STATEMENT

The Standard Operating Procedures (SOPs) in this document meet the guidelines contained in the National Health and Medical Research Council’s (NHMRC) National Statement on Ethical Conduct in Human Research (2007) Updated 2018 (The National Statement), and the Australian Therapeutic Goods Administration’s (TGA) Good Clinical Practice Guidelines.

The HREC’s primary role is to protect the welfare and the rights of individual participants in research within or in association with Greenslopes Private Hospital and Ramsay Health Care facilities operating in Queensland.

These SOPs apply to the conduct of all research involving human participants carried out at GPH facilities, or with patients, staff, data or records of the hospital.

1. JURISDICTION OF HREC

Sites that fall under the jurisdiction of the Greenslopes Research and Ethics Committee (GREC) are:

- Greenslopes Private Hospital (GPH)
- Any Ramsay Healthcare facility in Queensland
- Gallipoli Medical Research Foundation (GMRF)

2. Authority

GPH has established the HREC to advise the institution on human research ethics matters, to assist researchers in the design and conduct of high quality ethical research, and to facilitate the hospital’s compliance with the various regulatory frameworks which relate to the governance of human research ethics issues.

GPH human research ethics arrangements comply with the National Statement on Ethical Conduct in Human Research (2007 - Updated 2018). The Terms of Reference and functioning of this committee is in accordance with the provisions of the National Statement.

The HREC has no delegated authority in relation to budgetary or management issues, but can advise the Hospital on matters which may have budgetary implications.

3. Reporting

The HREC reports annually to the National Health and Medical Research Council and quarterly to the GPH Executive Committee.

4. Resourcing

The GPH Executive has appointed an Ethics Secretary to work with the GREC. The hospital allocates financial resources to the Chair and Deputy Chair of the Committee to facilitate their work on behalf of the Committee.
5. Membership

The “core” membership structure of a HREC is outlined by the National Statement on Ethical Conduct in Human Research. This structure should include a reasonable balance between internal and external members, a balance between male and female members, and there should also be a balance of expert and lay perspectives.

Where a member ceases to fulfil the criteria of their position (eg a nominee of an element ceases to be a staff member of that element), their membership immediately lapses.

Much of the membership of the Committee is appointed by the GPH Director of Medical Services.

The Director of Medical Services may determine the method by which his / her recommendation for nominations are made – which could include calling for expressions of interest, followed by whatever selection method which the Director of Medical Services deems appropriate.

A recommendation in relation to the filling of casual vacancies will be made by the GREC, and a final determination made by the Director of Medical Services.

6. Chair

The Chair of the HREC has the following authorities and responsibilities:

- considers applications for Expedited Ethical Review
- considers (and may award interim approval to) requests for minor changes to ethical clearances / projects;
- approves the draft outcome report /approval letters prepared by the Secretary following meetings of the Committee
- Chairs (or nominates the chair) of the various Audit panels, and such other working groups that may be established by the Committee.

The Chair has debate and voting rights for all matters before HREC – except in situations where a conflict of interest precludes them from exercising such rights.

7. Deputy Chair

The Deputy Chair of HREC is appointed by the Committee. The Deputy Chair undertakes the role of the Chair in her/his absence.

The Deputy Chair has debate and voting rights as per their position on the Committee.

8. Additional attendance at meetings

The constitution of the GREC permits the Committee to invite the attendance and participation in debate of additional persons, as required to enable the Committee to appropriately and efficiently conduct its business.
A co-opted member / invited expert has audience rights, but cannot exercise a vote or participate in debate unless specifically invited to do so on a particular matter.

9. Policy and administrative support

The Secretary to the Committee will have rights of audience and debate.

The Secretary will:

- receive and forward correspondence to GREC members, as appropriate, (such as applications for minor changes to ethical clearances / projects, etc);
- provide commentary and advice to assist in the consideration of matters before the GREC;
- receive progress reports and determines what, if any, further action is required;
- maintain the Hospital’s register of ethical clearances;
- assist in the preparation of internal and external reports, submissions and other corporate documents;
- provide advice to other officers on the governance of human research ethics, regulatory requirements, and compliance issues;
- provide advice and assistance directly to researchers and supervisors, where appropriate;
- initiate and progress the business and work of the Committee;
- directly handle requests for textual or administrative changes to active ethical clearances; and
- draft such reports, policies and documents as requested by the Chair or the Committee.

