**Clinical Trial Protocol**

**Investigational Medical Device**

[Insert clinical trial title]

[Insert version number and date]

[Insert the name of UNSW Coordinating Principal Investigator]

**Contents**

[**1.** **General Information** 4](#_Toc72309540)

[**2.** **Safety and Monitoring Contacts** 5](#_Toc72309541)

[**3.** **Delegation of Clinical Trial Duties** 7](#_Toc72309542)

[**4.** **Trial Objectives and Purpose** 8](#_Toc72309543)

[**5.** **Background Information** 8](#_Toc72309544)

[**6.** **Statement of Compliance** 8](#_Toc72309545)

[**7.** **Trial Design** 8](#_Toc72309546)

[**8.** **Sample Size** 8](#_Toc72309547)

[**9.** **Selection and Withdrawal of Subjects** 8](#_Toc72309548)

[**10.** **Treatment** **of Subjects** 9](#_Toc72309555)

[**11.** **Safety and Monitoring** 9](#_Toc72309556)

[**12.** **Non-compliance, Protocol Deviation and Serious Breaches of Good Clinical Practice** 13](#_Toc72309557)

[**13.** **Review of a Protocol Deviation and a Serious Breach** 15](#_Toc72309563)

[**14.** **Statistics** 15](#_Toc72309564)

[**15.** **Data Handling, Ownership and Access** 15](#_Toc72309565)

[**16.** **Data Ownership** 15](#_Toc72309566)

[**17.** **Recording and Reporting Data** 15](#_Toc72309567)

[**18.** **Monitoring Quality Control and Quality Assurance** 16](#_Toc72309568)

[**19.** **Clinical Trial Research Agreement** 16](#_Toc72309569)

[**20.** **Research Governance Site Authorisation** 16](#_Toc72309570)

[**21.** **Good Clinical Practice Requirements**  16](#_Toc72309571)

[**22.** **Essential Documents for the Conduct of a Clinical Trial** 16](#_Toc72309572)

[**23.** **Clinical Trial Delegation and Responsibilities Log** 17](#_Toc72309573)

[**24.** **Safety Monitoring Register Template** 21](#_Toc72309574)

# **General Information**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Protocol Title** | | | | | | | | |
|  | | | | | | | | |
| **Protocol identifying number** | |  | | | | | | |
| **Version Number** | |  | | **Version date** |  | | | |
| **Amendment History** | | | | | | | | |
| **Version Number** | |  | | **Version date** |  | | | |
| **Clinical Trial Sponsor** | | | | | | | | |
| **Sponsor Name** | |  | | | | | | |
| **Sponsor Contact** | |  | | | | | | |
| **Telephone** | |  | | | | | | |
| **Email** | |  | | | | | | |
| **Address** | |  | | | | | | |
| **Coordinating Principal Investigator** | | | | | | | | |
| **Name** | |  | | | | | | |
| **Telephone** | |  | | | | | | |
| **Email** | |  | | | | | | |
| **Type of Appointment with UNSW** | | UNSW Employee  UNSW Conjoint  Other (Please describe) | | | | | | |
| **Principal Investigator - 1** | | | | | | | | |
| **Name** | |  | | | | | | |
| **Contact** | | **Email** |  | | | **Telephone** | |  |
| **Site** | |  | | | | | | |
| **Principal Investigator - 2** | | | | | | | | |
| **Name** | |  | | | | | | |
| **Contact** | | **Email** |  | | | **Telephone** | |  |
| **Site** | |  | | | | | | |
| **Personnel authorised to sign the protocol and the protocol amendment(s) for the Sponsor** (ICH GCP 6.1.3) | | | | | | | | |
| **Name** | |  | | | | | | |
| **Telephone** | |  | | | | | | |
| **Email** | |  | | | | | | |
| **Address** | |  | | | | | | |
| **Human Research Ethics Committee** | | | | | | | | |
| **Name** |  | | | | | | | |
| **Status of ethical review** | **Approved**  **In progress**  **To be submitted** | | | | | | | |
| **Trial Sites** |  | | | | | | | |
| **Funding for the Clinical Trial** | | | | | | | | |
| **Funding Body Name** |  | | | | | | | |
| **Amount of Funding** |  | | | | | | | |
| **Regulatory Requirements** | | | | | | | | |
| **Therapeutic Goods Administration Clinical Trial Notification** | | | | | | | **Yes**  **No** | |
| **Insurance for Clinical Trial** | | | | | | | | |
| **Insurer** |  | | | | | | | |
| **Type of Insurance** | Clinical trials are not automatically covered by UNSW insurance, and confirmation must be obtained by completing the [Clinical Trials Spreadsheet](https://www.fin.unsw.edu.au/sites/default/files/content/clinicaltrials.xlsx) and sending it to the UNSW Insurance manager ([peter.mccarthy@unsw.edu.au](mailto:peter.mccarthy@unsw.edu.au)).  Once insurance has been confirmed, attach a copy of the insurance certificate to the trial protocol. | | | | | | | |
| **Confirmation of Insurance** | **Attached**  **In progress**  **To be submitted** | | | | | | | |

