PROCEDURE

Research Office Procedure Good Clinical Practice (GCP) Series of SOPs

Purpose:

This document integrates several standard operating procedures. The procedures describe the process, design, conduct, documentation, reporting requirements and preparation, responsibilities and maintenance of records of clinical trials.

Scope:

These procedures are applicable to all clinical research including drug and device trials.

Risks/Precautions:

None have been identified at the time of this review.

Procedure/Method:

This set of Standard Operating Procedures (SOPs) is provided with the aim of achieving Good Clinical Practice (GCP) in clinical research and provides the necessary tools to suppport researchers comply with relevent Good Clinical Practice guidelines (International Conference on Harmonisation GCP and/or ISO14155) . This document contains the following procedures:

SOP1 - Documentation of Investigational Site Qualifications, Adequacy of Resources and Training Records

Procedure/Method:

1. Documentation of Investigational Site Qualifications and Training Records

The investigator(s) must:

- Maintain an up-to-date *Curriculum vitae* and review on a yearly basis.
- Be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial. This should be evidenced in the CV.
- Meet all the qualifications specified by the applicable regulatory requirement(s). Current medical practitioner registration details and similar documentation should be referenced in the CV.
- Provide evidence of such qualifications through up-to-date *Curriculum vitae* and/or other relevant documentation requested by the sponsor, the HREC, and/or the regulatory authority(ies).
- Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties. The list is in the form of a Delegation Log and delegated duties should be captured and signed and dated by the investigator on a per person basis. The delegation log may be provided by the Sponsor but for investigator-initiated studies, a separate site log must be developed.

2. Adequacy of Resources

The investigator(s) must:

- Be able to demonstrate (if possible, based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period. This may be in the form of de-identified subject recruitment listings or other documented written evidence.
- Have sufficient time to properly conduct and complete the trial within the agreed trial period and have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
- Adequacy of resources is normally determined by a site feasibility assessment for commercially-sponsored studies.

3. Training Records

The investigator(s) must:

- Ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions. An initiation meeting may be held where all required staff are present and written evidence of study specific training is developed.
- Ensure that documentation of this training be kept current and available for review on request throughout the entire trial period.
- Ensure that tasks delegated to study staff are documented appropriately. This can be evidenced by the delegation log. However, study specific training records should be maintained to provide evidence that tasks were delegated following the correct training.

Outcome:

That Researchers have appropriate documentation of investigational site qualifications and training records as well as the provision of resources to perform research appropriately.

Definitions:

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Human Research Ethics Committee (HREC): A body that reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Council for Harmonisation (ICH): International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site ensuring that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Sub Investigator: 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).

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3).

NHMRC National Statement on Ethical Conduct in Human Research, (2023).

SOP2 - Trial Master Files and Essential Documents

Procedure/Method:

1. The Investigator Site File (ISF) and Essential Documents

   The investigator(s) must:

   - File essential documents at the site in a timely manner. All site-related materials should be made available for review by the sponsor's representatives (monitors and auditors) or regulatory authority(ies).
   - Keep a minimum list of essential documents -
   - Before the clinical phase of the trial
   - During the clinical conduct of the trial
   - After completion or termination of the trial.
   - Study documentation must be maintained for a minimum of 15 years for adult studies or 25 years for paediatric studies.
   - Written confirmation that records are no longer needed should be obtained prior to destruction.
   - For legal reasons, sites may consider indefinite archiving periods.
   - The TGA position on document retention states:
     - "The TGA requires records to be retained by the sponsor for 15 years following the completion of a clinical trial. However, in Australia the over-riding consideration for sponsors with respect to record retention is the issue of product liability and the potential need for sponsors of products to produce records at any time during, and possibly beyond, the life of a product in the event of a claim against the sponsor as a result of an adverse outcome associated with the use of the product."

2. The Investigator Site File (ISF)
   - The ISF should contain all the essential documentation.
   - For commercially sponsored studies, sponsoring companies will normally provide site file complete with tab separators for ease and consistency of filing.
   - For Studies conducted on behalf of smaller companies or for investigator-initiated studies, the site file should be structured in accordance with appropriate checklists deemed appropriate for the study.
   - Financial documentation such as the clinical trial agreement may be filed in a separate location to the Master Site File.
   - The site pharmacy will usually keep investigational product shipping, receipt and accountability documents. The site itself does not have to replicate these documents. However, the records must be made available to sponsors monitors, inspectors, and auditors.

Outcome:

That researchers be able to maintain the investigator site file and associated essential documents.

Definitions:

Essential Documents: Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

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Sub Investigator: 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).

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3)

NHMRC National Statement on Ethical Conduct in Human Research, (2023)

SOP3 - Communication with HREC, Trial Sponsor and Insurer

Procedure/Method

1. Communication with HREC

   The investigator(s) must:

   - Understand the Institutional HREC requirements and processes to better liaise with sponsors, e.g., on application process, documents, understanding legal requirements, understanding specific institutional site specifications on wording in consent forms, etc.
   - Be aware of how often the HREC meets, what documents are required in an initial application and when (time period prior to an ethics committee meeting), research governance site specific approval processes and what is the approval documentation and how to issue safety alerts.
   - Ensuring they are familiar with this process (e.g., does the HREC have subcommittees) since this may be required to be described to sponsors, auditors, inspectors.
   - Ensure the institutional ethics committee is registered with the National Health and Medical Research Council and is constituted in accordance with the National Statement.
   - Obtain written and dated approval/favourable opinion from the HREC for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects prior to the commencement of the trial. This is normally in the form of an ethics approval letter which should state the version number and dates of documentation submitted.
   - As part of the institution's written application to the HREC, provide the HREC with a current copy of the Investigator's Brochure and if updated

during the trial, the investigator/institution should supply a copy to the HREC.

- Be familiar with the procedure for submitting protocol amendments and changes to the informed consent form and understand the time periods associated to obtain approval following submission of amendments.
- Provide to the HREC all documents subject to review during the trial, including any serious or unexpected adverse events, proposed changes in the protocol and unforeseen events that might affect continued ethical acceptability of the project.
- Submit written summaries of the trial status to the HREC annually, or more frequently, if requested by the HREC. They should understand the reporting requirements for their ethics committee including protocol deviations and safety reporting.
- In addition, the Investigator must report to the HREC any serious, adverse drug/device effect that is experienced during the Trial by any participant within 24 hours of him or her becoming aware of same.

2. Communication with the Trial Sponsor

The investigator(s) must:

- Notify the sponsor within 24 hours of any serious AND unexpected adverse events involving trial subjects.
- Provide written reports promptly to the sponsor, the HREC and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.
- Notify the sponsor within 24 hours of any significant deviation from the protocol (this is individually defined by the sponsor).
- Be available during the study to meet with sponsor delegates to discuss study progress, issues and safety.
- Notify the sponsor promptly of any adverse effect that may reasonably be regarded as caused by, or probably caused by, the investigational product.
- Provide the Sponsor with copies of all correspondence from the reviewing HREC.
- Immediately notify the Research Office of any notification received from a research participant that they intend to initiate a claim against either the Sponsor and/or the Institution. In addition, the Sponsor, Insurer and the reviewing HREC must also be notified as soon as possible.

