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# Standard Operating Procedure

| Standard Operating Procedures for the Mater Misericordiae Ltd Human Research Ethics Committee Office Staff | | | |
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**Affirmation**

This governance document is consistent with Mater's Mission, Vision and Values.

# 1 Introduction

## 1.1 Purpose

The procedures in this document describe the role of the Mater Misericordiae Ltd (MML) Human Research Ethics Committee (HREC) and the administrative processes involved in relation to the ethics review of human research.

## 1.2 Scope and context

Human research conducted at MML or for which MML is responsible must be reviewed in terms of scientific and ethical validity and monitored in accordance with documents set out in Section 1.3.

These procedures apply to the conduct of all human research that is carried out in collaboration with MML, Mater Research (MR) facilities, or involving people human tissue and data (medical and personal records or information).

## 1.3 Fundamental guidelines

| Document ID | Document title |
|---|---|
| | NHMRC National Statement on Ethical Conduct in Human Research 2007 (updated 2015) |
| CT-RSH-300000 | Mater Misericordiae Ltd Human Research Ethics Committee (MML HREC) (EC00332) Terms Of Reference |

# 2 Procedure requirements

In general all proposals that do not qualify for exemption from the requirement of full HREC review, expedited review, or a review under exceptional circumstances (as described in section 3.1.4), must be submitted to the MML HREC for approval.

This requirement does not preclude the institution accepting an ethical approval conducted by another certified HREC.

The following procedures are to be followed:

## 2.1 New Applications for Ethical Review

### 2.1.1 Applications for ethical review

- All new applications for ethical review are to be submitted using the Online Forms version of the National Ethics Application Form (NEAF) or Low and Negligible Risk (LNR)or the new Human Research Ethics Application HREA (the HREA may be used for low risk research and greater than low risk)
- All studies with a risk level deemed by the HREC Coordinator and/or Chairperson as more than low risk *(NS 2.1.5-7),* satisfying criteria *National Statement* 5.1.6 (b), or requiring approval of a waiver of consent or an opt-out consent will be placed on the next agenda for full Committee review.
- Applications intended for review at the next HREC meeting must be delivered to the HREC Office by closing time on the closing day for applications. Late submissions will be held over until the following HREC meeting unless the CPI has negotiated the late submission with the HREC Office.

- Only those confirmed as valid applications by the HREC Coordinator or delegate will be placed on the agenda.

- Upon receipt of an application, the HREC Office must check the following:
    - The researcher has generated a submission code in the online forms application which appears in bottom right of the footer;
    - All required signatures are in the application – CPI or PI plus supervisor/s if the PI is a student or undertaking the research for the purpose of a higher degree;
    - Signature pages have the same submission code as the remainder of the document, or there is an accompanying explanation as to why the submission codes are different, and what amendments were made to the application form; and
    - All supporting documentation has been electronically uploaded to the application by the researcher.

### 2.1.2 Low and negligible risk (LNR) research (National Statement 2.1.6, 5.1.18 – 5.1.21)

- Low risk studies that seek participant consent and where the only foreseeable risk is one of discomfort, or negligible risk research in which there is no foreseeable risk of harm or discomfort may be reviewed by one or two HREC members plus the HREC Chairperson or one HREC member, one expert reviewer and the HREC Chairperson.
- Low risk studies requiring a waiver of consent (*National Statement* sections 2.3.9-11 and Section 95, 95A and 95AA of the Privacy Act), or an opt-out consent process (*National Statement* sections 2.3.6-8) and greater than low risk single site research will be reviewed by the full Committee.
- Even where the risk is considered low if described in *National Statement* 5.1.6 (b) it requires review by the full Committee. This includes:
    - *Chapter 3.3: Interventions and therapies, including clinical and non-clinical trials, and innovations*
    - *Chapter 3.5: Human genetics,*
    - *Chapter 4.1: Women who are pregnant and the human fetus,*
    - *Chapter 4.4: People highly dependent on medical care who may be unable to give consent,*
    - *Chapter 4.5: People with a cognitive impairment, an intellectual disability, or a mental illness,*
    - *Chapter 4.7: Aboriginal and Torres Strait Islander Peoples, and some categories of research*
    - *falling under Chapter 4.6: People who may be involved in illegal activities*
- Low risk applications must be submitted using the Online Forms LNR or the HREA. After the application has been completed the researcher should forward an email to the MML HREC office to advise the submission code.
- Additional information may be required before approval.
- All communication between the researcher and the MML HREC office prior to approval is via the Online Forms website and email. A hard copy of the approval letter (as well as electronic) is also provided to the researcher.
- Approval of the research project may be granted between meetings and noted by the MML HREC at the next meeting.
- The decision to grant the waiver of consent, or opt-out consent, and the reasons for the decision, and as appropriate the ethical and legal justification, must be recorded in the HREC approval letter.

