Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

STANDARD OPERATING PROCEDURE

HUMAN RESEARCH ETHICS & GOVERNANCE OFFICE (HREG) SOP004: MONITORING OF ONGOING RESEARCH

TARGET AUDIENCE

The target audience is Sponsors, Contract Research Organisations, Investigators, participating Institutions and their delegates, of human research projects that were approved by the Peter Mac HREC.

STATE ANY RELATED PETER MAC POLICIES, PROCEDURES OR GUIDELINES

POLICY Responsible Conduct of Research

SOP002 Peter Mac Governance Review Requirements for Human Research

SOP006 Safety Reporting

PURPOSE

The purpose of this SOP is to describe the Peter MacCallum Cancer Centre (Peter Mac) Ethics Committee process for monitoring of ongoing research reviewed by the Peter Mac Ethics Committee as the reviewing Human Research Ethics Committee (HREC).

This procedure applies to all research involving humans that has been approved by the Peter MacCallum Cancer Centre Ethics Committee. The reporting covered in this SOP includes amendments, safety reports, progress reports and auditing.

For monitoring requirements for research conducted at Peter Mac that was reviewed by an Ethics Committee other than Peter Mac HREC, refer to SOP002: Peter Mac Governance Review Requirements for Human Research.

This SOP is consistent with the *NHMRC National Statement on Ethical Conduct in Human Research* (*2023 and updates*), the *NHMRC/ARC Australian Code for the Responsible Conduct of Research (2018 and updates)* and other relevant national and international guidelines and standards.

PROCEDURE

Once a research proposal has been approved by the Ethics Committee, ongoing project reporting to the Ethics Committee is required. The Human Research Ethics & Governance office (Peter Mac HREG) receives submissions for the Peter Mac HREC. For submission instructions and required forms refer to the Peter Mac HREG website: www.petermac.org/research/research-support-services/ethics-and-governance

Project reports are required as described below:

1 AMENDMENTS

The Ethics Committee must be notified of any amendment to an ethically approved project.

This includes changes in:
MULTI-SITE ETHICAL REVIEW: Coordinating Principal Investigator or site Principal Investigators;

SINGLE-SITE ETHICAL REVIEW: Principal Investigator.

A full explanation of the scope of the amendment and the rationale for the amendment should be given. Tracked and clean copies of all amended documents should be submitted.

The amendment should be submitted by:

- MULTI-SITE ETHICAL REVIEW: Sponsor or Coordinating Principal Investigator (or delegate), once on behalf of all sites.
- SINGLE SITE ETHICAL REVIEW: Sponsor or Principal Investigator (or delegate) for Peter Mac site.

Single site ethical review amendments should also 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.

Amendments will be reviewed at the next available and suitable Ethics Committee or sub-committee/panel meeting. Administrative amendments will be reviewed by the Peter Mac HREG.

Any queries will be sent to the Coordinating Principal Investigator or Principal Investigator.

When approved, an amendment ethical approval will be issued.

2 URGENT AMENDMENTS

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.

Urgent Amendment requests usually fall into three categories:

i) Request to treat outside the protocol requirements

ii) Request to recruit outside the protocol eligibility requirements.
In accordance with ICH-GCP, a request to recruit outside protocol of eligibility requirements is only permitted if an amendment modifying the eligibility criteria is submitted within 30 days. Please note that although interim approval may be granted, once submitted the amendment will undergo full review at the next scheduled meeting of the Ethics Committee or subcommittee and any queries arising from the review will need to be addressed.

iii) Safety-related protocol changes affecting all participants.
These requests should be submitted as a formal amendment as per section 6.1 above. Please note that although interim approval may be granted the amendment will undergo full review at the next scheduled meeting of the Ethics Committee or subcommittee and any queries arising from the review will need to be addressed.

