dependent on Medical Care.
  - Consent should be obtained from their legally acceptable representative.
  - In circumstances where neither the potential clinical trial participant nor their legally acceptable representative can consider the clinical trial, the HREC may (having taken into account, relevant jurisdictional law) approve the clinical trial participant's involvement without prior consent, as detailed in the National Statement section 4.4.

## Informed consent via phone or Telehealth

- E-consent may be the preferable option for teletrials, as consent signatures can be obtained contemporaneously at both Primary and Satellite Sites.
- If Informed Consent is obtained by telehealth consultation, all persons who are not known to each other must produce identification to the other person to ensure verification of each person's identity and to confirm the identity of the participant who is giving valid consent.

- With telehealth, all measures will be taken to ensure privacy and confidentiality of the participant's identity.
- If Informed Consent is obtained by telephone, this must be recorded on the Informed Consent Form and in the participant's health and medical record, and/or Source Document.
- A description of how study procedures, visits, assessments, collection of data and medical consultations will be undertaken e.g. they may be conducted in person or via telehealth or a combination of both, are to be clearly detailed in the HREC application, the supervision plan and the PICF, and clearly described to the participant during the consent process.
- Following discussions with the PI or delegate and the patient, the PICF will be signed by the patient. The study team member present will document the informed consent discussion, event and format.
- If a witness is required, the witness will be asked to sign and date the witness section of the PICF.
- The original signed PICF will be returned to the study site in person (if participant is attending the site within an appropriate timeframe) or by registered mail.
- The Investigator must then sign the Consent Form on the date they received the Consent Form, NOT the date they obtained consent from the participant, and document this in the patient's medical record.
- When all parties have signed the PICF, the participant will receive a copy of the signed and dated PICF, and the original will be filed at the study site.

### **Informed Consent Documentation**

Ensure the essential elements are present as described in the National Statement, Chapter 2.2 and ICH GCP E6 (R2) Section 4.8.10.

- The Master PICF is supplied by the Sponsor. Any necessary national or local adaptation will be made as required for submission to the reviewing HREC and local governance office.
- The process of informed consent must be documented, and the documentation must include the following:
  - Patient name and unique identifier number.
  - Version number and date of PICF.
  - Date PICF(s) given to clinical trial participant, including details if emailed/mailed prior to visit.
  - A statement by the investigator obtaining informed consent confirming that the clinical trial participant has had full opportunity to read the PICF and ask questions (questions/issues raised should also be documented) and that all questions have been adequately addressed.
  - Date PICF was signed and dated by the clinical trial participant.
  - Use of witness, if required.
  - Use of an interpreter, if needed.
- Once the PICF is signed and dated by both participant and the Investigator, the original PICF is kept in the participant's health and medical record and a copy is given to the participant.
- Storage of Informed Consent documents may be at the Satellite Site, at the Primary Site or at both sites for a teletrial (refer to SOP 07 The Study Master File).
- Where consent has been obtained by telehealth or telephone, once the PICF is signed and dated by both the participant and the Investigator (and any other person present for example an interpreter), the participant is to record that consent was obtained by telehealth or telephone with the name of the Investigator. Similarly, the

Investigator is to record that consent was obtained by telehealth or telephone with the name of the participant. The participant's original PICF is kept in the participant's health and medical record (electronic or paper), a copy is given to the participant and:

- For a teletrial, where paper records are kept, a certified copy of the participant's signed and dated PICF is sent to the Primary Site for filing in the participant's health and medical record with the Investigator's signed and dated original. The Investigator is to add the date the participant's PICF was received.
- Where electronic records are kept, both signed PICFs are uploaded into the participant's electronic medical record and a certified copy of the PICF is not required.
- A copy of the PICF with the Investigator's signature is given to the participant.

## SOP 10 - Handling and Shipping of Biological Substances (Category B) and Dangerous Goods

### Purpose

To outline the procedures to follow when handling and shipping Biological Substances (Category B) and/or Dangerous Goods in clinical trials to ensure the safety of all staff when carrying out this activity. To also outline the regulations that govern this activity in clinical trials.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and or staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice.

This SOP covers the handling and shipment of biological substances category B and dangerous goods (dry ice) only. When references to biological samples/ specimen/ substances are made, category B is implied. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### Handling and Shipping of Biological Substance and Dry Ice in Clinical Trials

- This activity may be delegated to another staff member or third-party service provider, provided they hold a current certificate to do so. This duty is delegated as per SOP 03 Site Staff Qualifications, Training Records and Capability. It is still the Investigator's responsibility to ensure all procedures and regulations are adhered to.
- All personnel and students who perform any trial related laboratory work that require PC2 containment are required to comply with this SOP. Users are required to be deemed competent by the Laboratory Manager (or a suitably qualified person) and be registered on current training documentation.
- If samples potentially contain genetically modified organisms (GMO), the correct procedures for preparation, shipping, disposal and management of spills of the GMO must be followed in line with sponsor guidelines, the [Office of the Gene Technology Regulator \(OGTR\)](#) and local policy and procedures.

The Investigator must:

- Ensure all study staff, who have cause to handle or ship biological substances, hold a current certificate in the International Air Transport Association (IATA) Approved, Civil Aviation Safety Authority (CASA) Certified Dangerous Goods Packaging Course.
- Ensure specimens are collected and handled in accordance with local and Sponsor requirements as written in the Protocol and laboratory manual.
- Ensure specimens are packed and shipped in accordance with local and Sponsor requirements as written in the Protocol and laboratory manual and according to IATA requirements, including that a valid export permit is in place, if required.
- Ensure that in situations where research personnel do NOT hold current certification, arrangements for biological substance/dry ice shipment are made with IATA certified Pathology Laboratory staff or external third party.
- Ensure that the National Pathology Accreditation Advisory Council (NPAAC): Requirements for the Packaging and Transport of Pathology Specimens and Associated Materials are followed by relevant certified staff.
- Ensure any training is recorded on the Training Log as per SOP 03 Site Staff Qualifications, Training Records and Capability and copies of certificates are kept in the respective site file (SMF/SSSF).
- Ensure that site staff and sponsor provide sufficient shipping details for trial-specific packages (eg: name of person, department, delivery address and contact number).

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- Ensure that documentation (e.g. receipts, shipping records, order forms, proformas) related to handling and shipment of biological specimens is maintained and filed in the respective site file (SMF/SSSF) or patient medical record. Sites frequently take biological samples (e.g. tissue, blood, urine, and sputum) from trial participants that are then processed, stored, packed and transported to local or central laboratories. To ensure that the integrity of biological samples has been maintained, there should be evidence of the chain of custody from their point of collection through processing, storage, transport, through to disposal, with evidence of appropriate storage and transit conditions.

#### **Maintenance of equipment used for processing and storage of samples**

- Equipment used for processing and storage of samples (e.g. centrifuges, fridges and freezers) should be maintained by suitably qualified persons and periodically inspected, cleaned, and calibrated to the relevant standard according to local policy and manufacturer's manuals.
- Calibration certificates and temperature logs are available for all equipment mentioned above.
- Hospital biomedical services is responsible for ensuring associated facilities and equipment are maintained and serviced.
- Sample kits provided by sponsors will be stored in an appropriate environment. A tracking system may be used to review and periodically track kit stocks, to ensure there are sufficient for the purpose of the study and they remain in date.

#### **Temperature Records**

- All free-standing fridges and freezers used for clinical trial sample testing and storage must have a temperature log. The temperature is recorded periodically, and these records must be available upon request.

#### **Waste Disposal**

- All waste is to be discarded through the Austin Health waste management system in accordance with Austin Health Waste Disposal and Minimisation Policy.

#### **Emergency Procedures**

- Spills: Refer to Austin Health Management of Blood and Body Fluid & Substance Spills procedure.

#### **Notes regarding Certification to handle and transport biological substances and Dry Ice**

- To organise training for handling and shipping of biological substances and dry ice, staff should contact the Austin Health Pathology Service/Laboratory. The [CASA Certified Dangerous Goods Packaging Course](#) can be done by any media and must be recorded on the respective Training Log as per SOP 03 Site Staff Qualifications, Training Records and Capability.
- CASA Regulations have defined categories of personnel who should attend training and the subject matter in which they must be qualified. These regulations are mandatory and legally binding and consequently must be adhered to in full.
- Re-certification is required every two years. Certificates and any training records must be kept for a minimum period of 36 months from the most recent training completion date, and must be made available, upon request to the Sponsor, regulatory authority, and CASA.

### Purpose

To describe the procedures related to managing all aspects of Investigational Product (IP), either medicinal product or device. Management includes, but is not limited to, the receipt, storage, accountability, preparation and administration, shipment and destruction of IP.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and or staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice. This SOP must be read in conjunction with individual trial unit and pharmacy SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### Management of Investigational Product (Medicinal Product or Device)

Responsibility for IP management and accountability at the trial site rests with the PI. However, the PI may delegate responsibility for IP management to the site pharmacist or, where a pharmacist is not available or involved, to an appropriately qualified person (as per SOP 03 Site Staff Qualifications, Training Records and Capability).

The site pharmacist or the appropriately qualified person will undertake management of the IP at the Primary Site and/or the Satellite Site.

Where the responsibility is delegated (e.g. pharmacist or appropriately qualified person), the delegated activity is to be clearly documented on the Delegation and Training Logs, as well as the Supervision Plan if the trial is a teletrial, as outlined in SOP 03 Site Staff Qualifications, Training Records and Capability.

The task of prescribing IP should only be delegated, as appropriate and within a health practitioner's scope of practice, to medical practitioners, dentists or nurse practitioners. The task of administering IP should only be delegated to medical or clinical staff and within their scope of practice (e.g. registered nurses).

