Generic Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia

Based on ICH GCP and as developed by QLD Health

Government of South Australia
SA Health

Contents

Introduction

Good Clinical Practice (GCP) Guideline for Good Clinical Practice ICH E6 (R2) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of trials that involve participation of humans.

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

National Mutual Acceptance (NMA) is a national initiative for mutual acceptance of ethical and scientific review in public hospitals for multi-centre clinical trials. These generic Standard Operating Procedures, the Teletrials Clinical Consultation User Guide and Supervision Plan have been adapted from Queensland Health Standard Operating Procedures to provide this generic version.

The Australian ICH GCP (including Teletrials) SOPS were developed by the State of Queensland (Queensland Health) and incorporate the recommendations from the Clinical Oncology Society of Australia's (COSA) Australasian Teletrial Model – A National Guide to Implementation, September 2016.

Glossary

ADE	Adverse Device Effect
ADR	Adverse Drug Reaction
AE	Adverse Event
AHPRA	Australian Health Practitioner Regulation Agency
ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
CASA	Civil Aviation Safety Authority
CIOMS	International, non-governmental, non-profit organisation representing the biomedical scientific community
Code	Code of Practice - Exposure of Humans to Ionizing Radiation for Research (2005) published by ARPANSA
CPI	Coordinating Principal Investigator
CRA	Clinical Research Associate
CRC	Clinical Research Coordinator
CRF	Case Report Form
CRO	Contract Research Organisation
CTA	Clinical Trial Agreement
CTRA	Clinical Trial Research Agreement
CTN	Clinical Trial Notification
CTX	Clinical Trial Exemption
CV	Curriculum Vitae
DSMB	Data and Safety Monitoring Board
GCP	Good Clinical Practice
HHS	Hospital and Health Service

HREC	Human Research Ethics Committee
IATA	International Air Transport Association
ICH	International Council for Harmonisation of Technical requirements for Registration of Pharmaceuticals for Human Use
IMD	Investigational Medical Device
IMP	Investigational Medicinal Product
IVRS	Interactive Voice Response System
IWRS	Interactive Web Response System
National Statement	National Statement on Ethical Conduct in Human Research (NHMRC)
NHMRC	National Health and Medical Research Council
NMA	National Mutual Acceptance
PI	Principal Investigator
PICF	Participant Information and Consent Form
PMS	Post Registration or Marketing Surveillance Study
RGO	Research Governance Officer
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SI	Sub-Investigator
SMF	Study Master File
SSSF	Satellite Site Study File
SSI	Significant Safety Issue
SUSAR	Suspected Unexpected Serious Adverse Reaction
TGA	Therapeutic Goods Administration

UR	Unit Record Number
USM	Urgent Safety Measure
USADE	Unanticipated Serious Adverse Device Event

Terms

Please refer to terms in this section when reading the Generic Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia and other associated documents.

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)

Any untoward medical occurrence in a participant administered an investigational medicinal product or device and which does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or device, whether or not considered related to this medicinal product or device.

Australian Health Practitioner Regulation Agency (AHPRA)

The Australian Health Practitioner Regulation Agency (AHPRA) is the organisation responsible for the registration and accreditation of ten health professions 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.

Blue Card

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

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.

Certified copy

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

CIOMS form

A form used to report Serious Adverse Reaction reports that occur in Australia and sent to the TGA.

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 to monitor the sites conduct in a clinical trial.

Clinical Research Coordinator (CRC)

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. 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 Agreement (CTA)

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, input into further intellectual property. The agreement covers matters such as confidentiality, intellectual property, ownership of data, insurance and indemnity.

Clinical Trial Research Agreement (CTRA)

Medicines Australia Standard form

Clinical Trial 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 legally entity to the Primary site.

Clinical Trial Notification (CTN)

The CTN scheme is an online notification scheme run under the Therapeutic Goods Act, 1989 whereby information relating to a proposed clinical trial is submitted directly to the Therapeutic Goods Administration (TGA) by the Sponsor. Once a trial is notified to the TGA and the relevant fee has been

paid, the sponsor can supply the “unapproved” therapeutic goods to be used in the trial. 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.

CTN trials cannot commence until the trial has been notified to the TGA, the appropriate notification fee paid and acknowledgement is received.

Clinical Trial Exemption (CTX)

An approval process whereby 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 CTX 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 from the institution at which the trial will be conducted.

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 tele-health. 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)

This Code of Practice is designed to ensure that researchers proposing to expose research participants to ionizing radiation provide the participants and the Human Research Ethics Committees with information that allows consent to be properly considered by the research participants and approval considered by the Human Research Ethics Committee.

Coordinating Principal Investigator (CPI)

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, including coordination of all Human Research Ethics Committee (HREC) processes throughout the study, on behalf of the individual Primary and / or Satellite Site investigators.

Contract Research Organisation (CRO)

An organisation contracted by the sponsor to oversee the conduct of the clinical trial.

Curriculum Vitae (CV)

A resumé 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 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.

Delegation log

A list of appropriately qualified and trained persons to whom the Principal Investigator has delegated significant study – related duties and which documents study-specific roles and responsibilities assigned to each staff member on the study team. Each entry is signed and dated by the delegates and countersigned by the Principal Investigator.

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.

FDA 1572

A form that must be filed by an Investigator running a clinical trial to study a new drug or agent. The Investigator agrees to follow the United States Food and Drug Administration (FDA) Code of Federal Regulations for the clinical trial and verifies they have experience and background needed to conduct the trial.

The Statement of Investigator, Form FDA 1572 (1572), is an agreement signed by the investigator to provide certain information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic.

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.

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 trial participants are protected.

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

Human Research Ethics Committee (HREC)

A committee registered by the NHMRC and constituted under the guidance of the NHMRC National Statement on the Ethical Conduct in Human Research 2007 (Updated 2018) which reviews all research proposals involving human participants, and is responsible for assessing the scientific validity of the trial design, the safety and efficacy of the medicine or device and the ethical acceptability of the trial process, and grants approval of the trial protocol in accordance with relevant standards and national guidelines.

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

A process by which a participant voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the participant's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

International Air Transport Association (IATA)

An international organisation that develops the commercial standards globally, for the air transport system.

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 touch-tone key pad of 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 unblinding.

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 unblinding.

International Council for Harmonisation (ICH)

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Registration of Pharmaceuticals for Human Use is a joint initiative involving both regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration.

Conceived in 1990, ICH has gradually evolved, to respond to the increasingly global face of drug development. ICH's mission is to achieve greater harmonisation worldwide to ensure that safe,

effective, and high-quality medicines are developed and registered in the most resource-efficient manner.

International Organisation for Standardisation (ISO) 14155:2011 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 Medical Device (IMD)

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 authorization 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 group, or when used to gain further information about an approved use.

Investigational Product

Investigational Medical Device or Investigational Medicinal Product

Investigator

An individual responsible for 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 a Sub-Investigator.

Investigator Brochure (IB)

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.

Institutional Review Board (IRB)

An independent ethics committee.

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.

National Health and Medical Research Council (NHMRC)

The Council established to develop and maintain health standards and is responsible for implementing the National Health and Medical Research Council Act 1992.

National Mutual Acceptance (NMA)

NMA 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 NMA, 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.

Participant screening log

To document identification of participants who entered pre-trial screening.

Participant enrolment log

To document chronological enrolment of participants by trial number.

Participant identification list

To document that investigator/institution keeps a confidential list of names of all participants allocated to trial numbers on enrolling in the trial. Allows investigator/institution to reveal identity of any participant and to make future contact if required.

Participant Information and Consent Form (PICF)

The ethically approved document used for providing written patient information about a specific clinical trial and the documentation of Informed Consent in the form of the patient and the investigator signatures and date.

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

The Primary Site coordinates the trial across a cluster to enhance patient reach, recruitment and management. The Principal Investigator located in the Primary Site has full responsibility of conducting the clinical trial under ICH GCP.

Principal Investigator

Takes responsibility at their own site for the conduct, management, monitoring and reporting of a research project.

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.

Protocol Deviation

A deviation is any breach, divergence or departure from the requirements of Good Clinical Practice (GCP) or the protocol 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 trial sponsor.

Research Governance Officer (RGO)

The RGO is the individual appointed within an organisation who is responsible for the

management of applications for site authorisation and administrative oversight of authorised

research projects.

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

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 responsibility is delegated by the Primary Site (clinical trial site) to perform activities associated with the conduct of a clinical trial and to support trial accessibility of remote participants to a clinical trial.

Satellite Sites can be located in metropolitan, regional or rural settings. Delegated activities to be performed by the Satellite Site are trial specific and should be agreed and documented at the time of site selection via a delegation log and a supervision plan.

For each trial, infrastructure and training requirements for Satellite Sites 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 trial related activities including obtaining informed consent (if required). Study staff are trained in the protocol, IB, study procedures, 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.

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 prolongation of existing hospitalisation
- results in persistent or significant disability / capacity
- is a congenital anomaly / birth defect

Serious Adverse Event (SAE) – device

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

- results in death
- lead 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 Human Research Ethics Committee (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.

Source Documents

Original documents (where the 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. A sponsor should be designated for all clinical trials.

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

A folder containing all the study related Essential Documentation / Source Documents as defined by 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.

Sub Investigator (SI) or Associate Investigator (AI)

Any individual member of the clinical trial team designated and supervised by the 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:

- the SI when located at a Primary Site may be delegated some or all of the study related responsibilities by the PI according to their level of experience
- the SI 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.

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 study 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 Sub Investigator, other study staff and independent third party i.e. external service providers.

Clear delegation and supervision of roles documented in the Supervision Plan will be agreed with the team and the sponsor in advance to study start.

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

A teletrial uses TeleHealth technology to communicate between the Primary Site and Satellite site/s for all aspects of a clinical trial. This support a Principal Investigator to supervise Sub-Investigator/s to conduct a clinical trial at a Satellite Site 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. Trial participants may have trial visits at both the Primary and Satellite Sites, as determined by the protocol. The conduct of the trial is detailed under 'head agreement', being using a Clinical Trial Research Agreement/Clinical Trial Agreement between the Sponsor and the Principal Investigator's institution and a Sub-Agreement between the Primary Site and the Satellite Site institutions (see Terms).