Urgent Amendments should be submitted by:

- MULTI-SITE ETHICAL REVIEW: Coordinating Principal Investigator (or delegate) on behalf of all sites. A site Principal Investigator (or delegate) may directly request an Urgent Amendment on behalf of their own site.
- SINGLE SITE ETHICAL REVIEW: Principal Investigator (or delegate) for Peter Mac site.

NOTE: The submitting party must demonstrate that the affected Coordinating Principal Investigator and/or site Principal Investigator(s) are aware of the action being requested.

Urgent Amendment Review Procedure

The steps involved are:

1. First, obtain a written statement from the Sponsor that it agrees to the urgent amendment as requested. For Peter Mac-sponsored studies contact **crdo@petermac.org**

2. The CPI or site PI or project delegated treating clinician drafts a short memo addressed to the Ethics Committee detailing the rationale for the urgent amendment and providing an explanation for the changes/variations. The memo must be signed by the CPI or site PI or the delegate.

3. The CPI/site PI or project delegated treating clinician must obtain approval (via signature or email) from their Head of Department and then obtain the approval (via signature or email) of the Chair of the Clinical Research Committee (CRC) or suitable delegate (a member of the CRC able to assess the request).

4. The requested Urgent Amendment is considered approved upon receipt by the Peter Mac HREG of the items set out in point 1, 2 and 3 above.

5. The Peter Mac HREG issues the CPI/site PI an interim approval memo. The Ethics Committee ratifies the interim approval at the next scheduled Ethics Committee meeting and the Peter Mac HREG then issues the CPI/site PI a ratification memo.

3 SAFETY REPORTING

Throughout the life of a research project, safety reports must be submitted for review according to **SOP006 Safety Reporting.**

Clinical trials involving therapeutic goods that were approved by the Peter Mac HREC must also comply with the reporting requirements in the NHMRC document *Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016*.

4 SERIOUS BREACHES

Serious breach reporting replaces Protocol Deviation/Violation 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 Sponsor to determine whether any suspected breach meets the definition of a serious breach.

Third parties may report a serious breach directly to the HREC in the following situations:

- the investigator/institution has good evidence that a serious breach has occurred but the sponsor disagrees with their assessment and is unwilling to notify the HREC
- the investigator/institution has become aware that the sponsor may have committed a serious breach.

The items below required to be submitted to the Peter Mac HREC by the Sponsor or delegate will be acknowledged by the Peter Mac HREC.

The procedure to be followed is provided in the following table.

Reporting party	Report required and timeline	Supporting information required
SPONSOR or delegate	**Serious breaches** should be notified to the HREC **within 7 calendars days** of the sponsor confirming that a serious breach has occurred	*Details of the serious breach* *Impact of the serious breach on any of:* • *Participant safety* • *Participant rights* • *Reliability and robustness of data* *Details of any action taken to date:* • *Investigations being conducted* • *Outcome of investigations* • *How the serious breach will be reported in publications* • *Corrective and preventative actions to be implemented*
SPONSOR	Notify the reviewing HREC if a	*Reason for closure of site*

or delegate	serious breach leads to the closure of a site	*Ongoing plan for site participants* *Implications for other sites, if any*
Third party	Serious breaches can be reported directly to the reviewing HREC	*Details of the serious breach* *Impact of the serious breach on any of:* • *Participant safety* • *Participant rights* • *Reliability and robustness of data*

The Peter Mac HREC must notify as follows:

HREC	Advise TGA (if relevant) and the Sponsor, Investigators and their institutions of any decision to suspend or withdraw ethical approval	*State reasons for the suspension or withdrawal of approval and date of the suspension or withdrawal of approval*
HREC	Inform the Sponsor of any serious breach report from a third party	*Request an explanation from the sponsor*

5 PROJECT STATUS/INFORMATION UPDATES

Progress status/information updates are usually in the form of a letter or memo addressed to the Ethics Committee informing the committee of recent changes to an approved research project. The letter or memo will be noted at a subsequent committee meeting.