3. Communication with the Insurer

The institution must report the following to the VMIA (usually through the Research Office):

Reports of serious adverse events, [or which relate to a claim made against the Hospital/Institution (or member of its staff) and/or the occurrence of circumstances which may subsequently give rise to a claim against a Hospital/Institution], must be reported to VMIA in accordance with the provisions of the VMIA Public Liability and Medical Indemnity Policies.

Outcome:

That researchers know the procedures related to communicating with the HREC, trial sponsor and insurer.

Definitions:

Delegate: A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial. Delegation must be evidenced in writing.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Human Research Ethics Committee (HREC): A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Council for Harmonisation (ICH): International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site and ensures that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Serious Adverse Device Event (SADE): A device-related serious adverse event. (See Serious Adverse Event (SAE) – device)

Serious Adverse Event (SAE) – drug: Any untoward medical occurrence that, at any dose:

- results in death;
- is life-threatening;

NOTE: The term 'life-threatening' in the definition of 'serious' refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event, which hypothetically might have caused death if it were more severe.

- requires in-patient hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability/incapacity; or
- is a congenital anomaly/birth defect; and fits the SAE criteria as specified in the relevant clinical trial protocol.

Medical or scientific judgement should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also usually be considered serious. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalisation; or development of drug dependency or drug abuse.

Serious Adverse Event (SAE) – device: Serious Adverse Event for *medical devices*: any adverse medical occurrence that:

- lead to a death;
- lead to a serious deterioration in health of a patient 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 e) 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 has to be modified or temporarily/permanently taken out of service
- a factor (a deterioration in characteristics or performance) found on examination of the device

Sub Investigator: 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).

References:

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

VMIA Clinical Trials Risk and Insurance Guide August 2023

SOP4 - Protocol and Investigator's Brochure Content, Design, Amendments and Compliance

Procedures/Methods:

1. Protocol content and design

Specific content of a protocol will vary depending on whether the subject of investigation is a medicinal product, device or therapeutic intervention. The description below uses the case of a medicinal product, in the case of a device or therapeutic intervention the terms should be adapted appropriately and followed where applicable.

Where the investigator is responsible for the protocol design and/or is the sponsor they must (where applicable) provide the following information in the protocol:

2. General Information

- Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).
- Name and address of the sponsor, and monitor (if other than the sponsor).
- Name and title of the person(s) authorised to sign the protocol and the protocol amendment(s) for the sponsor.

- Name and title of the investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of the trial site(s).
- Name, title, address, and telephone number(s) of the qualified physician (who is responsible for all trial-site related medical decisions (if other than investigator).
- Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

3. Background Information
   - Name and description of the investigational product(s).
   - A summary of findings from non-clinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.
   - Summary of the known and potential risks and benefits, if any, to human participants.
   - Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).
   - A statement that the trial will be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s).
   - Description of the population to be studied.
   - References to literature and data that are relevant to the trial, and that provide background for the trial.
   - Trial Objectives and Purpose
   - A detailed description of the objectives and the purpose of the trial.
4. Trial Design
   - The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design. A description of the trial design should include:
     - A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.
     - A description of the type/design of trial to be conducted (e.g. double-blind, placebo controlled, parallel design) and a schematic diagram of trial design, procedures and stages.
   - A description of the measures taken to minimise/avoid bias, including:
     - Randomisation.
     - Blinding.

- A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s). Also include a description of the dosage form, packaging, and labelling of the investigational product(s).
- The expected duration of participant participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.
- Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.
- Maintenance of trial treatment randomisation codes and procedures for breaking codes.
- The identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.

Selection and Withdrawal of Participants

- Participant inclusion criteria.
- Participant exclusion criteria.
- Participant withdrawal criteria (i.e. terminating investigational product treatment/trial treatment) and procedures specifying:
  - When and how to withdraw participants from the trial/ investigational product treatment.
  - The type and timing of the data to be collected for withdrawn participants.
  - Whether and how participants are to be replaced.
  - The follow-up for participants withdrawn from investigational product treatment/trial treatment.

5. Treatment

- The treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.
- Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.
- Procedures for monitoring participant compliance.

6. Assessment of Efficacy

- Specification of the efficacy parameters.
- Methods and timing for assessing, recording, and analysing of efficacy parameters.

7. Assessment of Safety
   - Specification of safety parameters.
   - The methods and timing for assessing, recording, and analysing safety parameters.
   - Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.
   - The type and duration of the follow-up of subjects after adverse events.
8. Statistics
   - A description of the statistical methods to be employed, including timing of any planned interim analysis(ses).
   - The number of subjects planned to be enrolled. In multicentre trials, the numbers of enrolled subjects projected for each trial site should be specified.
   - Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.
   - The level of significance to be used.
   - Criteria for the termination of the trial.
   - Procedure for accounting for missing, unused, and spurious data.
   - Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).
   - The selection of subjects to be included in the analyses (e.g. all randomised subjects, all dosed subjects, all eligible subjects, evaluable subjects).
9. Direct Access to Source Data/Documents
   - The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, HREC review, and regulatory inspection(s), providing direct access to source data/documents.

Quality Control and Quality Assurance

1. Ethics
   - Description of ethical considerations relating to the trial.
2. Data Handling and Record Keeping

3. Financing and Insurance
    - Financing and insurance if not addressed in a separate agreement.
4. Publication Policy
    - Publication policy, if not addressed in a separate agreement.
5. Supplements
6. Amendments to the protocol

The investigator(s) must:

- Inform the HREC, and seek its approval, of amendments to the protocol including amendments that:
    - Are proposed or undertaken without prior HREC approval in order to eliminate immediate risks to participants;
    - May increase the risks to participants; or
    - Significantly affect the conduct of the trial.
- Inform the HREC as soon as possible of any new safety information from other published or unpublished studies that may have an impact on the continued ethical acceptability of the trial or may indicate the need for amendments to the trial protocol. Notification of the HREC is site specific and the investigator should be familiar with the processes of their ethics committee.

7. Protocol compliance

The investigator(s) must:

- Conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority(ies) and which was given approval/ favourable opinion by the HREC.
- Along with the sponsor, sign the protocol, or an alternative contract, to confirm agreement.
- Not implement any deviation from, or changes to the protocol without agreement by the sponsor and prior review and documented approval/favourable opinion from the HREC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change in monitor(s), change of telephone number(s)).
- Document and explain any deviation from the approved protocol.

The investigator(s) may:

- Implement a deviation from, or a change to the protocol to eliminate an immediate hazard(s) to trial subjects without prior HREC approval/favourable opinion.

As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted:

- To the HREC for review and approval/favourable opinion;
- To the sponsor for agreement and, if required; and
- To the regulatory authority(ies).