10. Meeting Procedures

A meeting schedule for GREC is determined at the end of the preceding year. Generally, the GREC will meet at least 10 times a year.

11. Committee papers

There are standard agenda items, and proformas to assist the GREC in the consideration of the following matters:

i. Reporting the actions taken on conditional ethical clearances and seeking the Committee’s ratification, amendment or modification of these actions.

ii. Reporting the decisions of Expedited Ethical Review and seeking the Committee’s ratification, amendment or modification of these decisions.

iii. Applications for full ethical clearance.

iv. Reporting the decisions of the Chair on requests for modifications to existing ethical clearances and seeking the Committee’s ratification, amendment or modification of the Chair’s decisions.

v. Presenting for action any progress reports which are deemed to require the attention of the Committee.

12. Distribution of committee papers

To enable appropriate processing, any matters for consideration by the Committee (such as applications for full ethical clearance) must be received by the Secretary of the GREC by the submission deadline, approximately two weeks prior to the meeting.
13. Quorum

The quorum provisions for the GREC are articulated in the Terms of Reference for the Committee.

14. Conduct of meetings

Meetings of the GREC follow the distributed agenda, and discussion and debate are directed through the Chair. Nevertheless, formal standing orders do not apply to the conduct of the meeting, and debate is largely conducted in an informal manner.

15. Basis for the consideration of issues

GPH is committed to the principle that the review of proposed human research should be transparent, consistent, and promptly communicated to the applicants. This process should have the objective of working collaboratively with researchers to facilitate excellent and ethical research.

The deliberations of the HREC and other ethics reviewers must be based upon the provisions of the National Statement, the GREC Guidelines and other regulatory issues which relate to the terms of reference articulated by the Committee's constitution. Members are asked to carefully consider proposed research, policy and other matters, with reference to the above guidelines, policies and regulations. Any review decision and/or advice must be based upon these documents.

16. Conflict of Interest identified during a meeting

If an HREC member, or Chairperson, identifies a conflict of interest during a meeting, they shall verbally declare the interest to the Committee, which shall be recorded in the minutes of the meeting. The Member/Chairperson shall withdraw from all related discussions and not participate in any decision making associated with the identified conflict of interest. Experts invited to meetings to assist in the review of research shall be subject to the same requirements to declare an identified conflict of interest.

If an HREC member, or Chairperson, are the Principal Investigator, or named as a co-investigator on a project that is reviewed by the HREC, they shall be required to declare in the application if there is a conflict of interest. When the project is reviewed by the HREC, the member/Chairperson may remain in the meeting to answer questions on the study protocol but shall withdraw from the meeting whilst the Committee makes its deliberation on whether or not to approve the research. The member, or Chairperson, shall not be informed of the Committee’s decision at the meeting.

Where a potential conflict of interest is identified relating to the Chair all correspondence will be signed by the Deputy Chair.

17. Method for reaching a decision
In most cases, the GREC reaches a decision by consensus, but this does not necessarily mean a unanimous view. In those circumstances where a consensus cannot be reached, the Chair will call for a vote. As noted previously, only core members may vote on an application for ethical clearance. Even if a majority of core members vote to grant a project ethical clearance, the Committee may elect not to grant clearance if a significant number of members are opposed.

18. Communicating the outcomes

Good communication is an important foundation of a sound approach to research ethics. After each meeting of the GREC, the Secretary will:

- Should clarifications or corrections be required the Secretary will make this request to the Principal Investigator or designee via email within 5 days of the meeting.
- (normally within five working days of receiving an endorsed outcome of a review or appropriate clarifications or corrections) email the outcomes of ethical clearance to the proponents;
- Provide a response with the full documentation to the Chair for action and sign off; and
- Forward the completed approval letter and associated documentation to the Principal Investigator, or designee

In the interests of timeliness, efficiency and sustainability, the described communication processes may make use of email. In addition, an electronic signature may be used on the approval letters if the chair is unavailable in person and he/she directs the Ethics Secretary to do so.

19. Observers

The attendance of observers at a meeting of the HREC is at the discretion of the Chair.

20. Invitations to researchers

Having decided that an application must be revised and resubmitted to a subsequent meeting, the GREC can elect to invite the proponents to attend the meeting to discuss their application with the Committee.

21. Format of submissions of applications for ethical clearance

To be considered for any level of ethical review, an application must conform to the minimum requirements in relation to having been submitted on the correct form, including the appropriate signatures and attachments. Any incomplete application or an application made using the incorrect form may be returned unprocessed.