Therapeutic Goods Administration (TGA)

Australia's regulatory agency for therapeutic goods.

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 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.

Urgent Safety Measure (USM)

One type of significant safety issue where sponsors or trial investigators act immediately to protect participants from an immediate hazard to their health and safety. Consequently, USMs are often instigated before the TGA and HREC are notified. In these cases, it is strongly recommended that the sponsor contact the TGA within 24 hours of the measure being taken. If this initial contact is by telephone, it should be followed-up with a written notification provided by facsimile or e-mail within 72 hours.

SOP 01 Standard Operating Procedure (SOP) Creation, Implementation and Revision

Purpose

To document the procedure for the creation and implementation of new Standard Operating Procedures (SOPs) and review of existing SOPs according to the principles of ICH GCP E6 (R2) and the NHMRC National Statement on Ethical Conduct in Human Research (2007) - Updated 2018.

Scope

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

This applies to all SOPs when a need is identified to either create a new SOP or modify an existing one.

Procedure

Review date is two years after the effective date. The time between SOP authorisation and the effective date may be reduced in special circumstances (e.g. urgent situations where procedures must be implemented immediately).

An earlier review date is permitted where necessary (e.g. changes to legislation, changes to NMA policy and procedures).

1.1 Initiating the creation of a new SOP or revision of an existing SOP

All researchers may:

- Identify the need for a new SOP or a deficiency or an improvement in an existing SOP and suggest appropriate modification
- Notify the jurisdiction health department (or equivalent) and discuss this need with the SOP number and title in the subject header

NMA members will

Delegate a responsible jurisdiction to coordinate the following:

- Assess and verify the need
- Use the provided template in Appendix 1 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, and 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 stakeholder for second review.
- If necessary repeat above 2 steps until a final version is ready for approval.
- Update the front-page identifier box and / or amendment history box as necessary, ensuring the 'SOP effective date' and 'SOP review by date' is in alignment with the timeframe identified in this SOP.
- Arrange for final review and incorporate any relevant comments.

1.2 Approval and Authorisation of the SOP

NMA members will:

- Print the final SOP and arrange for approval and authorisation and final sign off by the NMA jurisdictional working group.
- Ensure the original signature field and / or amendment history field is completed by the delegated coordinating jurisdictions.
- File the final approved (in writing) new/amended SOP electronically as a pdf file and distribute to all jurisdiction members to post on a website.
- Securely store the final, approved, new/amended master SOP.
- Once the authorised Generic Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia has been approved any changes can only be made by following the steps outlined in this SOP.

1.3 Training, Implementation, Distribution of the new or revised SOP

- All relevant jurisdiction stakeholders should be notified of the new/updated SOP between the authorisation and the effective date. This would include Health Services Human Research Ethics Committees (HRECs) and Research Governance Officers (RGOs).

1.4 Superseded SOPs

- NMA jurisdictions will notify relevant stakeholders including all HRECs and RGOs of superseded SOPs.
- The superseded SOP will be watermarked with SUPERCEDED and filed.
- The superseded hard copy master SOP shall be clearly marked as superseded and be securely stored as a record of previously used SOPs.
- The superseded SOP shall be removed from the relevant websites.

SOP 02 Investigator Responsibilities

Purpose

To define the Investigator responsibilities associated with undertaking a clinical trial which are not listed in other NMA Standard Operating Procedures.

Scope

This standard applies to all relevant employees but not limited to visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients, facilities and or staff. The responsibilities described in this SOP are extra to and are to be read in conjunction with investigator responsibilities defined in all other NMA SOPs.

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

Procedure

2.1 Investigator Responsibilities (CPI, PI and SI)

2.1.1 Before the Research Project Commences

The Investigator must:

- 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.
- Ensure any payment received 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.
- Be thoroughly familiar with the appropriate use of the investigational product as described in the protocol, in the current Investigator's Brochure for medicines or Product Information for devices and in other information sources provided by the Sponsor.
- Be provided with 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.

2.1.2 During the course and at the completion of the Research Project

The Investigator must:

- Sign all trial related documentation, 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 reports, eCRF/CRF, SAE reports, etc.
- Ensure all trial related staff and Third-Party Providers have been informed of research project closure, results and publication plan.
- Inform participant's primary care physician (where participant has consented to do so) of research project closure, results and, if applicable, the treatment the participant was allocated for notation in the participant's medical record.
- Record in the participant's medical record at the institution the treatment the participant was allocated (if applicable).
- Follow the Teletrials Clinical Consultation User Guide to enable the telehealth process to be successfully used and correctly reimbursed.
- Document any deviation from the Protocol as per sponsor's guide
- Ensure they notify the sponsor, HREC and RGO if they leave the institution, in writing with either their new place of employment and contact details or who their replacement is with contact details for recording on all archiving related documentation.
- Ensure study related documents are archived according to SOP 13 Site Close Out and Archiving.

SOP 03 Site Staff Qualifications, Training Records and Capability

Purpose

The purpose of this Standard Operating Procedure is:

a) to ensure the appropriate documentation of clinical research site staff qualifications and training records are completed and maintained up to date during the course of the study, and b) to ensure the provision of resources to perform clinical research at all clinical research sites, according to the principles of ICH GCP and the NHMRC *National Statement on Ethical Conduct in Human Research (2007) - Updated 2018*.

Scope

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

Procedure

3.1 Site Staff Qualifications

The Investigator must:

- Be qualified by education, training and experience, including GCP training, to assume ultimate responsibility for the proper conduct of the research.
- If required by the local site RGO submit a current Curriculum Vitae (CV) to the RGO if not submitted previously and at any time the CV changes including (see Appendix 2):
    - current Australian Health Practitioner Regulation Agency (AHPRA) registration details.
    - other relevant documentation requested by the sponsor, the HREC, and/or the regulatory authority (e.g. current GCP training).
    - Current workplace name and address
- Ensure all investigational site staff, at both Primary and Satellite Sites, or Independent Third Party, and External Service Providers are qualified by education, training and experience, including GCP training, to assume responsibilities to perform the delegated study-related duties and functions.

- Ensure all investigational site staff, at both Primary and Satellite Sites, or Independent Third Party, who has been delegated significant responsibilities has a current CV in the research office/SMF for sighting by sponsor and / or regulatory authority.
- Implement procedures to ensure the delegated study-related duties and functions performed are carried out safely.
- Implement procedures to ensure integrity of any data generated.

3.2 Site Staff Training Records

The Principal Investigator must:

- Ensure all required staff, including new staff involved during the course of 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. This can be in the form of an Initiation meeting held by any communication means e.g. via face-to-face, skype, videoconference, telehealth means etc.
- Record the study specific training given, documents and tools used, to whom and when e.g. on a training record or log. See Appendix 3 Training Record.
- Ensure that all required training is completed and the training record are kept up to date and a copy is kept at the Primary Site and/or Satellite Sites (when applicable) and available for review on request throughout the entire duration of the clinical research trial.

3.3 Capability

The Principal Investigator must:

- Demonstrate a potential for recruiting the required number of suitable participants, either from the Primary Site only or from 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.
- 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. See Appendix 4 Delegation Log.

- Where applicable ensure each Satellite Site maintains their own site Delegation Log separate to the Primary Site. The Sub-Investigator will delegate duties appropriately, sign and date the log and send a copy to the Primary Site, when requested (see Appendix 4 Delegation Log).
- Develop and complete a Supervision Plan before the commencement of a clinical research study that documents the manner and frequency of supervision to be undertaken between Primary Site and Satellite Site and other study staff, especially sub-investigators and other team members new to the role. The Supervision Plan must include cover for planned leave. See Appendix 5 Supervision Plan.
- 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.

SOP 04 Protocol and Investigational Brochure (IB) Requirements

Purpose

To describe the procedures related to the development of a research protocol, an investigational brochure, and amendments to these documents ensuring compliance to ICH GCP E6 (R2).

Scope

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

Procedure

4.1 Protocol content and development

Specific content of a protocol will vary depending on the subject of the research, the level of risk to participants, the phase of research and study design, whether a medicinal product is being researched or a device or a therapeutic intervention. Consequently, the terminology will be different and should be adapted appropriately.

Where the investigator is responsible for the protocol development they must ensure the protocol follows the outline as per ICH GCP E6 (R2) Section 6 CLINICAL TRIAL PROTOCOL AND PROTOCOL AMENDMENT(S). This protocol table of contents is not mandated but it is recommended 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.

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 manner in which Informed Consent will be taken is to be clearly described i.e. face-to-face, videoconference, via telehealth, skype, phone etc.
- 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 telehealth 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.

4.2 Investigational Brochure (IB) content and development

Where the investigator contributes to the content and development of the Investigator Brochure they must ensure the Investigator Brochure follows the outline as per ICH GCP E6 (R2) Section 7 INVESTIGATOR'S BROCHURE.

An example of an IB Table of Contents is found in Section 7.5 Appendix 2 section in the above link. This is not mandated but is recommended for use as it ensures adherence to ICH GCP E6 (R2). 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 that current and comprehensive information about the product under study is available to the investigators. If a product is registered, but is being trialled 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.

4.3 Amendment/s to the Protocol and IB

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:
    a) are proposed or undertaken without prior HREC approval in order to eliminate immediate risks to participants;
    b) may increase the risks to participants; or
    c) significantly affect the conduct of the trial (including changes to the Inclusion / Exclusion criteria).
- as soon as possible any new safety information from other published or unpublished studies 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 Human Research Ethics Committee (HREC), Research Governance (RGO), Sponsor and Institution's Insurer, regarding communication with the HREC.

The Investigator must provide to the RGO:

- the HREC approval letter for the amendment(s)
- a copy (if required by the RGO) of all HREC approved amended documents.

and obtain authorisation from the RGO to continue the project where a governance aspect has been affected (if required) including protocol amendments that:

a) are proposed or undertaken without prior HREC approval in order to eliminate immediate risks to participants
b) may increase the risks to participants
c) significantly affect the conduct of the trial (including changes to the Inclusion / Exclusion criteria)
d) pose a risk to the Institution.