8. Investigator's Brochure content and design

Specific content of an Investigator's Brochure will vary depending on whether the subject of investigation is a medicinal product, device or therapeutic intervention. The description below uses the case of a medicinal product, in the case of a device or therapeutic intervention the terms should be adapted appropriately and followed where applicable.

The Investigator's Brochure (IB) is a compilation of the clinical and non-clinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects.

Its purpose is to provide the investigators and others involved in the trial with the information to facilitate their understanding of the rationale for, and their compliance with, many key features of the protocol, such as the dose, dose frequency/interval, methods of administration and safety monitoring procedures.

The IB also provides insight to support the clinical management of the study subjects during the course of the clinical trial.

The information should be presented in a concise, simple, objective, balanced, and non-promotional form that enables a clinician, or potential investigator, to understand it and make his/her own unbiased risk-benefit assessment of the appropriateness of the proposed trial.

As part of their written application to the HREC, provide the HREC with a current copy of the Investigator's Brochure and if updated during the trial, the Investigator/institution should supply a copy to the HREC in accordance with that HRECs procedures.

In the case of a marketed product being studied, it may be acceptable to use the Product Information as a substitute for the Investigator's Brochure. The ICH guideline state:

"If the investigational product is marketed and its pharmacology is widely understood by medical practitioners, an extensive IB may not be necessary. Where permitted by regulatory authorities, a basic product information brochure, package leaflet, or labelling may be an appropriate alternative, provided that it includes current, comprehensive, and detailed information on all aspects of the investigational product that might be of importance to the investigator. If a marketed product is being studied for a new use (i.e, a new indication), an IB specific to that new use should be prepared."

9. The Investigator Brochure should provide the following information:

- Title Page
    - This should provide the sponsor's name, the identity of each investigational product (i.e., research number, chemical or approved generic name, and trade name(s) where legally permissible and desired by the sponsor), and the release date. It is also suggested that an edition number, and a reference to the number and date of the edition it supersedes, be provided.
- Confidentiality Statement
    - The sponsor may wish to include a statement instructing the investigator/ recipients to treat the IB as a confidential document for the sole information and use of the investigator's team and the HREC.
- Contents of the Investigator's Brochure
    - The IB should contain the following sections, each with literature references where appropriate:

Table of Contents

1. Summary
    - A brief summary (preferably not exceeding two pages) should be given, highlighting the significant physical, chemical, pharmaceutical, pharmacological, toxicological, pharmacokinetic, metabolic, and clinical information available that is relevant to the stage of clinical development of the investigational product or device.
2. Introduction
    - A brief introductory statement should be provided that contains:
    - The chemical name (and generic and trade name(s) when approved) of the investigational product(s).
    - All active ingredients, the investigational product (s) pharmacological class and its expected position within this class (e.g. advantages)

- The rationale for performing research with the investigational product(s), and the anticipated prophylactic, therapeutic, or diagnostic indication(s).
- The introductory statement should provide the general approach to be followed in evaluating the investigational product or device.

3. Physical, Chemical, and Pharmaceutical Properties and Formulation
   - A description should be provided of the investigational product substance(s) (including the chemical and/or structural formula(e)), and a brief summary should be given of the relevant physical, chemical, and pharmaceutical properties.
   - To permit appropriate safety measures to be taken in the course of the trial, a description of the formulation(s) to be used, including excipients, should be provided and justified if clinically relevant. Instructions for the storage and handling of the dosage form(s) should also be given.
   - Any structural similarities to other known compounds should be mentioned.

Non-Clinical Studies

1. Introduction

The results of all relevant non-clinical pharmacology, toxicology, pharmacokinetic, and investigational product metabolism studies should be provided in summary form.

- This summary should address:
  - The methodology used;
  - The results, and a discussion of the relevance of the findings to the investigated therapeutic; and
  - The possible unfavourable and unintended effects in humans.
- The information provided may include the following, as appropriate, if known/available:
  - species tested
  - number and sex of animals in each group
  - unit dose (e.g., milligram/kilogram (mg/kg))
  - dose interval
  - route of administration
  - duration of dosing

- information on systemic distribution
- duration of post-exposure follow-up
- results, including the following aspects:
- nature and frequency of pharmacological or toxic effects
- severity or intensity of pharmacological or toxic effects
- time to onset of effects
- reversibility of effects
- duration of effects
- dose response

Tabular format/listings should be used whenever possible to enhance the clarity of the presentation.

The following sections should discuss the most important findings from the studies, including the dose response of observed effects, the relevance to humans, and any aspects to be studied in humans.

If applicable, the effective and non-toxic dose findings in the same animal species should be compared (i.e., the therapeutic index should be discussed).

The relevance of this information to the proposed human dosing should be addressed. Whenever possible, comparisons should be made in terms of blood/tissue levels rather than on a mg/kg basis.

Non-clinical Pharmacology

- A summary of the pharmacological aspects of the investigational product and, where appropriate, its significant metabolites studied in animals, should be included.
- Such a summary should incorporate studies that assess potential therapeutic activity (e.g. efficacy models, receptor binding, and specificity) as well as those that assess safety (e.g., special studies to assess pharmacological actions other than the intended therapeutic effect(s)).

Pharmacokinetics and Product Metabolism in Animals

- A summary of the pharmacokinetics and biological transformation and disposition of the investigational product in all species studied should be given.
- The discussion of the findings should address the absorption and the local and systemic bioavailability of the investigational product and its metabolites, and

their relationship to the pharmacological and toxicological findings in animal species.

Toxicology

- A summary of the toxicological effects found in relevant studies conducted in different animal species should be described under the following headings where appropriate:
    - Single dose
    - Repeated dose
    - Carcinogenicity
    - special studies (e.g., irritancy and sensitisation)
    - Reproductive toxicity
    - Genotoxicity (mutagenicity)

Effects in Humans

1. Introduction

A thorough discussion of the known effects of the investigational product(s) in humans should be provided, including information on pharmacokinetics, metabolism, pharmacodynamics, dose response, safety, efficacy, and other pharmacological activities:

- Where possible, a summary of each completed clinical trial should be provided.
- Information should also be provided regarding results of any use of the investigational product(s) other than from in clinical trials, such as from experience during marketing.

2. Pharmacokinetics and Product Metabolism in Humans
    - A summary of information on the pharmacokinetics of the investigational product(s) should be presented, including the following, if available:
        - Pharmacokinetics (including metabolism, as appropriate, and absorption;
        - Plasma protein binding, distribution, and elimination);
        - Bioavailability of the investigational product (absolute, where possible, and/or relative) using a reference dosage form;
        - Population subgroups (e.g., gender, age, and impaired organ function);

- Interactions (e.g., product-product interactions and effects of food); and
- Other pharmacokinetic data (e.g., results of population studies performed within clinical trial(s).