### 2.1.3 Exemption from the requirement of HREC approval by the MML HREC

- The NHRMC National Approach recognises the need for Single Ethical Review for Multi-Centre research.
- In recognition of this, Mater Misericordiae Limited (MML) maintains a memorandum of understanding with Queensland Health public sector health services for matters related to HREC

approval. This MOU links Queensland Health facilities, MML, Mater Research and the Mater Research Institute University of Queensland (UQ).

- Therefore, if an application has been approved by another certified lead HREC that conforms with this MOU and lists Mater as a site on the HREC approval, further review by the MML HREC is not required. The application may proceed to the Research Governance Office for site authorisation requirements.
- Research considered exempt from HREC review must satisfy *National Statement* 5.1.22 (a) and (b) and 5.1.23.

### 2.1.4 Research that may be exempted from HREC review

Researchers should write to the HREC Chairperson and justify that their project is exempt in accordance with the National Statement guidance. If the HREC Chairperson agrees the researcher will be provided with a letter advising their project is exempt from the requirement of full ethical review in accordance with section 5.1.22 (a) and (b) and section 5.1.23. These projects are not exempt from the requirement of research governance review and authorisation.

### 2.1.5 Procedure for seeking exemption from HREC review for projects that are not research

- An activity where the primary purpose is to monitor or improve the quality of service delivered by an individual or an organisation is a quality assurance (QA) activity (e.g. an audit of practice against current standards). Terms such as “peer review”, “quality assurance”, “quality improvement”, “quality activities”, “quality studies” and “audit” are often used interchangeably and are considered part of a QA program, as is a project undertaken to understand the service provided (service evaluation).
- Undertaking a QA project does not require HREC approval and formal exemption from the requirement of full ethical review may be granted by the HREC Chairperson. This may occur when the project is recognised as not being research in accordance with the definition of research on page 6 of the *National Statement*.
- The project is registered on AU RED and given an HREC reference number, but should be categorised as a QA project.
- The HREC Chairperson will review the submitted documentation and do one of the following:
  - Consider the project, and provide a letter of exemption from the requirement of further ethical review stating that it does not meet the definition of research ; or
  - After review of the project recommend review by the HREC or sub-Committee because it is research and cannot be exempt from the requirement of ethical review. The researcher will then be required to prepare a NEAF or LNR application and submit under those requirements.
- If considered exempt, the project will be registered in AU RED conclusions as “not requiring HREC review”.
- Exemption from the requirement of full HREC review may be granted for presentations at conferences.
- Exemption from the requirement of full HREC review may be granted for case studies to be published. Many case studies are not research; and form part of clinical care and clinical training and they generally do not require any research ethics oversight. Where multiple case studies are presented they may constitute a case series, a form of research.
- Any presentation or publication outside of MML or MR of resulting information from a QA project requires oversight by the MML Privacy Office.
- Research governance authorisation is not required unless the project is considered research or has a research component however approval from the MML Privacy Office is required for all projects.
- Applicants should always follow hospital policy in regard to clinical governance requirements for National Safety and Quality Health Service Standards and an associated Australian Health Service and Quality Accreditation (AHSSQA) Scheme.

### 2.1.6 Exceptional circumstances

- Applications that may qualify for a review under exceptional circumstances can be made through the MML HREC Coordinator to the Chairperson. These include:
    - studies requiring an urgent review on the basis of maintaining, improving, sustaining or ensuring patient wellbeing and safety;
    - studies requiring an urgent review to identify, reduce, expose or eliminate a real or potential risk or burden to participant safety or wellbeing;
    - the necessity to eliminate an immediate hazard to the research participants;
    - the urgent need for research data where there is an imminent threat to public health and / or
    - the chance to capitalise on a unique opportunity for significant research where there is only a limited time to consider participation.
- The application is first reviewed and assessed for its validity and suitability by the HREC Office and the MML HREC Chairperson. If the MML HREC Chairperson is satisfied that the application qualifies for review under exceptional circumstances, the HREC Chairperson may:
    - Decide that expedited approval may be granted;
    - Refer the application to any other member of the MML HREC or expert reviewers for comment to assist in deciding whether approval should be given;
    - Require amendment of the application; or
    - Refuse to grant expedited approval.

  Exceptional circumstances review may be conducted on single site or multi-site applications.

All levels of review and approval undertaken outside the monthly meeting will be noted or ratified by the full HREC at its next available monthly meeting.

### 2.1.7 The National Approach – single ethical review for multi-centre research

- MML HREC, MML and MR will operate in accordance with certification and as outlined in the NHMRC National Approach to Single Ethical Review of Multi-centre Research and as outlined in the MOU with Queensland Health.