Notification to the RGO is site specific and the investigator should be familiar with the processes of their RGO.

SOP 05 Communication with Human Research Ethics Committee (HREC), Research Governance (RGO), Sponsor and Institution's Insurer

Purpose

To describe the procedures relating to communication with the HREC, RGO, Sponsor and Insurer.

Scope

Applies to all relevant employees but not limited to visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients, facilities and or staff. 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.

Procedure

Communication with the HREC and RGO is illustrated in a tabular form in the National Mutual Acceptance Single Ethical Review of Multi-centre Human Research Projects. MONITORING AND REPORTING TABLES.

5.1 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 term "FILE NOTE" 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).

5.1.1 Prior to study commencement, the Investigator (CPI/PI/SI) must:

- Choose a reviewing HREC whose approval is acceptable to the institution/s where the clinical study is being undertaken.
- 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 startup 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 Telehealth with Satellite Sites, if applicable, and that the informed consent process and/or some or all study assessments will be undertaken using Telehealth, face to face consultation or a combination of both.
- Submit any other application as per that process found on the relevant website.
- 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 body.

5.1.2 During the study, the Investigator (CPI/PI/SI) must:

- No longer submit individual reports of AEs, SAEs, SUSARs, USADEs and six-monthly line listings to the reviewing HREC unless otherwise advised.
- 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 violations; annual progress reports; and unforeseen events that might affect continued ethical acceptability of the trial.
- Immediately notify the reviewing HREC 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.
- File all documentation in the SMF/SSSF.

5.1.3 At the end of the study, the Investigator (CPI/PI/SI) 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.

5.2 Communication with the Research Governance Office (RGO)

For the purpose of this SOP the Clinical Trial Research Agreement (CTRA), 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 may be submitted to the RGO in parallel to the HREC submission if all governance related documentation is available and completed correctly. In this case 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.

5.2.1 Prior to study commencement, the Investigator (CPI/PI/SI) must:

- Submit the CTRA, the SSA Form 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 Principal Investigator or the same HHS) completes a clinical trial sub-contract and a SSA Form which is a subsection of the main SSA and submits to their RGO.
- 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.

5.2.2 During the trial, the Investigator (CPI/PI/SI) 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; budget; any change that might affect continued financial acceptability of the trial; any change that may increase institution risk.
- 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 the Satellite Site files all documentation in the SSSF.

5.2.3 At the end of the trial, the Investigator (CPI/PI/SI) must:

- Notify the RGO the trial has terminated/closed.

- File all documentation in the SMF/SSSF.

5.3 Communication with the Sponsor

- notify the sponsor within 24 hours of discovery 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/SI. Communication must be followed up with written report/email and filed in the SMF/SSSF
- notify the sponsor of any Protocol Violation (which may include significant deviation from the protocol) and where relevant notify the CPI/PI/SI (see Appendix 6 Protocol Deviation Log)
- 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 against either the sponsor and/or the Institution.

5.4 Communication with Institution's Insurer

If the Institution is notified or becomes aware that a trial participant intends to make a claim 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, the Institution must promptly notify the Institution's insurer in writing that such an action is intended.

5.4.1 Communication with Solicitor, Sponsor and CPI/PI/SI

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 as a result 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 relevant Solicitor
- the CPI/PI/SI as relevant, and
- the Sponsor.

SOP 06 Site Initiation

Purpose

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

Scope

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

Procedure

Site Initiation

Prior to initiation of the study, the Investigator must:

- mutually agree with the Sponsor a scheduled date, time and location for the Study Initiation Visit at the participating site or the Primary Site in the case of a teletrial.
- review all study related documentation and be familiar with the Investigational Product and protocol.
- ensure that all relevant staff involved with the study, (Sub-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.
- ensure a Supervision Plan 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 for each Satellite Site.
- under the teletrials model a Satellite Site is not initiated until such time a potentially eligible participant is identified.

For further guidance refer to Appendix 7 Example Initiation Checklist.

During the Initiation Visit the Investigator must ensure the following are available and/or addressed:

- Study Master File 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 curricula 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, 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 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 course of the trial
- a pharmacy manual clearly defining any activity linked to the handling or the IMP/IMD
- any specialised equipment required will be available throughout the period of the trial, e.g. centrifuge, freezer, etc.
- the eCRF, completion guidelines and that they are accessible by all sites
- training in all aspects required by the protocol is recorded on 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.
- Supervision Plan
- Under the teletrials model when a Satellite Site is initiated, the Satellite Site Study File is set up and all above steps apply at that time

At the conclusion of the initiation the Investigator must:

- File the sponsor's initiation visit report/letter in the SMF

- Ensure that the staff at the Satellite Site files all communication and documentation in the SSSF

SOP 07 The Study Master File

Purpose

To describe the procedures related to the maintenance of the Study Master File (SMF) held at all clinical research Sites/units, according to ICH GCP E6 (R2) Section 8 to ensure it is current at all times for the duration of the clinical study.

Scope

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

Procedure

7.1 The Study Master File

The Principal Investigator must:

- Ensure an SMF is created, if not provided by the Sponsor, prior to study commencement and it must contain at a minimum the Essential Documents listed in Appendix 8 Example of Study Master File Index and Contents. The SMF is stored at the Primary Site.
- Establish the maintenance rules of the SMF and relationship between Primary Site Study Master File (SMF) and Satellite Site Study File (SSSF). For example, the contents of the SSSF, how and which documents generated at the Satellite Site will be sent to the Primary Site and filed in the SMF and archiving of Satellite Site study file after study close out. When establishing the maintenance rules, it will be important to ensure that key documents from the SSSF are present in the SMF 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 is contained in the SMF.
- 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 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, search ability 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.

7.2 The Study Master File (SMF)

- Study related Essential and Source Documents generated for/by the Primary Site, as per Appendix 8 at a minimum, will be filed in the SMF.
- 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, 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, the location is to be recorded on the SMF index. See Appendix 9 for example of Study Master File Index. A copy may be filed in the SMF if requested by the Sponsor.
- Investigational Product handling documentation e.g. shipping, receipt, IVRS, 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 to be recorded on the SMF 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 after completion of the study.
- Sample handling procedures are to be clearly documented if performed e.g. in a laboratory manual. 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.
- Other study related materials handling documentation are filed in the SMF/SSSF as agreed.

7.3 The Study Master File (SMF)

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, similar to Appendix 8.
- All Source Documents generated 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
- Satellite Site Training Records
- Satellite Site, 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.

SOP 08 Case Report Forms and Source Documents

Purpose

To describe the procedures related to the completion of (electronic) case report forms, and maintenance of Source Documents.

Scope

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

Procedure

8.1 Completion of Case Report Forms (CRFs and eCRFs)

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 Investigator must:

- Ensure the accuracy, completeness, legibility, (including any changes or corrections) and timeliness of data recording adheres to the protocol and monitoring plan requirements and also 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 and explained (i.e. an audit trail should be maintained).

8.2 Source Documents

The Investigator must:

- Maintain adequate source documents and trial records including all key observations on each of the site's 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, Governance officer 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 that for telehealth consultations, the call is documented in the participant's medical record at each site by agreeing in the Supervision Plan where the original and Certified Copies are stored. The written record will include a brief summary of the consultation; follow up instructions and that the visit was conducted via telehealth as per current version of the Teletrials Clinical Consultation User Guide.
- For paper records, ensure that a Certified Copy of any key essential documentation generated at the Satellite Site is sent to the Primary Site for filing in the SMF e.g. SAE reports, to allow remote monitoring by sponsor and for auditing and inspection purposes. These can be sent via email or post.
- Where Electronic Medical Records (EMR) are in use, ensure that access to the patient's trial related information is limited to authorised users only. Where access cannot be limited measures must be put in place to ensure the patient's privacy and confidentiality are respected e.g. print the trial related information, sign as a Certified Copy and place in a paper record for access by Sponsor, regulatory inspectors and auditors etc.

SOP 09 Participant Informed Consent Process and Documentation

Purpose

To describe procedures and documentation management relevant to the Informed Consent process, including consenting via telehealth.

Scope

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

The consent form must be signed by hand and in ink by both parties (wet signature) or alternatively *e*-signatures may be acceptable in the consent process in some jurisdiction health services (as confirmed in ethics approval documentation).

Procedure

9.1 Informed Consent Process

- In obtaining and documenting Informed Consent, the investigator must comply with the NHMRC National Statement, Chapter 2.2 and adhere to ICH GCP E6 (R2) 4.8
- The principles of the Declaration of Helsinki inform the ethical principles of the National Statement. However, the National Statement is the primary statement on ethical principles related to human research in Australia.
- Obtaining Informed Consent from any participant is the responsibility of the Principal Investigator including consent from participants from each site under the responsibility of the Principal Investigator.
- Obtaining Informed Consent maybe delegated to an appropriately qualified medical practitioner as described in SOP 03 Site Staff Qualifications, Training Records and Capability.
- The Investigator must be in possession of both, the written approval from the relevant HREC and written authorisation from the local research governance office/r for:
    a) the Informed Consent form
    b) any other information to be provided to the Participant, and
    c) the Informed Consent process

before these documents may be used to obtain consent from any participant.

- When changes have been made to a HREC approved Informed Consent, the Investigator must have the relevant HREC's written approval (and if needed the written authorisation from the local research governance office/r) of the amended Informed Consent before it may be used to obtain consent from any participant.
- The Study Coordinator or other appropriately qualified person may initiate the process and discuss the intricacies of the clinical trial. However, all medical questions must be answered by and final consent signing must be carried out by the Investigator. This final step cannot be undertaken by anyone who is not a medical practitioner (or dentist if applicable).
- The manner in which Informed Consent will be obtained i.e. in person or via telehealth, is to be clearly documented in the HREC application and the Participant Information and Consent Form (PICF) and clearly described to the Sponsor and in other documents where this information is pertinent to the conduct of the clinical trial e.g. participant's medical record, Source document. With telehealth, all measures will be taken to ensure privacy and confidentiality of the participant's identity, as described in the Teletrials Clinical Consultation User Guide.
- 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 and the PICF and clearly described to the participant during the consent process.
- If Informed Consent is obtained by telehealth consultation, all persons who are not known to each other must produce photographic 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.
- If Informed Consent is obtained by telephone, this must be recorded on the Informed Consent form and in the participant's medical record, and/or Source document, stating (as an example):
    - "The protocol was discussed with [participant's name] via telephone on [DD/MMM/YYYY]. I received the participant's signed consent form on [DDMMMYYYY]."