Unless the proponent presents a compelling argument for action to the contrary, applications submitted after the due date for the meeting will normally be considered at the Committee’s next
meeting. At the discretion of the Chair of GREC, late applications may be considered outside of a meeting by flying minute.

22. Monitoring of research

As per s5.5.1 to 5.5.5 of the National Statement, the Hospital has established a number of strategies to monitor approved research, these include:

- Annual reports on progress (including compliance with any conditions of approval and maintenance and security of records). These are due on the anniversary of when ethics approval was granted.
- Final report on completion (including a copy of the results and any publications).
- Reports of adverse/serious adverse events, according to the Committee’s SAE Reporting Guidelines (SOP No. 8).
- Protocol amendments, or changes to informed consent documents.
- Any significant deviation from, or violation of, the study protocol impacting the safety of participants or the integrity of the data collected
- If the study is withdrawn, terminated or suspended before the expected date of completion

Further information about the Hospital’s monitoring processes, including the handling of serious adverse events, can be found in GREC Guidelines.

23. Suspension or withdrawal of ethical approval

The GREC may suspend or withdraw its ethical approval for a study if it is satisfied that circumstances have arisen such that a research project is not being or cannot be conducted in accordance with its ethical approval and that, as a result, the welfare and rights of participants are not or will not be protected.

Where the GREC considers it appropriate that the serious adverse event/s and / or monitoring report requires the immediate suspension or discontinuation of the research ethics approval, the HREC should immediately notify the Principal Investigator (PI) and instruct them to:

- Immediately cease all study related activities;
- Ensure the health and wellbeing of participants are not compromised;
- Notify any study sponsor of the GREC’s decision, and
- Notify the authorising Research Governance Office.

Upon suspension, the GREC Chair, with the support of the Ethics Secretary and other nominated members of the GREC, will investigate the conduct of the project and compile a report for consideration by the full HREC and the PI. The PI will be requested to respond to the report. The full HREC will consider the response of the PI to the report and decide on the conditions for reinstatement of approval or whether approval will be withdrawn. The PI will be notified of the decision by the GREC. A PI will discontinue research following suspension or withdrawal of ethical approval and will comply with the special conditions imposed by the GREC. Any other HRECs involved in the project will be notified of the suspension or withdrawal as required by the National Statement.
24. Confidentiality

Each member of the GREC agrees to accept the Terms of Reference and Standard Operating Procedures of the Committee confirming that they will not disclose any confidential information to third parties.

This agreement means that, outside of a meeting, members should only discuss matters relating to the Committee’s deliberations if they are discharging an official responsibility / role. Members must never compromise intellectual property, commercial-in-confidence, or participant confidentiality.

The Ethics Secretary maintains hard copy and electronic records in relation to ethical clearance applications and related activity. Any access to these records is limited to members of the research team (including supervisors), members of the GREC, and authorised officers.

25. Hospital indemnification of members

In accordance with Australian requirements and international guidelines, the Hospital provides indemnification to the members of the HREC on the basis of them being either:

(i) staff, voluntary worker, foundation, institute, centre or other body, affiliated to or operating within the framework of the Hospital and formed by or with the knowledge and consent of the Hospital; or

(ii) any person acting in an honorary (academic or otherwise) capacity for the Hospital and includes honorary research fellows and voluntary workers who occupy a duly recognised position in the business of the Hospital.

This indemnification covers activities that are officially approved and undertaken with the knowledge of the Hospital or under the direction or control of, or at the request of, or which are activities relevant to that person’s position with the Hospital.

26. Handling of initial complaints and investigations

Institutions are required to have processes regarding the handling of complaints in relation to the ethical conduct of their research. The expectations in relation to these processes are articulated in the National Statement.

The Hospital has established mechanisms in relation to the following matters:

- concerns / complaints from anyone participating in the research;
- alleged breaches of the Hospital's research ethics arrangements; and
- requests for a review of a decision of HREC.

The Ethics Secretary is the initial contact for any concerns in relation to the ethical conduct of the research and attempts to resolve these matters in liaison with the complainant, the respondent, and the Chair of the GREC. The Director of Medical Services is responsible for handling formal complaints.
27. Fees for submitting proposals

The GREC has a processing fee for the consideration of any application for ethical clearance proposed where there is industry Sponsorship. No fee is charged for student projects, university collaborations or Investigator Initiated Research Projects.