### 2.1.8 Memorandums of Understanding (MOU)

- MML and the MML HREC have formal mutual acceptance/recognition agreements with Queensland Health. The ethics approval procedure is set out in the agreement.
- The following advised procedures will be followed in the case of studies also involving QH sites.

**SOP for QH HREC Administrators (External documents, reference 13)**

Queensland Health advises:

- *Only one HREC review is required for multi-centre research studies being undertaken in Queensland Health and MML.*
- *The HREC review from the MML HREC is accepted throughout Queensland Health for all types of research, and is not restricted to clinical trials.*
- *The MML HREC is not a signatory to the National Mutual Acceptance (NMA) and, therefore the review of the MML HREC will not be accepted in public institutions outside of Queensland.*
- *All participating sites for which the HREC review is valid must be listed on the HREC Approval letter.*

- Outside the context of a formal MOU, MML HREC and individual institutions may still undertake single ethical review of a multi-centre research study in keeping with the *National Statement* Chapter 5.3, and MML HREC TOR Section 3.5.

### 2.1.9 Approving multi-centre research to be conducted at a Mater site when a lead National Mutual Acceptance (NMA) HREC is unable to add Mater as a site

Because MML is not a signatory to the NMA (see 2.1.8) research projects may require the MML HREC to also review and approve the study in order to participate in the research when the lead certified HREC is unable to add Mater as a site. As MML will take full responsibility for the research to be conducted at a Mater site, full HREC review is required.

In general, this type of review is required to approve Catholic wording in a PICF.

A new NEAF or HREA is not required. A letter outlining the reasons for the submission in the light of approval by another Committee and the management of relevant ethical and other issues should be provided. Researchers may submit a copy of the approved application and all supporting documents including site Participant Information Sheet and Consent Form (PICF) to a MML HREC monthly meeting.

### 2.1.10 Multi-centre Studies

- All multi-centre studies must have a Coordinating Principal Investigator (CPI).
- The HREC may communicate with the CPI or nominated Study Coordinator or contact person.
- Multi-centre research applications of all risk levels will be reviewed by the MML HREC in accordance with its certification and the Memorandum of Understanding between MML and QH.

### 2.1.11 Student Research

- Student research includes undergraduate and postgraduate including PhD research for the purpose of a higher degree.
- All students undertaking research at MML or MR require a supervisor.
- If the student's primary supervisor is not an MML or MR employee, this supervisor must nominate a Mater contact.

### 2.1.12 Reviewing research for other private institutions

- Participating sites that will be monitored by the MML HREC must be listed in the application form (NEAF, HREA or LNR). If these sites are private institutions, the following points must be satisfied:
    - Will the private institution accept the review of the MML HREC?
    - Is there an agreement in place between MML and the private institution to allow HREC monitoring of the project in the private institution, including access to patient data?
    - If commercially sponsored research, has the private institution been listed on the Form of Indemnity – HREC Review Only?; and
    - If investigator initiated research, has the private institution offered indemnity to the MML HREC?
- Researchers will be referred to the Research Compliance Officer, Mater Research, to establish the adequacy of agreement / indemnity requirements.

### 2.1.13 Uploading and checking new applications and supporting documents to AU RED

- If the application and supporting documentation have not been uploaded via the Online Forms website, the HREC Office will request that the researcher upload the application and supporting documents. The application will not be validated until all supporting documents have been uploaded by the researcher and may be held over to a future meeting if this cannot be achieved in a reasonable timeframe.
- The HREC Office must check all submitted documentation has correct version details and descriptors when registered on AU RED, so that the approval documentation will be correct and

complete. Where inconsistencies are found, the HREC Office should contact the researcher to notify them that the application will be deemed invalid until corrected.