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.

9.1.1 Research involving Participants who are unable to give consent

The investigator must ensure that, in addition to ICH GCP E6 (R2) 4.8.15 and NHMRC National Statement, Chapter 2.2., the following is taken into consideration.

The Declaration of Helsinki states that research involving participants who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving Informed Consent is a necessary characteristic of the research group. In other words, in these cases, the study must be relevant to the physical or mental condition of the participant that prevents them from being able to consent to participate in the study.

Where an adult is unable to give consent to participate in a study, once the Investigator has received HREC approval, the Investigator may apply under the relevant jurisdictional Act to obtain consent for the adult to participate in research that involves a 'medical research procedure' or 'experimental health care' – provided the relevant legislated criteria apply.

9.1.2 Informed Consent Documentation

Ensure the essential elements are present as described in the NHMRC National Statement, Chapter 2.2 (https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) and ICH GCP E6 (R2) Section 4.8.10

- The Master PICF is supplied by the Sponsor. Any necessary national or local adaptation for the ethics review process will be made as required for submission to the reviewing HREC. An HREC may approve a Master PICF amended with preapproved local site PICF adaptations such as
  - *By signing this consent form, I give permission for the study investigator to obtain information from the following:*
    - *ambulance transportation,*
    - *any admission to any hospital,*
    - *Emergency Department visits,*
    - *stays in an observation unit,*
    - *information from my local doctor,*

    for the term of the study period. The information collected from these places / persons will only be requested if it is required for this study and will only be used for the purpose of this study

- The appropriate pre-approved wording relating to the use of contraception where a site has a specific requirement.

- Where the Investigator has delegated obtaining Informed Consent to another appropriately qualified medical practitioner, this must be recorded on the Delegation Log
- Once the PICF is signed and dated by both participant and the Investigator, the original PICF is kept in the participant's medical record and a copy is given to the participant.
- Storage of Informed Consent documents maybe at the Satellite Site, at the Primary Site or at both sites (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 tick the statement identifying that consent was obtained by telehealth or telephone with the name of the Investigator. Similarly, the Investigator is to tick the statement identifying 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 medical record (electronic or paper), a copy is given to the participant and:
  - 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 medical record with the Investigator's signed and dated original. The investigator 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, a certified copy of the PICF is not required.
  - If the participant requests a copy of the PICF with the Investigator's signature, obtain a copy of the Investigator's signed PICF and give to the participant.
- Examples of pre-approved statements that may be added to the PICF where consent is obtained by telehealth/telephone:
  - Consent was obtained using telehealth with "Name of Investigator", whose photographic identification was sighted by the participant who observed the Investigator's signature being written
  - Consent was obtained using telehealth with "Name of participant", whose photographic identification was sighted by the Investigator who observed the participant's signature being written
  - Consent was obtained via telephone with "Name of Investigator", on [DD/MMM/YYYY].
  - Consent was obtained via telephone with "Name of participant", on [DD/MMM/YYYY].
  - participant's signed consent form received by the Investigator on [DDMMMYYYY].

- Discussed with [participant] via telephone on [insert date] and received signed consent form on [insert date]. Signed by [Investigator]

SOP 10 Handling and Shipping of Biological Substances (Cat B) and/or Dangerous Goods in Clinical Trials

Purpose

To outline the procedures to follow when handling and shipping Biological Substances (Cat 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.

Scope

This standard applies to all relevant employees but not limited to visiting health professionals, contractors, consultants and volunteers who propose to undertake, administrate, review and/or govern human research involving patients, facilities and or staff. 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 biological samples/specimen/substances are written, category B is implied.

Procedure

10.1 Handling and Shipping of Biological Substances 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 3 Site Staff Qualifications, Training records and Capability. It is still the Investigator's responsibility to ensure all procedures and regulations are adhered to.

The Investigator must:

- Ensure all study staff, who have cause to handle or ship biological substances, hold a current certificate in the IATA Approved, Civil Aviation Safety Authority (CASA) Certified Dangerous Goods Packaging Course.
- Ensure specimens are 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

International Air Transport Association (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 documentation (e.g. receipts, shipping records, order forms, proformas etc.) related to handling and shipment of biological specimens is maintained and filed in the respective site file (SMF/ SSSF).

10.2 Notes regarding Certification to handle and transport biological substances and dry ice

- Organise training for handling and shipping of biological substances and dry ice, staff should contact their Pathology Service/Laboratory. The Civil Aviation Safety Authority (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, 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 sponsor, regulatory authority, and CASA.

SOP 11 Management of Investigational Product

Purpose

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

Note: Relabelling of investigational product is not covered here as it will follow the procedures sent to the sites by the sponsor or follow the institution's pharmacy procedures for relabelling.

Scope

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

Procedure

11.1 Management of Investigational Product (Medicinal Product or Device)

Responsibility for Investigational Product (IP) management and accountability at the trial site rests with the Principal Investigator (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 Investigational Product at the Primary Site and / or the Satellite Site.

Where the delegation of this activity requires supervision (e.g. pharmacist or appropriately qualified person new to the role), the delegated activity is to be clearly documented on the Supervision Plan, the Delegation and Training Logs. (see SOP 03 Site Staff Qualifications, Training Records and Capability).

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

- Ensure the Investigational Product is used only in accordance with the approved protocol.
- Maintain records of all aspects of the management of the Investigational Product. 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 investigational product throughout the trial period; the set of unique code numbers assigned to the Investigational Product and to the trial participant; and record of destruction/return. See Appendix 10 for Example of Individual Participant Investigational Product (IP) Accountability Record.
- Provide maintenance and calibration records for storage equipment (e.g. refrigerators, thermometers) in accordance with sponsor requirements.
- Ensure that the Investigational Product 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 Investigational Product, with restricted access to approved personnel.
- Ensure any deviation to required temperature, storage conditions, potential defect / issue with IP is notified to sponsor in a timely manner and in accordance with study Protocol. Follow study site quarantine process as applicable.
- Explain the correct use of the Investigational Product to each participant and should check, at intervals appropriate for the trial, that each participant is following the instructions properly. Instruct participant 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.
- Follow the trial's randomisation procedures, if any, and 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 Investigational Product.
- Where the Investigational Product is shipped to, and/or returned from, a Satellite Site, a written working instruction or procedure documenting the manner in which 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 Study Site Master File.

SOP 12 Safety Data Monitoring and Reporting Requirements for Clinical Trials

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 Devices (IMD), conducted under the Clinical Trial Notification (CTN) or Clinical Trial Exemption (CTX) Scheme. This also includes company sponsored post registration/post marketing surveillance studies.

Scope

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

In 2016, the NHMRC released important changes to regulatory and 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. See Appendices 11 – 15.

Procedure

Where Satellite Sites 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 Site Master File. The rules will be pre-determined as per SOP 07 The Study Master File.

NOTE: where a sponsor delivers 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 but only after the sponsor confirms that the report has no bearing on participant safety or trial conduct. There no longer is a requirement for Investigators to print, review and file these reports. See *NHMRC Safety Monitoring and Reporting In Clinical Trials Involving Therapeutic Goods (November 2016)*.

12.1 Sponsor responsibilities

The two documents the *Australian clinical trial handbook (October 2018)* and the *NHMRC Safety Monitoring and Reporting In Clinical Trials Involving Therapeutic Goods (November 2016)* give clear direction to sponsor responsibilities.

A sponsor:

- must be identified for all clinical trials
- 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:
    a) the assessment and management of risk (if not in an alternative document);
    b) safety reporting definitions, procedures, responsibilities and reporting timelines;
    c) 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), 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 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).

12.1.1 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 Principal Investigator 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.

12.1.2 Sponsor Reporting Requirement

The outcome of various safety reviews is reported directly to HRECs, investigator and the Therapeutic Goods Administration (TGA), by the Sponsor and must indicate the impact of each report on patient 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.

12.1.2.1 Sponsor to provide to Investigator

- updated Investigator's Brochure 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 in order to eliminate an immediate hazard to a participant's health or safety measure) should be notified within 72 hours, and all other significant safety issues should be notified within 15 calendar days of the sponsor instigating or being made aware of the issue.

12.1.2.2 Sponsor to provide to Therapeutic Goods Administration (TGA)

- significant safety issues that meet the definition of an urgent safety measure (i.e. a measure required to be taken in order to eliminate an immediate hazard to a participant's health or safety measure) should be notified within 72 hours, and all other significant safety issues should be notified within 15 calendar days of the sponsor instigating or being made aware of the issue
- all suspected unexpected serious adverse reactions (SUSAR) 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

12.1.2.3 Sponsor to provide to HREC

- updated Investigator's Brochure 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 in order to eliminate an immediate hazard to a participant's health or safety measure) should be notified within 72 hours, and all other significant safety issues should be notified within 15 calendar days of the sponsor instigating or being made aware of the issue.

12.2 Investigator 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 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.

12.2.1 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 a device safety issues arise.
- review the adverse outcome in the context of known information on the medicine / device and make a determination 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.

12.2.2 Reporting Requirement

The reporting of safety reviews by the investigator should be as per *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.

12.2.2.1 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 Investigator 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 in order 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

12.2.2.2 To Therapeutic Goods Administration (TGA)

Use the Australian Government Department of Health Report of suspected adverse reaction to medicines or vaccines commonly known as the "Blue Card", CIOMS form or equivalent to report to the TGA. When submitting a SUSAR report to the TGA, submit via the TGA Business Services (TBS) ADR submission portal by email using a "Blue Card" or sponsor provided CIOMS form to adr.reports@tga.gov.au

- Advise TGA of any safety issues which emerge during this process. Such data do not need to be submitted on a routine basis to the TGA during the trial but should be available for submission to the TGA on request, and where applicable, submitted as part of an application for registration.

