

**Human Ethics**

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**MACQUARIE UNIVERSITY**

|  |
| --- |
| Protocol Title: |

***NOTE****: This template is a guide. Sections that are not applicable (e.g. randomisation) can be deleted as required.*

*Sections that are strongly recommended are: Hypothesis, Primary Objective, Inclusion and Exclusion criteria, Statistical Consideration for sample size, and Adverse Reporting if the study involves an intervention.*

|  |  |
| --- | --- |
| **Principal Investigator:** |  |
| **Contact Details:** |  |
| **Protocol Number:** |  |
| **Protocol Authors:** |  |
| **Protocol Version #:** |  |
| **Protocol Date:** |  |
| **Proprietary Notice**  ***(if applicable):*** |  |

**Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Ethics Statement:**

The study will be conducted in accordance with the [*National Statement on Ethical Conduct in Human Research*](https://www.nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research) *2023*, the [CPMP/ICH Note for Guidance on Good Clinical Practice](http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm) and consistent with the principles that have their origin in the Declaration of Helsinki. Compliance with these standards provides assurance that the rights, safety, and well-being of trial participants are respected.

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## Summary

**Study title:**

**Protocol version:**

**Objectives** Primary objective

Secondary objectives

**Study design**

**Planned sample size**

**Selection criteria**

**Study procedure**

**Statistical considerations** Sample size calculation

Analysis plan

**Duration of the Study**

# 1. BACKGROUND AND INTRODUCTION

### 1.1. Disease/Proposed Intervention Background

Provide a brief history of the disease or the proposed intervention including prognostic factors (for diseases) and an explanation of the proposed intervention. This history should be based on a literature review and include the investigators' experiences. References must be supplied.

### 1.2. Rationale For Performing the Study.

State clearly why the study is being undertaken and what it is hoped to achieve.

# 2. HYPOTHESIS

Cleary state the study hypothesis.

# 3. STUDY OBJECTIVES

### 3.1. Primary Objectives

### 3.2. Secondary Objectives

# 4. STUDY DESIGN

### 4.1. Design

Provide information about the study design, for example, whether the study is a randomised control trial, case control study etc.

### 4.2. Expected Participant Numbers

### 4.3. Duration Of the Study

Specify the expected study duration (start date and end date).

In this section specify the expected time period for participant recruitment.

### 4.4. Endpoints

Primary Endpoints

Secondary Endpoints

### 4.5. Centres

Include the number of centres and the expected number of participants at each site.

Indicate whether the procedures and participants will be the same across all sites. State any site-specific requirements.

# 5. STUDY PARTICIPANTS

### 5.1. Inclusion Criteria

List all inclusion criteria, for example:

1. Disease status/ or disease group for study:
2. Gender:
3. Age range:
4. :
5. Concomitant disease status:
6. Laboratory parameters: e.g. Adequate renal function as defined by .... Adequate liver function as defined by ....
7. Others: radiograms, electrocardiograms, CT-scan, ultrasound, etc.
8. Willingness to provide informed consent and willingness to participate and comply with the study requirements.

### 5.2. Exclusion Criteria

List all exclusion criteria, for example:

1. Women lactating, pregnant or of childbearing potential who are not willing to avoid becoming pregnant during the study.
2. Participants with a history of XXXX disease(s) that are likely to interfere with the metabolism or excretion of test medications.
3. Participants who may have received an investigational new drug within the last XX days/weeks.
4. Participants with a history of a psychological illness or other conditions which may interfere with their ability to understand the study requirements.
5. Participants with XXXX disease that is likely to interfere with the evaluation of the participant’s safety and of the study outcome.
6. As the following medication(s) can have interactive effects and may interfere with the participant’s ability to meet the study requirements, they cannot be administered during the clinical study (list any prohibited concomitant medications here)

# 6. STUDY PROCEDURES

### 6.1. Study Flow Chart

Diagram of the study design (example below)

Enrolment

Randomisation

Treatment Phase

(e.g. 12 weeks)

Group A Group B

### 6.2. Investigation Plan

Methodology

In this section clearly describe how the study procedures/interventions will be conducted in order to ensure the results are reproducible.

This section should include a table listing all the potential study visits and the procedures that will be conducted at each visit.