- Applications must be accompanied by a cover letter and must contain the required number of copies of all documents as specified in the HREC Checklist.
- Photocopying and collating the required number of copies of documents is the responsibility of the applicant and not the HREC Office. If bundles are submitted uncollated, they will be deemed to be invalid until collated by the research team.
- Every application should contain a study proposal or protocol. The application form is not the protocol.
- All studies must be registered in AU RED within two business days of the documentation being delivered to the HREC office. Registration of the study allocates the unique identifying number - HREC number - for the project.
- Guidance on uploading an Online Forms application can be found in the AU RED user Manual, accessed via the *Help* tab in AU RED.
- If there is no submission code on the application it is still in draft format and will be considered invalid. The HREC Coordinator or Administrator will contact the researcher and request they create a submission code for their application and to inform the HREC Office of the submission code to enable uploading into AU RED. The HREC Coordinator can decide whether to request new copies of the application with the submission code on each page (and new signature pages) or accept a statement from the PI or CPI that no changes have been made to the application form between submitting it and later obtaining a submission code.
- The HREC Coordinator or Administrator must ensure that all documents for review by the HREC have been uploaded by the researcher and are listed in the checklist on AU RED. This ensures that the HREC Office receives and has a record of all supporting documentation. Names, dates and version numbers of uploaded documents from this list will also be automatically populated into the HREC approval letter.
- The HREA application form is available at https://hrea.gov.au/. It is not yet available at the Online Forms website. Emailed applications will be accepted and researchers are asked to prepare a "dummy" NEAF via the Online Forms site and request a submission code. The HREA application can then be uploaded together with supporting documentation in the "Documents" tab in the "dummy" NEAF. The submission code is then provided to the HREC Office.
- If the applicant has uploaded their supporting documentation to their Online Forms application, these documents will automatically be uploaded when the HREC Coordinator or Administrator imports the Online Forms application by entering the submission code into AU RED.

### 2.1.14 Validation of applications

**Valid application**

Upon receipt of an application, the MML HREC Office will check that the application meets the criteria for validity. An application is accepted as valid if it meets all the following criteria:

- All documents relevant to the particular application have been submitted electronically and hard copies posted and / or delivered in person (see *Checklist* on the website).
- All relevant sections and questions in the NEAF, HREA or the LNR application are in English and the print is clearly legible.
- Only the signature of the CPI is required on the application, unless the applicant is a student, in which case, the signature of the Student Supervisor is also required.
- The Head of Department is not required to sign the application form.
- The applications may be signed electronically via the Online Forms site by the CPI (multi-centre applications) or PI (single site applications). Applications with original signatures can be submitted. All hard copy signatures should be scanned and uploaded into AU RED.
- Some documents must have original signatures e.g. and Forms of Indemnity.

**Invalid application**

Applications are invalid when:

- Discrepancies are present e.g. the submission code is not on the NEAF, the NEAF or HREA is incomplete, online and other provided copies are not the same.
- The required relevant supporting documentation, such as protocol, information sheet and consent form, questionnaires and other tools, are not submitted with the online NEAF / LNR.
- The documentation is not signed.

The decision whether or not an application is valid may be made by the MML HREC Coordinator, although if in doubt the HREC Chairperson would be consulted.

For invalid applications the PI will then be notified by the MML HREC Coordinator that:

- The application will not be accepted for the next meeting and that the application will require further documentation prior to HREC review, or
- The PI must supply further information in relation to an application by a specific date for the application to be reviewed at the next meeting.

An email acknowledging receipt of the application and notifying the applicant if the application is 'valid' and able to be reviewed, or 'invalid' and requires amendment and/or additional documentation, will be sent by the HREC Administrator in the week following the relevant closing date. The acknowledgement email includes the specific identifying number allocated to the protocol.

### 2.1.15 Allocation of applications for full ethics review

- The HREC Coordinator in consultation with the HREC Chairperson will allocate each valid application to a minimum of two HREC members to lead the review.
- Additional expert review may be sought from a panel of expert reviewers.
- All applications will be made available to reviewers in hard copy and electronically on the AU RED Members' Portal.
- When an application has been assigned to a meeting a letter/ email should be sent to the investigator, by the reviewing HREC, notifying them of the need to attend the meeting if required.

### 2.1.16 Revision of applications following submission

- Once a valid application has been made, no revisions may be made prior to HREC review except with the approval of the HREC Chairperson.
- If the applicant considers it necessary to revise the application form or the supporting documentation prior to review by the HREC, the applicant must justify their request to the HREC Chairperson who then makes one of two determinations:
    - review of the study should proceed, or
    - the study should be withdrawn and resubmitted at a later date.

### 2.1.17 Withdrawal of applications

If an applicant withdraws an application at any time, the application should be treated as no longer valid and the 60 day time frame will no longer apply. If the applicant wishes to re-submit the application, it should be treated as a new submission.

## 2.2 MML HREC meetings

### 2.2.1 Meeting frequency (*National Statement* sections 5.1.37, 5.2.28 – 5.2.31)

- Meetings will be held monthly, except for January when there will be no scheduled meeting (*National Statement* section 5.1.37).
- A timetable for meetings will be prepared by the MML HREC office and endorsed by MML HREC Chairperson and committee members prior to its circulation by November of the preceding year. Meeting dates, closing dates and checklist will be published on the MML website.