- Significant safety issues: those that meet the definition of an urgent safety measure (i.e. a measure required to be taken immediately in order to eliminate an immediate hazard to a participant's health or safety measure) should be notified within 72 hours, and all other significant safety issues should be notified within 15 calendar days of the sponsor instigating or being made aware of the issue.

12.2.2.3 To Institution/Research Governance Officer

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 in order 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.

SOP 13 Site Close Out and Archiving

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.

Scope

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

Procedure

13.1 Site close-out

13.1.1 Premature Termination or Suspension of a 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/Sub-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.

13.1.2 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:

- Provide a summary report of the trial's outcome to the HREC, RGO, any Satellite Site and the TGA.
- File documentation and correspondence in the SMF.
- Arrange for archiving of SMF/SSSF.

- Ensure appropriate final disposition of any Investigational Product/and other trial related material. This may include return to the Sponsor or destruction of remaining materials.
- Where a Satellite Site was 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 with the Satellite Site staff during the study (e.g. minutes of calls with Satellite staff to review patients 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 Primary Site.

See Appendix 16 Example Close Out Check-List as a reference guide.

13.2 Archiving

Study documentation is to be archived as specified in:

(i) ICH GCP E6 (R2) 4.9.5, 5. 5.12

(ii) Australian Code for the Responsible Conduct of Research. Part A, section 2.1

- 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.
- Jurisdiction requirements for clinical trial records where the participants are minors must be adhered to.
- Jurisdiction requirements for clinical trial records where the participants are adults must be adhered to.

13.2.1 For Paper Records

- Original documents or Certified Copies are to be retained.
- Evident identification (e.g. a document retention sticker) that the medical record forms part of a clinical trial is to be placed on all volumes of the participant's medical record in an appropriate position, without obscuring any information, as guided by local health information management services practice.
- For commercially sponsored research, archiving arrangements are negotiated with the study sponsor (and the site's health information management services) prior to study commencement. These details are to be noted in the study contract.

- Identifiable information (e.g. Participant Identification Log and Participant Information Sheet and Consent Forms) is to be archived separately from the main study documents, e.g. with the Principal Investigator – 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 site as per above and send a certified copy to the Primary Site for archiving with the Primary Site participant identifiable information.
- Where the study documentation will be filed by the sponsor, the identifiable information (e.g. Participant Information Sheet and Consent Forms) site records are **NOT TO BE** filed with the sponsor study records.

13.2.2 For Electronic Records

- Electronic Medical Records will be archived indefinitely

Appendix 1 SOP Template

SOP Number: SOP Title

Amendment History

Version	Effective Date	Review Date	Author/s	Amendment Details
March 2020	xx March 2020			New

Footer of the SOP is to note:

Generic Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia

Based on ICH GCP and as developed by Queensland Health

Version: xxxxx

Appendix 2 Example CV

Please see this link to the TransCelerate CV Template

http://www.transceleratebiopharmainc.com/wp-content/uploads/2018/03/CV-Template-1.pdf

Appendix 3 Training Record

Example Internal Training Record

Complete, sign, date and retain the original form at the site. Provide a copy of the completed form to the sponsor representative.

<table>
<tr><td>Trainee Name:
(Printed)</td><td></td><td>Trainee Role:</td></tr>
<tr><td>PI Name:</td><td></td><td rowspan="4">☐ Principal Investigator (PI)
☐ Study Coordinator (SC)
☐ Sub-investigator (Sub-I)
☐ Pharmacist
☐ Other (Specify role e.g. Study Nurse)</td></tr>
<tr><td>Protocol:</td><td></td></tr>
<tr><td>Site Number:

☐ Primary

☐ Satellite</td><td></td></tr>
<tr><td>Training Method:</td><td colspan="2">☐ Classroom face to face
☐ Video / teleconference
☐ eLearning
☐ Self-directed
☐ Other (see below)</td></tr>
<tr><td>Other description:</td><td colspan="2"></td></tr>
</table>

	Trainer(s) Name & Role **(Printed) if applicable**	**Training method**	**Training Completed** **DDMMMYYYY**
Protocol Version NN DDMMMYYYY			
Investigator Responsibilities Version NN DDMMMYYYY			
Informed Consent Version NN DDMMMYYYY			
Interactive Web response System (IWRS/IVRS) Version NN DDMMMYYYY			
ICH GCP E6 R2 Version NN DDMMMYYYY			
CRF completion Version NN DDMMMYYYY			
EDC system Version NN DDMMMYYYY			
Serious Adverse Event (SAE) Reporting Version NN DDMMMYYYY			

	Trainer(s) Name & Role (Printed) if applicable	Training method	Training Completed DDMMMYYYY
Safety Monitoring Plan Version NN DDMMMYYYY			
IMP handling Version NN DDMMMYYYY			
Laboratory Manual Version NN DDMMMYYYY			
Source Documentation Version NN DDMMMYYYY			
Monitoring Plan Version NN DDMMMYYYY			

By signing this certificate, I attest that I have completed all training topics listed above for my role in the trial. I agree to follow TGA, NHMRC National Statement and ICH GCP guidelines as well as instructions provided in these training topics when conducting this trial. This training was completed before performing any trial responsibilities, and trial related activities. I was given the opportunity to ask questions and received satisfactory clarification.

_____ _____

Signature of Trainee Date (dd-mmm-yyyy)

Appendix 4 Delegation Log

Example Site Signature and Delegation of Responsibility Log

Please access this link to see the TransCelerate / SCRS Site Signature and Delegation of Responsibility Log. Scroll down to the Forms section.

https://myscrs.org/learning-campus/site-management-modules/

Appendix 5 Supervision Plan

Please see: **Teletrials Supervision Plan – Based on the Generic Standard Operating Procedures for Clinical Trials, including Teletrials, In Australia.**

Appendix 6 Protocol Deviation Log

Example Protocol Deviation Log:

Purpose

This tracking log should provide a comprehensive list of all protocol deviations that occur at a study site. It is required for both observational and interventional clinical research studies.

This tool is complementary to, and does not replace, the form reporting individual protocol deviations to the Ethics Committee and others as required.

Definition

A deviation is any breach, divergence or departure from the requirements of Good Clinical Practice (GCP) or the protocol 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 trial sponsor.

Reporting

The Principal Investigator is responsible for the reporting of protocol deviations. Site staff or a study monitor may prepare a protocol deviation form, but this form should be signed by the PI. This form should be kept in the Trial Master File for the relevant site. Once signed by the PI a new form is required for any further breaches even if the previous form was filled to the end.

Protocol Deviation Codes

A – Consent Procedures

B – Inclusion/Exclusion Criteria

C – Concomitant Medication/Therapy

D – Laboratory Assessments/Procedures

E – Study Procedures

F – Serious Adverse Event Reporting/Unanticipated Adverse Device Effect

G – Randomization Procedures/Study Drug Dosing

H – Visit Schedule/Interval

I – Efficacy Ratings

J – Other

Protocol Deviation Tracking Log (Can use Sponsors)

Page Number __

Please use one sheet per Site. If signed by the Principal Investigator, please file and use a new form even if all 6 rows are not completed

- *Each page should be separately numbered to allow cross-referencing (e.g., deviation #3 on page 9)*
- *Deviation Type: (A-J) See codes below—enter the appropriate deviation code from the list.*

Protocol Number:		Primary Site Name/Number:	
Protocol Title (abbreviated):		Principal Investigator:	
		Satellite Site Name/Number (if applicable)	
		Sub-Investigator (if applicable)	

No.	Subject ID	Site No	Date of Deviation	Date Identified	Description	Type of Deviation See Codes	Resulted in AE?	Did Subject continue in study?	Ethics reporting requirements (Yes / No)	Ethics reporting date
1										

2										
3										
4										

Investigator Signature: _____ **Date:** _____

Appendix 7 Example Initiation Check-list

Activity	Complete
Ensure the Site Initiation Meeting is scheduled and all relevant staff are able to attend - • Investigator, Clinical Research Coordinator, Sponsor or CRA, Pharmacist, other relevant people such as laboratory staff. • It is usual for the Sponsor to confirm the initiation by letter	
Review Investigational Product overview and background	
Review with investigator and relevant staff their understanding of the protocol, study procedures, randomisation procedures, un-blinding procedures, sampling handling procedures and study timelines	
Review that site resources are adequate to conduct the trial	
Review with investigator and relevant staff Safety Reporting procedures and principles of Good Clinical Practice (ICH-GCP), including informed consent procedures, investigator responsibilities, record keeping, ethics and governance reporting.	
Review contents of Site Master File to ensure it complies to Australian ICH GCP	
Review source documentation location for Satellite sites	
Complete site signature and delegation of responsibilities log	
Review investigational product shipment records	

Appendix 8 Example Study Master File Index and Contents

File Section	Documentation	Location	Responsible	
			Primary	**Satellite**
Contact List	Contact list table for study related personnel at Primary and Satellite Sites, including the cluster contact details to all sites		**Holds for all sites**	Site only. Copy to Primary Site Request full list if needed
Correspondence	General correspondence with sponsor, CRO, teleconference and meeting notes		All sites	Copy from Primary
Agreements	Clinical trial agreement location, site indemnities, confidentiality agreement(s) location, letters of intent, Health Service Directive for clinical trial regulatory process for Satellite sites		Held at Primary Site	Copy from Primary
Finance	Financial disclosure forms for any person listed on the FDA Form 1572 (IND study only)		Held at Primary Site	Copy from Primary