A flat fee of $4400.00 (including GST) will be charged to all commercial companies submitting research proposals. This fee is common to all ethics committees and is to cover costs of assessment. A cheque made payable to “Gallipoli Medical Research Foundation” should be submitted with the proposal. Arrangements can also be made for direct debit.

<table>
<thead>
<tr>
<th>Initial application:</th>
<th>$4400 (incl GST)</th>
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<tbody>
<tr>
<td>With full or partial industry sponsorship</td>
<td></td>
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<tr>
<td>Amendment to protocols for studies with industry sponsorship requiring consideration by the committee</td>
<td>a) $550 (incl GST) for an standard Amendment (requiring no review of revisions to the ICF)</td>
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<tr>
<td></td>
<td>b) $825 (incl GST) for a more substantial Amendment, where an amendment to the ICF needs to be reviewed and approved</td>
</tr>
<tr>
<td>Investigator initiated, NHMRC grants etc, scholarship, student and unsponsored research</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

28. Member training

Greenslopes Private Hospital is committed to the training and ongoing development of the members of the GREC. Consequently, the Hospital or Research Foundation will support the attendance of a delegation of the Committee to the biannual national research ethics conference. The Hospital/Foundation will also, where possible, support and fund the attendance of members at other training, developmental and networking opportunities. New members of the HREC will be provided with a resource kit of materials.
HUMAN RESEARCH ETHICS COMMITTEE MEMBERSHIP 2019

<table>
<thead>
<tr>
<th>Name</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor Darrell Crawford</td>
<td>Chair</td>
</tr>
<tr>
<td>Dr Mellissa Naidoo</td>
<td>Director of Medical Services</td>
</tr>
<tr>
<td>Ms Claire Carsley</td>
<td>Assistant Director of Medical Services (Deputy Chair)</td>
</tr>
<tr>
<td>Ms Jude Rowe</td>
<td>Assistant Director of Clinical Services</td>
</tr>
<tr>
<td>Ms Monica Rider</td>
<td>Laywoman</td>
</tr>
<tr>
<td>Dr Rebecca Mello</td>
<td>Researcher</td>
</tr>
<tr>
<td>Mr Pat Mullins</td>
<td>Legal Representative</td>
</tr>
<tr>
<td>A. Prof Andrew Nicol</td>
<td>Researcher</td>
</tr>
<tr>
<td>Ms Petra Milaudi</td>
<td>Chaplain</td>
</tr>
<tr>
<td>Ms Anousheh Page</td>
<td>Pharmacist</td>
</tr>
<tr>
<td>Dr Roderick Whybird</td>
<td>Layman</td>
</tr>
<tr>
<td>Dr Luke Spence</td>
<td>Medical Representative</td>
</tr>
<tr>
<td>Ethics Secretary – Mrs Julie Greaves</td>
<td></td>
</tr>
</tbody>
</table>
EMPLOYEE / VISITOR CONFIDENTIALITY AGREEMENT

I, _____________________________________________________________

hereby confirm that I fully understand my obligation to the hospital and to any patient, to respect in

confidence, any personal information which becomes available to me during the course of my
duties / visit.

I also understand that any unauthorised disclosure of patient, or other hospital and health service
information, is considered an act of misconduct that would be dealt with in accordance with
standard award disciplinary procedures.

I am also aware that, under the provisions of the Criminal Code, legal action may be taken against
me for any unauthorised disclosure of confidential information concerning the patient.

___________________________________ ____________________________

Signature (Employee / Visitor) Date

_____________________________ ____________

Signature (Manager / Head of Department / Chairperson) Date
Title: HREC Terms of Reference

| Purpose | To provide a forum to consider the ethical aspects of proposed research, to examine and debate ethical and legal issues arising in the care of patients and to advise the Chief Executive Officer of the recommendations in matters of ethical significance. |
| Functions | • To consider ethical implications of all proposed research projects and to determine whether or not they are acceptable on ethical grounds.  
• To provide for surveillance of research projects until completion so that the Committee may be satisfied that they continue to conform to approved ethical standards.  
• To maintain a register of all research projects.  
• To make recommendations on the ethical implications of institutional policies brought to the notice of the committee from Executive.  
• Provide a perspective to Executive pertaining to the management of specific ethical issues arising in patient care.  
• To maintain communication with the NHMRC Australian Health Ethics Committee and to provide access, upon request, to information in the Institutional Ethics Committee’s records.  
• To provide advice to the Gallipoli Research Foundation on the ethical implications of research grant submissions. |