*The Investigator, Pharmacist or appropriately qualified non-pharmacist must:*

- Ensure the IP is used only in accordance with the approved Protocol.
- Confirm IP certification and all relevant trial approvals/notifications are in place before releasing IP for dispensing to participants (i.e. ethics and governance approval, CTN/CTA, drug committee approvals and product compliance with guidance documents and legislation).
- Maintain records of all aspects of the management of the IP. These records at a minimum should include: shipping documents; date of each transaction; quantities; batch/serial numbers; expiration dates/retest dates (if applicable); temperature logs showing the storage conditions of IP throughout the trial period; the set of unique code numbers assigned to the IP and to the trial participant; and record of destruction/return. Study teams may use templates provided by the sponsor or internal log templates to maintain these records.
- Provide maintenance and calibration records for storage equipment (e.g. refrigerators, thermometers) in accordance with Sponsor requirements.
- Ensure that the IP is received, stored respecting correct temperature control, prepared, administered, shipped and destroyed as specified by the Sponsor in accordance with the Protocol, pharmacy manual and applicable regulatory requirement. Consideration must be given to security of the IP, with restricted access to approved personnel.
- Ensure IP is transported, stored and supplied according to jurisdictional and Institutional policies.

- The majority of IP will be received, stored and managed within a pharmacy. However, exceptionally, it may be necessary for IMP to be stored in a ward or facility (e.g. for trials where IP is administered in the emergency setting or outside of pharmacy opening hours). Arrangements for IP storage outside of the pharmacy should only occur following consultation with the local pharmacy service. Where organisational policy allows delivery directly to storage areas outside pharmacy, these should be assessed by staff (e.g. pharmacy) to ensure storage conditions are adequate, temperature monitoring is in place and accountability (including an area for returns) meets Protocol/pharmacy manual requirements.
- Where IP is logged out of pharmacy and transferred to a department/facility/area (or other location) for administration to the patient/participant (e.g. IV infusion in a ward or administration of a vaccination at a participant's home), appropriate chain of custody records should be maintained.
- Where IP (compounded or reconstituted in pharmacy or for immediate use by nursing or other qualified staff) has limited stability/short half-life, records should be able to demonstrate that it was transported and administered within the specified timeframe.
- Ensure IP is not destroyed without prior written authorisation by the Sponsor. IP that is unused, expired or returned by patients/participants should be stored in an appropriately controlled area, until ready for return to the Sponsor (usually at intervals) or disposal at site. Returned IP should be stored separately to unused IP. Where IP is to be returned to the Sponsor, all patient/participant identifiers must be removed beforehand.
- Ensure any deviation to required temperature, storage conditions, and potential defect/issue with IP is notified to the Sponsor in a timely manner and in accordance with the study Protocol. Follow study site quarantine process as applicable.
- Explain the correct use of the IP to each participant and check, at intervals appropriate for the trial, that each participant is following the instructions properly. Instruct participants where relevant to return empty and partially used medication containers at their next visit. Extra counselling by the Investigator or delegate, for study participants regarding poor medication compliance, may be required.
- Ensure all staff follow the trial's randomisation procedures, if any.
- In a teletrial, the Primary Site will normally be responsible for the randomisation of Satellite Site participants and for the notification of the result of randomisation to the Satellite Site. The Satellite Site should be provided with the randomisation codes or access to Interactive Response Technology (IRT) (and appropriate training) for trials where emergency unblinding may be required, as outlined in the supervision plan.
- Ensure, for blinded studies, the blind is broken only in accordance with the Protocol. For a blinded study, the Investigator must promptly document and explain to the Sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the IP.
- If the investigational product is a GMO, the correct procedures for preparation, administration, disposal and management of spills of the GMO product must be followed in line with sponsor guidelines, the [Office of the Gene Technology Regulator](#) (OGTR) and local policy.
- For a teletrial, where the IP is shipped to, and/or returned from, a Satellite Site, a written working instruction or procedure documenting the way this process is to occur must be in place at the Primary Site pharmacy. The Sponsor will require evidence of this document for the Primary Site to manage the Satellite Site stock. The document must address, at a minimum, aspects of IP shipment such as: the appropriate transfer method, respecting temperature control and monitoring thereof; clear identification of what is being shipped; that the IP is to be used according to the Sponsor's guidelines; relevant documentation to accompany the shipment; acknowledgement of receipt by Satellite Site or Primary Site; delivery information of IP from or to the Primary Site; filing of relevant documentation at both

sending and receiving sites.

- File all relevant trial related documentation in the SMF/SSSF as per SOP 07 The Study Master File.

### Purpose

To describe the procedures and requirements related to the safety data collection, verification and reporting requirements for clinical trials involving Investigational Medicinal Products (IMP) and Investigational Medicinal Devices (IMD). This also includes post registration/post marketing surveillance studies.

### Target Audience

This SOP applies to all health employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and/or staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice.

In 2016, the NHMRC released important changes to safety guidance documents pertaining to the Sponsor's responsibilities, which change the Sponsor's reporting responsibilities to the Australian regulatory body, the TGA, and to HRECs. Refer to [NHMRC Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods \(November 2016\)](#). Consequently, this SOP refers to both the Sponsor's and Investigator's responsibilities relating to safety monitoring.

Reporting of all serious suspected adverse reactions that occur in post registration/marketing surveillance studies undertaken in Australia follow the same reporting lines and timelines as for serious adverse reactions.

ICH-GCP guidelines define the requirement to ensure that all clinical trial participants taking part in a clinical trial are safe and their rights are protected. The National Health and Medical Research Council (NHMRC), local Human Research Ethics Committees and ICH-GCP safety reporting guidelines should be followed for the reporting of all internal and external safety information.

This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### Sponsor Responsibilities

Two documents, the [Australian Clinical Trial Handbook](#) and the [NHMRC Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods](#) give clear direction to Sponsor responsibilities.

NOTE: Sponsor responsibilities are transferred to Coordinating Principal investigators (CPI) for Investigator Initiated clinical trials who must have a Safety Monitoring Plan in place that covers all study sites and includes a Data Safety Monitoring Board (DSMB) or equivalent.

A Sponsor:

- Must be identified for all clinical trials. Joint sponsorship between two or more institutions is not accepted.
- Has ultimate responsibility for the ongoing safety evaluation of the IMP/IMD.
- Is responsible for generating and disseminating all safety communications.
- Must ensure that the trial Protocol has clear sections describing:
  - the assessment and management of risk (if not in an alternative document)
  - safety reporting definitions, procedures, responsibilities and reporting timelines, and
  - Any serious adverse events that do not require immediate reporting.
- Must ensure the conduct of the trial, including the monitoring of safety and reporting of adverse outcomes, complies with the study Protocol as well as applicable guidelines.

- May delegate functions and duties to individuals or third parties, such as a Contract Research Organisation (CRO), or Data Safety Monitoring Board (DSMB), provided arrangements are in place for oversight of the delegated functions and duties, to ensure the integrity of the functions and duties performed and any data generated.
- Should evaluate and categorise all safety information that is reported by Investigators as well as safety information received from other sources.
- Keep detailed records of all reported adverse events and maintain up-to-date tabulations and/or line listings.
- Review the Investigational Brochure (IB)/Instruction for Use or Clinical Investigation Plan (CIP) at least annually and update it when new and relevant information becomes available.
- Prepare and submit to relevant parties an annual safety report/Development Safety Update Report (DSUR).

### **Safety Data Monitoring**

The Sponsor's plans for safety data monitoring should be documented in a Safety Monitoring Plan or similar document and be given to the PI prior to the commencement of the clinical trial. It must be continually reviewed and updated during the trial, as real-time assessments of safety data are performed, and outcomes are made available.

A Sponsor may utilise an independent safety monitoring committee (e.g. Data Safety Monitoring Board) or independent individuals (e.g. a medical monitor) to:

- Review accruing trial safety data in either an unblinded or blinded manner to assess treatment exposure.
- Access, assess and review emerging efficacy data for the trial.
- Assess the balance of risks and benefits within the trial.
- Document the outcome of these reviews.

### **Sponsor Reporting Requirements**

The outcome of various safety reviews is reported directly to HRECs, the Investigator and the Therapeutic Goods Administration (TGA), by the Sponsor and must indicate the impact of each report on patient/participant safety, trial conduct or trial documentation. The reporting of safety reviews by the Sponsor should be as per NHMRC Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods (November 2016) pages 7 and 17 or as detailed in the Protocol. The safety reporting requirement in the Protocol cannot be less than that required by the NHMRC.

Sponsor to provide to Investigator:

- Updated IB at least annually.
- Spontaneous reports of significant safety issues i.e. an issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.
- Outcomes of analyses of accumulating safety data.
- Significant safety issues: those that meet the definition of an Urgent Safety Measure (i.e. a measure required to be taken to eliminate an immediate hazard to a participant's health or safety measure) must be notified within 72 hours, and all other significant safety issues must be notified within 15 calendar days of the Sponsor instigating or being made aware of the issue.

Sponsor to provide to Therapeutic Goods Administration:

- Significant safety issues that meet the definition of an Urgent Safety Measure (i.e. a measure required to be taken to eliminate an immediate hazard to a participant's health or safety measure) must be notified within 72 hours, and all other significant safety issues must be notified within 15 calendar days of the Sponsor instigating or being made aware of the issue. It is strongly recommended that the Sponsor contact the TGA within 24 hours of an Urgent

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Safety Measure being taken, and if initial contact is by telephone, it should be followed-up with a written notification provided by facsimile or e-mail within 72 hours.

- All SUSARs occurring in Australian participants.
- For fatal or life threatening Australian SUSARs, immediately, but no later than 7 calendar days after being made aware of the case, with any follow-up information within a further 8 calendar days.
- For all other Australian SUSARs, no later than 15 calendar days after being made aware of the case.
- Where Austin Health is acting sponsor, TGA notification is facilitated by the Research Development Unit.

