STANDARD OPERATING PROCEDURE

HUMAN RESEARCH ETHICS & GOVERNANCE OFFICE (HREG) SOP002 PETER MAC GOVERNANCE REVIEW REQUIREMENTS FOR HUMAN RESEARCH

TARGET AUDIENCE

The target audience is Investigators, Sponsors, Contract Research Organisations and their delegates, of human research projects that are seeking authorisation or that have been authorised to be conducted at the Peter MacCallum Cancer Centre.

RELATED PETER MAC POLICIES, PROCEDURES OR GUIDELINES

POLICY Responsible Conduct of Research

PURPOSE

The purpose of this document is to describe the governance review system implemented by the Peter MacCallum Cancer Centre (Peter Mac) to ensure that human research is conducted safely and responsibly and is scientifically and ethically sound.

This SOP applies to all human research to be conducted at the Peter Mac that required ethical review in accordance with the *National Statement on Ethical Conduct in Human Research (2023 and as amended)* (National Statement). Human research is research conducted with or about people, or their data or tissue. This SOP complies with the requirements set out in the National Statement and the *Australian Code for the Responsible Conduct of Research (2018 and as amended)* and other relevant national and international guidelines and standards.

This SOP applies to the governance review of single site and multi-site ethical review submissions by the Peter Mac Human Research Ethics & Governance office (Peter Mac HREG).

PROCEDURE

A. GOVERNANCE REVIEW OF A NEW RESEARCH PROJECT

A project requiring ethical approval may not commence at Peter Mac until it has also undergone governance review and received authorisation to commence at Peter Mac.

Governance review is the process by which Peter Mac determines that a research project proposed to be conducted at a Peter Mac site is scientifically and ethically sound and can be conducted responsibly and safely. Ethical review and approval of a project for Peter MacCallum Cancer Centre as a site by a reviewing HREC satisfies the requirement that the project is scientifically and ethically sound.

Governance review of a project satisfies the requirement that the project is conducted responsibly and safely. Governance review of projects proposed to be conducted at Peter Mac is undertaken by the Peter Mac HREG and submissions/enquiries should be directed to the Research Governance Officer, Peter Mac HREG. Governance review of new project submissions can occur concurrently with the ethical review.

Governance review is undertaken to ensure that Peter Mac has the appropriate resources, expertise, legal compliance, financial management, accountability and risk management to undertake the proposed project. During the governance review Peter Mac staff and external agencies may be consulted for advice in determining whether submitted documents are acceptable to Peter Mac.

Submission instructions are posted on the Peter Mac HREG website: www.petermac.org/research/research-support-services/ethics-and-governance

B. GOVERNANCE MONITORING OF ONGOING RESEARCH PROJECTS

Once a research proposal has been approved by an Ethics Committee ongoing reporting to the responsible Ethics Committee should be in accordance with the advice of that Ethics Committee (for the Peter Mac Ethics Committee see: SOP004 Monitoring of Ongoing Research and SOP006 Safety Reporting).

Once an ethically approved research proposal has undergone governance review and been issued an Authorisation to Conduct a Research Project at Peter Mac certificate/letter, reporting for governance of ongoing research at Peter Mac is required as outlined in sections 6.2.1 to 6.2.9 below.

Submission requirements for governance monitoring of ongoing research projects are posted on the Peter Mac HREG website: www.petermac.org/research/research-support-services/ethics-and-governance

If the Peter Mac HREG has any queries regarding the amendments or notifications they will communicate with the PI.

All required project reports will be acknowledged. *If the reporting requirement is satisfied by submission to the Peter Mac Ethics Committee, the acknowledgment issued for the report also serves as acknowledgment by Research Governance*.

The Peter Mac HREG maintains an electronic file of all project submissions.

B1: AMENDMENTS

The Peter Mac HREG must be notified of any amendment to an ethically approved project.

The amendment submission must include a detailed explanation on the impact of the amendment on Peter Mac resources. Any change in type or increase in frequency of a service provided by a supporting department must be notified to the supporting department and the signoff/agreement of the supporting department must be included with the amendment submission for governance review.

Once the governance review has been completed and all governance requirements satisfied, an amendment governance approval will be issued to the Principal Investigator. The approved amendment may then commence at Peter Mac.