### 2.2.2 Agenda

- The agenda will include the date, time and venue for the meeting;
- Members will be provided minutes of the previous meetings;
- A hard or electronic copy (AURED Members' Portal) of the applications for consideration will be made available to members approximately 12 days before the meeting, except in exceptional cases decided by the Chairperson where submissions or items for discussion may be tabled at the meeting.
- New applications are provided in hard copy to lead reviewers. All other members may view the application electronically on the AU RED Members' Portal online website.

### 2.2.3 Standing agenda items include:

- Welcome
- Reflection
- Apologies
- Statements of disclosure
- Confirmation of minutes
- Items for discussion
- Business arising from minutes
- Submissions
    - Status of studies
    - Late tabling
    - Resubmissions of proposals previously considered
    - New proposals for review
        - New proposals – expedited approval between meetings as per *National Statement* Chapter 5.3
    - Changes to approved projects – amendments for review
    - Minor amendments of approved protocols (approved by HREC Chairperson between meetings – for information only)
    - Low or negligible risk research projects (LNR)
        - LNR applications approved between meetings – for information only
        - LNR submissions requesting a waiver of consent either approved between meetings or for discussion at the meeting
        - LNR invalid applications – for information only
- Investigators brochures for review
- Protocols exempt from ethical review – for information only
- Serious adverse events and safety data review
- Protocol Violations
- Progress Reports
- Items for Noting
- General Business

- Date Time and Place of Next Meeting

### 2.2.4 Lead reviewers

- The MML HREC Coordinator in consultation with the MML HREC Chairperson appoints two or more lead reviewers for each new application.
- The HREC Chairperson and Coordinator will determine if additional expert review may be required at the time of allocation of studies to lead reviewers.

### 2.2.5 Expert reviewers – internal or external

- The MML HREC may seek the written advice of an expert reviewer on any aspects of an application that are relevant to the formation of an ethical decision, and which lie beyond the expertise of the members or on which the Committee is unable to agree. This may necessitate going outside the membership of the HREC. These expert reviewers may be specialists in ethics, specific diseases or methodologies, or they may be representatives of communities, patients or special interest groups.
- For multi-centre research, the opinion of the external expert may not be used to allow the HREC to review research outside of its NHMRC certification categories.
- For commercially sponsored studies, the cost of an external expert review (if applicable) may be borne if agreed, by the sponsor.
- Advice from expert reviewers may be sought at any time by the HREC.
- Expert reviewers are not voting members of the HREC, and will not be involved in the business of the Committee other than that related to the application on which their advice is sought.
- Communication between the MML HREC and the expert reviewer about the substance of the study is conducted by the MML HREC Chairperson or MML HREC Coordinator after first ensuring that the reviewer does not have any conflicting interests or other matters to declare which would affect their ability to objectively review the submission.
- A signed Confidentiality Agreement and Conflict of Interest Disclosure Statement are required prior to an expert advisor being appointed. Conflicts of interest should be disclosed as they arise or are recognised.
- A copy of the advice received will be made available to members prior to the meeting on the AU RED Members' Portal or tabled at the meeting. The substance of the advice should be recorded in the minutes.

### 2.2.6 Attendance of the PI or CPI at the meeting

- At the request of the HREC, after discussion with the Chairperson, the CPI or PI may be invited to attend a meeting (in person or remotely) at which his/her application is to be reviewed, or at a subsequent meeting. The purpose of this meeting is for the CPI or PI to respond directly to requests from the Committee for further information, clarification or reassurance but would be required to leave the meeting before a decision is made on the outcome. It is not the purpose of the CPI or PI's attendance to make a formal presentation of the study,
- Where the CPI or PI is unable to attend, it is acceptable for another key investigator or collaborator to attend in their place. It is not ethically acceptable for a representative of the sponsor to attend in place of the CPI or PI. Other members of the research team or representatives of the sponsor may also express an interest in attending alongside the CPI or PI and may do so at the discretion of the Chairperson.
- In the case of applications submitted by students, the HREC should consider inviting the academic or clinical supervisor.

### 2.2.7 Minimum membership requirements and meeting attendance (*National Statement* section 5.1.29 – 5.1.30)

- The minimum membership is made up from six (6) categories (a to f):

  a) *a chairperson, with suitable experience, whose other responsibilities will not impair the HREC's capacity to carry out its obligations under this National Statement;*
  b) *at least two lay people, one man and one woman, who have no affiliation with the institution and do not currently engage in medical, scientific, legal or academic work;*
  c) *at least one person with knowledge of, and current experience in, the professional care, counselling or treatment of people; for example, a nurse or allied health professional;*
  d) *at least one person who performs a pastoral care role in a community, for example, an Aboriginal elder, a minister of religion;*
  e) *at least one lawyer, where possible one who is not engaged to advise the institution; and*
  f) *at least two people with current research experience that is relevant to research proposals to be considered at the meetings they attend. These two members may be selected, according to need, from an established pool of inducted members with relevant expertise.*