Sponsor to provide to HREC:

- Updated IB at least annually which supports trial oversight, depicts a clear picture of evolving safety profile of the trial and provides evidence that the Sponsor is conducting its safety monitoring appropriately.
- Significant safety issues: those that meet the definition of an Urgent Safety Measure (i.e. a measure required to be taken immediately to eliminate an immediate hazard to a participant's health or safety measure) must be logged immediately in RiskMan at the Health Service in which the patient is enrolled, notified within 72 hours, and all other significant safety issues must be notified within 15 calendar days of the Sponsor instigating or being made aware of the issue.

### **Investigator's Responsibilities**

The role of the Investigator with regard to safety reporting is to:

- Provide the Sponsor with all relevant information so that an appropriate safety analysis can be performed.
- Capture and assess all local safety events and report adverse events that occur at the site as further clarified below.
- Ensure safety monitoring complies with the study Protocol, safety monitoring plan if there is one as well as Institutional and national policies, procedures and guidelines.
- Act on any events as clinical care dictates.
- Maintain responsibility for oversight of the ongoing safety evaluation of the IMP/IMD.
- Ensure that if signing of safety documents has been delegated to another medical officer, that this is documented on the Delegation Log as per SOP 03 Site Staff Qualifications, Training Records and Capability.
- Ensure safety events are reported to relevant parties as they occur including Sponsor, DSMB, and HREC, site RGOs, TGA, and Riskmans are completed promptly within the timeframe in accordance with their category (eg. SAE, SUSAR, SSI, USM) and protocol, ICH-GCP, NHMRC guidelines and local guidelines

### **Safety Data Monitoring**

- Keep detailed records of safety management.
- In the instance of device trials, maintain a permanent record of participant identification, study Protocol number and device serial number or other tracking detail for the lifetime of the device, to enable a rapid response, if device safety issues arise.
- Review the adverse outcome in the context of known information on the medicine/ device and decide as to whether the event was drug/device-related (i.e. an adverse reaction).
- Ensure that the immediate and follow-up reports identify participant by unique code number assigned to the trial participant and not by the participant's name, personal identification number, and/or address.

- Ensure any new information regarding safety events is updated on the adverse event page in the CRF/eCRF and/or with a follow up Serious Adverse Event Form (paper or electronic), within 24 hours of the site becoming aware of the change of information and send to Sponsor.

### Reporting Requirements

The reporting of safety reviews by the Investigator should be as per Austin Health's Incident and Feedback Procedure, *NHMRC Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods (November 2016)* or as detailed in the Protocol. The safety reporting requirement in the Protocol cannot be less than that required by the NHMRC.

#### *To Sponsor:*

Within 24 hours of instigating or becoming aware of the event:

- All SAEs and SUSARs except those that are identified in the Protocol, safety monitoring plan or similar document or Investigational Brochure as not needing immediate reporting.
- Any occurrences of congenital anomaly/birth defect arising from any pregnancy of a participant (or partner).
- Within 72 hours of instigating or becoming aware of the event:
  - Significant safety issues which meet the definition of an Urgent Safety Measure instigated by the Investigator (i.e. a measure required to be taken immediately to eliminate an immediate hazard to a participant's health or safety measure).
  - All Urgent Safety Measures instigated by the site as specified in the Protocol.
  - All safety critical events/laboratory abnormalities identified in the Protocol as "critical to safety evaluations".
  - Any additional requested information relating to reported deaths (e.g. autopsy reports and terminal medical reports).
  - Additional requested information relating to reported deaths.
- Within 15 days of instigating or becoming aware of the event:
- All other significant issues.

#### *To Therapeutic Goods Administration:*

- Sponsor is responsible for reporting safety items to the TGA.
  - Where Austin Health is acting sponsor, TGA notification is facilitated by the Principal Investigator.

**NOTE:** Prompt reporting of Urgent Safety Measures to these units is important to allow time to meet the 'within 72 hours' reporting timelines to TGA.

#### *To Institution/Research Governance Office:*

- Within 72 hours of instigating or becoming aware of the event:
  - Significant safety issues that meet the definition of an Urgent Safety Measure (i.e. a measure required to be taken immediately to eliminate an immediate hazard to a participant's health or safety measure).
  - SUSARs arising from the local site.
  - Any information received from the Sponsor that may be new and have an impact on the continued ethical acceptability of the trial or may indicate the need for amendments to the trial Protocol, including monitoring of safety.

- Complete a Riskman where appropriate as per the Austin Health Incident Management Policy

*Electronic reporting – additional information:*

Where a Sponsor delivers Suspected Unexpected Serious Adverse Reactions (SUSARs), analyses of accumulating safety data, annual safety reports and other safety communication through a web portal delivery system or via e-mail, as opposed to paper reports, acknowledgement of receipt by the Investigator/HREC/Institution/TGA of such information will be required by the Principal Investigator (PI), but only after the Sponsor confirms that the report has no bearing on participant safety or trial conduct. There is no longer a requirement for Investigators to print, review and file these reports.

*Satellite Sites – additional information:*

Where a Satellite Site(s) is/are involved, staff will report safety issues directly to the Sponsor as per the timelines specified in the Protocol and the safety monitoring plan or similar document in the same way as the Primary Site. Certified copies of the relevant safety reports/documentation generated at the Satellite Site will be sent to the Primary Site for filing in the SMF. The rules will be pre-determined as per SOP 07 The Study Master File and as documented in the Supervision Plan.

### Purpose

To describe the procedures related to close-out of a clinical trial at all sites and archiving of trial related documentation at the end of the clinical trial.

### Target Audience

This SOP applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants and staff at Austin Health. All study personnel involved in the clinical study must operate within their scope of practice. This SOP must be read in conjunction with individual trial unit SOPs or work practice guidelines (WPG), as well as the Austin Health Research Policies and Procedures.

### Site Close-Out

#### Premature Termination or Suspension of Trial

If the Trial is prematurely terminated or suspended for any reason, the Investigator must:

- Promptly inform the relevant parties of Sponsor, HREC, RGO, Associate Investigator, any Satellite Site and the TGA by providing a detailed written explanation of the premature termination or suspension.
- Promptly inform the trial participant and their primary care physician where the trial participant has consented, of the termination or suspension and, if applicable, of the Investigational Product and dose they were administered.
- Assure appropriate therapy and follow-up for the participant's continued care.

#### *Site Close-Out*

A final close out of a trial can only be done when the Sponsor has reviewed both Investigator/Institution and Sponsor files and confirmed that all necessary documents are in the appropriate files. The Sponsor notifies the Investigator close-out can occur.

The Investigator must:

- Supervise all staff carrying out close-out activities to ensure they are undertaken in accordance with Sponsor requirements, the Delegation Log and the Supervision Plan.
- Provide a summary report of the trial's outcome to the HREC, RGO and any Satellite Site.
- File documentation and correspondence in the SMF/ISF.
- Arrange for archiving of SMF/SSSF.
- Ensure appropriate final disposition of any IP/and other trial related material. This may include return to the Sponsor or destruction of remaining materials.
- Where a Satellite Site is involved: ensure the Satellite Site Supervision Plan is followed regarding the disposition of Essential Documents during the study. Also ensure that evidence of the manner and frequency of supervision to be undertaken by the Principal Investigator (PI) with the Satellite Site staff during the study (e.g. minutes of calls with Satellite Site staff to review patients/participants and study progress) is filed in the Primary Site SMF.
- Ensure any Satellite Site retains documentation and correspondence in their SSSF with original or certified copy of pre-determined documents sent to the Primary Site.

## Archiving

Study documentation is to be archived as specified in the [Australian Code for the Responsible Conduct of Research](#). Part A, section 2.1 and [ICH GCP E6 \(R3\)](#) 4.9.5, 5 and 5.12.

- Where the specified archiving period is conflicting, documentation is to be archived for whichever period is the longest.
- For legal reasons, sites may consider archiving for longer periods or indefinitely.
- Jurisdictional and Institutional requirements for clinical trial records where the participants are minors must be adhered to.
- Jurisdictional and Institutional requirements for clinical trial records where the participants are adults must be adhered to.
- Archived material should be enduring (e.g. fax thermal paper copied to standard paper to prevent fading) and protected from damage or destruction in a secure, environmentally controlled location (e.g. protection from fire, water damage, pest infestation, and theft).
- Study teams may archive study documents locally provided all requirements are met.
- Access to archives should be restricted to authorised personnel. Any change in the ownership and location of the archived materials should be tracked. The PI should make the Sponsor aware of the storage arrangements for the Essential Documents and if at any stage these arrangements can no longer be maintained, the Sponsor should be notified in writing so that alternative storage arrangements can be agreed.
- Ensure appropriate Austin Health Department identifying information is provided to archive company to enable contact before destruction of archived material.

### *For Paper Records:*

- Original documents or certified copies are to be retained.
- Evident identification (e.g. a document retention sticker) that the health and medical record forms part of a clinical trial may be placed on all volumes of the participant's health and medical record in an appropriate position, without obscuring any information, as guided by the local health information management services practice.
- For commercially sponsored research, archiving arrangements are negotiated with the study Sponsor prior to study commencement. These details are to be noted in the study specific CTRA and/or the Satellite Site Sub-Contract.
- Identifiable information (e.g. Participant Identification Log and Participant Information Sheet and Consent Forms) may be archived separately from the main study documents, e.g. with the PI – in case identification of participants is required later. A reference to the type and location of these documents is to be filed with the SMF.
- Satellite Sites will archive the original participant identifiable information at the Satellite Site if the archiving requirements can be met and send a certified copy to the Primary Site for archiving with the Primary Site participant identifiable information (or as outlined in the Supervision Plan).
- Where the study documentation will be filed by the Sponsor, the Identifiable information (e.g. Participant Identification Log and Participant Information Sheet and Consent Forms) site records are NOT TO BE filed with the Sponsor study records.

### *For Electronic Records:*

- Where electronic documents and data are archived, they must be suitably protected from unauthorised changes.
- Electronic Medical Records may be archived indefinitely.