3. Safety and Efficacy

- A summary of information should be provided about the investigational product's/products' (including metabolites, where appropriate) safety, pharmacodynamics, efficacy, and dose response that were obtained from preceding trials in humans (healthy volunteers and/or patients).
- The implications of this information should be discussed.
- In cases where a number of clinical trials have been completed, the use of summaries of safety and efficacy across multiple trials by indications in subgroups may provide a clear presentation of the data.
- Tabular summaries of adverse drug reactions for all the clinical trials (including those for all the studied indications) would be useful.
- Important differences in adverse drug reaction patterns/incidences across indications or subgroups should be discussed.
- The IB should provide a description of the possible risks and adverse drug reactions to be anticipated on the basis of prior experiences with the product under investigation and with related products. A description should also be provided of the precautions or special monitoring to be done as part of the investigational use of the product(s).

4. Marketing Experience

- The IB should identify countries where the investigational product has been marketed or approved.
- Any significant information arising from the marketed use should be summarised (e.g., formulations, dosages, routes of administration, and adverse product reactions).
- The IB should also identify all the countries where the investigational product did not receive approval/registration for marketing or was withdrawn from marketing/registration.

5. Summary of Data and Guidance for the Investigator

This section should provide a brief summary of the fundamental requirements or information available for a particular investigational product in order to allow a quick reference for the investigator. Summaries included in this section should not replace the information to be contained in the main body of the document.

Special emphasis should be placed on provision of quick reference safety aspects in order to find information as efficiently as possible.

SOP5 - Receipt and Handling of Investigational Product

Procedures/Methods:

1. Receipt and handling of investigational product

Responsibility for investigational product(s) accountability at the trial site(s) rests with the investigator/institution.

The investigator(s) must:

- (Where allowed/required), assign some or all of the investigator's/institutions duties for investigational product(s) accountability at the trial site(s) to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.

The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, must:

- Ensure that the investigational product(s) are used only in accordance with the approved protocol.
- Maintain records of the product's delivery and receipt to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product(s). These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product(s) and trial participant.
- Ensure that the investigational product(s) are stored as specified by the sponsor in accordance with applicable regulatory requirement(s). Consideration should be given to how the investigational product shall be securely stored, including restricting access to approved personnel. Records of accountability and storage monitoring (i.e., temperature logs) shall be maintained.
- Maintain records that document adequately that the participants were provided the doses specified by the protocol and reconcile all investigational product(s) received from the sponsor.

- Explain the correct use of the investigational product(s) to each participant and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
- A compliance check could include instructing the subjects to return empty and partially used containers at their next visit. An assessment would then be made of how much medication has been taken versus the expected amount of medication to be taken. The compliance check will usually also involve asking the subject to describe how and when they are taking the medication.

The investigator(s) should:

- Ensure that the investigational product(s) are used only in accordance with the approved protocol including the quarantine of investigational product(s) that have expired, and return them to the sponsor or destroy upon written instruction from the sponsor. Investigational products that have been exposed to temperature ranges outside the allowable range must also be quarantined and the temperature deviation documented and a decision sought from the sponsor regarding the use of the investigational product. Any destruction of investigational product requires the sponsors written permission.
- Follow the trial's randomisation procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should 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(s).

Outcome:

That researchers comply with the correct receipt and handling of the investigational product.

Definitions:

Delegate: A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Human Research Ethics Committee (HREC): A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Council for Harmonisation (ICH): International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigational Product: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site and ensures that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Protocol: A document that describes the objective(s), design, methodology, statistical considerations and organisation of a clinical trial.

Sub-Investigator: 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).

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3).

NHMRC National Statement on Ethical Conduct in Human Research, (2023).

Investigational medicinal products (Annex 13).

RVEEH Pharmacy Department SOP Destruction of Investigational Products

SPO6 – Informed Consent Procedures and Writing Patient Informed Consent Forms

Procedures/Methods:

1. Informed consent procedures

The investigator(s) must:

- Comply with local HREC requirements, NHMRC National Statement on Ethical Conduct in Human Research (2023) and other applicable regulatory requirement(s), and adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki.
- Obtain the HREC's written approval/favourable opinion of the written informed consent form and any other written information to be provided to subjects prior to the beginning of the trial.
- Ensure that the written informed consent form and any other written information to be provided to subjects is revised whenever important new information becomes available that may be relevant to the participant's consent.
- Obtain the HREC's approval/favourable opinion in advance of use for any revised written informed consent form, and written information.
- Ensure the person or persons taking the informed consent have an adequate understanding of the trial and of the informed consent process and is the person(s) identified to conduct the process on the delegation log.
- Inform the participant or the participant's legally acceptable representative in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.
- Not, nor permit trial staff to coerce or unduly influence a subject to participate or to continue to participate in a trial.
- Not permit any of the oral and written information concerning the trial, including the written informed consent form, to contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
- Or a person designated by the investigator), fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval/ favourable opinion by the HREC.

- Ensure that language used in the oral and written information about the trial, including the written informed consent form is as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable. The information that forms part of the informed consent process should be written in layman's terms and generally to the level of a 13 year old.
- Ensure that before informed consent is obtained, they, or a person designated by the investigator, provide the participant or the participant's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the participant or the participant's legally acceptable representative.
- Ensure prior to a participant's participation in the trial, that the written informed consent form is signed and personally dated by the participant or by the participant's legally acceptable representative, and by the person who conducted the informed consent discussion.
- Ensure if a participant is unable to read or if a legally acceptable representative is unable to read, that an impartial witness be present during the entire informed consent discussion, and that discussion be held in an appropriate language.
- Ensure that after the written informed consent form and any other written information to be provided to participants, is read and explained to the participant or the participant 's legally acceptable representative, and after the participant or the participant's legally acceptable representative has orally consented to the participant's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form.
- Ensure prior to participation in the trial, the participant or the participant's legally acceptable representative receive a copy of the signed and dated written informed consent form and any other written information provided to the participants.
- Ensure during a participant's participation in the trial, the participant or their legally acceptable representative receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects.
- Ensure that when a clinical trial (therapeutic or non-therapeutic) includes participants who can only be enrolled in the trial with the consent of the participant's legally acceptable representative (e.g., minors, or patients with severe dementia), the subject is informed about the trial to the extent compatible with the subject's understanding and, if capable, the participant should sign and personally date the written informed consent.

- Ensure that (except as described immediately below), a non-therapeutic trial (i.e., a trial in which there is no anticipated direct clinical benefit to the subject), is conducted in participants who personally give consent and who sign and date the written informed consent form.

Note: Non-therapeutic trials may be conducted in subjects with consent of a legally acceptable representative provided the following conditions are fulfilled:

- The objectives of the trial cannot be met by means of a trial in participants who can give informed consent personally.
- The foreseeable risks to the subjects are low.
- The negative impact on the subject's well-being is minimised and low.
- The trial is not prohibited by law.
- The approval/favourable opinion of the HREC is expressly sought on the inclusion of such subjects, and the written approval/ favourable opinion covers this aspect.