Example: (this is often in landscape orientation – if so ‘use section breaks’)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Interventions** | **Enrolment Visit** | **Visit 1** | **Visit 2** | **Visit 3** | **Final Study Visit** |
| Participant Consent | ✓ |  |  |  |  |
| Inclusion / Exclusion criteria | ✓ |  |  |  |  |
| Physical examination |  | ✓ |  |  |  |
| CXR | ✓ |  |  |  | ✓ |
| Adverse Event & Serious Adverse Event Assessment |  | ✓ | ✓ | ✓ | ✓ |

If a study procedure is not performed as part of normal practice, please outline how the procedure will be performed for this study.

### 6.3. Study Procedure Risks

Describe all possible risks relating to the study interventions/procedures

### 6.4. Participant Recruitment and Screening

Explain how potential participants will be identified and from where (for example, hospital patients, community members, clinic patients etc).

Participants can also be identified via the following means:

1. Review of existing databases or databanks (please identify the database/databank and the custodian
2. Review of clinic files (please include who will be reviewing these files, for example a research coordinator).
3. Advertisements (please include where the advertisement will be placed for example, in a newspaper, poster in a clinic or hospital foyer, radio announcements, website etc)
4. Information Letter to Medical practitioners
5. Explain how potential participants will be screened for the study
6. Any other potential recruitment methods.

### 6.5. Participant Enrolment

Explain how a potential participant will be enrolled into the study

For example: Potential participants will be enrolled into the study after the informed consent process has been completed and the participant has been assessed to meet all the inclusion criteria and none of the exclusion criteria. Study participants will receive a study enrolment number, and this will be documented in the participant’s medical (or personal) record and on all study documents.

### 6.6. Information and Consent

Explain the process, how this process will be documented and whether there are any site-specific requirements (i.e. in NSW Clinical trials require review by the Guardianship Tribunal in order for delegation of consent)

### 6.7. Randomisation Procedure

Provide details regarding the method of randomisation to be used; i.e. computer generated etc.

As relevant, explain how participants will be randomized.

An example: The participant will be randomized at study visit X after they have met the randomization criteria (e.g. baseline enrolment bloods are within normal range and the CT scan confirms disease). At this visit the participant will be randomised to study procedure A or Study procedure B and receive a Randomisation Number allocated by pharmacy.

### 6.8. End of Study Treatment/Withdrawal Procedure

### 6.9. Patient Withdrawal

# 7. OUTCOMES

### 7.1. Definition of Outcomes

# 8. STATISTICAL CONSIDERATIONS

### 8.1. Sample Size or Power Calculation

### 8.2. Provide A Detailed Analysis Plan

# 9. DATA COLLECTION

### 9.1. Participant Registration

### 9.2. Forms and Procedure for Collecting Data

### 9.3. Case Report Forms and Schedule for Completion

### 9.4. Data Flow

# 10. QUALITY CONTROL AND ASSURANCE

### 10.1. Control of Data Consistency

### 10.2. Audits

### 10.3. Protocol Amendments

# 11. ETHICS

### 11.1. Investigator Authorisation Procedure

Explain what authorisation is required before authorisation is granted to commence recruiting to the study. For instance, ethics approval, approved versions of the participant information and consent form, Clinical Trial Notification (CTN) if required.

### 11.2. Patient Protection

The responsible investigator/s will ensure that the study is completed in accordance with the guidelines set out in the [*National Statement on Ethical Conduct in Human Research*](https://www.nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research) *2023* (the *National Statement*) and the [*CPMP/ICH Note for Guidance on Good Clinical Practice*](http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm)and any other relevant legislation/guidelines.

# 12. SAFETY

### 12.1. Adverse Event Reporting

Adverse event

[*The Australian Clinical Trial Handbook*](https://www.tga.gov.au/resources/resource/guidance/australian-clinical-trial-handbook)(*The Handbook*) defines an adverse event (drugs) as:

any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational/experimental) product, whether or not related to this product. *[[1]](#footnote-2)*

**Adverse drug reaction**

[*The Handbook*](https://www.tga.gov.au/resources/resource/guidance/australian-clinical-trial-handbook) defines an adverse drug reaction as:

For unapproved medicines: all noxious and unintended responses to a medicinal product related to any dose should be considered ADVERSE DRUG REACTIONS. The phrase “responses to a medicinal product” means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility.