*Transfer of Paper Records into an Electronic Format:*

- When original records are transferred to other media for the purpose of archiving, the system of transfer should be validated to ensure that information will not be lost or altered.
- Filing systems should allow review (e.g. by an auditor) in an efficient manner, analogous to that possible with paper study files.
- Paper records must be scanned in a logical order (e.g. in accordance with the Study Master File index) to ensure that trial reconstruction is possible.
- There should be a quality control process to certify that the scanned image has been captured without error and so is a suitable record of the original document.

## Authorised/endorsed by:

Research Steering Committee

## Document Writer/Contributor

This Standard Operating Procedure has been adapted from the [National Standard Operating Procedures for Clinical Trials, Including Teletrials, in Australia](#)

The authors wish to acknowledge the Standard Operating Procedures of the Barwon Health Research Development Unit, Northern Health Development and Governance Unit and the Epworth Research Development and Governance Unit, from which parts of this document were based.

## Legislation/References/Supporting

### References:

ACSQHC National Clinical Trials Governance Framework:

<https://www.safetyandquality.gov.au/standards/national-clinical-trials-governance-framework>

Aged Care Quality Standards:

<https://www.agedcarequality.gov.au/providers/quality-standards>

Australian clinical trial handbook:

<https://www.tga.gov.au/resources/resource/guidance/australian-clinical-trial-handbook>

Australian Code for the Responsible Conduct of Research: <https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018>

Common Terminology Criteria for Adverse Events:

[https://ctep.cancer.gov/protocoldevelopment/electronic\\_applications/docs/ctcae\\_v5\\_quick\\_reference\\_5x7.pdf](https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf)

Drug Information Association (DIA) TMF reference model

<https://tmfrefmodel.com/>

Drugs, Poisons and Controlled Substances Act 1981.

[http://classic.austlii.edu.au/au/legis/vic/consol\\_act/dpacsa1981422/](http://classic.austlii.edu.au/au/legis/vic/consol_act/dpacsa1981422/)

ICH Guideline for Good Clinical Practice:

<https://www.tga.gov.au/resources/publication/publications/ich-guideline-good-clinical-practice>

Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2):

<https://www.tga.gov.au/publication/note-guidance-good-clinical-practice>

National Safety and Quality Health Service Standards:

[https://www.safetyandquality.gov.au/sites/default/files/2021-05/national\\_safety\\_and\\_quality\\_health\\_service\\_nsqhs\\_standards\\_second\\_edition\\_-\\_updated\\_may\\_2021.pdf](https://www.safetyandquality.gov.au/sites/default/files/2021-05/national_safety_and_quality_health_service_nsqhs_standards_second_edition_-_updated_may_2021.pdf)

National Standards for Mental Health Services: <https://www.safetyandquality.gov.au/our-work/mental-health/national-standards-in-mental-health>

National Standard Operating Procedures for Clinical Trials, Including Teletrials, in Australia:

<https://www.health.gov.au/resources/publications/national-standard-operating-procedures-for-clinical-trials?language=en>

National Statement on Ethical Conduct in Human Research: <https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018>

NDIS Practice Standards: <https://www.ndiscommission.gov.au/providers/registered-ndis-providers/provider-obligations-and-requirements/ndis-practice-standards>

NHMRC Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods: <https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods>

Primary and Community Healthcare Standards: <https://www.safetyandquality.gov.au/standards/primary-and-community-healthcare>

Victorian legislation <https://www.legislation.vic.gov.au/>

**Primary Person/Department Responsible for Document**

Discovery & Innovation Unit

### Adverse Device Effect (ADE)

Adverse event related to the use of an Investigational Medical Device.

Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the Investigational Medical Device. This definition includes any event resulting from use error or from intentional misuse of the Investigational Medical Device.

### Adverse Drug Reaction (ADR)

Any untoward and unintended response to an Investigational Medicinal Product or device related to any dose administered. All adverse events judged by either the reporting Investigator or the Sponsor as having a reasonable possibility of a causal relationship to an Investigational Medicinal Product or device, would qualify as adverse reactions. The expression “reasonable possibility of a causal relationship” means to convey in general that there is evidence or argument to suggest a causal relationship.

### Adverse Event (AE)

In the Australian context, an adverse event (AE) is any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An adverse event is an incident that results, or could have resulted, in harm to a patient/participant or consumer. An unintended near miss is a type of adverse event.

### ARPANSA Code of Practice for the Exposure of Humans to Ionizing Radiation for Research Purposes (2005)

See Code of Practice.

### Amendment

Change in a clinical trial document i.e. protocol, patient informed consent form, and investigator brochure etc.

### Associate Investigator (AI)

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.

*Where the Teletrial Model is implemented:*

- An AI when located at a Primary Site may be delegated some or all of the study related activities by the PI according to their level of experience and documented in the Delegation Log.
- An AI when located at the Satellite Site is the local contact for study related matters at the Satellite Site and will be under the supervision of the PI at the Primary Site.

### Audit

An audit is a systematic and independent examination of trial activities to determine whether a trial is conducted in accordance with applicable requirements. May be scheduled periodically at sites to confirm Protocol compliance and adherence to GCP and regulatory requirements. Routine audits often involve an opening meeting and are conducted according to a pre-prepared plan, which may be revised based on initial findings as the audit proceeds. Audits normally include interviews with the trial team, supporting department staff and the research office, document review, and facility tours.

- HREC audit: The act by the approving HREC of conducting an official review of a clinical trial site during a study to ensure study participant safety and ethical guidelines are being followed.

- **Regulatory inspection:** The act by a regulatory authority of conducting an official review of documents, facilities, records and any other resources that are deemed to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's/contract research organisation (CRO) facilities, or at any other establishments deemed appropriate by the regulatory authority.
- **RGO audit:** The act by the approving RGO of conducting an official review of a clinical trial site during a study to ensure study participant safety and ethical guidelines are being followed.
- **Sponsor audit:** The Sponsor may conduct a systematic and independent examination of clinical trial related activities and documents to determine whether the evaluated clinical trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor's written procedures, ICH GCP and applicable regulatory requirements.

### **Auditor/Inspector**

The individual(s) responsible for conducting an audit at site, on behalf of the regulatory authority, sponsor or HREC.

### **Audit Trail**

Documentation that allows for reconstruction of the course of events throughout a research trial.

### **Australian Health Practitioner Regulation Agency (AHPRA)**

Working with 15 National Health Practitioner Boards, the Australian Health Practitioner Regulation Agency (AHPRA) is the national organisation responsible for implementing the National Registration and Accreditation Scheme (the National Scheme) across Australia.

### **Australian Radiation Protection and Nuclear Safety Agency (ARPANSA)**

The Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) is the Australian Government's primary authority on radiation protection and nuclear safety. ARPANSA regulates Commonwealth entities using radiation with the objective of protecting people and the environment from the harmful effect of radiation.

### **Biopsy**

The process involves extraction of sample cells or tissues for examination to determine the presence or extent of a disease. A tissue sample might be taken for genetic studies.

### **Blinding/Masking**

A clinical trial design strategy in which one or more parties involved in the trial, such as the investigator or participants, do not know which participants have been assigned which interventions. Types of masking include: open label, single blind masking, and double-blind masking.

### **Blue Card**

An Adverse Reaction reporting form to report suspected adverse reactions to vaccines and prescription, over-the-counter and complementary medicines to the Therapeutic Goods Administration.

### **Case Report Form (CRF and e-CRF)**

A printed, optical, or electronic document designed to record all of the Protocol required information to be reported to the study Sponsor on each trial participant. The data collected in the CRF is used as the basis of the trial report and any publications, as well as making up part of the data for regulatory approval for the unapproved therapeutic goods.

## Central Samples

Refers to any sample available for research purposes, this may include pharmacokinetics, pharmacodynamics and pharmacogenetics and molecular testing.

## Certified copy

A certified copy is a copy of an original document that has been verified to be a true copy of the original document by an authorised witness after they have sighted the original document.

## Civil Aviation Safety Authority (CASA) Training

Part 92 of the *Civil Aviation Safety Regulation* (CASR) prescribes the minimum safety requirements for the consignment and carriage of dangerous goods by air. It includes training, documentation, record keeping and incident reporting as well as provisions for packaging, marking, labelling, loading of and stowage in aircraft. Staff involved in the preparation, safe handling and carriage of dangerous goods on aircraft, are required to undertake CASR Part 92 training.

## Clinical Research Associate (CRA)

An individual designated by a Sponsor or Contract Research Organisation (CRO) to monitor the sites conduct in a clinical trial.

## Clinical Research Coordinator (CRC)/ Clinical Trial Coordinator (CTC)

A research worker who works at a clinical research site under the immediate direction of a Principal Investigator, whose research activities are conducted in accordance with Good Clinical Practice guidelines, the National Statement, and the National Clinical Trials Governance Framework. May also be called “Clinical Study Coordinator” or “Trial Coordinator” or “Research Coordinator” or “Research Nurse”.

Where Teletrials is engaged, the CRC at the Primary Site is the contact for coordinators at both Primary and Satellite Sites. Their duties are extended to include Satellite Sites in all aspects of their role (these roles can be delegated to Satellite Site coordinators).

## Clinical Trial

Any investigation in humans intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

## Clinical Trial Agreement

See Clinical Trial Research Agreement.

## Clinical Trial Approval (CTA) scheme- (previously Clinical Trials Exemption (CTX) scheme)

The CTA scheme is established under the Therapeutic Goods Act 1989 and is administered by the TGA. Under the CTA scheme, therapeutic goods are permitted to be used for experimental purposes if the relevant clinical trial is approved by the TGA.

Under the CTA scheme, a Sponsor submits an application to the TGA for evaluation and comment requesting to administer an investigational agent to participants under specified conditions of a particular research study in a clinical setting such as in clinical trials.

A Sponsor cannot commence a CTA trial until written advice has been received from the TGA regarding the application, and approval for the conduct of the trial has been obtained from an ethics committee, and authorisation has been obtained from the Institution at which the trial will be conducted.