| REPORTING STRUCTURE & PROCESS | Provides regular feedback to the Executive Management Committee and submit an annual summary report of research activities to NHMRC. |
| Sub committees | Nil |
| Chair | Appointed by the CEO |
| Deputy Chair | Elected annually. Delegated the responsibility of the Chair in the Chair’s absence or if a conflict of interest is perceived. |
| MEMBERSHIP | Director Medical Services  
Assistant Director of Medical Services  
Assistant Director of Clinical Services  
Minister of Religion  
Legal Representative  
Researchers  
Medical Representatives  
Pharmacist  
Laypersons (not associated with institution) x 2 |
| QUORUM | 5 people |
| SECRETARY | Ethics Secretary |
| Frequency of Meetings | Monthly (except for January when there will be no meeting). |
| Formulated | March 1995 |
| Last Revised | January 2019 |
### PERFORMANCE INDICATORS

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Responsibility</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Ethics proposals are tabled on a timely basis.</td>
<td>Ethics Secretary</td>
<td>Monthly</td>
</tr>
<tr>
<td>Annual review of submission approvals and turn-around times.</td>
<td>Ethics Secretary</td>
<td>Annually</td>
</tr>
<tr>
<td>Report annually on compliance with the NHMRC guidelines.</td>
<td>Ethics Secretary</td>
<td>Annually</td>
</tr>
<tr>
<td>The function and outcomes of the Research &amp; Ethics Committee is reviewed quarterly and a written report summarising outcomes of the committee is provided to Executive.</td>
<td>Ethics Secretary</td>
<td>Quarterly</td>
</tr>
</tbody>
</table>
Investigators are responsible for conducting research in accordance with all applicable national and state regulations and specific requirements of the Greenslopes Research Ethics Committee (GREC). During the conduct of the study, changes to the protocol may be proposed, or unintentional changes may be discovered. Changes to the GREC-approved protocol, planned or otherwise, are governed by national regulations and Institutional policies and procedures.

The GREC is required to review proposed changes in a research activity and to ensure that such changes in approved research are not initiated without GREC review and approval, except when necessary to eliminate apparent immediate hazards to the research subject. Research activity includes all aspects of the conduct of the research study, eg. recruitment methods, consent process, procedures used to protect privacy and confidentiality, etc (ie. all of the information outlined in the protocol submission and reviewed and approved by the GREC. Non-compliance with these regulations, policies and procedures, or GREC requirements during the conduct of a research study results is a protocol violation, and as such should be reported to the GREC.

Planned changes to the GREC approved protocol should be submitted as formal protocol amendments to the GREC and should be approved prior to initiation or implementation of the change. Any protocol deviation or protocol violation should be reported to the GREC as outlined below.

**DEFINITIONS:** The following definitions apply throughout this guidance document:

**Protocol Deviation:** Any alteration/modification to the GREC-approved protocol that does not impact on the safety of the subject, compromise the integrity of study data and/or affect the subject’s willingness to participate in the study.

Examples *(the list of examples is intended as a guide and is not all-inclusive)*

- Implementation of unapproved recruitment procedures
- Missing original signed and dated consent form (only a photocopy available)
- Missing pages of executed consent form
- Inappropriate documentation of informed consent, including
  - missing subject signature
  - missing investigator signature
  - copy not given to the person signing the form
  - someone other than the subject dated the consent form
- Use of invalid consent form, ie. consent form without GREC approval, or outdated/ expired consent form
- Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity
- Study procedure conducted out of sequence
- Omitting an approved portion of the protocol
- Failure to perform a required lab test
- Missing lab results
- Enrolment of ineligible subject (eg. subject’s age was 6 months above age limit)
- Study visit conducted outside of required timeframe
**Title:** Protocol Deviations and Violations  

**SOP No.:** 5  
**Version No.:** 1  
**Effective Date:** 12 February 2019

**Protocol Violation:** Any protocol deviation that is not approved by the GREC prior to its initiation or implementation that may impact on the safety of the subject, affect the integrity of study data and/or affect the subject’s willingness to participate in the study.