File Section	Documentation	Location	Responsible	
			Primary	Satellite
Ethics Committee • Approvals • Acknowledgements • Composition • Correspondence	All ethics correspondence and documentation including all versions of the informed consent form, ethics committee composition, statement of committee compliance to NH&MRC National Statement, approval letters, reports to ethics committee, correspondence as applicable to commercial sponsorship, submission package(s), sample informed consent form, approved advertising materials/wording, other information provided to study participants and approved by ethics, tracked changes to protocol and summary tables, insurance certificate		Held at Primary Site	Copy from Primary
Investigator Brochure and safety updates	All versions as provided to ethics, safety updates from sponsor		Held at Primary Site	Copy from Primary
Protocol	All versions as provided to and as approved by ethics, signed protocol signatory page should also be in this		Signed by Primary Site	Copy from Primary
Regulatory documents	Australian CTX or CTN form (fully executed), IND form 1572, other regulatory agency forms, all correspondence to the regulatory agencies		Held at Primary site	Copy from Primary

File Section	Documentation	Location	Responsible	
			Primary	Satellite
Sample CRF	Approved version of sample CRF (a blank set that can be duplicated)		Held at Primary Site	Copy from Primary
Serious Adverse Events	Documentation tracking the incidence and reporting of SAEs, reports to ethics, reports to the applicable agency (interim and final)		Site specific Primary notified of any SAEs at the same time as sponsor	Site specific Primary notified of any SAEs at same time as sponsor
Monitoring	All general monitoring correspondence unless specifically belonging in another file section, pre-trial monitoring report, feasibility assessments, monitoring visit reports and follow-up letters, monitor-site correspondence, close-out visit reports		Sponsor visit face-to-face	Via telehealth or face-to-face
Audit	Auditor correspondence, audit reports (if available) and auditor follow-up letters		Held at Primary Site	Only if requested
Laboratory	Clinical laboratory certification (NATA, CLIA), laboratory normal values for medical/laboratory/technical procedures and/or tests included in the protocol, all provided		From Primary Site	Only if used
Curriculum Vitae	Signed and dated copies of CVs for all medical staff, (Principal Investigator, Sub-Investigators) and other staff delegated significant duties as listed on the delegation log for the duration of the research project		All Investigators and staff with significant duties from all sites	Site specific staff and key Primary

File Section	Documentation	Location	Responsible	
			Primary	Satellite
Signature Log	Site personnel signature sheet with a list of signatures and initials of all persons authorised to make entries and/or corrections on the CRFs and e-CRFs and certain delegated tasks		All staff from all sites	Site only
CRF completion guidelines	Any correspondence, presentations and/or CRF completion guidelines provided by the Sponsor		Sent to Primary Site	Copy to Secondary
Shipping records for IMP and other study related materials	Shipment records, date of shipment, batch numbers, method, shipment receipt records, certificate of analysis for Investigational Product, storage conditions		Site specific and on ward to Satellite	Site specific receipt, use and return
Accountability and destruction records	Investigational Product accountability and destruction correspondence and records		Site specific and on ward to Satellite	Site specific receipt, use and return
Decoding and Unblinding	Any correspondence relating to decoding and unbinding. Documents how identity of blinded investigational product can be revealed in case of emergency.		Site specific and Satellite information stored	Site specific
Participant Screening Logs	Screening logs including participant identification logs (site only for identification in case of emergency), participant registration/screening logs containing a chronological listing of screening/enrolment of participants.		Site specific (Primary has copy of Satellite Site for emergency)	Site specific

File Section	Documentation	Location	Responsible	
			Primary	Satellite
Participant identification code list	A confidential list of names of all participants allocated to trial numbers upon enrolment in the trial. Allows investigator/institution to reveal participant identity in the case of emergency or for reasons of safety		Primary has all details	Site specific only
Participant enrolment logs	Chronological enrolment of participants by participant number		Site specific only	Site specific only
Visit log	Records for all site visits, monitoring visits, sponsor visits, auditor visits, agency audits		Sponsor visit	Only if sponsor visits
Data query tracking	Data query tracking, monitors site queries and correspondence		Sponsor visit	Remotely accessed
Clinical study report	Final clinical study report (signed copy) if provided		Sent to Primary	Copy from Primary
Signed Informed Consent Forms	Informed Consent forms should be fully signed with all signatories dating their own signature. In addition, time of consent should be recorded in order to establish that consent was obtained prior to any trial procedures. Where informed consent is placed in the medical record, a file note stating this must be added to this section of the file		All sites	Held at site, witnessed and processed by telehealth if required
Other-study specific	Other documents not included in the previous sections			Copy from Primary

File Section	Documentation	Location	Responsible	
			Primary	Satellite
			All	where relevant
Supervision Plan	A plan recording the oversight for the project and staff involved in the study and the role of the Primary Site overseeing the Satellite sites and reporting structure for the study.		Held at site	Explained to all site staff
Monitoring Plan			At Primary Site	Copy from Primary
Safety Monitoring Plan			At Primary Site	Copy from Primary

Appendix 9 Example Study Master File Index

1. Contact List
2. Project Documents incl. IP and safety

   2.1 Investigator Brochure

   2.2 Safety Updates (reports, expedited safety letters/notifications, etc.)

   2.3 Protocol

   2.4 CRF (blank)

   2.5 CRF completion guidelines

   2.6 IP Shipping records (refer to Pharmacy Folder/Records)

   2.7 Accountability records (refer to Pharmacy Folder/Records)
3. Contracts

   3.1 Site Agreements (CTRA, Indemnities, Confidentiality Agreements, Staff personal information consent, etc.)
4. Regulatory Authority Documents

   4.1 Regulatory Agreements (e.g. FDA 1572)

   4.2 Financial Disclosure Forms (FDFs)

   4.3 Other Regulatory Documents (CTX, CTN, etc.)
5. Ethics Committee (EC) / Institutional Review Board (IRB)

   5.1 Initial Submissions/Approval

   5.2 Other Submissions/Approval

   5.3 Composition and Registration

   5.4 EC and IRB guidance documents

   5.5 Clinical Study Report

   5.6 Correspondence
6. Site Staff Qualification

   6.1 Curriculum Vitae and Medical Licences

   6.2 Training (GCP, study specific, vendor specific)

   6.3 Delegation of Authority log

6.4 Supervision Plan

7. Subject Documents

7.1 Blank informed Consent Forms (signed forms in patient files)

7.2 Screening Log

7.3 Enrolment Log

7.4 Subject Identification Log

7.5 Other (subject diaries, emergency card, recruitment material, etc.)

8. Safety Documents

8.1 Safety Monitoring Plan

8.2 Risk Management Plan

8.3 Serious Adverse Events Log

8.4 Serious Adverse Events Form(s)

8.5 SUSARs

8.6 Safety Reports

9. Laboratory

9.1 Central and Local Lab Accreditation/Certification (NATA, CLIA)

9.2 Central and Local Lab normal ranges

9.3 Central Lab Manual/Instructions

9.4 Other (calibration certification, freezer logs, pathology records/shipment) – refer to Pathology records

10. Monitoring

10.1 Site visits (incl. initial)/Monitoring Visits/Sponsor Visits

10.2 Data query tracking

10.3 Protocol deviation log

10.4 Audit (correspondence, reports, follow up letters, etc.)

10.5 Monitoring Plan

11. Correspondence

11.1 General with Sponsor, CRO, teleconference, meeting notes

Appendix 10 Example of Individual Participant Investigational Product (IP) Accountability Record

Section 1 – Investigational Product Details **Page ____ of ____**

Investigational Product:		**Dosage Form:**		**Lot Number:**	
Study Protocol Number:		**Strength / Unit:**		**Expiry Date:**	
Participant ID:		**Research Coordinator:**		**Used IP:**	

Section 2 - Storage Details

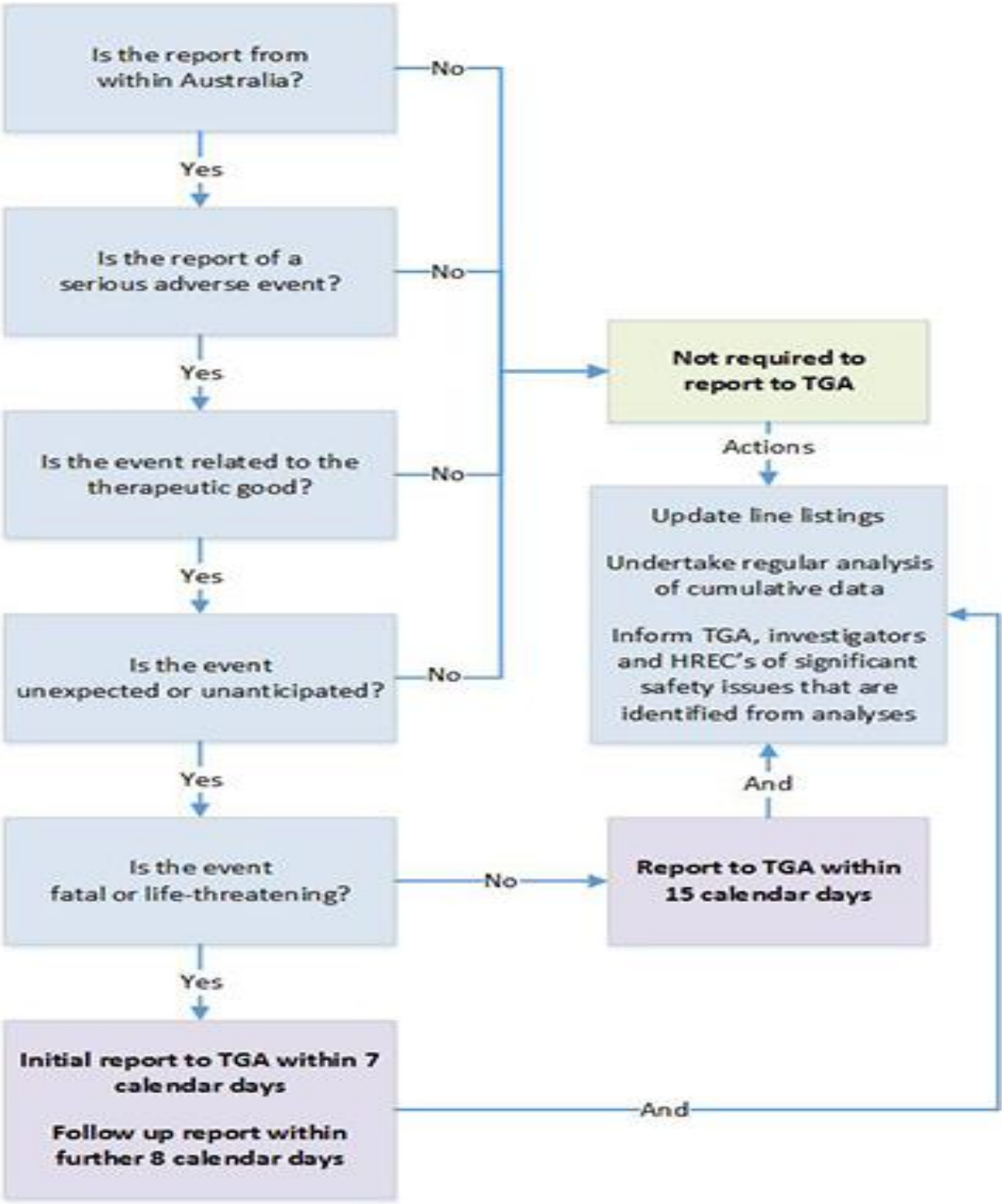
Room / Location:		**Storage Requirements:**	☐ Ambient ☐ 2 – 8 ° C ☐ Other ----------

