**FULL STUDY TITLE**

**SHORT STUDY TITLE**

**CONFIDENTIAL**

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# STATEMENT OF COMPLIANCE

This document is a protocol for a clinical research study. The study will be conducted in compliance with all stipulations of this protocol, the conditions of ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95).

NOTE: Guidance for completing this template: Some sections may not apply to your study. You should delete those sections that are N/A. Delete all guidance text (marked in RED) and margin comments prior to submission. Contents

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PROTOCOL SYNOPSIS

|  |  |
| --- | --- |
| Title |  |
| Objectives | Primary:Secondary: |
| Study Design |  |
| Planned Sample Size |  |
| Selection Criteria |  |
| Study Procedures |  |
| Statistical ProceduresSample Size Calculation:Analysis Plan: |  |
| Duration of the study |  |

# GLOSSARY OF ABBREVIATIONS

|  |  |
| --- | --- |
| **ABBREVIATION** | **TERM** |
|  |  |
|  |  |
|  |  |

# Study Management

* 1. **Principal and Associate Investigators**

Please include the name of the Principal Investigator and all Associate Investigators with their title, telephone number, department they work in and their primary email.

* 1. **Statistician**

Please include the name of the statistician and title, address, telephone number and email.

* 1. **Internal Trial Committees**
	2. **Independent Safety and Data Monitoring Committee**

If applicable, describe the membership and responsibilities – refer to the ‘National Statement’ for information regarding Data Safety Monitoring Boards.

* 1. **Sponsor**

|  |
| --- |
| Investigator-Initiated |
| Royal North Shore Hospital | Sponsor: Northern Sydney Local Health District |
| North Shore Private Hospital | Sponsor: North Shore Private Hospital |

The study sponsor is not necessarily the same as the funding body.

The sponsor is the company, institution or organisation that takes overall responsibility for the conduct of the trial and usually initiates, organises and supports the clinical trial. The sponsor usually owns the study protocol and study data. For example, in the following situation - *an employee of NSLHD who is conducting a study with an NHMRC project grant* – NSLHD is the study sponsor, NHMRC is the funding body.

* 1. **Funding and resources**

Please explain how the study is being funded. (eg Commercial sponsor, Departmental funds etc)

# INTRODUCTION AND BACKGROUND

* 1. **Background Information**

Include information based on literature review, investigators’ experiences and a brief history of the disease including prognostic factors. All references must be listed at the back of the protocol.

* 1. **Research Question**

Clearly state the question the study intends to answer.

* 1. **Rationale for Current Study**

The rationale specifies the reasons for conducting the research in light of current knowledge. It should include a well-documented statement of the need/problem that is the basis of the project, the cause of this problem and its possible solutions. It is the equivalent to the introduction in a research paper and it puts the proposal in context. It should answer the question of why and what: why the research needs to be done and what will be its relevance.

# STUDY OBJECTIVES

* 1. **Primary Objective**
	2. **Secondary Objectives**

Your research question needs to be further refined into one or more study objectives. The study objective(s) should be single and quantifiable statement(s) that will allow you to answer your research question. Objectives should be simple, specific, and stated in advance, e.g. to determine if socioeconomic status is associated with excess childhood asthma in Istanbul.

# STUDY DESIGN

 **4.1 Type of Study**

For example a randomised control trial, qualitative study, case control study etc.

* 1. **Study Design**

The scientific integrity of the study and the credibility of the study data depend substantially on the study design and methodology. The methodology section is the most important part of the protocol. It should include detailed information on the interventions to be made, procedures to be used, measurements to be taken, observations to be made, laboratory investigations to be done etc. The design of the study should include information on the type of study, the research population or the sampling frame, and who can take part (e.g. inclusion and exclusion criteria, withdrawal criteria etc.), and the expected duration of the study

* 1. **Number of Participants**

XXX participants will be recruited OR the data of XXX patients will be collected.

* 1. **Expected Duration of Study**

Expected start and stop date.

Include the expected time period for the recruitment phase of the study and the expected time period for the follow up phase of the study.

* 1. **Primary and Secondary Outcome Measures**

The primary outcome should be the most important and clinically relevant outcome (e.g. clinical, psychological, economic, or other) of the study. This is the measure used to answer your study aim. It is also the outcome used to calculate study sample size and power. (e.g. caesarean/no caesarean; blood loss ≥500mL/blood loss <500mL; weight - kg; pain - mild, moderate, severe; time to event (e.g. survival); and counts (e.g. number of infections).