Examples (the list of examples is intended as a guide and is not all-inclusive):

- Failure to obtain informed consent, ie, there is no documentation of informed consent/informed consent obtained after initiation of study procedures
- Informed consent is obtained by someone other than individuals authorised to obtain consent, eg. someone other than a licensed physician investigator
- Enrolment of a subject who did not meet all inclusion/exclusion criteria
- Performing study procedure not approved by the GREC
- Failure to perform a required lab test that, in the opinion of the PI, may affect subject safety or data integrity
- Drug/study medication dispensing or dosing error
- Failure to follow safety monitoring plan

**REPORTING REQUIREMENTS**

**Protocol violations** - must be reported to the GREC within ten (10) working days of discovery (Note: the Principal Investigator (PI) must review and sign off before being submitted to the GREC).

**Protocol deviations** – must be reported at the time of the annual report to the GREC. These may be reported to the Committee in list format.

- It is the responsibility of the PI to determine whether a deviation or violation has occurred and to ensure proper reporting to the GREC. Reports of protocol deviations and violations should be submitted to the Sponsor as outlined in the Sponsor’s protocol.
Authorised Prescriber Scheme

There are circumstances where patients may require access to medicines, biologicals or medical devices that have not been approved for supply by the Therapeutic Goods Administration (TGA). In these circumstances a medical practitioner may be granted authority to become an 'Authorised Prescriber' of a specified unapproved therapeutic good (or class of unapproved therapeutic goods) to specific patients (or classes of recipients) with a particular medical condition.

Medical practitioners wishing to become Authorised Prescribers submit their clinical justification to a human research ethics committee (HREC) for endorsement prior to submitting the Authorised Prescriber Scheme Application Form to the TGA.

The Greenslopes Research and Ethics Committee (GREC) can review applications from medical practitioners engaged in clinical practice in a Queensland Ramsay Health Care facility. The application should include:

- A cover letter providing complete and accurate information in support of the application including an appropriate clinical justification.
- Name of Medical Practitioner
- Site where goods/device will be used
- Details of unapproved goods
- Copy of informed consent form template to be used for patients prior to prescribing.

On successful review a letter of endorsement will be provided to the applicant for inclusion in their application to the TGA.

If the application to the TGA is unsuccessful you should provide the HREC with a copy of the letter from TGA stating reasons for authorisation not being granted.

See https://www.tga.gov.au/form/authorised-prescribers
REPORTING OF ADVERSE / SERIOUS ADVERSE EVENTS - GUIDANCE NOTES

During clinical investigations, adverse events may occur which, if considered to be serious or unexpected and if suspected to be related to an experimental drug/device, might be significant enough to lead to important changes in the way the drug/device is developed. As a result changes to the clinical trial protocol and/or to the subject information sheet may be required. Therefore, when reporting such events to the GREC, the Investigator must give consideration to the significance of the event and how it impacts on the Hospital/Site’s participation in the trial.

WHAT SHOULD BE REPORTED TO THE GREC?

Events at Queensland Ramsay Hospitals/Sites approved by the Greenslopes Research and Ethics Committee
All related adverse events that occur at hospitals/sites should be reported to the GREC.
Researchers are required to keep a list of all adverse events.

How to Report Adverse Events
All related, or probably related, internal SAEs (occurring in participants at Queensland Ramsay approved Hospitals/Sites) must be reported to the GREC within 72 hours of study staff being notified (or being made aware) of the event using the GREC’s SAE Form.

All other locally occurring events should be reported to the Committee at the time of annual reporting using the GREC’s Annual Questionnaire and Adverse Events Form.

If a serious adverse event occurs at a Hospital/site that results in death, all steps necessary should be taken to ascertain the cause of death and at times this may require a post mortem.

Definitions:
Serious Adverse Event (SAE): A SAE is defined at any untoward medical occurrence, whether it is considered to be related to the study or not, that:
- results in death
- is life-threatening
- requires in-patient hospitalisation (≥24 hours) or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- results in a congenital abnormality or birth defect

 Suspected Unexpected Serious Adverse Reactions (SUSARs): A SUSAR is defined as a SAE which is both suspected as being related to the drug/device and where the nature and severity is not consistent with known information about the drug/device in questions i.e. reasonable suspected causal relationship and unexpected.

Adverse Event (AE): Any expected event as defined in the protocol. This event should be managed by the research team using their risk and safety procedures. The events should be recorded in the case report forms, but there is no reporting requirement to the GREC.

It is the responsibility of Sponsors, Contract Research Organisations, Investigators, Institutions and their delegates, of clinical trials involving therapeutic goods that were approved by the Greenslopes Research and Ethics Committee to comply with the reporting requirements in Safety Monitoring and Reporting in Clinical Trials NHMRC Nov 2016.