Project status updates should be submitted by:

- MULTI-SITE ETHICAL REVIEW: Sponsor or Coordinating Principal Investigator (or delegate), once on behalf of site or all sites.
- SINGLE SITE ETHICAL REVIEW: Sponsor or Principal Investigator (or delegate) for Peter Mac site.

If not submitted as a safety report, in accordance with SOP006 Safety Reporting, a project status update must be submitted in the following circumstances:

- When termination or suspension of a research project has occurred along with the reason for the termination or suspension.

- When there is a significant divergence between actual progress or outcomes and the project's original objectives, hypotheses or expectations. *This only is required if there is no amendment that will be submitted to address the divergence*.

- There have been any changes to a project, having significant implications for project participants or the conduct of the trial. *This only is required if there is no amendment that will be submitted to address the implications*.

<u>These items will be acknowledged</u>.

6 ANNUAL PROGRESS REPORTS

A progress report must be submitted annually to the Ethics Committee. This report includes information about the project at all participating sites included under the Ethics Committee approval.

Progress reports are due annually in the month of the initial ethical approval.

The Ethics Committee has the discretion to request more frequent reporting for specific trials, such as early phase trials. Such a request may be stated on the initial Ethical Approval for a trial or may be instituted during the conduct of the trial.

Progress reports should be submitted by:

- MULTI-SITE ETHICAL REVIEW: Sponsor or Coordinating Principal Investigator (or delegate), to submit a progress report prepared by the project sponsor (or delegate) on behalf of all participating sites.

- SINGLE SITE ETHICAL REVIEW: Sponsor or Principal Investigator (or delegate) to submit a progress report for Peter Mac site.

Failure to submit the annual progress report within 30 days of the due date may result in the suspension of the project by the Ethics Committee.

These items will be acknowledged.

7 SITE CLOSURE REPORTS/FINAL REPORTS

Once a project has been closed at a site, i.e. no further contact with participants required and no further access to source data/medical record required, a site closure report must be submitted to the Ethics Committee. When the overall project is closed at all sites included under the Ethics Committee approval a final report must be submitted.

These Reports should be submitted by:

- MULTI-SITE ETHICAL REVIEW: Sponsor or Coordinating Principal Investigator (or delegate), to submit a site closure report prepared by the project sponsor (or delegate) on behalf of a site.
- MULTI-SITE ETHICAL REVIEW: Sponsor or Coordinating Principal Investigator (or delegate) to submit a final report prepared by the project sponsor on behalf of all sites included under the Ethics Committee approval.
- SINGLE SITE ETHICAL REVIEW: Sponsor or Principal Investigator (or delegate) to submit a final report/site closure report.

These items will be acknowledged.

8 COMPLAINTS

Any complaints regarding the conduct of a research project or the conduct of the Peter MacCallum Cancer Centre Ethics Committee in the ethical review of a research project should be promptly reported to the Peter Mac HREG. Information on how to lodge a complaint can be found on the Peter Mac HREG website and SOP003 Handling Clinical Research Project Participant and Prospective Participant Queries/Complaints.

Complaints reported to the research project team should be submitted by:

- MULTI-SITE ETHICAL REVIEW: Coordinating Principal Investigator (or delegate), once on behalf of site or all sites.

- SINGLE SITE ETHICAL REVIEW: Principal Investigator (or delegate) for Peter Mac site.

Complaints made by project participants and prospective participants or their representatives, such as a family member or carer, must be dealt with according to SOP003 Handling Clinical Research Project Participant and Prospective Participant Queries/Complaints.

These items will be acknowledged.

9 AUDITING OF RESEARCH PROJECTS

The Ethics Committee or its delegate 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 committee's findings.

10 WITHDRAWAL OF ETHICAL APPROVAL

In the event of serious deficiencies in the conduct of a research project, deficiencies in reporting, or failure to comply with Ethics Committee conditions of approval, the Ethics Committee may withdraw its approval of that project. Withdrawal may also occur if it is believed a participant's welfare is compromised in any way.