# **Safety and Monitoring Contacts**

|  |  |
| --- | --- |
| **Clinical Trials Involving Investigational Medical Device** | |
| **Qualified Physician/Medical Expert** | |
| **Name** |  |
| **Telephone** |  |
| **Email** |  |
| **Address** |  |
| **Sponsors Independent Physician/Medical Expert** | |
| **Name** |  |
| **Telephone** |  |
| **Email** |  |
| **Address** |  |
| **Pharmacy, Clinical Laboratory, Radiology, Pathology and other medical and technical departments involved in the trial** | |
| **Name** | **(add or remove additional boxes where necessary)** |
| **Telephone** |  |
| **Email** |  |
| **Address** |  |
| **Independent Safety Monitoring Board or Data Safety Monitoring Board Members** | |
| * List the members of the safety monitoring board. | |
| **Trial Management Group** | |
| * List the members of the trial management group. | |
| **Sponsors Independent Physician/Medical Expert** | |
| **Name** |  |
| **Telephone** |  |
| **Email** |  |
| **Address** |  |
| **Pharmacy, Clinical Laboratory, Radiology, Pathology and other medical and/or technical departments involved in the trial** | |
| **Name** |  |
| **Telephone** |  |
| **Email** |  |
| **Address** |  |

# **Delegation of Clinical Trial Duties**

Responsibilities for the conduct and oversight for the trial are delegated to you as the Coordinating Principal Investigator. You may delegate trial related responsibilities to the listed Principal Investigator(s) and any trial-related personnel. All trial-related duties delegated by the Coordinating Principal Investigator or Principal Investigator(s) and trial-related personnel must only be delegated to those that are qualified by experience and training. Delegated responsibilities must be retained in the [UNSW Clinical Trial Delegation Log](https://research.unsw.edu.au/document/Clinical%20Trial%20Delegations%20Log.docx). The UNSW Sponsor’s Delegate is to be notified of the following:

* Protocol deviation reports outlined in the UNSW Research Misconduct Procedure.
* Any serious breach of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that is likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Significant safety issues that are likely to (or have the potential to) affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Urgent safety measures implemented to remove or prevent a significant safety issue.
* Safety reports relating to the continuation, suspension, or discontinuation of the clinical trial for safety reasons.
* Non-compliance with the protocol, SOPs, GCP, and applicable regulatory requirement(s) significantly affects or has the potential to affect human subject protection or reliability of trial results significantly.
* Participant complaints or concerns received concerning the conduct of the research.
* Significant modifications to the clinical trial that is likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial.
* Addition of participating trial sites, contractual arrangements at participating sites or modifications to legal agreements.
* The intention to conduct the trial in other countries.

# **Trial Objectives and Purpose**

* Describe the aim(s) of the clinical trial and specify the research questions that the trial will address.
* Specify the primary endpoints and the secondary endpoints to be measured during the trial.

# **Background Information**

* Describe the theoretical background for the clinical trial and describe the disease or medical condition that the trial aims to prevent, detect, treat, or manage and provide supporting background literature references.
* Provide theoretical background information for the investigational medical product, investigational medical device, or the health intervention. Justify the use of these interventions, the route of administration, dosage, treatment regimen or treatment periods by including a summary of findings from non-clinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial. Include supporting provide background literature references.
* Describe the population to be studied in the clinical trial and provide background literature references to justify their inclusion in the trial.

# **Statement of Compliance**

The clinical trial will be conducted in compliance with the following guidelines and documentation:

* [ICH Guidelines for Good Clinical Practice (GCP)](https://www.tga.gov.au/publication/note-guidance-good-clinical-practice)
* [National Statement on Ethical Conduct in Human Research](https://nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018) (National Statement)
* As approved by the Human Research Ethics Committee (HREC), the clinical trial protocol is responsible for monitoring the trial’s conduct.
* The responsibilities set out by the UNSW Sponsors Delegate.