Secondary outcome(s) are measures of additional or less important research interest. They may include additional clinical, psychological, economic, or safety outcomes (e.g. treatment related side effects/adverse events). However, as these endpoints are not used to calculate study power and sample size it is often not possible to draw robust conclusions from the results.

# STUDY TREATMENTS

* 1. **Treatment Arms**

**5.1.1 Description**

**5.1.2 Dosage and Route of Administration**

**5.1.3 Dose modification**

* 1. **Preparation and administration of study drug**

 **Dispensing and Product Accountability**

* 1. **Measurement of participant compliance**
	2. **Excluded medications and treatments**

# PARTICIPANT ENROLLMENT AND RANDOMISATION

* 1. **Recruitment**

Explain how potential participants will be identified for the study and where.

For record review, explain how records will be identified.

Examples include the following:

* review of databases (please identify the database and the custodian)
* review of outpatient clinic files, Emergency Department admissions, inpatients (please include who will be reviewing the notes e.g. research coordinator)
* advertisements (include where the advertisement will be e.g. newspaper, poster in outpatients area or hospital foyer, radio announcements)
* Information Letter to Medical practitioners

Explain how potential participants will be screened for the study.

* 1. **Eligibility Criteria**
		1. **Inclusion Criteria**

List each criterion, eg. gender, age range, weight, height, disease status, laboratory parameters.

* + 1. **Exclusion Criteria**

List each criterion, eg:

* Women lactating, pregnant or of childbearing potential who are not willing to avoid pregnancy during the study
* Patients with a history of xxx disease(s) that is (are) likely to interfere with the metabolism or excretion of the test medication
* Patients who had an investigational new drug within the last xx days /weeks
* Patients with a history of psychological illness or condition such as to interfere with the patient’s ability to understand the requirements of the study.
* Patients with xxx disease that is likely to interfere with the evaluation of the patient’s safety and of the study outcome.

List the prohibited concomitant medications.

## Informed Consent Process

Explain the process and how it will be documented.

The following fundamental conditions for a valid informed consent should be met for each participant: Disclosure of relevant information, comprehension of the information provided, voluntary agreement of the participant (free from coercion).

State who will obtain consent.

* 1. **Enrolment and Randomisation Procedures**

Explain how a potential participant will be enrolled into the study.

Example: The participant will be enrolled into the study after the informed consent process has been completed and the participant has met all inclusion criteria and none of the exclusion criteria. The participant will receive a study enrolment number and this will be documented in the participant’s medical record and on all study documents.

* 1. **Blinding Arrangements**

As relevant, provide information on how the study will be blinded. Provide a description of stopping rules for individuals, for part of the study or entire study, the procedures and conditions for breaking the codes etc. should also be described.

* 1. **Breaking of the Study Blind**
		1. **On Study**
		2. **Following Completion of the Study**
	2. **Participant Withdrawal**
		1. **Reasons for withdrawal**

List any possible circumstances that may lead to early termination of the study and outline how this will be managed, i.e. who will be responsible for what in the process of terminating the study (informing participants, correspondence to HREC, compiling a final study report, unblinding if applicable)?

* + 1. **Handling of withdrawals and losses to follow-up**
		2. **Replacements**
	1. **Trial Closure**

Outline any follow up that will be provided to the research participants and for how long. This may include a follow up, especially for adverse events, even after data collection for the research study is completed.

* 1. **Continuation of therapy**

# STUDY VISITS AND PROCEDURES SCHEDULE

## Study Flow Chart

Diagram of the study design (example below)

Enrolment

Randomisation

Treatment Phase

(e.g. 12 weeks)

Group A Group B

Include all study visits and all study procedures conducted at each visit. This information can also be displayed in a table.

Example below

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| List Interventions | Enrolment Visit | Visit 1 | Visit 2 | Visit 3 | Final Study Visit |
| Informed Consent | ✓ |  |  |  |  |
| Inclusion / Exclusion criteria | ✓ |  |  |  |  |
| Physical examination |  | ✓ |  |  |  |
| CXR | ✓ |  |  |  | ✓ |
| SAE /SSI/ USM/ USADE/SUSAR or URSAE Assessment |  | ✓ | ✓ | ✓ | ✓ |

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

# CLINICAL AND LABORATORY ASSESSMENTS

# SAFETY REPORTING:

# MANAGEMENT and REPORTING

# Explain how Safety Reporting will be managed and reported.

For example, *Participants are encouraged to report significant safety issues (SSIs) to a member of the research team as they occur. Contact details of research team members are provided on the Participant Information Sheet in addition to the procedure for reporting injuries and complications.*

*The CPI will report SSIs to the HREC no later than 72 hours after becoming aware of the event.*

*Definitions:*

Significant Safety Issues (SSI) A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.