Section 3 – Transaction History

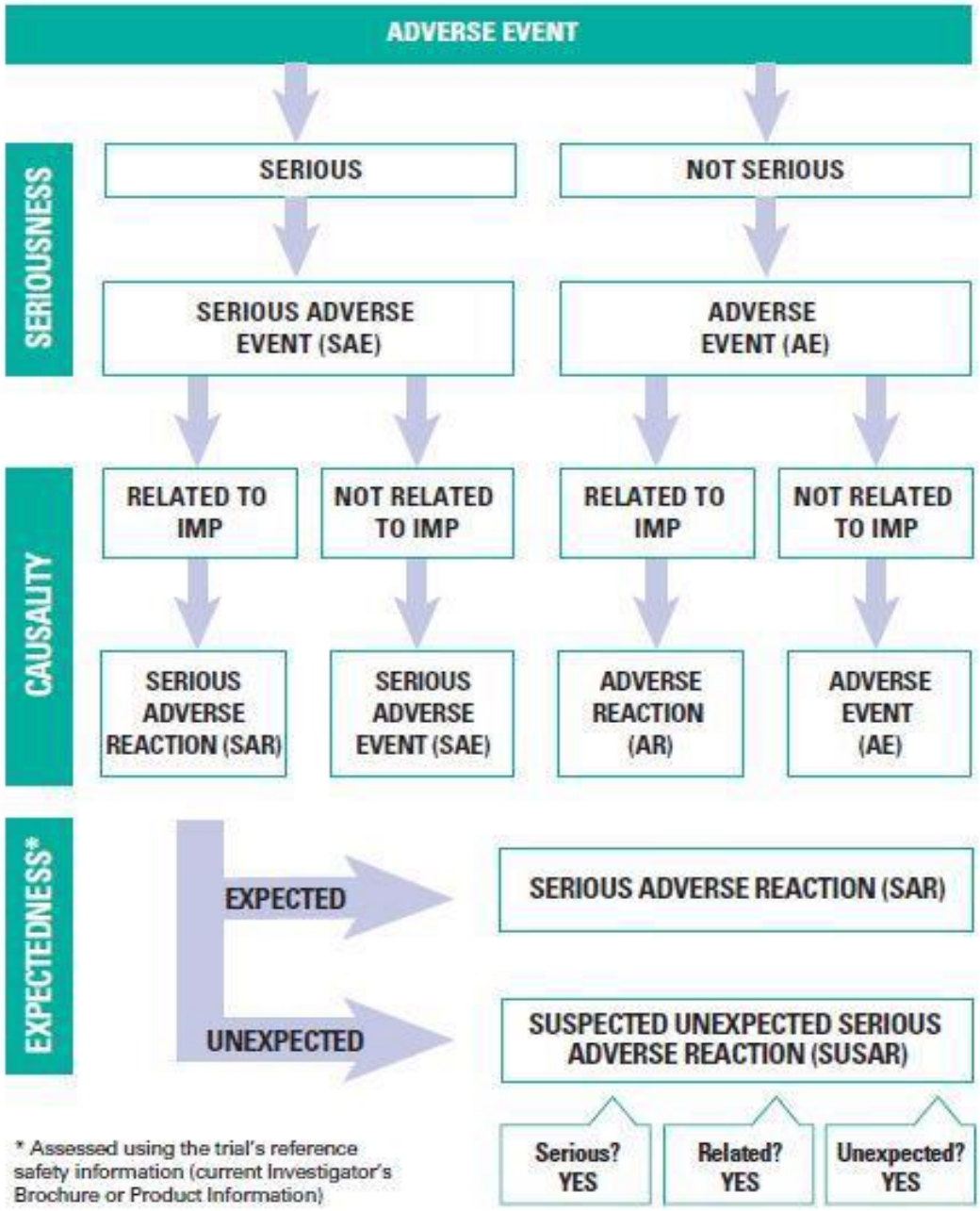
Date / Time		**Transaction Details**				**Balance of IP**			**Balance of used IP** ☐ **NA**			**If Transaction = RECEIVE or RETURN**	**Comments**
Date	Time	Received, Dispensed, Destroyed or Returned	Participant ID	Performed by (initials)	Checked by (initials)	IN	OUT	TOTAL	IN	OUT	TOTAL	**Indicate LOCATION received or returned to**	

		☐ Received ☐ Balance carried over											

Appendix 11 Sponsor reporting of SUSAR and USADEs to TGA (for trials conducted under the CTN or CTX schemes)

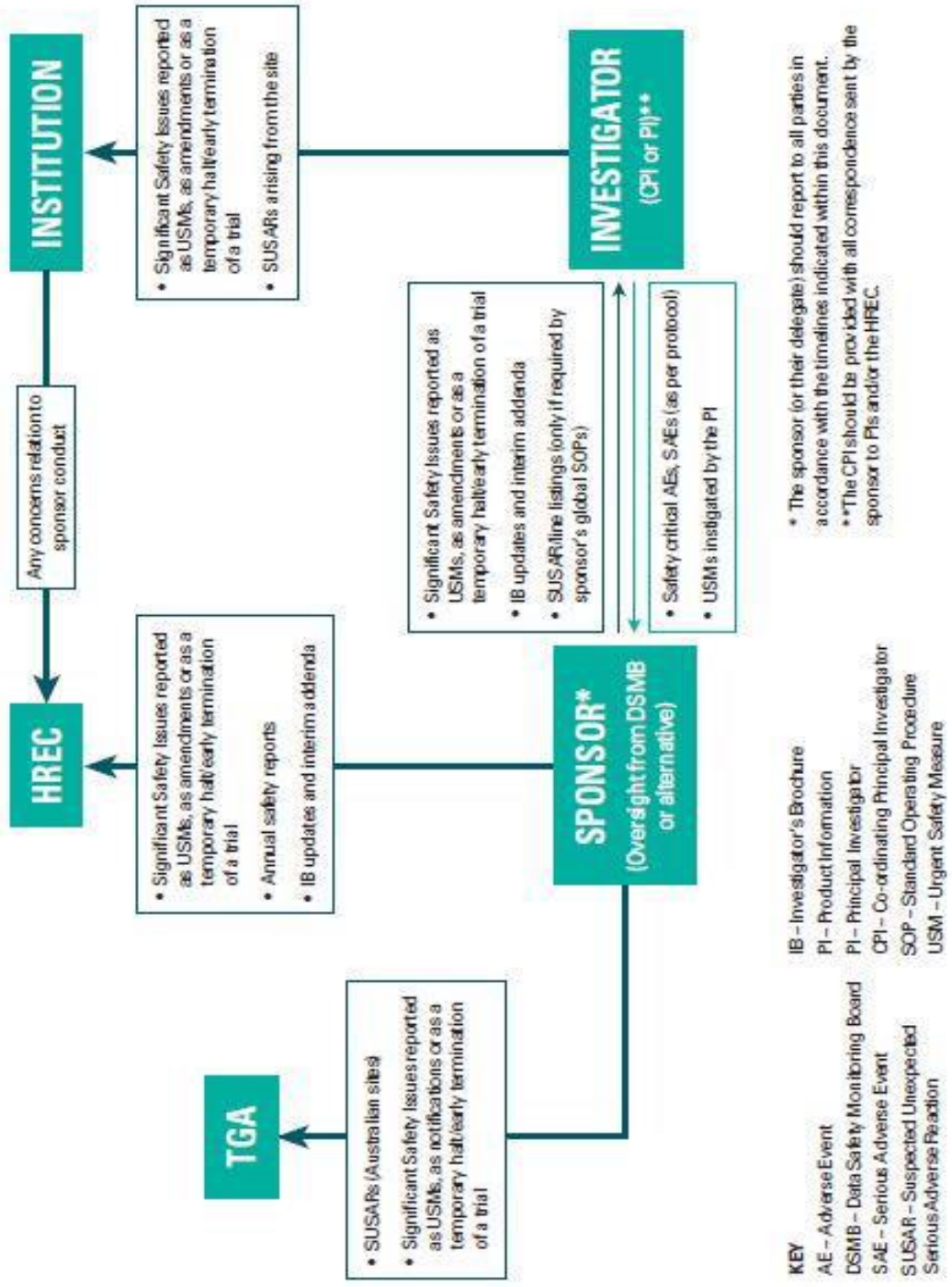


Appendix 12 Safety Reporting Assessment Flow Chart Investigational Medicinal Product Trial