The onsite or remote monitoring standard operating procedures as put in place by the clinical trial sponsor.

# **Conflicts and Interests**

# **Trial Design**

* Describe the selected trial design (e.g., double-blind, placebo-controlled, parallel design) and justify how it will meet the aims of the clinical trial.
* Describe the measures to be implemented to minimise and avoid bias (e.g. randomisation, blinding)
* Provide a schematic diagram of trial design, procedures, and stages.

# **Sample Size**

The plan is to enrol [x] subjects to complete the trial. The nominated sample is based on [insert sample size calculation].

Multicentre trials

Each participating site is required to recruit and enrol [x] subjects.

# **Selection and Withdrawal of Subjects**

## **Inclusion Criteria**

State the inclusion criteria. If there are multiple study groups, define each group in table format criteria or use dot points.

## **Exclusion Criteria**

State the exclusion criteria. If there are multiple study groups, define each group in table format criteria or use dot points.

Ensure that the criteria for inclusion and exclusion are provided in lay terminology within the recruitment materials, participant information statement and consent form and the human ethics application.

## **Recruitment Strategy**

Describe the recruitment strategy in detail and explain how this strategy will identify the population studied in this clinical trial.

## **Screening**

Describe the screening process and explain how the research team will inform participants that are not eligible to participate in the trial.

## **Consent**

Describe the process for collecting consent.

## **Withdrawal of Consent or Participant**

Describe the subject withdrawal process and describe the procedures to ensure participants safety is monitored throughout the withdrawal process.

Provide detailed procedures for informing participants of the risks and the ongoing safety monitoring required in circumstances when terminating the trial interventions including:

* When and how to withdraw subjects from the trial or the investigational medical product treatments.
* The type and timing of the data to be collected for withdrawn subjects.
* Whether and how subjects are to be replaced
* The follow-up for subjects withdrawn from investigational product treatment/trial treatment.

# **Treatment of Subjects**

Provide a detailed description of the following:

* All trial treatments, measures, and procedures that participants will complete or used to collect trial data and detail the instructions for administering these procedures.
* Describe the follow-up period(s) for subjects for each type of intervention.

## Investigational Medical Product and Trial Intervention

Provide the details of the investigational medical products used in the trial.

* List the medication(s)/treatment(s) permitted (including rescue medication) and not permitted before or during the trial.
* Specify any differences between the trial intervention, treatment, placebo arms for the trial.
* Describe the trial interventions, specify the qualifications and experience required by personnel delegated these responsibilities.

## **Storage, dispensing and product accountability.**

* Describe how investigational medical products, investigational medical devices, or placebo will be ordered, stored, dispensed, and destroyed.
* The accountability of investigational products will be managed.
* Specify the qualifications and experience required by personnel delegated these responsibilities.

## **Randomisation and Allocation**

* Describe the randomisation and allocation procedure.
* Describe the procedure for unblinding.
* Specify the qualifications and experience required by personnel delegated these responsibilities.

## **Treatments, Dosing, Dosage Schedules, and Route of Administration**

* Describe all trial treatments, measures, and procedures that participants will complete or used to collect trial data and detail the instructions for administering these procedures.
* Specify how and when the investigational medical product or investigational medical device will be administered to trial participants. Indicate the names of the products to be used and provide the instructions for administration.
* Specify the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s).
* List the medication(s)/treatment(s) permitted (including rescue medication) and not permitted before or during the trial.
* Describe the follow-up period(s) for subjects for each investigational product treatment, trial treatment.
* Specify any differences between the trial intervention, treatment, placebo arms for the trial.
* State the experience and qualifications required to administer the above procedures.

# **Safety and Monitoring**

## **Assessment of Safety Event Report Forms**

Safety reports will be assessed on the seriousness, causality, and expectedness of the event to the trial treatment(s), intervention(s), investigational medical product(s), investigational medical device(s). The following are known and expected adverse effects, harms, risks, or discomforts associated with trial procedures, treatments, or interventions.

1. Known Adverse Effects

Provide a detailed list of all adverse effects associated with the trial investigational medical device, intervention or trial procedure that participants may (or have the potential) to experience.

1. Known Harms, Risks or Discomforts

Provide a detailed list of all adverse effects associated with the trial investigational medical device, intervention or trial procedure that participants may (or have the potential) to experience.