B2: URGENT AMENDMENT TO A PROTOCOL

An Urgent Amendment is a request for urgent review of a proposed amendment to a protocol. The request for urgency of the amendment review must be adequately justified. Usually this justification will be related to participant safety. The urgent amendment can be for the benefit of all research participants or a specific research participant. The requests usually fall into three categories:

- Request to treat a specific participant outside the protocol requirements
- Request to recruit a specific participant who falls outside the protocol eligibility requirements.
- Safety related protocol changes affecting all participants

The Peter Mac HREG must be notified of any urgent amendments that are approved for research participants at the Peter Mac site as follows:

a) If Peter Mac Ethics Committee is not the reviewing HREC once the Ethical Approval has been issued by the external HREC the Urgent Amendment may then be conducted at Peter Mac. A copy of the request to the external reviewing HREC for the Urgent Amendment and the Approval issued by the reviewing HREC must be submitted to the Peter Mac HREG.

If the external reviewing HREC requests any follow up or action to be taken please forward a copy of these communications to the Peter Mac HREG.

b) If Peter Mac Ethics Committee is the reviewing HREC *this requirement is satisfied by the submission to the Peter Mac Ethics Committee*. For information on the Urgent Amendment request procedures for Peter Mac as reviewing HREC, refer to Ethics Committee SOP004 Monitoring of Ongoing Research.

B3: SAFETY REPORTING

It is the responsibility of Sponsors, Contract Research Organisations, Investigators, Institutions and their delegates, of clinical trials involving therapeutic goods to also comply with the reporting requirements in NHMRC document *Safety monitoring and reporting in clinical trials involving therapeutic goods November (2016 and as amended)*.

Definitions stated in the NHMRC document *Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016* are the governing definitions for Investigational Medicinal Product (IMP) Trials and Investigational Medical Device (IMD) Trials. The Definitions provided below are broader in scope to allow inclusion of clinical research outside the scope of an IMP or IMD trial in this SOP.

Significant Safety Issue (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.
Urgent Safety Measure (USM)	A measure required to be taken in order to eliminate an immediate hazard to a participant's health or safety. *Note: This type of significant safety issue can be instigated by either the investigator or sponsor and can be implemented before seeking approval from HRECs or institutions.*
Adverse Event/Reaction (AE/AR)	Any untoward and unintended response to an investigational medicinal product related to any dose administered
Serious Adverse Event/Reaction (SAE/SAR)	An adverse event/adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect.
Unexpected Adverse Reaction	An adverse reaction, the nature or severity of which is not consistent with the Reference Safety Information (Investigator's Brochure, Product Information or equivalent)
Suspected Unexpected Serious Adverse Reaction (SUSAR)	An adverse reaction that is both serious and unexpected i.e. any untoward and unintended response to an investigational medicinal product related to any dose administered, that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect, the nature or severity of which is not consistent with the Reference Safety Information (Investigator's Brochure, Product Information or equivalent)
Adverse Device Event (ADE)	Adverse event related to the use of an investigational medical device
Serious Adverse Device Effect (SADE)	An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event
Unanticipated Serious Adverse Device Effect (USADE)	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

The Peter Mac HREG must be notified of safety reports for a research project, as follows:

Reporting party	**Report required and timeline**	**Supporting information required**
Principal Investigator or delegate	Notify the RGO of all Significant Safety Issues **occurring at the Peter Mac site** that adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial:	

	I. All **Significant Safety Issues occurring at the Peter Mac site, including Urgent Safety Measures,** should be notified **within 72 hours** of the PI instigating or being made aware of the issue. II. **Significant Safety Issues** often result in safety-related changes to trial documentation. Any resulting **amendment** should be submitted to the reviewing HREC and Peter Mac RGO **without undue delay**. III. **Temporary halt of trial for safety reasons at the Peter Mac site** should be notified **within 72 hours** of the decision to halt the trial. IV. **Early termination of a trial for safety reasons at the Peter Mac site** should be notified without undue delay and **within 72 hours** of the decision to terminate the trial	*I. Details of the significant safety issue; reason for the urgent safety measure; measures taken; further actions planned* *II. Submit amendment* *III. Reasons for the halt; the scope of the halt (e.g. suspension of recruitment or cessation/interruption of trial treatment); measures taken; further actions planned.* *IV. Reasons for the early termination; measures taken; further actions planned*
Principal Investigator or delegate	Notify the RGO of all **SUSARs/USADEs** arising at the Peter Mac site within **72 hours**	*Details of the event, further actions planned, copy of notification to sponsor*