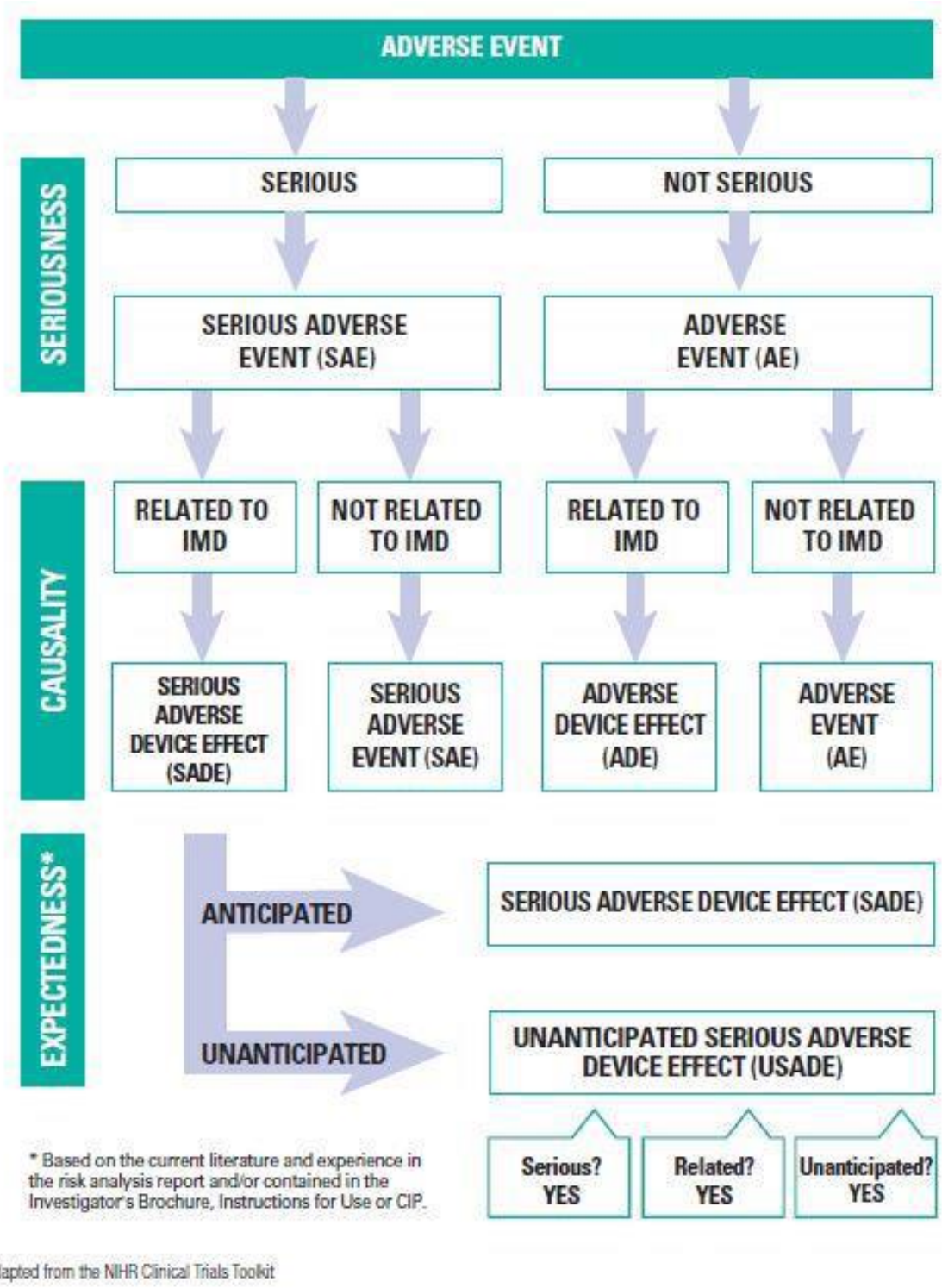


Adapted from the NIHR Clinical Trials Toolkit

Appendix 13 Report Flowchart for Investigational Medicinal Product Trial

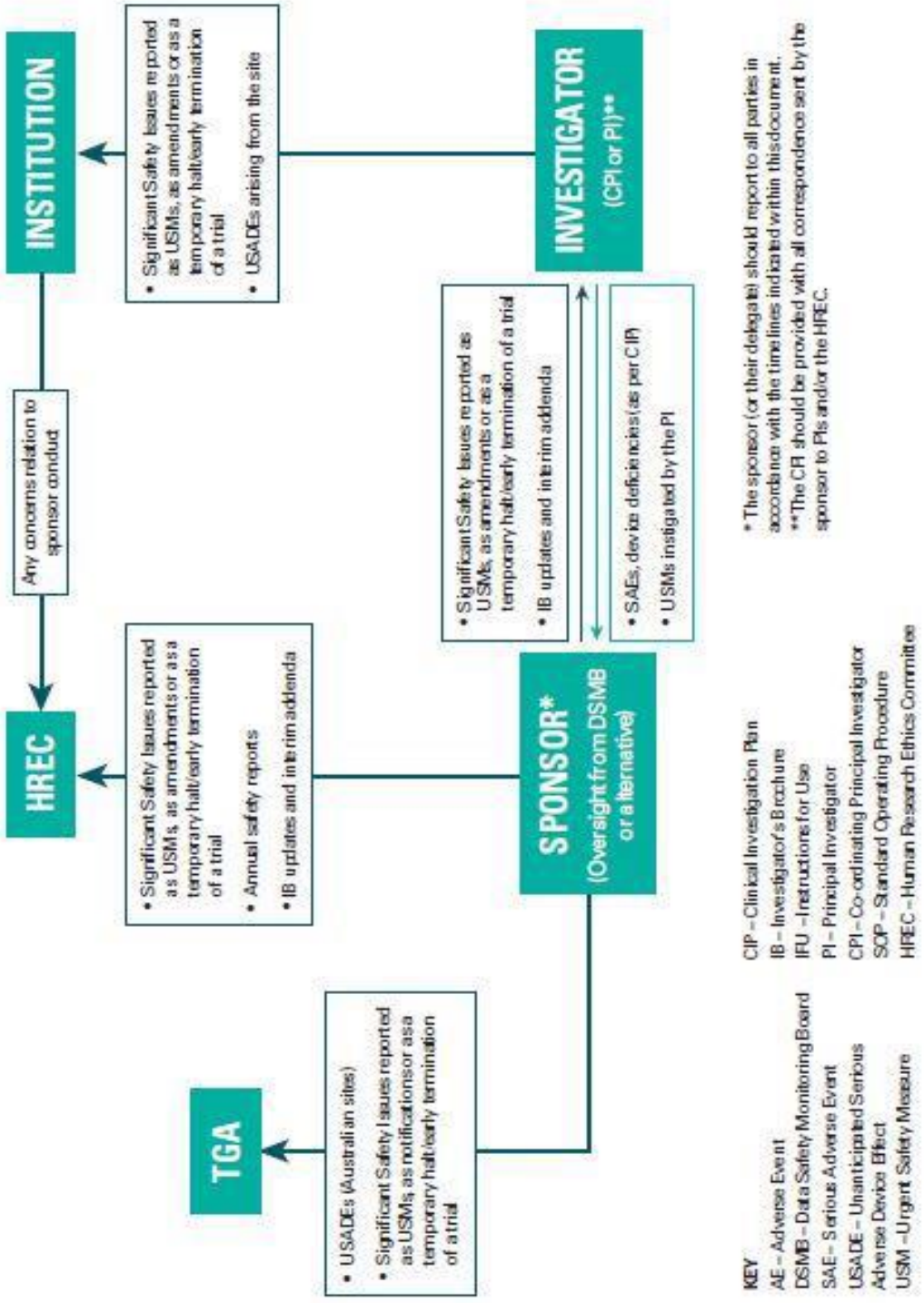


Appendix 14 Safety Reporting Assessment Flowchart Investigational Medicinal Device Trial



Adapted from the NIHR Clinical Trials Toolkit

Appendix 15 Report Flowchart for Investigational Medicinal Device Trial



Appendix 16 Example Close Out Check-List

Activity	Complete
Ensure all protocol required data has been collected	
Finalise accountability and disposition of investigational product (medicine/device)	
Verify that all study files are complete	
Discuss overall study conduct at the site	
Collect final signatures for any delegation or training logs or reports	
Discuss archiving of original data and documents	
Dispose of or return any remaining trial specific supplies including biological samples	
Formally close the site	
Notify the HREC and /or Governance Office that the study has been closed, and study materials returned/destroyed/archived	

Appendix 17 Jurisdictional Contact Details

Australian Capital Territory

Research Office

Phone: 02 6174 7968

Email: acthealth-hrec@act.gov.au

Web: www.health.act.gov.au/datapublications/research/human-research-ethics-committee

New South Wales

The Office for Health and Medical Research

Email: researchethics@doh.health.nsw.gov.au

Website: www.health.nsw.gov.au/ethics/Pages/nma.aspx

Northern Territory

Royal Darwin Hospital and Flinders University

Email: lewis.campbell@gmail.com

Queensland

Research, Ethics and Governance; Health Innovation, Investment and Research Office

Phone: 07 3708 5071

Email: hiiro_reg@health.qld.gov.au

Website: www.health.qld.gov.au/ohmr/html/regu/regu_home.asp

South Australia

Office for Research

Phone: 08 8226 7231

Email: Health.DHAResearch@sa.gov.au

Website: www.sahealth.sa.gov.au/researchethics

Tasmania

Dr Jodi Glading

Office of the Principal Medical Advisor

Phone: (03) 6166 0413

Email: Jodi.johnson-glading@dhhs.tas.gov.au

Victoria

Coordinating Office for Clinical Trial Research

Phone: 03 9096 7394

Email: multisite.ethics@health.vic.gov.au

Website: www2.health.vic.gov.au/about/clinical-trials-and-research

Western Australia

Clinical Services and Research

Phone: 08 9222 4332

Email: ResearchDevelopment@health.wa.gov.au

Website: https://rgs.health.wa.gov.au/Pages/Multi-centre-Research.aspx

For more information

SA Department for Health and Wellbeing
Office for Research
Level 5, Citi Centre
11 Hindmarsh Square
Adelaide SA 5000
Health.DHAResearch@sa.gov.au
www.sahealth.sa.gov.au

www.ausgoal.gov.au/creative-commons