## Clinical Trials Governance Framework

The National Clinical Trials Governance Framework is a key initiative of the Revitalised clinical trials agenda endorsed by all Health Ministers in March 2017. It has been developed by the Australian Commission on Safety and Quality in Health Care on behalf of all jurisdictions to support the delivery and integration of high-quality clinical trials service provision into routine hospital care for improved patient outcomes.

The National Clinical Trials Governance Framework is aligned with the National Safety and Quality Health Service (NSQHS) Standards. Once embedded, just as health service organisations need to meet requirements of the NSQHS Standards when they are accredited, the actions in the National Clinical Trials Governance Framework will also be mandatory for health service organisations and trial sites providing clinical trial services.

## Clinical Trial Notification (CTN) scheme

The CTN scheme is an online notification scheme established under the Therapeutic Goods Act 1989 and is administered by the TGA under the CTN scheme, therapeutic goods are permitted to be used for experimental purposes if the relevant clinical trial is notified to the TGA.

CTN trials cannot commence until the trial has been notified to the TGA, the appropriate notification fee paid and Human Research Ethics Committee (HREC) approval has been received. Information relating to a proposed clinical trial is submitted directly to the TGA by the Sponsor. The Institutions where the clinical trial will be undertaken are also documented on the CTN. As it is a notification scheme, the TGA does not review any data relating to the clinical trial.

Once a trial is notified to the TGA, the Sponsor can supply the “unapproved” therapeutic goods to be used in the trial.

## Clinical Trial Participant

An individual participating in a clinical trial.

## Clinical Trial Research Agreement (CTRA)

A legally binding agreement that manages the relationship between Sponsor and Institution where the Sponsor may be providing the study drug or device, the financial support and/or proprietary information and the Institution may be providing data and/or results, publication or input into further intellectual property. The agreement covers matters such as confidentiality, intellectual property, and ownership of data, insurance and indemnity. The Medicines Australia CTRA is the recommended Standard form.

## Clinical Trial Team

The clinical trial team includes individuals, identified by the Investigator, who are responsible for study coordination, data collection and data management. Members of the clinical trial team may also be the research coordinator, study coordinator, research nurse, study nurse or Associate Investigator, clinical trial pharmacist and may have respective roles in the clinical trial as per the Delegation Log, including:

- Participant recruitment and enrolment
- Obtaining consent from prospective participants
- Meet with research participants
- Collect and record information from research participants
- Maintain consistent study implementation.
- Data management, and to ensure integrity
- Dispensing and administering the Investigational Product
- Compliance with regulatory and reporting requirements.

## Cluster

A group of sites involved in undertaking the same study, consisting of a Primary Site who assumes overall responsibility for the conduct of the same study and one or more Satellite Sites, which conduct the study under the direction of the Primary Site using telehealth. A cluster can be made up of sites in the same Hospital Health Service or across different Hospital Health Services.

## Code of Practice for the Exposure of Humans to Ionizing Radiation for Research Purposes (2005) (ARPANSA Code of Practice)

This Code of Practice is designed to ensure that researchers proposing to expose research participants to ionizing radiation provide the participants with relevant information as part of the informed consent process as approved by a HREC.

## Clinical Research Associate (CRA)

An individual designated by a sponsor or contract research organisation (CRO) to monitor the sites conduct in the clinical trial.

## Clinical Trial Site

A clinical setting that is utilised for the examination and/or treatment of participants in a clinical study. The site must provide security for the storage of the test article and must be a facility that is clinically appropriate to perform required procedures described in the protocol. In addition, this site must provide adequate storage for all study related materials with appropriate working space for sponsor monitoring.

## Cohort

A group or subgroup of participants in an observational study that is assessed for biomedical or health outcomes, who have certain characteristics in common, such as sex, a defined age range, or particular severity of disease.

## Common Terminology Criteria for Adverse Events (CTCAE)

Refer: [Common Terminology Criteria for Adverse Events \(CTCAE\)](#)

## Compliance (in relation to clinical trials)

Adherence to all the trial related requirements, good clinical practice (GCP), and the applicable regulatory requirements.

## Concomitant medication (con-meds)

Other prescription medication, over-the-counter drugs or dietary supplements that a study participant takes in addition to the drug under investigation.

## Confidentiality

Prevention of disclosure of proprietary information to unauthorised individuals.

## Confidentiality and disclosure agreement (CDA)

A legal agreement to protect confidential information being revealed during discussions or negotiations with another party; applicable where either or both [parties are individuals or an organisation. The agreement also containing the following clauses:

- Protection against the copying or retention of confidential information
- Protection against disclosure to third parties of information not already in the public domain
- Remedy for any breach of the agreement.

## **Contract**

Written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate on financial matters. The protocol may serve as the basis of a contract.

## **Contract Research Organisation (CRO)**

A person or an organisation (commercial, academic, or other) contracted by the Sponsor to perform one or more of a Sponsor's trial related duties and functions.

## **Coordinating Principal Investigator (CPI)**

In Australia, and specifically in the context of the National Mutual Acceptance (NMA) scheme, this term is sometimes used to describe the health professional, whether or not they are an Investigator at any particular site, who is assigned the responsibility for the conduct of the study and coordination of Investigators at different sites participating in a multicentre trial. This includes coordination of all HREC processes, such as the initial submission and any required notifications throughout the trial, on behalf of the individual Primary and/or Satellite Site Investigators.

The term Coordinating Principal Investigator (CPI) is a term used in Australia in the context of the NMA scheme to describe the Investigator responsible for coordinating the ethics application and related notifications associated with a trial, and so this role has been included in these SOPs. However, the CPI cannot be responsible for trial activity at a site (except where they are also the Principal Investigator). Further, for the avoidance of doubt, the role of the CPI is not relevant for the purposes of teletrials, and the only relationship is between the PI and the AI.

## **Corrective preventative action (CAPA)**

A CAPA consists of improvements to an organization's processes taken to eliminate causes of non-conformities or other undesirable situations. It is usually a set of actions, laws or regulations required by an organization to take in manufacturing, documentation, procedures, or systems to rectify and eliminate recurring non-conformance.

## **Council for International Organizations of Medical Sciences (CIOMS) form**

The CIOMS form provides a standardised format for the reporting of suspected adverse reactions to any particular medical product, including Suspected Unexpected Serious Adverse Reactions (SUSARs) from Australian clinical trials sites.

## **Credentialing**

Credentialing is the formal process used by a health service organisation to verify the qualifications, experience, professional standing, competencies and other relevant professional attributes of clinicians, so that the organisation can form a view about the clinician's competence, performance and professional suitability to provide safe, high-quality healthcare services within specific organisational environments.

## **Curriculum Vitae (CV)**

A résumé of academic and professional training, work history and other qualifications.

## **Dangerous Goods**

Articles or substances which are capable of posing a risk to health, safety, property or the environment and which are shown in the list of dangerous goods in the International Air Transport Association (IATA) Regulations or which are classified according to the IATA Regulations as such.

## **Data and Safety Monitoring Board (DSMB), or Independent Data Monitoring Committee (IDMC) or Monitoring Committee or Data Monitoring Committee**

An independent data-monitoring committee that may be established by the Sponsor (or the Institution acting as Sponsor) to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the Sponsor whether to continue, modify, or stop a trial. The composition and operations of the IDMC must be approved as part of the ethical review process by a HREC.

### **Delegation Log**

A list of appropriately qualified and trained persons to whom the Principal Investigator has delegated significant study-related duties and functions. The Log details related duties and documents which study-specific roles and responsibilities are assigned to each staff member on the study team.

Delegation Logs should be actively maintained (not constructed retrospectively) so there is evidence of appropriate delegation before any trial activities are undertaken. Each entry is signed and dated by the delegates and countersigned by the Principal Investigator.

### **Development Safety Update Report (DSUR)**

A periodic analysis of investigational product safety information crucial to the ongoing assessment of risk to clinical trial participants.

### **Deviation**

A deviation is any breach, divergence or departure from the ICH Good Clinical Practice (GCP), the approved Protocol, SOPs or applicable regulatory requirements that does not have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the research project. GCP requires all deviations to be reported to the Investigator and trial Sponsor.

### **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. They may be subject to, and should be available for, audit by the Sponsor's auditor and inspection by the regulatory authority/ies.

Essential Documents for the trial should be supplemented or may be reduced where justified (in advance of study initiation) based on the importance and relevance of the specific documents to the study.

### **Electronic Medical Record (EMR)**

An electronic medical record (EMR) is a digital version of a paper chart that contains all of a patient's medical history.

### **Eligibility criteria**

The key requirements that people who want to participate in a clinical study must meet or the characteristics they must have. Eligibility criteria consist of both inclusion criteria (which are required for a person to participate in the study) and exclusion criteria (which prevent a person from participating). Types of eligibility criteria include whether a study accepts healthy volunteers, has age or age group requirements, or is limited by sex.

### **Endpoint**

Occurrence of a disease, symptom, sign or test result that constitutes one of the target outcomes of a clinical trial.

### **Exclusion criteria**

A type of eligibility criteria. These are reasons that a person is not allowed to participate in a clinical study.

## **Experimental arm**

An arm type in which a group of participants receives the intervention/treatment that is the focus of the clinical trial.

## **European Medicines Agency (EMA)**

EMA is an agency of the European Union (EU) in charge of the evaluation and supervision of medicinal products.

## **Financial Disclosure Form (FDF)**

A statement form in compliance with the U.S Code of Federal Regulations for which clinical investigators are required to disclose to the study Sponsor their financial interests for the period of time they participated in the study and for one year following the end of the study.

## **Genetically modified organism (GMO)**

A genetically modified organism (GMO) is defined as an organism whose genetic material has been altered using genetic engineering techniques and is capable of transferring genetic material and/or reproduction. The office of the Gene Technology Regulator (see OGTR) has specific requirements in relation to practices and procedures involving GMOs.