The investigator(s) must ensure:

- That such trials, unless an exception is justified, are conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
- That in emergency situations, when prior consent of the participant is not possible, the consent of the participant's legally acceptable representative, if present, is requested. When prior consent of the participant is not possible, and the subject's legally acceptable representative is not available, enrolment of the participant should require measures described in the protocol and/or elsewhere, with documented approval/favourable opinion by the HREC, to protect the rights, safety and well-being of the participant and to ensure compliance with applicable regulatory requirements.
- That the participant or the participant's legally acceptable representative are informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

Please refer to the ***National Statement on Ethical Conduct in Human Research, 2023*** for details on obtaining consent in special cases.

2. Writing patient informed consent forms

The investigator(s) must:

- Ensure the written informed consent form and any other written information provided to participants include explanations of the following:
  - That the trial involves research.
  - The purpose of the trial.
  - The trial treatment(s) and the probability for random assignment to each treatment.
  - The trial procedures to be followed, including all invasive procedures.
  - The subject's responsibilities.
  - Those aspects of the trial that are experimental.
  - The reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, foetus, or nursing infant.
  - The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this.
  - The alternative procedure(s) or course(s) of treatment that may be available to the participant, and their important potential benefits and risks.
  - The compensation and/or treatment available to the participant in the event of trial related injury.
  - The anticipated prorated payment, if any, to the participant for participating in the trial.
  - The anticipated expenses, if any, to the participant for participating in the trial.
  - That the participant's participation in the trial is voluntary and that the participant may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled.
  - That the monitor(s), the auditor(s), the HREC, and the regulatory authority(ies) will be granted direct access to the participant's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or the participant's legally acceptable representative is authorising such access.
  - That records identifying the participant will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will

not be made publicly available. If the results of the trial are published, the participant's identity will remain confidential.

- That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue participation in the trial.
- The person(s) to contact for further information regarding the trial and the rights of trial participants, and whom to contact in the event of trial-related injury.
- The foreseeable circumstances and/or reasons under which the participant's participation in the trial may be terminated.
- The expected duration of the participant's participation in the trial.
- The approximate number of participants involved in the trial.

3. Training Records

The investigator(s) must:

- Ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.
- Ensure that documentation of this training be kept current and available for review on request.

Outcome:

That researchers comply with procedures relating to informed consent and writing patient inform consent forms.

Definitions:

Delegate: A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Human Research Ethics Committee (HREC): A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

Informed Consent: 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 Council for Harmonisation (ICH): International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site and ensures that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Protocol: A document that describes the objective(s), design, methodology, statistical considerations and organisation of a trial.

Sub Investigator: 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).

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3).

NHMRC National Statement on Ethical Conduct in Human Research, (2023).

SOP7 – Case Report Forms, Source Documents, Record Keeping and Archiving

Procedures/Methods:

1. Completion of case report forms (CRFs)

The investigator(s)/ institution should:

- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Ensure that data reported on the CRF, that are derived from source documents, be consistent with the source documents or the discrepancies should be explained.
- Ensure that any change or correction to a CRF is dated, initialled, and explained (if necessary) and should not obscure the original entry (i.e., an audit trail should be maintained); this applies to both written and electronic changes or corrections.
- Retain records of the changes and corrections.

2. Source documents, record keeping and archiving

The investigator(s) must:

- Keep original source documents (where the data was first recorded) and take measures to prevent accidental or premature destruction of these documents.
- Maintain the trial documents , as required by the applicable regulatory requirement(s) and take measures to prevent accidental or premature destruction of these documents.
- Ensure that financial aspects of the trial are documented in an agreement between the sponsor and the investigator/institution.
- Ensure that upon request of the monitor, auditor, HREC, or regulatory authority, make available for direct access all requested trial related records.
- Study documentation should be maintained for a minimum of 15 years for adult studies or 25 years for paediatric studies.
- For legal reasons, sites may consider indefinite archiving periods.
- The TGA position on document retention states:

  "The TGA requires records to be retained by the sponsor for 15 years following the completion of a clinical trial. However, in Australia the overriding consideration for sponsors with respect to record retention is the issue of product liability and the potential need for sponsors of products to produce records at any time during, and possibly beyond, the life of a product in the event of a claim against the sponsor as a result of an adverse outcome associated with the use of the product"

- ICH-GCP requirements for record retention state:

"Ensure that essential documents are retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor".

- Original documents should be retained, scanned copies are not yet generally accepted as archives.
- Ensure written confirmation from the sponsor is obtained prior to destruction of study documentation.

Outcome:

That researchers complete case report forms, source documents, record keeping and archiving in compliance with GCP principles.

Definitions:

Case Report Form (CRF): A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial participant.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Human Research Ethics Committee (HREC): A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Council for Harmonisation (ICH): International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site and ensures that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may

be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Source Documents: Original documents (where the data was first recorded), data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, participants' 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, participant files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

Sub Investigator: 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).

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3)

SOP8 - Site Initiation and Close-Out

Procedures/Methods:

1. Site initiation

The procedure outlined below refers to a "sponsored" study. Where the investigational study is "investigator initiated" and the "sponsor" is the institution, the investigator should undertake both investigator and monitor roles unless an external monitor has been assigned by the institution.

Prior to initiation the investigator(s) must:

- Arrange with the monitor the scheduled date, time and location of the study initiation visit.
- Review the Investigator's Brochure and any up-to-date information on the investigational product. The Investigator(s) must be familiar with the product, including pre-clinical toxicology, pharmacology, pharmacokinetics and up-to-date clinical data if applicable.
- Ensure that the procedures stated in the study protocol are applicable in their centre and fully understood.

- Ensure that sub-Investigator(s), pharmacist(s), research coordinators and any other relevant staff involved with the study have been advised of the meeting and are able to attend.

During the initiation the investigator(s) or delegate must:

- Establish that the Investigator's Site File contains all the required regulatory documents.
- Provide a list of study personnel and functions in the study to the clinical monitor.
- Provide curricula vitae of the Sub Investigators involved.
- Ensure that the names and contact numbers of the relevant medical and study personnel of the sponsor are available and documented clearly.
- Ensure that all relevant study site personnel fill out and sign the Delegation Log.
- Check that the procedures and plans for storage, dispensing and return of investigational product have been agreed and finalised with the Sponsor and Pharmacist (if applicable).
- Review the documents used in the shipment of the investigational products to the study site.
- Check that the quantity of CRFs that have been requested or shipped to the study site are sufficient for the number of participants/patients that are likely to be recruited into the study.
- Check that other related supplies are available, or are to be shipped to the study site at a later date, and that they are available in sufficient quantities.
- Check that laboratory facilities and arrangements for the dispatch of samples to the laboratory are organised and that any specialised equipment that may be required will be available throughout the period of the trial, e.g., centrifuge, freezer, etc.
- Establish who will be responsible for CRF completion and clarify the procedure for entering data in the CRF, as well as making changes and corrections.
- Ensure an understanding of the requirements that source documents and raw data will need to be available during monitoring visits to enable the monitor to perform source data verification at each monitoring visit.
- Review the arrangements for organising and maintaining study files.
- Ascertain that the procedures relating to the archiving of study records at the end of the study is agreeable to the sponsor.

- Establish the next monitoring visit with the Monitor.