## **Adverse Events**

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users or other persons, whether or not related to the investigational medical device.

AEs are assessed using the safety monitoring flow chart. Those classified as “not serious” are assessed by the qualified physician/medical expert specified in section 2 of the protocol. The Qualified Physician cannot delegate this responsibility to other research personnel.

Adverse event reports must be reported to the Coordinating Principal Investigator within [insert the reporting time frame]. All adverse event reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

## **Adverse Device Effect**

An adverse device effect (ADE) is related to the use of an investigational medical device. Including adverse events resulting from insufficient or inadequate Instructions for Use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

ADE are assessed using the safety monitoring flow chart. Those classified as “not serious” are assessed by the qualified physician/medical expert specified in section 2 of the protocol. The Qualified Physician cannot delegate this responsibility to other research personnel.

ADE must be reported to the Coordinating Principal Investigator within [insert the reporting time frame]. All adverse event reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

## **Serious Adverse Events**

Serious Adverse Events (SAEs) that result in or lead to one or more of the following and the event is not related to the investigational medical product, the trial intervention, or procedures:

* The death of a trial participant.
* A life-threatening illness or injury involving a trial participant.
* A participant’s permanent impairment of body structure or body function.
* In-patient or prolonged hospitalisation (not for a pre-existing condition or an elective surgery) of a trial participant.
* Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or function of a trial participant.
* Fetal distress, fetal death or congenital abnormality or birth defect.

SAE reports are classified following the safety assessment flowchart and are assessed by Sponsors Independent Medical specified in section 2 of the protocol. The Sponsors Independent Medical cannot delegate this responsibility to other research personnel. SAE reports are reported to the Coordinating Principal Investigator within [insert the reporting time frame] for multicentre clinical trials. SAR reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

## **Serious Adverse Device Effects**

A Serious Adverse Device Effect (SADE) is an SAE that is related to the investigational medical product, the trial intervention, or procedures. SAR reports are classified following the safety assessment flowchart and are assessed by Sponsors Independent Medical specified in section 2 of the protocol. The sponsors independent medical expert must determine whether the SAR was expected or unexpected. The Sponsors Independent Medical cannot delegate this responsibility to other research personnel.

#### **Expected Serious Adverse Reaction**

A serious adverse reaction by its nature, incidence, severity, or outcome is anticipated and identified in the current version of the investigational medical product or intervention safety information are classified as a SAR report. SAR reports are reported to the Coordinating Principal Investigator within [insert the reporting time frame] for multicentre clinical trials. Serious Adverse Reaction reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

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

A serious adverse reaction by its nature, incidence, severity, or outcome is unanticipated and not identified in the investigational medical product, the trial intervention, or procedures for use safety information are classified as a SUSAR.

Fatal or life-threatening Australian SUSAR reports are reported to the Therapeutic Goods Administration, the Coordinating Principal Investigator, and the sponsor’s delegate within 7 calendar days after being made aware of the case follow up information reported within a further 8 calendar days.

All other Australian SUSAR reports are to be reported to the Therapeutic Goods Administration, the Coordinating Principal Investigator, and the sponsor’s delegate within 15 calendar days after being made aware of the case follow up information reported within a further 8 calendar days. SUSAR reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

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

A safety issue that could adversely affect participants’ safety or materially impact the continued ethical acceptability or conduct of the trial. The Therapeutic Goods Administration, Human Research Ethics Committee and Sponsor’s Delegate must be notified of all significant safety issues within 15 calendar days of the sponsor instigating or being made aware of the issue**.** SSI reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