- Where there is less than full attendance of the minimum membership at a meeting, the Chairperson must be satisfied, before a decision is reached, that the views of those absent who belong to the minimum membership have received all papers and have had an opportunity to contribute their views and that these have been recorded and considered.
- The MML HREC Chairperson can reschedule a meeting, convene additional meetings to consider urgent matters or as workload necessitates, or cancel a meeting if there is insufficient business or if unable to constitute a quorum.
- All applications may be reviewed on the AU RED Members' Portal. Members can upload their reviews for all other members to read and make comment on. If a meeting is cancelled review using this electronic media makes it possible to review and approve new projects in the 60 day clock period and not cause unnecessary delay for the researcher/s.
- Members who are unable to attend a meeting will be encouraged to contribute and advise their opinion via electronic submission on the AU RED Members' Portal or by email to the Chairperson or HREC Coordinator prior to the meeting.
- If members are unable to attend three or more consecutive meetings they should consider their availability to remain on the MML HREC.
- Members must contact the HREC Chairperson to request a leave of absence.

### 2.2.8 Conflict of interest

- Members of the Committee and observers will be required to declare any conflict of interest prior to or at any time during a meeting.
- When a research application involves a Committee member or observer, that member or observer will be required to leave the meeting prior to discussion taking place.
- Members are required to disclose any actual or potential conflicts of interest, which exist or may arise during tenure on the MML HREC, and that bears on any research coming before the review body [*National Statement* section 5.2.4]. This includes any:
  - Personal involvement or participation in the research;
  - Financial or other interest or affiliation, or
  - Involvement in competing research [*National Statement* section 5.4.5]
- Declarations of any conflicts of interest by members, expert reviewers and observers are called for at the beginning of each meeting.
- Where such disclosure is made the Chairperson will determine, with the assistance of the Committee, the action to be taken, including exclusion from the meeting, or from some or all of the deliberations [*National Statement* section 5.4.5].
- The outcome and the action taken by the Committee is recorded in the Minutes.

### 2.2.9 Confidentiality of proceedings

- The Agenda; content of applications, documents associated with submissions, proceedings and all discussions of the meeting, or HREC sub-Committees of the full Committee; expert reviews and identity of reviewers, and Minutes will remain confidential and confined to the Committee, those responsible for the administration of the HREC Office and those with authority to access the HREC AU RED database and Members' Portal.
- Before appointment to the MML HREC, members acknowledge in writing their acceptance of the Terms of Reference of the Committee and any requirements for confidentiality required by MML.
- Members are required to sign an agreement and declaration at the time of appointment and thereafter every three (3) years or earlier should their situation change, undertaking that all matters of which members, observers or expert reviewers become aware in the course of involvement with the MML HREC will be kept confidential.
- Observers are required to sign a declaration prior to the commencement of the meeting undertaking that all matters of which they become aware of in the course of the meeting will be kept confidential.
- Expert reviewers are required to sign an agreement to maintain confidentiality of all documents provided to them by the HREC office.

### 2.2.10 Conduct of business and decision-making

- The Chairperson is responsible for the conduct of the business and for ensuring that the Committee reaches clearly agreed decisions on all matters. In the absence of the Chairperson, the Deputy Chairperson will perform the duties of the Chairperson: i.e. chairing the meeting and/or fulfilling the other duties of the Chairperson as set out in the Position Description.
- In the absence of both the Chairperson and Deputy Chairperson, the Chairperson or HREC Coordinator may appoint an Acting Chairperson to chair the HREC meeting.
- All members present, both expert and lay, should be allowed reasonable opportunity to express relevant views on matters on the agenda. As per Section 5.2.30 of the *National Statement*, the written opinions of absent members should be tabled at the meeting and considered as part of the deliberation of a research project.
- The HREC should endeavour to reach decisions by general agreement (Section 5.2.31 of the *National Statement*). Generally, the minutes will record discussion of significant issues and the decision given.
- Where any member wishes to record his/her formal dissent from the Committee's decision, this should also be recorded in the minutes.

### 2.2.11 Decisions available to the HREC (National Statement section 5.2.21)

The *National Statement* advises: *"a review body may approve, request amendment of, or reject a research proposal on ethical grounds".*

- It is the role of the HREC Chairperson to ensure one of these decisions has been reached.
- It is the role of the HREC Coordinator to clearly minute the decisions reached and record or collate any further information requested by the Committee.
- Questions or issues raised should be linked by members and reviewers to the relevant section of the *National Statement*.
- Decisions by the Committee about whether the research project meets the requirements of the *National Statement* must be informed by the exchange of opinions from each of the members that constitute the minimum membership of the MML HREC.