When communicating safety information to our HREC the Sponsor, or their representative, must clarify the impact of each report on patient safety, study conduct and study documentation. This may include a list of likely documents that will be forthcoming for submission to the HREC.

Reports should be forwarded as a double-sided paper copy and also emailed in pdf format to researchandethics@ramsayhealth.com.au. These submissions should be copied to the Principal Investigator at the relevant Ramsay site and clearly provide the following details:

- the GPH HREC Reference Number,
- Study Protocol Number,
- Study Protocol Title,
- Name of Principal Investigator with submission.

The Sponsor must ensure that the Principal Investigator has been made aware of any significant updates to safety by being copied into the advice to the HREC.

The Sponsor should advise on the time of the submission how the HREC acknowledgment should be communicated back after committee review. The Principal Investigator should be copied into the acknowledgement response and/or receive the hard copy for filing.

<table>
<thead>
<tr>
<th>REPORT REQUIRED AND TIMELINE</th>
<th>To be reported by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual update of the Investigator’s Brochure (IB). Including any additions to the IB or, where applicable, product information.</td>
<td>Sponsor or representative</td>
</tr>
<tr>
<td>Notification of all Significant Safety Issues that adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.</td>
<td>Sponsor or representative</td>
</tr>
<tr>
<td>Drug/Development Safety Update Reports (DSURs) on an annual basis including a clear summary of the evolving safety profile of the study.</td>
<td>Sponsor or representative</td>
</tr>
<tr>
<td>All related internal SAEs (occurring in GPH participants) must be reported to the HREC within 72 hours of study staff being notified (or being made aware) of the event. An annual summary including related and unrelated internal SAEs to be provided with the Annual Questionnaire.</td>
<td>Principal Investigator</td>
</tr>
</tbody>
</table>
Title: Participant Consent

SOP No.: 9  |  Version No.: 1  |  Effective Date: 12 February 2019

Consent

The following outlines the requirements for written consent which must be obtained prior to participation in a research study as per Chapter 2.2 of the National Statement and TGA Note for Guidance on Good Clinical Practice section 4.8.

- Consent is required for participants that are 18 years and older and able to consent.
- Third party Consent is provided by a Legally Authorised Representative (LAR) when an adult is unable to consent and for participants aged under 18 years.
- If a participant, or that person’s Legally Authorised Representative (LAR) is unable to read, an impartial person must be present during the entire informed consent process and may assist the participant or LAR during that process, such as by reading aloud the informed consent form. As part of the informed consent process the impartial person must attest in writing that the consent form, and any other relevant information, was appropriately explained to and apparently understood by the participant or the LAR, and that informed consent was freely given. (Refer GCP Guideline 4.8.9 and 1.26)
- If the research involves women who are pregnant and the human foetus, children and young people, people in dependent or unequal relationships, people highly dependent on medical care who may be unable to give consent, people with a cognitive impairment, an intellectual disability or a mental illness, people who may be involved in illegal activities, Aboriginal and Torres Strait Islander Peoples or people in other countries, please refer to the NHMRC National Statement on Ethical Conduct in Human Research (2007) – incorporating all updates, Section 4.
- The Principal Investigator is responsible for ensuring that the Participant Information Sheet and Consent Form (PICF) used has been approved by the GREC.

Re-consenting of patients in Long-Term Follow-up:

In keeping with the ICH-GCP 4.8.2 ‘The subject or the subject’s legally acceptable representative should be informed in a timely manner if the new information becomes available that may be relevant to the subject’s willingness to continue participation in the trial’ participants currently enrolled in the follow-up period of a clinical trial in the following cases need not be re-consented.

- It has been approximately 3 months or more since the participant’s last dose of the study treatment and the only PISICF updates are related to study treatment safety information (unless the update is deemed relevant by the investigator) or a part of the study that is irrelevant (such as screening);
- It has been less than 3 months (approximately) since the participant has received study treatment, however there are no updates related to study treatment safety, the follow-up period they are participating in or any generic PISICF sections;
- The participant is involved in the long-term or survival follow-up period only and it is deemed by the Investigator that it is not in the participant’s best interest (such as they have a poor prognosis and under palliative care) to seek re-consenting to the updated PISICF.
- The reason for not re-consenting should be added to the participant’s study file.