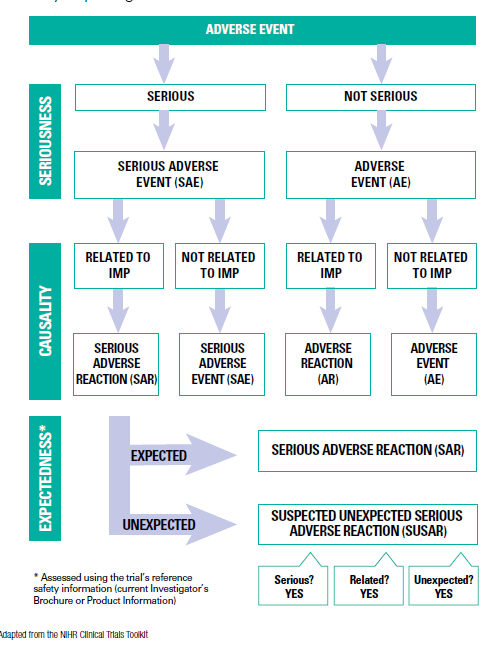
## **Urgent Safety Measure (USM)**

A measure that is taken to eliminate an immediate hazard to a participant’s health or safety. Significant safety issues where an urgent safety measure is required to be taken to eliminate an immediate hazard must be classified as a significant safety issue requiring an urgent safety measure. The Therapeutic Goods Administration, Human Research Ethics Committee and the Sponsor’s Delegate must be notified of any significant safety issues that meet the definition of an urgent safety measure should be notified within 72 hours. Examples include:

* a serious adverse event that could be associated with the trial procedures and that requires modification of the conduct of the trial.
* a patient population hazard, such as lack of efficacy of an intervention used for the treatment of a life-threatening disease.

USM reports must be recorded in the [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx).

## **Safety** **Assessment Flow Chart Investigational Medical Device Trials**



## **Register of Clinical Trial Safety Monitoring Reports**

A register of all event reports assessed and classified is to be retained by the Coordinating Principal Investigator and reported to the trial sponsor annually and the HREC if required.

## **Reporting of Clinical Trial Safety Monitoring Reports**

Single case reports of Adverse Events Adverse Reactions, Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs), reports do not need to be reported to the UNSW Sponsor’s Delegate or the HREC. All single case reports must be recorded in a safety monitoring register and are reported to the UNSW Sponsor’s Delegate annually.

#### **Emerging Safety Issues**

## The Trial Management Group, Trial Safety Committee or the Data Safety Monitoring Board is responsible for reviewing the safety information to identify any serious emerging safety concerns. If safety concerns are identified, this body will establish a plan to minimise the time participants may be placed at excess risk of harm. Before implementing the plan, the Trial Management Group, Trial Safety Committee or the Data Safety Monitoring Board must seek the advice of the human research ethics committee and sponsor’s delegate.

#### **Annual assessment of safety**

The following information must be provided in a report to the sponsors delegate annually:

* Documented evidence that the Trial Management Group, Trial Safety Committee or the Data Safety Monitoring Board (e.g., meeting minutes) confirming that regular reviews of safety occurred.
* Analysis of the trial intervention(s) and its implications for participants considering all available safety data and relevant clinical or non-clinical studies results.
* Any reports of emerging safety issues and a description of any measures taken or proposed to minimise risks.
* A copy of the safety monitoring register.

# **Non-compliance, Protocol Deviation and Serious Breaches of Good Clinical Practice**

## **Protocol Deviation**

A protocol deviation is defined as any breach, divergence or departure from the requirements of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that does not have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the research or clinical trial. Protocol deviations are events that do not occur persistently or systematically and do not potentially result in participant harms. Examples of protocol deviations include but are not limited to:

* Deviations because of participant adherence to the protocol, including rescheduled study visits, participants refusal to complete scheduled research activities or failure to complete self-report questionnaires required by the study protocol.
* Blood samples obtained or clinical trial testing occurring at times close to, but not precisely at the time points specified in the protocol.
* The completion of consent forms, safety monitoring report, case report forms or data collection tools in a manner that is not consistent with the protocol instructions or failure to make reports within the required reporting timeframes.
* Administration of the clinical trial investigational medical product or device in a manner that is not consistent with the manufacturer’s instructions for use.
* Use of an unapproved version of the participant information statement or recruitment of participants using unapproved recruitment procedures.
* Inclusion of a participant that does not meet the inclusion criteria.
* An urgent safety measure must be taken to eliminate an immediate hazard to a participant’s health or safety.

## **Serious Breach of Good Clinical Practice**

A serious breach is defined as a breach of Good Clinical Practice, the clinical trial protocol, the clinical trial standard operating procedures, or the human ethics approval that is likely to affect to a significant degree the safety or rights of participants or the reliability and robustness of the data generated in the clinical trial. Examples of serious breaches include but are not limited to:

* Persistent or systematic non-compliance with the instructions for completing consent forms, safety monitoring forms, case report forms or data collection tools that result in continued missed or incomplete data collection.
* Failure to record or report adverse events, serious adverse events, suspected unexpected serious adverse reactions, significant safety issues where urgent safety measures were implemented.
* Failure to conduct clinical trial procedures following the clinical trial delegation log.
* Widespread and uncontrolled use of protocol waivers affecting eligibility criteria, which leads to harm to trial subjects.
* Failure to report investigational medical product or device defects to the clinical trial sponsor or any relevant regulatory body.
* Failure to conduct research following the issued approvals, permits or licences by required laws, regulations, disciplinary standards, and UNSW policies relating to the responsible or safe conduct of research.
* Concealing or facilitating breaches (or potential breaches) of the Research Code by others.
* Researching without the requisite approvals, permits or licences required by laws, regulations, disciplinary standards, and UNSW policies related to the responsible or safe conduct of research.
* Failure to conduct research as approved by an ethics review body where that conduct leads to (or has the potential to) results in participant harms.
* Researching without ethics approval as required by the National Statement on Ethical Conduct in Human Research where that conduct leads to (or has the potential to) result in participant harms.
* Any breaches as outlined in the UNSW Research Misconduct Procedure or the Australian Code for responsible conduct of research that leads to (or has the potential to) result in participant harms.

## **Reporting Protocol Deviations**

* Protocol deviations occurring at a site must be documented in site files and reported by the principal site investigator to the Coordinating Principal Investigator.
* The Coordinating Principal Investigator must review the protocol deviation and the clinical trial protocol to establish the corrective actions and preventative steps to prevent the deviation from reoccurring.
* The protocol deviation and corrective action plan must be reported to the UNSW Sponsor’s Delegate by the Coordinating Principal Investigator or Coordinating Research Team using the protocol deviation report form.

## **Reporting of a Serious Breach**

* A serious breach occurring at a participating site must be reported by the site Principal Investigator to the Coordinating Principal Investigator within a specified timeframe.
* The Coordinating Principal Investigator must review the serious breach, along with the clinical trial protocol, to develop a Corrective and Preventive Action (CAPA) that defines the steps to prevent the serious breach from reoccurring.
* The serious breach report and the CAPA must be provided to the approving HREC, and the UNSW sponsors delegate for review and approval.

## **Reporting of Serious Breaches by Third Parties**

* A Suspected Breach is a report judged by the reporter as a possible serious breach but has yet to be formally confirmed as a serious breach by the sponsor.
* A Suspected Breach form must be completed when a third party (e.g., individual/institution) wishes to report a suspected breach of Good Clinical Practice or the protocol and should be reported directly to the reviewing HREC without reporting through the sponsor.
* Recording of Protocol Deviation and Serious Breach Reports
* A register of protocol deviation and serious breach reports must be recorded. Written records and copies of documentation sent to the sponsor must be retained in the Investigator Site File.
* Copies of protocol deviation and serious breach reports must be recorded, written records and copies of documentation sent to the sponsor, referrals made to the HREC or establishing whether a breach of the Australian Code for Responsible conduct of research must be retained in the Master Site File.

# **Review of a Protocol Deviation and a Serious Breach**

* The UNSW Sponsor’s Delegate will review reports to establish whether the event meets the definition of a protocol deviation or serious breach, to establish whether the proposed CAPA is appropriate and establish whether there is or will be an ongoing impact on the reliability and robustness of the data generated.
* The UNSW Sponsor’s Delegate will seek advice from the approving HREC on the corrective and preventive actions.
* Protocol deviation or serious breach reports where a UNSW researcher, staff or student is responsible for the protocol deviation or the serious breach will be reviewed as per the [UNSW Research Misconduct Procedure](https://www.gs.unsw.edu.au/policy/documents/researchmisconductproc.pdf) to establish whether a breach of the [UNSW Research Code of Conduct](https://www.gs.unsw.edu.au/policy/documents/researchcode.pdf) has occurred.
* Protocol deviation or serious breach reports where the UNSW Sponsor’s Delegate determines that site personnel are responsible for a protocol deviation or the serious breach will be referred onto their responsible institution for review under their Research Misconduct procedures to establish whether a breach of the [Australian Research Code for the Responsible Conduct of Research](https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018) has occurred.

# **Statistics**

* Describe the statistical plan for analysing the trial data.
* Indicate the timing of any planned interim analyses.

# **Data Handling, Ownership and Access**

# **Data Ownership**

All research data collected during this trial is governed and handled following the Research Data Governance and Materials Handling [policy](https://www.gs.unsw.edu.au/policy/documents/researchdatagovernancepolicy.pdf). UNSW, rather than any individual or Organisational Unit, is the Custodian of data and materials and any information derived from the data. Original research data and primary materials generated in the research conducted at the University will be owned and retained by the University subject to any contractual, statutory, ethical, or funding body requirements.