## **Good Clinical Practice (GCP) ICH GCP E6 (R2)**

An international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that involve participation of humans. GCP provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of clinical trial participants are protected.

Compliance with this standard provides public assurance that the rights, safety and well-being of trial participants are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data generated from the clinical trials are credible.

These SOPs rely upon the carefully considered Clinical Trials Governance Framework which uses ICH GCP as an objective international minimum standard for clinical practice - as does the TGA over areas for which it has legislative control. The TGA is fully supportive of the approach taken and the matter has been considered by all Health Ministers. The National Statement remains an important contributor.

The National Statement exceeds the minimum requirements for ethics committees set out in ICH GCP and is the Australian standard against which all research involving humans, including research, is reviewed. For the purposes of these SOPs, the National Statement effectively replaces ICH GCP E6 (R2) Section 3.

## **Human Research Ethics Committee (HREC)**

Human Research Ethics Committees review research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines, such as the National Statement. HRECs are usually established by organisations (public, not-for-profit or private) which conduct research involving humans. Universities and hospitals are the most common of these organisations.

In accordance with the Clinical Trials Governance Framework, a HREC is required to have notified its existence to the Australian Health Ethics Committee (AHEC) of the NHMRC to provide assurance that it is operating within NHMRC guidelines. HRECs in Australia (sometimes with the assistance of sub-committees) generally provide both an ethical and scientific review, which may be supplemented on an as-needed basis by external expert advice as the committee(s) concerned sees fit. Applications to a HREC for approval of a clinical trial are usually made using a standardised form that includes a number of essential elements.

In addition to the National Statement the HREC considers other guidance material including: Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders (2018), Keeping research on track: a guide for Aboriginal and Torres Strait Islander peoples about health research ethics, and the Australian Code for the Responsible Conduct of Research (the Code). Other guidance material may also be referred to including, but not limited to: Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and the Consolidated Standards of Reporting Trials (CONSORT).

HRECs also consider relevant national and jurisdictional legislation including guardianship legislation and the roles of civil and administrative tribunals for participation of people without the capacity to provide consent. HRECs also monitor compliance with the approved Protocol during the conduct of the trial and provide advice on strategies to promote awareness of the ethical conduct of clinical trials and research more broadly.

### **Independent Third-Party Provider**

An individual or group of individuals contracted by and external to a clinical trial site to provide a service related to a clinical trial, who is/are qualified to perform those trial related duties and functions. The individual or group of individuals provide the service under supervision of the Principal Investigator who ensures the integrity of the trial related duties and functions performed and any data generated by them.

### **Informed Consent**

Informed consent is a process of communication between a patient/participant and a clinician about options for treatment, care processes or potential outcomes. This communication results in the patient/participant's authorisation or agreement to undergo a specific intervention or participate in planned care. The communication should ensure that the patient/participant has an understanding of the care they will receive, all the available options and the expected outcomes, including success rates and side effects for each option.

Informed Consent may be expressed orally, in writing or by some other means depending on: the nature, and complexity of the research; and the participant's personal and cultural circumstances.

Research is 'low risk' where the only foreseeable risk is one of discomfort. Where the risk, even if unlikely, is more serious than discomfort, the research is not low risk. The greater the risks to participants in any research for which ethical approval is given, the more certain it must be both that the risks will be managed as well as possible, and that the participants clearly understand the risks they are assuming.

Potential participants who wish to participate in research will provide a record of their agreement, either through physically signing a paper copy of the consent form or electronically signing a consent form using an approved format that accurately documents the time, date and authenticity of their signature. The PI/ delegate will countersign and date that the consent process has occurred. Ideally this will be done contemporaneously; however, under special circumstances related to the nature of the study the HREC may approve this signature to occur at a later time with appropriate documentation.

### **Inspection**

An official review of trial related activities by a regulatory authority that has rights conferred by regulation (e.g. to enter premises and to request documents) to determine whether a trial is conducted in accordance with applicable requirements. May be scheduled periodically at sites to confirm Protocol compliance and adherence to GCP and regulatory requirements. Regulatory inspections normally require more extensive planning and input from the organisation than routinely conducted trial audits. Inspections often involve an opening meeting and are conducted according to a pre-prepared plan, which may be revised based on initial findings. Inspections normally include interviews with the trial team, supporting department staff and research office, document review, and facility tours.

### **Institutional Review Board (IRB)**

A term used to refer to an independent research ethics committee used in some countries, particularly the United States. In Australia, the term Human Research Ethics Committee should be used.

### **Insurance or indemnity**

Refers to a contract of insurance, a contract of indemnity, a guarantee, a surety, a warrant and a bond and which in any case shall be available to cover the liability of the sponsor and the investigator to provide for compensation in the event of any injury, loss or damage to tot the death of any subject arising out of the arrangement for or conduct of the clinical trial and which the sponsor or investigator shall become liable to pay to such subject or in respect of such subject by the way of damages or costs

### **Interactive Voice Response System (IVRS)**

Interactive Voice Response System is an interactive technology that allows a computer to interact with a human to detect voice and keypad inputs. These can be accessed via telephone. Users respond/provide their responses via the touch-tone keypad of a telephone.

This system is used to proactively manage the key aspects of their clinical trials which includes enrolment/randomization, dosing/drug dispensation, clinical supplies, drug inventory management, and un-blinding.

### **Interactive Web Response System (IWRS)**

Interactive Web Response System is an interactive technology that allows a computer to interact with a human through data input using a web browser. Users respond/provide their responses via the internet site. This system is used to proactively manage key aspects of their clinical trials which includes enrolment/randomization, dosing/drug dispensation, clinical supplies, drug inventory management and un-blinding.

### **International Air Transport Association (IATA)**

An international organisation that develops the commercial standards globally, for the air transport system. In the context of this document, IATA sets the standards for training personnel in the packing and shipping of Dangerous Goods including Dry Ice, e.g. packing and shipping of biological samples in clinical trials.

### **International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)**

The ICH is a joint initiative involving both regulatory authorities and the pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines.

Since its inception in 1990, ICH has gradually evolved, to respond to increasingly global developments in the pharmaceutical sector and the increasingly global face of drug development, and these ICH guidelines are applied by a growing number of regulatory authorities.

ICH's mission is to achieve greater harmonisation worldwide to ensure that safe, effective, and high- quality medicines are developed, registered and maintained in the most resource-efficient manner whilst meeting high standards.

Harmonisation is achieved through the development of ICH Guidelines via a process of scientific consensus with regulatory and industry experts working side-by-side. Key to the success of this process is the commitment of the ICH regulators to implement the final Guidelines.

The National Statement exceeds the minimum requirements for ethics committees set out in ICH GCP and is the Australian standard against which all research involving humans, including research, is reviewed. For the purposes of these SOPs, the National Statement effectively replaces ICH GCP E6 (R2) Section 3.

International Organisation for Standardisation (ISO) 14155 Clinical Investigation of Medical Devices for Human Subjects.

The international standard which addresses good clinical practice for the design, conduct, recording and reporting of clinical investigations carried out in human subjects to assess the safety or performance of medical devices for regulatory purposes.

### **Investigational Brochure (IB)**

A compilation of the clinical and non-clinical data available on the experimental products intended for use in the clinical trial in question. It provides trial organisers and staff with an understanding of the rationale of the trial, in order to inform their compliance with the Protocol requirements. The information enables a risk/benefit assessment of the appropriateness of the proposed trial, of vital importance to HREC considerations.

- **Medicine:** A compilation of the clinical and non-clinical data on the Investigational Product that is relevant to the study of the product in human participants. For marketed products it may be acceptable to use the Product Information.
- **Device:** A compilation of the current clinical and non-clinical information on the Investigational Medical Device relevant to the clinical investigation.

### **Investigational Medicinal Device (IMD)**

A medical device is any instrument, apparatus, implement, machine, appliance, implant, software, material or other similar or related article that is being assessed for safety or performance in a clinical investigation.

This includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes.

### **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 a new patient/participant group, or when used to gain further information about an approved use.

### **Investigational Product**

The Investigational Product (IP) includes any product, or intervention being investigated, tested or used as a placebo or reference point in a clinical trial. This includes 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. The Sponsor or their delegate, is responsible for the provision and maintenance of the IP.

An investigational product can be an Investigational Medicinal Device or Investigational Medicinal Product.

### **Investigator**

An individual engaged in the conduct of a clinical trial research study at a study site and ensures that the study complies with ICH GCP E6 (R2) guidelines. An Investigator can be either a Coordinating Principal Investigator, Principal Investigator, or an Associate Investigator.

It should be noted that in ICH GCP the term Sub Investigator is used to refer to an individual member of the clinical trial site to perform critical trial related procedures and/or to make important trial related decisions (e.g. associates, resident's research fellow). For the purposes of the Teletrials Compendium, the term Associate Investigator is used to refer to the Sub Investigator role and to reflect the Australian context.

Under the Teletrials Compendium, and in accordance with ICH-GCP, the Principal Investigator is the Investigator responsible for all aspects of the clinical trial at a site and within a cluster. An Associate Investigator cannot be responsible for trial conduct at a site but may be delegated duties according to expertise and scope of practice.

The term Coordinating Principal Investigator (CPI) is a term sometimes used in Australia in the context of the National Mutual Acceptance (NMA) scheme to describe the Investigator responsible for coordinating the ethics application and related notifications associated with a trial, and so this role has been included in these SOPs. However, the CPI cannot be responsible for trial activity at sites. Further, for the avoidance of doubt, the role of the CPI is not relevant for the purposes of teletrials, and the only relationship is between the PI and the AI.

### **Medical Monitor**

The medical monitor, usually a representative from the sponsor, is the person responsible for the safety surveillance of a clinical trial.

### **Medicines and Healthcare products Regulatory Agency (MHRA)**

MHRA is an executive agency of the Department of Health and Social Care in the United Kingdom which is responsible for ensuring that medicines and medical devices work and are acceptably safe.