2. Premature Termination or Suspension of a Trial

If the trial is prematurely terminated or suspended for any reason, the investigator/institution must:

- Promptly inform the trial participants, should assure appropriate therapy and follow-up for the participants, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority(ies).

In addition, If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator must:

- Inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the HREC.
- Provide the sponsor and the HREC with a detailed written explanation of the termination or suspension.

If the sponsor terminates or suspends a trial, the investigator must:

- Promptly inform the institution where applicable and the investigator/institution should promptly inform the HREC and provide the HREC a detailed written explanation of the termination or suspension.

If the HREC terminates or suspends its approval/favourable opinion of a trial the investigator must:

- Inform the institution where applicable and the investigator/ institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.

3. Site close-out

The investigator(s) must:

- Provide a summary report of the trial's outcome to the ethics committee and the regulatory authorities, if required.
- Keep documentation and correspondence in the ISF.Inform the sponsor of the completion of the study.
- Ensure arrangements for archiving of trial documents are clarified (see section 6 of SOP 007).

- Ensure appropriate final disposal of any investigational product. This may include return to the sponsor or destruction of remaining materials. Refer to SOP 005 for details.

Outcome:

That researchers comply with these procedures related to site initiation and close-out of a clinical trial.

Definitions:

Case Report Form (CRF): A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial participant.

Delegate: A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Human Research Ethics Committee (HREC): A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Council for Harmonisation (ICH): International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site and ensures that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Investigator initiated trial: A clinical trial that is undertaken by the investigator whereby the investigator and/or their institution takes on the role of the sponsor in addition to their role as investigator.

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

Sponsor: An individual, company, institution or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Source Documents: Original documents, data, and records (e.g., hospital records, clinical and office charts ,laboratory notes, memoranda, participants' 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, participant files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

Sub Investigator: 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).

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3).

SOP9 - TGA Notification and SAE Reporting Requirements

Procedures/Methods:

1. TGA Notification and SAE Reporting Requirements

The investigator has a responsibility to ensure the conduct of the trial, including the monitoring of safety and reporting of adverse outcomes, complies with the study protocol. In the case of an investigator-initiated study the investigator must complete the sponsor section of the eCTN form, and the Institution is usually listed as the sponsor. The sponsor and the principal investigator should review all adverse outcomes in the context of known information on the medicine and make a determination as to whether the event was drug-related (i.e., an adverse reaction).

The investigator(s) must:

- Report immediately (within 24 hours of learning of the event) to the sponsor (or the TGA if an Investigator Initiated Trial) all serious adverse events (SAEs) except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports.
- Ensure that the immediate and follow-up reports identify participants by unique code numbers assigned to the trial participants rather than by the participants' names, personal identification numbers, and/or addresses.
- Comply with the applicable regulatory requirement(s) related to the reporting of SAEs and SUSARs to the regulatory authority(ies), insurers and the HREC. At a minimum this includes six-monthly listings of all SUSARs occurring with a compound, and annual update of the IB/Product Information or equivalent.
- Notify the HREC of any information (either received form an external sponsor or collected as obliged as a sponsor for an investigator initiated trial) 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.
- Ensure that adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations are reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
- Ensure that for reported deaths, supply the sponsor and the HREC with any additional requested information (e.g., autopsy reports and terminal medical reports).
- Record non-serious and expected adverse reactions and adverse events as part of GCP. It is imperative that, in accordance with GCP principles, an internal statistical analysis of these data is performed. The TGA should be advised 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.

Outcome:

That researchers comply with the procedures for TGA notification and SAE reporting.

Definitions:

Clinical Trials Notification (CTN): A notification scheme whereby all material relating to the proposed trial, including the trial protocol is submitted directly to the HREC, by

the researcher, at the request of the sponsor. The TGA does not review any data relating to the clinical trial.

The HREC 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 for approval of the trial protocol.

The institution or organisation at which the trial will be conducted, referred to as the 'Approving Authority', gives the final approval for the conduct of the trial at the site, having due regard to advice from the HREC.

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

Clinical Trials Approval (CTA): An approval process whereby a sponsor submits an application to conduct clinical trials to the TGA for evaluation and comment.

A TGA Delegate decides whether or not to object to the proposed Usage Guidelines for the product. If an objection is raised, trials may not proceed until the objection has been addressed to the Delegate's satisfaction.

If no objection is raised, the sponsor may conduct any number of clinical trials under the CTA application without further assessment by the TGA, provided use of the product in the trials falls within the original approved Usage Guidelines. Each trial conducted must be notified to the TGA.

A sponsor cannot commence a CTA trial until written advice has been received from the TGA regarding the application and approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted. There are two forms, each reflecting these separate processes (Parts), that must be submitted to TGA by the sponsor.

Part 1 constitutes the formal CTA application. It must be completed by the sponsor of the trial and submitted to TGA with data for evaluation.

Part 2 is used to notify the commencement of each new trial conducted under the CTA as well as new sites in ongoing CTA trials. The Part 2 form must be submitted within 28 days of the commencement of supply of goods under the CTA. There is no fee for notification of trials under the CTA scheme.

Good Clinical Practice (GCP); A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Human Research Ethics Committee (HREC): A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Council for Harmonisation (ICH):

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site ensuring that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Serious Adverse Device Event (SADE): A device-related serious adverse event.

Serious Adverse Event (SAE) – drug: Any untoward medical occurrence that, at any dose:

- results in death;
- is life-threatening;

  NOTE: The term 'life-threatening' in the definition of 'serious' refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event, which hypothetically might have caused death if it were more severe:

- requires in-patient hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability/incapacity; or
- is a congenital anomaly/birth defect, and fits the SAE criteria as specified in the relevant clinical trial protocol.

Medical or scientific judgement should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also usually be considered serious. Examples of such events are intensive treatment in an

emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalisation; or development of drug dependency or drug abuse.

Serious Adverse Event (SAE) – device: Serious Adverse Event for *medical devices*: any adverse medical occurrence that:

- Led to a death.
- Led to a serious deterioration in health of a patient 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 e) 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 has to be modified or temporarily/permanently taken out of service
  - a factor (a deterioration in characteristics or performance) found on examination of the device.

Co Investigator: 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).

Therapeutic Goods Administration (TGA); Australia's regulatory agency for therapeutic goods, including medicinal products and devices.

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

Sponsor: An individual, company, institution or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Source Documents: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, participants' 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, participant files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

Sub Investigator: 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).

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3).

Australian clinical trial handbook, v2.4 August 2021.

NHMRC National Statement on Ethical Conduct in Human Research (2023)

SOP10 - Investigator Responsibilities

Procedures/Methods:

1. Investigator Responsibilities

   The investigator(s) must:

   - Ensure that clinical studies are carried out according to International Council for Harmonisation (ICH), regulatory authorities requirements and any other local requirements.
   - Have an understanding that when a trial is sponsored by an agency/pharmaceutical company, they may be requested to follow their procedures in order to comply with company obligations. Agreement between all parties should be discussed before initiating the trial.
   - Ensure that they are appropriately qualified to conduct the trial.
   - Inform the participant's primary physician about the participant's participation in the trial if the participant has a primary physician and if the participant agrees to the primary physician being informed.