# **Authorship**

Describe the requirements for authorship.

# **Recording and Reporting Data**

Principal Investigators are responsible for maintaining adequate and accurate source documents and trial records that include all pertinent observations on each site’s trial subjects. Source data must be attributable, legible, contemporaneous, original, accurate, and complete.

Trial subjects will be assigned a participant ID, and data will be reported using the [case report form].

Data will be reported on the [case report form], derived from source documents, should be consistent with the source documents, or the discrepancies must be explained. Any change or correction to a [case report form] should be 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.

Data is collected at the following timepoints [insert timepoints] and entered into the case report form in [written or electronic format] and transferred to the sponsor using [insert the platform to be used e.g. Qualtrics or RedCap]

1. Confidentiality

Information collected in the trial must be handled following the requirements of the Privacy and Personal Information Protection Act 1998 (NSW). Trial subjects have right of access to personal information held about them by the UNSW and can request correction and amendment of it. The UNSW requirements to ensure that personal information is protected is available in the [UNSW Privacy Management Plan](https://www.legal.unsw.edu.au/compliance/privacyhome.html).

1. Direct Access to Source Data and Documents

Site principal investigator(s) and institution(s) will permit trial-related monitoring, audits, HREC review, and regulatory inspection(s), providing direct access to source data/documents. The sponsor will not have access to source data however, site(s) and institutions will allow the sponsors monitor or auditor access to source documentation for auditing purposes.

# **Trial Management Group, Data Safety Monitoring Board, Independent Safety Committee**

Describe the terms of reference for the trial management group or safety committee. The information must include the frequency of meetings and specify how the information will be documented.

# **Monitoring Quality Control and Quality Assurance**

The Coordinating Principal Investigator and Principal Investigator(s) ‘responsibility are to monitor the clinical trial. The Coordinating Principal Investigator and Principal Investigator(s) are responsible for undertaking or participating in site initiation or protocol-specific training before recruitment and data collection commences. A monitoring report demonstrating regular compliance monitoring with the clinical trial protocol, procedures, and HREC approval is provided to the UNSW Sponsor’s Delegate annually.

Root, cause, analysis reports are to be completed by the Coordinating Principal Investigator for reports of non-compliance and serious breaches. A corrective and preventative action plan must be developed and actioned for any reports of non-compliance and serious breaches.

# **Clinical Trial Research Agreement**

The Coordinating Principal investigators must ensure that agreements are executed at each of the following sites before site initiation, recruitment, and data collection commences.

Templates for clinical trial research agreements can be downloaded using the following link:

* <https://www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements/>
* All agreements are to be negotiated with [Research Grants and Contracts](https://research.unsw.edu.au/research-grants-and-contracts-rgc) once the clinical trial protocol has been developed, human ethics approval has been established, and, where applicable, the UNSW Clinical Trials Sponsor’s Delegate has confirmed that UNSW will act as clinical trial sponsor.
* Signed CTRAs and other agreements must be included in the list of GCP essential documents. Recruitment and data collection for a clinical trial must not commence without an executed CTRA in place.

# **Research Governance Site Authorisation**

Site authorisation is to be obtained, or if a research site is added, a site authorisation letter from the delegated authority of an institution responsible for any participating site is obtained. It is to be stored as a GCP essential document before participants are recruited at a participating site.

# **Site Closure or Termination of Trial**

* Describe the procedure for closing trial sites.
* Describe the procedure for terminating the trial conduct.

# **Good Clinical Practice Requirements**

Coordinating Principal Investigators, Principal Investigators and all site personnel or trial-related staff must have current Good Clinical Practice Training. Evidence of training confirmation is to be stored as a GCP essential document.

It is the responsibility of the Coordinating and Principal Investigators to familiarise themselves with the requirements of the [Guideline for Good Clinical Practice (E6, R2)](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf)

# **Essential Documents for the Conduct of a Clinical Trial**

All essential documents referred to in section 8.2 of the [Guideline for Good Clinical Practice (E6, R2)](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf)   are retained by all trial investigators.

## **Qualifications and Curriculum Vitae**

Copies of CVs for all principal investigators will be stored as an essential document. The [TransCelerate CV template](https://research.unsw.edu.au/document/TransCelerate%20CV%20template.pdf) can be used as a template.