### **Monitoring**

The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the Protocol, Standard Operating Procedures (SOPs), GCP, and the applicable regulatory requirement(s).

### **Monitoring Plan**

A document developed by the Sponsor that is tailored to the specific human subject protection and data integrity risks of the trial. The plan should 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. The plan should also emphasize the monitoring of critical data and processes. Particular attention should be given to those aspects that are not routine clinical practice and that require additional training. The monitoring plan should reference the applicable policies and procedures.

### **Multi-Centre Trial**

A clinical trial conducted according to a single protocol but at more than one site, and therefore carried out by more than one investigator.

### **National Health and Medical Research Council (NHMRC)**

The NHMRC is Australia's leading expert body for supporting health and medical research; for developing health advice for the Australian community, health professionals and governments; and for providing advice on ethical behaviour in health care and in the conduct of health and medical research.

### **National Mutual Acceptance (NMA)**

The NMA scheme provides the framework for single scientific and ethical review of multi-centre human research projects in publicly funded health organisations of participating jurisdictions.

In order for ethics reviews of human research to be accepted under the NMA scheme, the HREC conducting the review must be under the authority of an Institution certified under the NHMRC National Certification Scheme, and also a Certified Reviewing HREC under the NMA scheme.

There will be some exceptions to single scientific and ethical review and details can be found on jurisdictional health websites.

## **National Statement on Ethical Conduct in Human Research 2007 (Updated 2018) (National Statement)**

The National Statement is the principal ethical guideline setting out the requirements for the ethical design, review and conduct of human research in Australia (including clinical trials). It is authored by the NHMRC, the Australian Research Council (ARC) and Universities Australia.

The National Statement exceeds the minimum requirements for ethics committees set out in ICH GCP and is the Australian standard against which all research involving humans, including research, are reviewed. For the purposes of these SOPs, the National Statement effectively replaces ICH GCP E6 (R2) Section 3.

### **New Drug Application (NDA)**

An NDA is the registration document through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing. The application includes detailed reports of pharmacology, toxicology, manufacturing, and chemistry, as well as data from clinical trials.

### **Observational study**

A type of clinical study in which participants are identified as belonging to study groups and are assessed for biomedical or health outcomes. Participants may receive diagnostic, therapeutic, or other types of interventions, but the investigator does not assign participants to a specific interventions/treatment. A patient registry is a type of observational study.

### **Open-label study**

A study in which the participants and the investigators know which treatment is being given. In an open-label study, there is no blinding and none of the participants receives a placebo.

### **Participant**

A participant is a clinical trial subject, patient/participant or consumer who is enrolled to participate in a clinical trial.

### **Participant screening log**

A document used to record the identification of participants who entered pre-trial screening.

### **Participant enrolment log**

A document used to record the chronological enrolment of participants by trial number.

### **Participant identification list**

A confidential document that the Investigator/Institution keeps of the names of all trial participants linked to their corresponding unique clinical trials identifier code. It allows an Investigator/Institution to reveal the identity of any participant and to make future contact if required.

### **Participant Information and Consent Form (PICF)**

The written information approved for use to provide information to potential participants and to record their decision to participate. The PICF must be approved by an HREC prior to use.

### **Patient registry**

A type of observational study that collects information about patients' medical conditions and/or treatments to better understand how a condition or treatment affects patients in the real world.

### **Pharmacodynamics (PD)**

PD describes drug response in terms of biochemical and physiological effects of drugs, and mechanisms of drug action, and relationship between drug concentration and effect.

## **Pharmacogenomics (PG)**

PG is the study of how genes affect a person's response to drugs. This relatively new field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and doses that will be tailored to a person's genetic makeup.

## **Pharmacokinetics (PK)**

PK describes a drug's exposure by characterizing absorption, distribution, bioavailability, metabolism, and excretion as a function of time.

## **Phase**

The stage of a clinical trial studying a drug or biological product, based on definitions developed by the

U.S. Food and Drug Administration (FDA). The phase is based on the study's objective, the number of participants, and other characteristics. There are five phases: Early Phase 1 (formerly listed as Phase 0), Phase 1, Phase 2, Phase 3, and Phase 4.

### **Phase 1**

A phase of research to describe clinical trials that focus on the safety of a drug. They are usually conducted with healthy volunteers, and the goal is to determine the drug's most frequent and serious adverse events and, often, how the drug is broken down and excreted by the body. These trials usually involve a small number of participants.

### **Phase 2**

A phase of research to describe clinical trials that gather preliminary data on whether a drug works in people who have a certain condition/disease (that is, the drug's effectiveness). For example, participants receiving the drug may be compared to similar participants receiving a different treatment, usually an inactive substance (called a placebo) or a different drug. Safety continues to be evaluated, and short-term adverse events are studied.

### **Phase 3**

A phase of research to describe clinical trials that gather more information about a drug's safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs. These studies typically involve more participants.

### **Phase 4**

A phase of research to describe clinical trials occurring after FDA has approved a drug for marketing. They include post market requirement and commitment studies that are required of or agreed to by the study sponsor. These trials gather additional information about a drug's safety, efficacy, or optimal use.

## **Placebo**

An inactive substance or treatment that looks the same as, and is given in the same way as, an active drug or intervention/treatment being studied.

## **Post Registration or Marketing Surveillance Study (PMS)**

The term "post-marketing surveillance (PMS) study" implies a scientifically rigorous study of a product that is approved for registration in Australia designed to produce reliable information about drug safety. PMS studies are generally performed on the initiative of the sponsoring company but may be suggested or requested by other parties. They should generally be designed to address a specific drug safety question or hypothesis (the latter often identified initially by voluntary reporting).

## Primary Site

Under the Teletrials Model, the Primary Site coordinates the trial across a cluster to enhance participant reach, recruitment and management. The Principal Investigator located at the Primary Site has full responsibility for conducting the clinical trial at their site and any Satellite Site within their cluster under ICH GCP.

## Principal Investigator

The Principal Investigator (PI) is the Investigator responsible for the conduct, management, monitoring and reporting of a trial at their own site.

Where the Teletrial Model is implemented, the Principal Investigator at the Primary Site assumes overall responsibility and provides oversight to Satellite Site(s) within a cluster. Associate Investigators at Satellite Site(s) operate under the direction and responsibility of the Principal Investigator at the Primary Site.

## Protocol

A detailed clinical trial plan that includes the purpose and procedures of the research and who can be part of the trial. The Protocol provides the rationale, design, methodology for the trial conduct, who may participate in a trial, the length of a trial and the schedule of tests, procedures, medications and dosages, method of analysis, monitoring of data safety and quality. The Sponsor of the trial is responsible for the Protocol.

The structure and minimum contents of a trial Protocol is defined in ICH GCP (refer to SOP 04 Protocol and Investigational Brochure Requirements).

The Protocol must be formally approved by the HREC prior to trials commencement.

## Protocol Amendment

A written description of a change(s) to or formal clarification of a Protocol. The Protocol amendment must be formally approved by a HREC prior to being enacted, except where participant safety is threatened.

## Quality Assurance (QA)

Planned and systematic actions that are established to ensure that the trial is performed, and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

## Quality Control (QC)

The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

## Randomisation

The process of assigning trial participants to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

## Randomisation List

A decoded list of randomisation identifiers that is locked away from all personnel who must remain blinded during the clinical trial.

## Recruitment status

- Not yet recruiting: The study has not started recruiting participants.
- Recruiting: The study is currently recruiting participants.
- Enrolling by invitation: The study is selecting its participants from a population, or group of people, decided on by the researchers in advance. These studies are not open to everyone who meets the eligibility criteria but only to people in that particular population, who are specifically invited to participate.

- **Active, not recruiting:** The study is ongoing, and participants are receiving an intervention or being examined, but potential participants are not currently being recruited or enrolled.
- **Suspended:** The study has stopped early but may start again.
- **Terminated:** The study has stopped early and will not start again. Participants are no longer being examined or treated.
- **Completed:** The study has ended normally, and participants are no longer being examined or treated (that is, the last participant's last visit has occurred).
- **Withdrawn:** The study stopped early, before enrolling its first participant.

### **Regulatory Authority**

Bodies having the power to regulate. This includes the Therapeutic Goods Australia (TGA), United States Food and Drug Administration (FDA), European Medicines Agency (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA).

### **Research Development and Governance Unit (RDGU)**

The RDGU at Austin Health manages the many aspects of research compliance, including research governance applications and review processes.

### **Research Governance Officer (RGO)**

The RGO is the individual appointed within an organisation who is responsible for the assessment of applications for site authorisation and who provides administrative oversight of authorised research projects.

Research Governance considers legal compliance, financial management, accountability and risk management associated with research at a participating site.

### **Risk Assessment**

Risk assessment is the assessment, analysis and management of risks. It involves recognising which events may lead to harm in the future and minimising their likelihood and consequence.

### **Risk Management**

Risk management is the design and implementation of a program to identify and avoid or minimise risks to patients/participants, employees, volunteers, visitors and the organisation.

### **Safety Monitoring Plan**

A description of the methods, roles and responsibilities and requirements for monitoring the safety data of the trial.

### **Satellite Site**

A Satellite Site is located in a geographically separate health facility and trial activities are delegated by the Primary Site (clinical trial site) to the Satellite Site, to enable performance of activities associated with the conduct of a clinical trial at the Satellite Site and to support trial accessibility of remote participants to a clinical trial.

A Satellite Site can be located in metropolitan, regional or rural settings. Delegated activities to be performed by a Satellite Site are trial and Satellite Site specific. The Primary Site must consider a Satellite Site's personnel and facilities in developing a Delegation Log and Supervision Plan suitable for a trial. The proposed delegation of duties and Supervision Plan must be agreed at the time of site selection and must be documented before the study is initiated at each Satellite Site.

For each trial, infrastructure and training requirements are the same for both the Primary and Satellite Sites.