### 2.2.12 Reporting responsibilities of the HREC Chairperson

- The MML HREC Chairperson reports to the MML Group CEO regarding the constitution and function of the Committee, associated processes and the ethical acceptability of research applications submitted for consideration;
- The MML HREC Chairperson operationally liaises with the CEO/Director MR relating to Mater researchers and research services and functions where the Chairperson considers no material conflict of interest exists.

### 2.2.13 Responsibilities of the HREC Coordinator

- The secretary to the meeting will be the HREC Coordinator or delegate.
- The responsibilities of the HREC Coordinator in relation to HREC meetings includes the following activities:
    - publish the schedule of HREC meetings;
    - manage the preparation of the agenda;
    - allocate lead reviewers, in conjunction with the HREC Chairperson;
    - arrange for distribution of the agenda and papers;
    - invite CPI's, PI's and, where appropriate, supervisors to attend the meeting and making the necessary arrangements;
    - manage the preparation of the venue;
    - record apologies for absence prior to the meeting;
    - raise with the Chairperson any concern that a meeting may not be quorate;
    - record attendance by members and referees for the discussion of each application for ethical review;
    - advise the meeting as necessary on compliance with Terms of Reference, relevant policy or standard operating procedures;
    - take the Minutes of the meeting for review and approval at the following meeting
    - forward draft Minutes to the Chairperson within 48 hours of the meeting;
    - finalise the Minutes within four (4) working days of the meeting;
    - forward HREC recommendations, usually in the form of the relevant meeting minute, via AU RED email to researchers within four (4) working days of the HREC meeting, or notify researchers of a delay and the expected timeframe for completion of the review/minute;
    - advise the researcher/s how to submit their response i.e. by email and / or hard copy to the MML HREC office and providing both tracked and clean documents with revised version details.

### 2.2.14 Minutes

- The minutes of the HREC meeting should be prepared by the HREC Coordinator or delegate in consultation with the Chairperson and other members as necessary, and approved by the HREC Chairperson within three (3) days following the meeting.
- The minutes of the HREC meeting should be uploaded and saved in AU RED under the relevant meeting documents tab.
- In relation to applications for ethical review or notices of substantial amendment, the minutes should contain an accurate record of the following, whether in the main text of the minutes or in attachments:
    - the members and external expert reviewers present for the review;
    - any conflicts of interest declared, and the decision of the Committee regarding the allowable level of participation of the member concerned;
    - the submission of reviews by members;
    - the substance of any advice given by an expert reviewer;
    - the decision of the HREC regarding the application;

- a summary of the main ethical issues considered and referenced to the *National Statement*;
- in the case of further information being requested, any special approval conditions or additional advice to be given to the applicant; as well as the arrangements for considering the information and confirming the final decision of the HREC;
- where a deficiency is identified by the HREC or additional information is required, the HREC may recommend the HREC Chairperson or another delegate approve the proposal on behalf of the full Committee when the HREC Chairperson or delegate is satisfied that the deficiency has been addressed or the additional information has been provided;
- in the case of a "Not Approved" decision (also known as rejected), the reasons for the decision with reference to the *National Statement*;
- where the opinion of an external expert is sought, the issues on which further advice is required; and
- any formal dissent from the decision of the HREC by a named member, with reasons for their dissent.

- The MML HREC provides unconfirmed minutes of each Committee meeting to Mater Misericordiae Ltd Group Executive Committee, once approved by the Committee Chairperson for distribution.
- The minutes should be submitted to the next meeting of the HREC for ratification and to be signed by the Chairperson as a true record. Any necessary revisions should be incorporated in the final version of the minutes, which should be signed and dated by the HREC Chairperson.
- Where a deficiency is identified by the MML HREC or additional information is required, the MML HREC may recommend the HREC Chairperson or another delegate to approve the minutes as confirmed on behalf of the full Committee when the HREC Chairperson or delegate is satisfied that the deficiency has been addressed or the additional information has been provided.
- The minutes are confidential to the HREC and should not be disclosed to applicants, sponsors or host organisations. In addition the Minutes may be provided to the MML Board of Directors if requested.

### 2.2.15 Delegation of responsibility by the MML HREC

- Where the MML HREC requests further information from the researcher/s it should decide at the meeting the process for reviewing the response i.e. the Chairperson or delegate (i.e. Deputy or Acting Chairperson) may approve on behalf of the Committee; a sub-Committee of the HREC may review responses either electronically on the AU RED Members' Portal or in a face-to-face meeting with or without the researcher/s present; or further full Committee review at the next available meeting after the researcher/s have provided responses.