In the event that approval is withdrawn, the following must occur:

- a memo must be sent to the Coordinating Principal Investigator or Principal Investigator informing them of the Committee's decision;
- a copy of the memo must also be sent to the Research Governance Office of each institution included under the ethical approval;
- the memo should include a set of conditions for re-activation of ethics approval; and
- the researcher is required to stop the project and inform staff and participants that ethical approval of the project has been withdrawn.

11 RE-ACTIVATION OF ETHICAL APPROVAL

Once ethical approval is withdrawn, an investigator cannot continue with the research. The research may only continue if and when conditions, set out by the Ethics Committee, have been satisfied.

This can be done in one of two ways:

- The Coordinating Principal Investigator or Principal Investigator demonstrates to the HREC that the continuance of the research will not compromise participants' welfare and is to be conducted in accordance with the original ethical approval, or
- The research has been modified to provide sufficient protection for participants.

Any modifications made will need to undergo ethical review. The HREC will discuss and consider the corrective steps taken by the Coordinating Principal Investigator or Principal Investigator. Following consideration, the HREC will make a final decision with regards to reinstatement or withdrawal of ethical approval.

The Coordinating Principal Investigator or Principal Investigator and the Research Governance Office of each institution included under the ethical approval will be notified in writing of the HREC's final decision and with reference to the relevant section of the National Statement.

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. These multiple sites will be named in the initial Ethical Approval or be added as an amendment to the initial Ethical Approval. This "reviewing HREC" is then responsible for the ongoing monitoring of the project at those sites.
SINGLE SITE ETHICAL REVIEW	Projects that have been ethically reviewed by the Peter Mac Ethics Committee as a single site project for the Peter MacCallum Cancer Centre. The Peter Mac Ethics Committee is only responsible for monitoring the project at the Peter MacCallum Cancer Centre.
MULTI-SITE ETHICAL	Projects that have been ethically reviewed by the Peter Mac Ethics Committee for multiple sites. The Peter Mac Ethics Committee is responsible for

REVIEW	monitoring the project at all sites listed on the ethical approval.
Coordinating Principal Investigator (CPI)	A CPI must be nominated for each **multisite ethical review** project. The CPI is the contact point for Ethics Committee correspondence. The CPI or project Sponsor (or delegate) is responsible for submitting all documents requiring ethical review during the life of trial to the reviewing HREC i.e. amendments, safety reports, protocol violations/deviations, complaints, progress reports, final reports for all sites. The CPI is usually also the Principal Investigator (PI) for their own site.
Principal Investigator (PI)	**Single site ethical review**: The PI is the contact point for Ethics Committee correspondence. The PI or project Sponsor (or delegate) is responsible for submitting all documents requiring ethical review during the life of trial to the reviewing HREC i.e. amendments, safety reports, protocol violations/deviations, complaints, progress reports, final reports. **Multisite ethical review**: As directed by the Sponsor and/or CPI, the PI is responsible for providing the sponsor and/or CPI with information relating to their study site for submission to the reviewing HREC. The PI is also responsible for submitting to their site Research Governance Officer (RGO) initial governance documents, HREC approved amendments and other reports as required by their site RGO (For Peter Mac see Guideline 001).

RESPONSIBILITIES

It is the responsibility of Sponsors, Contract Research Organisations, Investigators, Institutions and their delegates, conducting research projects that were approved by the Peter Mac HREC and all Peter Mac HREG staff members to follow and adhere to the procedures set out in this SOP.

Failure to comply with Ethics Committee requirements may result in the suspension or withdrawal of Ethics Committee approval for research.

LEGISLATION/REFERENCES/SUPPORTING DOCUMENTS

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

FURTHER INFORMATION

For enquiries related to this Procedure please email ethics@petermac.org
Consult the Peter MacCallum Cancer Centre website**:** Ethics and governance - Peter MacCallum Cancer Centre

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