The Peter MacCallum Cancer Centre must notify as follows:

Institution	I. Report any concerns regarding sponsor conduct to the reviewing HREC. II. Notify the Victorian Managed Insurance Authority (VMIA) of any SUSARs/USADEs that occur at the Peter Mac site	*I. Consult HREC for submission advice* *II. Submit per VMIA advice*

B4: SERIOUS BREACH REPORTING

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

i) The safety or rights of a research participant, or

ii) The reliability and robustness of the data generated in the research project.

It is the responsibility of the Principal Investigator (or delegate) to report any suspected breaches to the Sponsor within 72 hours.

It is the responsibility of the Sponsor to determine whether any suspected breach meets the definition of a Serious Breach.

The Principal Investigator (or delegate) must notify the Peter Mac HREG of any Serious Breach at a Peter Mac site within **72 hours** of the Sponsor notifying the Principal Investigator (or delegate) that a Serious Breach has occurred at a Peter Mac site.

For information on the procedures for Peter Mac as reviewing HREC, refer to Ethics Committee SOP004 Monitoring of Ongoing Research.

B5: PROJECT STATUS/INFORMATION UPDATES

The Peter Mac HREG must be notified of the following status/information updates for research projects at Peter Mac.

- Changes in Principal Investigator or Associate Investigators at Peter Mac.
- Termination or suspension of a research project has occurred along with the reason for the termination or suspension**.**
- Changes to a research project, having significant implications for use of Peter MacCallum Cancer Centre resources. *This only is required if there is no amendment that will be submitted to address the implications*.
- Updated Insurance Certificates of Currency for commercially sponsored trials only.

a) If Peter Mac Ethics Committee is not the reviewing HREC a copy of the notification must be submitted to the Peter Mac HREG. It is sufficient to submit a copy of the report as submitted to the external reviewing HREC or to submit in the format normally required for Peter Mac as reviewing HREC.

If the external reviewing HREC requests any follow up or action to be taken please forward a copy of these communications to the Peter Mac HREG.

b) If Peter Mac Ethics Committee is the reviewing HREC *this requirement is satisfied by the submission to the Peter Mac Ethics Committee, if required*. For information on the reporting procedures for Peter Mac as reviewing HREC, refer to SOP004 Monitoring Ongoing Research.

B6: ANNUAL PROGRESS REPORT - PETER MAC SITE

Researchers are required to complete an annual Progress Report for each project where they are named as the Principal Investigator.

a) If Peter Mac Ethics Committee is not the reviewing HREC the Site Progress Report for the Peter Mac site must be submitted to the Peter Mac HREG.

b) If Peter Mac Ethics Committee is the reviewing HREC:

MULTI-SITE ETHICAL REVIEW: Principal Investigator (or delegate) to submit a Site Progress Report for the Peter Mac site.

SINGLE SITE ETHICAL REVIEW: Principal Investigator (or delegate) to submit a Progress Report for Peter Mac site. *This requirement is satisfied by the submission of the progress report to the Peter Mac Ethics Committee in accordance with SOP004 Monitoring of Ongoing Research*.

B7: SITE CLOSURE REPORTS/FINAL REPORTS - PETER MAC SITE

Once a project has been closed at Peter Mac, i.e. no further contact with participants required and no further access to source data/ medical record required, the Principal Investigator must submit a Site Closure Report/Final Report for the Peter Mac site to the Peter Mac HREG.

a) If Peter Mac Ethics Committee is not the reviewing HREC the Site Closure Report/Final Report for the Peter Mac site must be submitted to the Peter Mac HREG. It is sufficient to submit a copy of the report for the Peter Mac site as submitted to the external reviewing HREC.

b) If Peter Mac Ethics Committee is the reviewing HREC *this requirement is satisfied by the submission of the Site Closure Report/Final Report for the Peter Mac site to the Peter Mac Ethics Committee*. For information on the reporting procedures for Peter Mac as reviewing HREC, refer to SOP004 Monitoring Ongoing Research.