A Satellite Site should have the following:

- Appropriately contracted qualified and trained Investigator(s) and delegated staff to undertake delegated trial related activities including obtaining informed consent (if required). Study staff are trained in the Protocol, IB, study procedures and Adverse Event (AE)/Serious Adverse Event (SAE) reporting. A system for safety reporting duties is in place for all study staff.
- Study related documentation including a Satellite Site Study File, procedures for managing the security of information and trial data and a process for managing data security or privacy breaches.
- An understanding of the process for securely and suitably storing and ensuring accountability for the Investigational Medicinal Product (IMP).

### **Satellite Site Study File (SSSF)**

A folder containing all the Satellite Site study relevant documents generated during the course of the trial. The content of the Satellite Site Study File can be decided with the study team and the Sponsor. The SSSF may be a sub-set of the Study Master File (SMF) and should be prefaced with an index of contents as well as indicate the location(s) of all Essential/Source Documents.

### **Scope of Clinical Practice**

Scope of clinical practice is the extent of an individual clinician's approved clinical practice within a particular organisation, based on the clinician's skills, knowledge, performance and professional suitability, and the needs and service capability of the organisation.

### **Serious Adverse Device Effect (SADE)**

An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

### **Serious Adverse Event (SAE) – drug**

Any untoward medical occurrence that, at any dose:

- Results in death
- Is life-threatening
- Requires inpatient hospitalisation or prolonging existing hospitalisation
- Results in persistent or significant disability/capacity
- Results in or is associated with a congenital anomaly/birth defect.

### **Serious Adverse Event (SAE) – device**

Serious Adverse Event for medical devices: any adverse medical occurrence that:

- Led to a death
- Led to a serious deterioration in health of a study participant user or other. This would include:
  - A life-threatening illness or injury
  - A permanent impairment of body function or permanent damage to a body structure
  - A condition requiring hospitalisation or increased length of existing hospitalisation
  - A condition requiring unnecessary medical or surgical intervention
  - Foetal distress, foetal death or a congenital abnormality/birth defect
  - Might have led to a death or a serious deterioration in health had suitable action

or intervention not taken place.

This includes:

- A malfunction of a device such that it must be modified or temporarily/permanently taken out of service
- A factor (such as a deterioration in the characteristics or performance) found on examination of the device.

### **Serious Breach**

A breach of Good Clinical Practice (GCP) or the Protocol that is likely to affect to a significant degree the safety or rights of a research participant or the reliability and robustness of the data generated in the research project.

A Serious Breach must be notified to the reviewing HREC.

### **Significant Safety Issue (SSI)**

A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.

### **Site Close-out Visit**

A visit conducted at the end of a study. The purpose is to ensure the completeness of all activities including the collection and verification of study data, the final counting and disposition of the investigational product and the verification of complete and accurate investigator files of essential documents.

### **Site Initiation Visit**

A visit conducted at the start of a study. The purpose is a thorough review of the protocol and study related procedures. All study site personnel meet together to clarify the actual process of implementing the protocol.

### **Site Qualification Visit**

A process to determine that the clinical investigational site is adequately equipped and has appropriate facilities to conduct a specific study. Qualified sites should have ample secured storage for all study related materials, access to patient population under study, sufficient staffing to conduct study related procedures, data collection and reporting, and have space for sponsor monitoring.

### **Site-Specific Assessment Officer**

The site-specific assessment officer responsibilities are distinct from those of the HREC and the Research Governance Officer. The granting of ethical approval by a HREC does not oblige an approving authority to grant authorisation at their site as the site may not have the capacity or capability to undertake the trial based on the Protocol requirements. As part of the process to confirm whether authorisation should be granted, the site-specific assessment officer confirms the clinical trial has undergone HREC review and received approval prior to commencement. Specifically, this position is responsible for undertaking authorisation activities in a timely manner.

### **Source Data**

All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source Data are contained in Source Documents (original records or certified copies).

Collection of accurate Source Data (contained in Source Documents) is essential for compliance with GCP. The format used (whether paper or electronic) should permit the reconstruction of the clinical care given to the participant and describe any significant participant-related events that may occur during the conduct of the trial. Source Data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to Source Data should be traceable, should not obscure the original entry, and should be explained if necessary. In addition, Source Data in electronic Form should be complete, consistent, enduring, and available (ALCOA+).

### **Source Documents**

Original documents (where the Source Data was first recorded), data, and records (e.g. medical/hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial). The principles apply to all records referenced irrespective of the type of media used.

Source Documents substantiate the existence of the participant and integrity of trial data collected.

### **Sponsor**

An individual, company, Institution or organisation which takes on the responsibility for securing the arrangements, the initiation, management, and/or financing of a clinical trial.

All clinical trials conducted in Australia must have a trial Sponsor that is an Australian entity (an overseas company cannot be the Sponsor of a trial in Australia). Sponsors of trials under the TGA CTN or CTA schemes may include individuals, companies, Institutions, or organisations. The ultimate responsibility for the quality and integrity of the clinical trial data resides with the trial Sponsor. The trial Sponsor retains overall responsibility for all delegated functions in accordance with the Guideline for Good Clinical Practice and the International Organisation for Standardisation for trials under the CTN or CTA schemes. This also applies when a non-commercial trial Sponsor delegates activities to a Coordinating Principal Investigator, trial coordinating centre or clinical research organisation.

The Sponsor is also responsible for ensuring that appropriate approvals are obtained prior to the commencement of the clinical trial, that conditions of any approvals are adhered to during the course of the clinical trial, and that the ethics principles of research merit and integrity, justice, beneficence and respect are applied to the conduct of clinical trials.

### **Standard of Care treatment (SOC)**

Treatment currently in wide use, often approved by regulatory agencies, and generally considered effective in the treatment of a specific disease or condition.

### **Standard Operating Procedures (SOPs)**

Detailed written instructions to achieve uniformity of the performance of a specific process.

### **Study Master File (SMF) or Investigator Site File (ISF)**

A folder containing all the study related Essential Documentation/Source Documents as defined by the study team and in accordance with ICH GCP E6 (R2), Section 8.2, 8.3 and 8.4 that should be established at the beginning of a trial both at the Investigator/Institution's site and at the Sponsor's office.

The SMF should also be prefaced with an index of contents as well as indicate the location(s) of all Essential/Source Documents. The storage system used during the trial and for archiving (irrespective of the type of media used) should provide for document identification, version history, search, and retrieval.

Where the Teletrial Model is implemented, the Primary Site should have control of all Essential Documents and records generated by the Investigator/Institution before, during, and after the trial.

### **Study Team**

This incorporates all staff members listed on the delegation log of an individual study.

### **Supervision Plan**

A plan that outlines processes for a Principal Investigator in the supervision of any individual or party to whom he/she delegates study-related duties and functions conducted at a Satellite Site, which includes, but is not limited to, details on joint consultations using telehealth, collation and monitoring of documents, frequency of joint trial meetings across a cluster (with minutes of these meetings) and clarification of activities performed by the PI and the AI, other study staff and independent third party i.e. external service providers.

### **Suspected Unexpected Serious Adverse Reaction (SUSAR)**

An adverse reaction that is both serious and unexpected and possibly, probably or likely related to the drug/device.

### **Teletrial**

Teletrials are defined as follows: A teletrial uses telehealth technology to communicate between the Primary Site and Satellite Site/s and enable delivery of aspects of a clinical trial as defined in the Supervision Plan. This technology supports a Principal Investigator to supervise Associate Investigator/s to conduct a clinical trial at a Satellite Site which is geographically remote from the Principal Investigator's Primary Site. The Principal Investigator remains responsible for the trial.

A detailed Supervision Plan is required, in addition to a Delegation Log required by ICH GCP for all Satellite Sites regardless of experience. Trial participants may have trial visits at both the Primary and Satellite Sites, as determined by the Protocol and Supervision Plan.

The conduct of the trial is detailed under the 'head agreement', (Clinical Trial Research Agreement/Clinical Trial Agreement between the Sponsor and the Principal Investigator's Institution) and a Sub-Contract between the Primary Site and the Satellite Site Institutions (see Teletrial Sub- Contract).

### **Teletrials Compendium**

Set of documents for teletrials that includes National Principles and National Standard Operating Procedures endorsed by all Australian jurisdictions through the Clinical Trials Project Reference Group intended to support nationally consistent and high-quality implementation of the Teletrials Model in Australia.

### **Teletrial Sub-Contract**

A legally binding agreement that manages the relationship between the Primary Site and the Satellite Site where the Satellite Site is a separate legal entity to the Primary Site.

### **Therapeutic Goods Administration (TGA)**

The Therapeutic Goods Administration (TGA) is the Australian Government Department of Health agency responsible for the regulation of, supply, import, export, manufacturing and advertising of therapeutic goods in Australia.

### **Training Log**

A record of all training relating to a specific clinical trial undertaken by a trial staff member who has been delegated clinical trial related duties. The log documents the date, the training undertaken, who gave the training with a signature of both trainer and trainee and is kept current for the duration of the clinical trial.

**Unanticipated Serious Adverse Device Effect (USADE)**

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

**Unexpected Adverse Drug Reaction**

An adverse reaction, the nature or severity of which is not consistent with the available product information (e.g., Investigator Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product).

**Urgent Safety Measure (USM)**

A measure not defined by the Protocol but required to be taken in order to eliminate an immediate hazard to a participant's health or safety. This type of procedure can be instigated by either the Investigator or Sponsor and can be implemented before seeking approval from HRECs or Institution.

**U.S. Food and Drug Administration (FDA)**

An agency within the U.S. Department of Health and Human Services. The FDA is responsible for protecting the public health by making sure that human and veterinary drugs, vaccines and other biological products, medical devices, the Nation's food supply, cosmetics, dietary supplements, and products that give off radiation are safe, effective, and secure.

**Work Practice Guideline (WPG)**

A tool to be used for reference.