For marketed medical products: a response to a drug which is noxious and unintended, and which occurs normally used in man for prophylaxis, diagnosis or therapy of diseases of for modification of physical function.[[2]](#footnote-3)

**Serious adverse event (SAE) or Serious Adverse Drug Reaction is defined as:**

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/reaction 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;

• is a congenital anomaly/birth defect; or

• is a medically important event or reaction.[[3]](#footnote-4)

**Devices Events**

[*The Handbook*](https://www.tga.gov.au/resources/resource/guidance/australian-clinical-trial-handbook)defines an Adverse Event (Device) as:

Any devices is any undesirable clinical occurrence in a subject whether it is considered to be device related or not, that includes a clinical sign, symptom or condition and/or an observation of an unintended technical performance or performance outcome of the device.[[4]](#footnote-5)

For devices is any adverse medical occurrence that:

• led to a death;

• led to a serious deterioration in health of a participant, including:

* 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; or
* foetal distress, foetal death or a congenital abnormality/birth defect;

• might have led to 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; or
* a factor deterioration in characteristics or performance) found on examination of the device.

An adverse event or serious adverse reaction can also be any event or experience which compromises the ethical acceptability of the protocol. This can be a non-medical event for clinical trials that are not medical or testing drugs or devices, such as those clinical trials conducted in different fields such as psychology.

Researchers are advised to consult [*The Handbook*](https://www.tga.gov.au/resources/resource/guidance/australian-clinical-trial-handbook)and the [*National Statement*](https://www.nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research) for further information regarding adverse events and adverse event recording.

### 12.2. Serious Adverse Event Reporting

All serious adverse events should be reported immediately to the sponsor and the HREC. The reports should be followed by a detailed written report. Follow-up reports should identify the participant/s by unique code assigned to participants (rather than by name).

### 12.3. Data Safety and Monitoring Board (Dsmb)

If applicable describe the membership and responsibilities – refer to the [National Statement](https://www.nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research) [[5]](#footnote-6) for information regarding DSMBs.

### 12.4. Early Termination

Detail the possible circumstances for early termination of the study and how will this be managed. Include who is responsible for what aspect in the process of terminating the study (informing participants, correspondence to HREC, compiling a final study report, unbinding if applicable).

# 13. BLINDING AND UNBLINDING

As relevant, describe how the study will be blinded.

# 14. DATA MANAGEMENT PLAN

# A data management plan needs to be developed in accordance with the following documents and any other relevant documentation or legislation:

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

# The National Statement on Ethical Conduct in Human Research: (<https://www.nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research>)

# CPMP/ICH Note for Guidance on Good Clinical Practice: (<https://www.tga.gov.au/resources/publication/publications/ich-guideline-good-clinical-practice>)

Include information under the following headings:

* Data ownership and custody
* Data collection or generation
* Data access, use, analysis
* Data disclosure, sharing and re-use
* Data storage, retention, or disposal
* Any risks associated with the data management plan and the strategies for minimising those risks.

# 15. TRIAL SPONSORSHIP AND FINANCING

If relevant, indicate who is funding/sponsoring the study and what costs are being covered.

# 16. INDEMNITY

16.1. Compensation

Indicate that reasonable precautions against harms are being taken and what steps are taken to mitigate risks. In the event of a harm occurring, indicate the compensation arrangements. For example, the administering institution agrees to follow the [Medicines Australia Guidelines for Compensation for Injury Resulting from Participation a Company-Sponsored Clinical Trial.](http://medicinesaustralia.com.au/issues-information/clinical-trials/indemity-and-compensation-guidelines/)

# 17. REFERENCES

# 18. APPENDICES

**List all appendices i.e.:**

1. Advertisement(s)

2. Questionnaires

3. Data collection sheet / Case Report Form

4. All protocol-specific appendices

1. <https://www.tga.gov.au/resources/resource/guidance/australian-clinical-trial-handbook> (new link for trial handbook but cant find references)

   <http://www.tga.gov.au/industry/clinical-trials-handbook.htm> (definitions of adverse events are on 28-29). [↑](#footnote-ref-2)
2. Ibid. [↑](#footnote-ref-3)
3. Ibid. [↑](#footnote-ref-4)
4. Ibid. [↑](#footnote-ref-5)
5. <http://www.nhmrc.gov.au/guidelines/publications/e72> (s 3.3.20(a)—(d)) [↑](#footnote-ref-6)