B8: COMPLAINTS

Any complaints regarding the conduct of a research project at the Peter MacCallum Cancer Centre should be promptly reported to the Peter Mac HREG, and if required to the reviewing HREC.

a) If reported to an external reviewing HREC please forward a copy of communications with the HREC to the Peter Mac HREG.

b) If Peter Mac Ethics Committee is the reviewing HREC refer to SOP003 Clinical Research Project Queries/Complaints.

B9: AUDITING OF RESEARCH PROJECTS

The Peter Mac HREG may conduct random or targeted audits of approved research projects.

These audits may be carried out by one or a combination of the following methods:

i) a request for information via an audit form,
ii) an interview with researchers.
iii) an examination of any or all records associated with the research project, including completed consent forms and computer files.

Researchers will be given limited notice of an impending audit and will receive written notification of the findings.

B10: WITHDRAWAL OF PROJECT AUTHORISATION AT PETER MAC

In the event of serious deficiencies in the conduct of a research project, deficiencies in reporting, or failure to comply with reviewing Ethics Committee conditions of approval, the reviewing Ethics Committee may withdraw its approval of that project. If the reviewing Ethics Committee withdraws approval for a project, the Peter Mac Project Authorisation is automatically withdrawn.

The Peter Mac HREG may also withdraw Peter Mac Project Authorisation independently of a reviewing Ethics Committee, on behalf of Peter Mac.

In the event that Project Authorisation is withdrawn, the following must occur:

- a memo must be sent to the Principal Investigator informing them of the decision;
- the memo should include a set of conditions for re-activation of Project Authorisation; and
- the researcher is required to stop the project

B11: RE-ACTIVATION OF PROJECT AUTHORISATION AT PETER MAC

Once Project Authorisation is withdrawn, an investigator cannot continue with the research. The research may only continue if and when Ethical Approval has been reactivated by the reviewing HREC and the Peter Mac HREG, has assessed that any reviewing HREC requirements for restarting the project and any Peter Mac requirements for restarting the project at Peter Mac can be complied with by the project team at Peter Mac.

DEFINITIONS

Reviewing HREC	The Human Research Ethics Committee (HREC) that issued the Ethical Approval for the project. Under the multisite review system a NHMRC certified HREC can review and issue ethical approval for a project at multiple sites. This "reviewing HREC" is then responsible for the ongoing monitoring of the project at those sites in accordance with the National Statement.
Multi-site ethical review	A project is reviewed by a reviewing HREC for multiple sites. All required ethics reporting for each site included in the review and approval must be submitted to that reviewing HREC in accordance with the National Statement. However each site included in the review is still responsible for the governance of the project at that site.
Single site	A project is reviewed by the Peter Mac HREC as a single site project for the Peter

ethical review	MacCallum Cancer Centre. The Peter Mac HREC is only responsible for the ongoing monitoring of the project at the Peter MacCallum Cancer Centre in accordance with the National Statement.
Research governance	A site is responsible for the conduct of research at that site. Research governance should address the management of site risk, management of site resources, and any required regulatory reporting.

RESPONSIBILITIES

It is the responsibility of Sponsors, Contract Research Organisations, Investigators, Institutions and their delegates and other staff involved in the conduct of research at the Peter Mac to follow and adhere to this SOP. It is the responsibility of the Human Research Ethics & Governance office to understand and comply with this SOP.

In addition, all research conducted at Peter Mac or by Peter Mac staff which is subject to governance review by the Human Research Ethics & Governance office must conform to the National Statement, the *Australian Code for the Responsible Conduct of Research (2018 and updates)* and other relevant national and international guidelines and standards.

Failure to comply with governance requirements may result in the suspension or withdrawal of authorisation for research conducted at Peter Mac or using Peter Mac resources.

LEGISLATION/REFERENCES/SUPPORTING DOCUMENTS

NHMRC National Statement on Ethical Conduct in Human Research (2023 and as amended)
NHMRC Australian Code for the Responsible Conduct of Research (2018 and as amended)
NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods (2016 and as amended)
NHMRC Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods (2018 and as amended)

AUTHORISED BY

Dianne Snowden, Manager Human Research Ethics & Governance

AUTHOR/CONTRIBUTORS

Dianne Snowden, Manager Human Research Ethics & Governance October 2024