Note: Although a participant is not obliged to give his/her reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the participant's rights.

Further, investigators must:

- Declare any conflicts of interest, payments etc. from other parties.
- Maintain a list of any delegated duties with respect to the trial, and the persons and qualifications of those persons to whom the duties are assigned.
- Be able to demonstrate that adequate participant recruitment is likely to be possible, with necessary time available to conduct the study to GCP requirements, and with adequate facilities and trial staff.
- Provide medical care to trial participants that is necessary as a result of any adverse events experienced during or following the trial that are related to the trial, and must be responsible for all trial-related medical decisions
- Possess, prior to trial commencement, a favourable HREC endorsement of trial protocol, patient information and consent documents, recruitment procedures, consent form updates and any other information given to participants.
- Present all trial related documents to the HREC for review including the Investigator's Brochure as well as updates.
- Ensure that the trial is conducted according to the approved protocol.
- Document any deviation from the protocol for later review.
- Ensure that no deviation from the protocol occurs without HREC endorsement, unless it is required to prevent imminent harm to participants. If the protocol deviation results in the creation of a "separate and distinct" therapeutic good as defined in section 16 of the Therapeutic Goods Act 1989, a new notification is required for CTN or CTA trials.
- Ensure a new CTN form is completed, or in the case of CTA a new "notification of intent to conduct clinical trial" form, for any new trial site subsequently added to a study.

Note: The CTN can be submitted online through the TGA Business Services web portal. A copy should be kept in the Trial Master File. For investigator-initiated trials where the Eye and Ear is sponsor, please contact the Research Office regarding completing the online CTN.

- Ensure accountability of the investigational product at the trial site.

- Ensure that participants have made fully informed, written consent, with all trial procedures and risks adequately explained and that the principles and essential elements of Informed consent are up held and included in the information document;
- Be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
- Ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.
- Submit written summaries of the trial status to the HREC annually, or more frequently, if requested by the HREC.
- Provide written reports to the sponsor, the HREC and, where applicable, the institution promptly on any changes significantly affecting the conduct of the trial, and/or increasing the risk to participants.
- Comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the HREC.
- Promptly inform the trial participants if the trial is prematurely terminated or suspended for any reason as well as the institution and should assure appropriate therapy and follow-up for the participants, and where required by the applicable regulatory requirement(s), inform the regulatory authority(ies).

Note: if the investigator terminates or suspends a trial without prior agreement of the sponsor, they should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the HREC, and provide the sponsor and the HREC a detailed written explanation of the termination or suspension.

- Upon completion of the trial, where applicable, inform the institution; the investigator/institution should provide the HREC with a summary of the trial's outcome, and the regulatory authority(ies) with any reports required.

Outcome:

That all investigators understand their responsibilities and are able to comply with all applicable regulatory requirements when performing a clinical study.

Definitions:

Adverse event (AE): Any untoward medical occurrence in a patient administered a medicinal product and which does not necessarily have to 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, whether or not considered related to this medicinal product.

Clinical Trials Notification (CTN) A notification scheme whereby all material relating to the proposed trial, including the trial protocol is submitted directly to the HREC by the researcher at the request of the sponsor. The TGA does not review any data relating to the clinical trial.

The HREC 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 for approval of the trial protocol.

The institution or organisation at which the trial will be conducted, referred to as the 'Approving Authority', gives the final approval for the conduct of the trial at the site, having due regard to advice from the HREC.

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

Clinical Trials Approval (CTA): An approval process whereby a sponsor submits an application to conduct clinical trials to the TGA for evaluation and comment.

A TGA Delegate decides whether or not to object to the proposed Usage Guidelines for the product. If an objection is raised, trials may not proceed until the objection has been addressed to the Delegate's satisfaction.

If no objection is raised, the sponsor may conduct any number of clinical trials under the CTA application without further assessment by the TGA, provided use of the product in the trials falls within the original approved Usage Guidelines. Each trial conducted must be notified to the TGA.

A sponsor cannot commence a CTA trial until written advice has been received from the TGA regarding the application and approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted. There are two forms, each reflecting these separate processes (Parts) that must be submitted to TGA by the sponsor.

Part 1 constitutes the formal CTA application. It must be completed by the sponsor of the trial and submitted to TGA with data for evaluation.

Part 2 is used to notify the commencement of each new trial conducted under the CTA as well as new sites in ongoing CTA trials. The Part 2 form must be submitted within 28 days of the commencement of supply of goods under the CTA. There is no fee for notification of trials under the CTA scheme.

Delegate: A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Human Research Ethics Committee (HREC): A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Council for Harmonisation (ICH): International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site ensuring that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Sub Investigator: 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).

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3).

Australian clinical trial handbook, v2.4 August 2021.

SOP11 - Sponsor Responsibilities in Investigator Initiated Studies

Procedures/Methods:

1. Sponsor Responsibilities

The sponsor for an investigator-initiated study may be an individual (e.g., the investigator or department head), a company (e.g., a not-for-profit) an organisation (e.g., a charity) or an institution (e.g., a public hospital). Each institution will have its own policy regarding the sponsorship role.

The sponsor is responsible for:

- Ensuring that Quality Assurance and Quality Control systems are in place to ensure trials are conducted, data is gathered, and subsequently reported, in compliance with GCP, the trial protocol, and any TGA requirements.
- Securing agreement from all involved parties to ensure direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities.
- Ensuring that no omissions occur which might disentitle themselves, the Hospital or HREC, to such indemnity as could otherwise be available under the Medical Indemnity and Public Liability Policies.
- Selection of the appropriate investigator(s) and institution(s) to conduct and complete the trial according to GCP standards.
- Definitive, unambiguous allocation of trial-related duties and responsibilities to trial-related staff.
- The provision of appropriate insurance and indemnity for the trial and trial-related staff, as well as measures for participant compensation for trial-related injury.
- Ensuring the confirmation of endorsement from the relevant HREC(s) and notification of the approval *etc.* to the TGA.
- Ensuring that funding arrangements are declared in the protocol submissions to warrant that the clinical trial retains its "investigator initiated" status under the VMIA policy.
- Ensuring medical expertise is on hand for trial-related medical queries or patient care.
- Trial design and appropriate analysis.
- Data handling, record keeping, and overall trial management.

- Must maintain all records relating to the study for a period of at least 15 years from the end of the Trial (i.e., completion of data analysis) in the case of adults and at least 25 years from the end of the Trial (i.e., completion of data analysis) in the case of children.
- Ensuring that agreements made with the investigator/institution and any other parties involved with the clinical trial, are in writing, as part of the protocol or in a separate agreement.
- Ensuring that Investigational Products available to participants free of charge.
- Taking appropriate urgent safety measures (with investigator) where necessary.
- Keeping records of all adverse events reported by investigators.
- Ensuring appropriate manufacture, packaging, labelling/coding and distribution to trial sites of all investigational medicinal products.
- Ongoing safety evaluation and AE/ADR reporting.
- Submission to the TGA of all safety updates and periodic reports, as required.
- Compliance with Monitoring/Audit/Inspection requirements.
- Notification of any premature termination or suspension of the trial in question.
- Completion of the Clinical Study Report.