Suspected Unexpected Serious Adverse Events (SUSARs) An adverse reaction that is both serious and unexpected.

Unanticipated Serious Adverse Device Effects (USADEs) A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report (and/or Investigator's Brochure/Instructions for Use).

Unexpected & Related SAEs (URSAE)

An adverse event that is:

* Serious – meets the definition of a serious adverse event
* Related – resulted from administration of the trial intervention
* Unexpected – the event is not described in the protocol as an expected occurrence.

For further information on the safety reporting requirements;

<https://www.nslhd.health.nsw.gov.au/Research/ResearchOffice/Pages/Safety-Reporting-for-Clinical-Trials.aspx>

* 1. **Specific Safety Considerations (Eg. Radiation, Toxicity)**

Radiation risks outlined in the **Code of Practice** from the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) must be followed for all Exposure of Humans to Ionizing Radiation for Research Purposes.

[***www.arpansa.gov.au/Publications/codes/rps8.cfm***](http://www.arpansa.gov.au/Publications/codes/rps8.cfm)

The following should be detailed:

* Why the participants are exposed to ionizing radiation.
* The number of participants to be exposed.
* The precautions to be taken to keep exposure to a minimum.
* The exposure to radiation needs to be addressed with a formal **Radiation Safety Report.**

# STATISTICAL METHODS

* 1. **Sample Size Estimation**
	2. **Population to be analysed**
	3. **Statistical Analysis Plan**
	4. **Interim Analyses**

The statistical methods proposed to be used for the analysis of data should be clearly outlined, including reasons for the sample size selected, power of the study, level of significance to be used, procedures for accounting for any missing or spurious data etc. For projects involving qualitative approaches, specify in sufficient detail how the data will be analysed.

# DATA MANAGEMENT

* 1. **Data Collection**

Details of how the data will be collected.

* 1. **Data Storage**

Outline where and how the data or database will be stored. Describe all procedures for handling data, how data are coded, who has access to the source data and database, by whom the key to the code is safeguarded, which steps will be taken to ensure data security, and how the participants’ privacy is protected, such as de-identification. If the research is multi-site include the data storage at all sites, eg, at Hornsby, data will be stored within the XXX Department and at RNSH data will be stored within the XXX Department.

* 1. **Data Confidentiality**

Explain how participants’ privacy will be protected and how data confidentiality will be maintained during the study, for archiving and storage, and for publication. Specify if records will be identifiable, re-identifiable (ie. coded), or de-identified/anonymised.

**NB: De-identified data is data that can never be linked back to the participant. Coded data is NOT de-identified.**

* 1. **Study Record Retention**

The minimum period for retention of research data is 5 years for non-clinical research, (this includes health and social science research), 15 years for clinical research and until participants are at least 25 years of age for research involving children/adolescents under the age of 16.

#  ADMINISTRATIVE ASPECTS

All clinical trials must be registered in a publicly accessible trials registry prior to enrolment of the first participant. This is the responsibility of the investigator. If possible, you should include the registration number here.

* 1. **Independent HREC approval**

This study has been approved by the Northern Sydney Local Health District HREC, 202X/ETHXXXXX.

* 1. **Amendments to the protocol**

Any amendments will be submitted to the HREC for review prior to implementation as per HREC guidelines.

* 1. **Serious Breach Reporting**

Serious Breaches will be submitted to the HREC for review.

Serious Breach definition; A breach of Good Clinical Practice or the protocol that is likely to affect to a significant degree;

a) The safety or rights of a trial participant, or

b) The reliability and robustness of the data generated in the clinical trial.​

Serious breaches must be reported by the sponsor through the CPI within 7 calendar days of the breach. The breach must be submitted as a general amendment via Regis.

* 1. **Participant reimbursement**

Details of participant reimbursement, if any.

* 1. **Financial disclosure and conflicts of interest**

Details of any conflicts of interest and how they will be addressed.

#  USE OF DATA AND PUBLICATIONS POLICY

The protocol should specify not only dissemination of results in the scientific media, but also to the community and/ or the participants, and consider dissemination to the policy makers where relevant. Publication policy should be clearly discussed, for example, who will take the lead in publication and who will be acknowledged in publications, etc.

# REFERENCES

This is the bibliography section for any information cited in the protocol.

List MUST INCLUDE: national and international guidelines on the conduct of research in humans (eg National Statement).