# **Clinical Trial Delegation and Responsibilities Log**

| **Protocol / Study Number:** |  | **Sponsor Name:** |  |
| --- | --- | --- | --- |
| **Principal Investigator Name:** |  | **Site Number:** |  |
| **Site Name (if applicable)** |  | | |

**\*THIS FORM IS TO BE COMPLETED BY ALL PERSONNEL INVOLVED IN THE STUDY AFTER RECEIVING PROPER STUDY TRAINING AND BEFORE TAKING PART IN ANY STUDY ACTIVITIES**

**Principal Investigator (PI)**

By signing, I confirm/acknowledge that the tasks listed below will only be delegated to appropriately trained, skilled and qualified staff. I will remain responsible for the overall study conduct and reported data, ensuring study oversight. All associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations and have not performed any study tasks before appropriate delegation and completion of appropriate training. Mechanisms are in place to ensure that site staff receives the appropriate information and training throughout the study and that a 2-way communication channel exists between staff and self. Any changes in staff or delegation in staff will be recorded promptly.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Name** | **Principal Investigator’s Signature** | **Initials** | **Start**  **(dd/mmm/yyyy)** | **End**  **(dd/mmm/yyyy)**  **(complete only if prior to end of study)** |
|  |  |  |  |  |
|  |  |  |  |  |

Site Staff

| **Name** | **Signature** | **Initials** | **Study Role** | **Key Study Task(s)**  **(choose from list below)** | **Start**  **(dd/mmm/yyyy)** | **End**  **(dd/mmm/yyyy) (complete only if prior to end of study)** | **PI Initials & Date**  **(dd/mmm/yyyy)** |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |
|  |  |  |  |  |  |  | \_\_/\_\_\_/\_\_\_\_\_ |

|  |
| --- |
| **Comments:** |
|  |

|  |
| --- |
| **Electronic Signature Declaration for Principal Investigator and Site Staff**   1. My electronic signature as it applies to entering electronic data or signing records in sponsor-owned or sponsor -outsourced computer systems is the legally binding equivalent of my handwritten signature. 2. I will not share password(s) assigned to me for this study with any other persons. |

|  |
| --- |
| **Principal Investigator’s End of Study Declaration**  I hereby confirm that the above information is accurate and complete, and that I authorised the delegation of study-related tasks to each individual as listed above.  **Principal Investigator’s Signature:** **Date:** |

**Task Key:**

|  |  |
| --- | --- |
| 1. Obtain informed consent \* | 12. Sample collection |
| 2. Subject selection/recruitment\* | 13. Sample processing and/or shipment |
| 3. Confirm eligibility (review inclusion/exclusion criteria)\* | 14. Evaluate study-related test results \* |
| 4. Obtain medical history (source documents) | 15. Use IWRS/IVRS |
| 5. Perform physical exam\* | 16. Make entries/corrections on (e)CRFs |
| 6. Conduct study visit procedure as outlined in the protocol\* | 17. Sign- off (e)CRFs\* |
| 7. Make study-related medical decisions\* | 18. Maintain essential documents |
| 8. Assess AEs/SAEs\* | 19. Perform study-related assessments as per protocol \* |
| 9. Dispense study drug\* | 20. Complete company- specific log ( if applicable) |
| 10. Perform drug accountability | 21. Other (specify)\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| 11. Study drug storage and temperature monitoring | 22. Other (specify) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

\*These tasks may only be performed by qualified individual as permitted by local law, medical or standard of care practices, or applicable required training as per job description or designation.

# **Safety Monitoring Register Template**

* [UNSW Safety Monitoring Register Template](https://research.unsw.edu.au/document/UNSW%20Safety%20Monitoring%20Register%20Template.xlsx)
* [UNSW Adverse Event or Incident Event Case Report Form](https://research.unsw.edu.au/document/Adverse%20Event%20Incident%20Report%20Form%20September%202019%20.docx) Example.

# **Corrective and Preventive Action Form**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Raised by: | Assigned to: | | | Date: | Remarks: |
| Description: | | | | | |
| Proposed immediate action (correction): | | | | | |
| Completed by: | | Date: | Remarks: | | |
| Root cause analysis required: Yes  No | | | | | |
| Underlying / root cause: | | | | | |
| Determined by: | | Date: | Remarks: | | |
| Proposed action for long term solution (corrective/preventive action): | | | | | |
| Completed by: | | Date: | Remarks: | | |
| Comments on effectiveness of action taken: | | | | | |
| Closed out by: | | Date: | Remarks: | | |