Outcome:

That researchers understand the responsibilities of the sponsor in the conduct of Investigator driven studies. In Investigator-Initiated studies the Investigator is acting in the capacity of Sponsor.

Definitions:

Adverse drug reaction (ADR): Adverse drug reactions concern noxious and unintended responses to a medicinal product.

Adverse event (AE): Any untoward medical occurrence in a patient administered a medicinal product and which does not necessarily have to 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, whether or not considered related to this medicinal product.

Clinical Trials Agreement (CTA): An agreement governing the safety and efficacy of outside collaborators, proprietary biologics or pharmaceutical compounds in clinical studies.

European Union (EU): An organisation of European countries.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Human Research Ethics Committee (HREC): A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Council for Harmonisation (ICH): International Coimcil for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site ensuring that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Investigator initiated trial: A clinical trial that has the following characteristics:

- A pharmaceutical/device company is not acting as the sponsor for the purposes of the CTN application.
- A pharmaceutical/device company is not fully funding the conduct of the study, that is, making payment to the relevant hospital or investigator.
- The clinical trial addresses relevant clinical questions and not industry needs.
- The principal investigator or the Hospital/Institution is the primary author and custodian of the clinical trial protocol.

Serious adverse event (SAE): Any untoward medical occurrence that at any dose:

- Results in death.
- Is life-threatening.

(NOTE: The term "life-threatening" in the definition of "serious" refers to an event/reaction in which the patient was at risk of death at the time of the event/reaction; it does not refer to an event/ reaction which hypothetically might have caused death if it were more severe).

- Requires inpatient hospitalisation or results in prolongation of existing hospitalisation.
- Results in persistent or significant disability/incapacity.
- Is a congenital anomaly/birth defect.
- Is a medically important event or reaction.

Sponsor: An individual, company, institution, or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Sub Investigator: 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).

Therapeutic Goods Administration (TGA): Australia's regulatory agency for medical drugs and devices.

References:

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice ICH E6(R3).

Australian clinical trial handbook, v2.4 August 2021.

VMIA Clinical Trials Risk and Insurance Guide August 2023.

SOP12 – Handling and Shipping of Infectious Substances for Clinical Trials

Procedures/Methods:

1. Handling and Shipping of Infectious Substances for Clinical Trials

The investigator(s) must:

- Ensure that clinical specimens are handled and packed in accordance with local, sponsor and, if being shipped by air ICAO requirements This includes the confirmation that staff involved in packaging and shipping of infectious waste/dangerous goods are appropriately qualified and trained. If shipped by other modes of transport, please refer to the Requirements for Packaging and Transportation of Pathology Specimens and Associated Materials by the National Pathology Accreditation Advisory Council.

- (Identify patient specimens for which there is minimal likelihood that pathogens are present are not subject to the ICAO requirements if the specimen is transported in Packaging for Exempt Patient Specimens.
- Exercise professional judgement in determining whether a patient specimen has a minimal likelihood that pathogens are present. That judgement should be based on the known medical history, symptoms and individual circumstances of the source, human or animal, and endemic local conditions.

Examples of specimens which may be transported as a patient specimen for which there is a minimal likelihood that pathogens are present include:

- blood or urine tests to monitor cholesterol levels, blood glucose levels or hormone levels;
- tests required to monitor organ function such as heart, liver or kidney function for humans with non-infectious diseases;
- therapeutic drug monitoring;
- pregnancy tests;
- biopsies to detect cancer; and
- antibody detection.

Patient specimens that have a minimal likelihood of containing pathogens must be packaged appropriately to further minimise the risk of exposure. While these specimens have a minimal likelihood of containing infectious pathogens in a form that would cause infection, appropriate packaging further minimises the risk of exposure (see appendix 1).

2. Tracking of Handling and Shipping of Infectious Substances for Clinical Trials The investigator/delegate must ensure that documentation related to handling and shipping of infectious substances is maintained and filed to facilitate tracking and to satisfy GCP requirements.

Outcome:

That researchers comply with the correct procedures for the handling and shipping of infectious substances in clinical trials.

Definitions:

Delegate: A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides

assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Infectious substances: Those substances which are known to contain, or are reasonably expected to contain, pathogens.

International Civil Aviation Organisation (ICAO): A specialised agency of the United Nations which sets international standards and regulations necessary for the safety, efficiency and regularity of air transport.

International Council for Harmonisation (ICH): International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator: An individual responsible for the conduct of a clinical trial at a trial site ensuring that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Medical or clinical wastes: Those derived from the medical treatment of animals or humans or from bio-research.

Pathogens: Micro-organisms (including bacteria, viruses, rickettsiae, parasites, fungi) and other agents such as prions, which can cause disease in humans or animals.

Patient specimens: Those collected directly from humans or animals, including, but not limited to, excreta, secreta, blood and its components, tissue and tissue fluid swabs, and body parts being transported for purposes such as research, diagnosis, investigational activities, disease treatment and prevention.

Sub Investigator: 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).

References:

International Civil Aviation Organisation Technical Instructions for the Safe Transport of Dangerous Goods by Air, 2023-2024 edition.

Requirements for Packaging and Transportation of Pathology Specimens and Associated Materials - Australian Commission on Safety and Quality in Health Care Fifth Edition 2022.)

Standard:


NSQHS Standard 1: Clinical Governance


NSQHS Standard 2: Partnering with Consumers


NSQHS Standard 3: Preventing and Controlling Healthcare Associated Infections


NSQHS Standard 4: Medication Safety


NSQHS Standard 5: Comprehensive Care


NSQHS Standard 6: Communicating for Safety


NSQHS Standard 7: Blood Management


NSQHS Standard 8: Recognising and responding to acute deterioration

Legislation:

Current Legislation may be sourced at: http://www.austlii.edu.au/ or Victorian legislation at: https://www.legislation.vic.gov.au/

None have been identified at the time of this review.

Linked Policy & Procedure:

- Research Policy

This series of SOPs is based on a generic set of GCP procedures developed by the VMIA to promote GCP compliance and further refined by CERA, Clinical Trial Research Unit procedures and Eye and Ear Research Office review.

Approval/Committees:

These procedures are authorised by the Executive Director Medical Services/Chief Medical Officer.

Responsible Executive:

Executive Director Medical Services/Chief Medical Officer

Document Author:

Manager Research

Evaluation:

Processes and procedures are evaluated within the context of organisation risk management accreditation and legislative standards.

Procedure Review:

This procedure will be reviewed at least every 3 years.

Author/ Co-Authors:

Name	Position	Service /Directorate
Dr Birinder Giddey	Executive Director Medical Services/Chief Medical Officer	Medical Services
Associate Professor Peter Keller	Research Manager	Research Office

Version Details:

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