### 2.2.16 Meetings with researchers

- The MML HREC and HREC Office encourages informal communication with researchers and face-to-face meetings to encourage good understanding of research ethics, submission requirements and discourage delays in approval due to miscommunication or misunderstanding of these requirements.
- If a study does not receive approval researchers are invited to a sub-Committee meeting to discuss and plan a way forward should they wish to resubmit a new application in the future.

### 2.2.17 60 day clock - time period to HREC approval

- The clock starts when a new application is validated. The clock runs until the study has been approved and the approval letter signed and sent / emailed. If the researcher is asked questions the clock stops when those questions are sent. The clock will re-start immediately the "response to further information" is received and actioned in AU RED. All research ethics applications should be approved within this 60 day time period.

- LNR applications may be completed in a shorter time frame as they are reviewed between meetings however this is not the case for all LNR applications as some require full Committee review.
- Applications for exemption from the requirement of full HREC review should generally have a decision made within a two (2) week time frame.

### 2.2.18 Approval of an application

- The MML HREC approval letter is based on the NHMRC templates.
- The letter includes standard conditions of approval and:
    - a list of all documents approved and the sites where the research will be conducted in the case of a multi-centre application or when the research is not being conducted at MML or MR;
    - period of approval;
    - date of first progress report and any specific reporting requirements; and
    - specific approval such as a waiver of consent in accordance with the Privacy Act.
- The letter is signed by the HREC Chairperson or delegate (i.e. Deputy or Acting Chairperson).

### 2.2.19 When the application is not approved

- The MML HREC provides a detailed explanation referencing the *National Statement*. The researcher/s is/are invited to a meeting to discuss.
- Researcher/s may choose to submit a new application taking into account the HREC recommendations.
- Researcher/s may choose to submit to another HREC however in accordance with questions raised in the NEAF, should provide the new reviewing HREC a copy of the initial review.

## 2.3 Other considerations

### 2.3.1 Studies requiring Queensland Civil and Administrative Tribunal (QCAT) opinion

- Sections 65, 68, 72 and 74 of the *Guardianship and Administration Act 2000 (Qld)* cover participation in "special medical research or experimental health care".
- In accordance with the designation of the study under this definition, the PI (or CPI for multi-centre research) is required to obtain approval from the Queensland Civil and Administrative Tribunal (QCAT) in circumstances where the participant of the trial may be, by reason of physical or mental incapacity, incompetent to give informed consent to participate in the study. This approval process occurs after HREC approval and forms part of the governance process.
- The *National Statement* provides guidance on obtaining consent where capacity to provide consent is limited or non-existent whether it is considered to be temporary or permanent.
- For persons under the legal age of consent, written approval must be obtained from the person's parent(s) or guardian(s). Where a person is over the legal age of consent but is unable to provide informed consent for participation, written application to the QCAT must be undertaken.
- Approval from QCAT does not provide consent for a person who has impaired decision making capacity to participate in a research project. QCAT Approval determines whether a clinical trial is appropriate for a person of impaired decision making capacity to participate in. However, consent for participation is still required from the Legally Authorised Representative (Substitute Decision Maker).

### 2.3.2 Clinical Trial Notification Scheme (CTN) and Clinical Trial Exemption Scheme (CTX)

- HREC's play an important role in the regulation of the supply of unapproved goods under the *Therapeutic Goods Act 1989* in connection with the operation of clinical trials (both CTN and CTX schemes), the "Special Access Scheme" and approval of "Authorised Prescribers".
- Unapproved therapeutic goods have undergone little or no evaluation of quality, safety or efficacy by the Therapeutic Goods Administration (TGA). These products are considered to be experimental and potentially carry some risks that have not been defined in the Australian context. HREC's should be guided by the principles outlined in the *National Statement* in assessing the risks and precautions in research involving humans.
- HREC roles and responsibilities are in accordance with the Therapeutic Goods legislation.
- This section should be read in conjunction with the *National Statement*, Chapter 3.3: Interventions and Therapies, including clinical and non-clinical trials, and innovations and *Good Clinical Practice (GCP) Guidelines.*

### 2.3.3 Research involving coronial material

- Research involving access to coronial material must be referred to the Queensland Forensic and Scientific Services Human Research Ethics Committee for ethical and legal approvals.

### 2.3.4 Indemnity

- The MML Board of Directors accepts legal responsibility for decisions made and advice given, and indemnifies all members of the HREC, sub-Committees of the HREC and expert reviewers appointed to advise the HREC against liabilities incurred as a result of carrying out authorised HREC tasks.
- For research which is not being conducted at MML, which is being undertaken by non-affiliated researchers, and where an MML or MR employee has not been nominated as a Principal Investigator or Mater contact:
    - The MML HREC must be provided with independent legal indemnity;
    - Documentation of legal indemnity must be provided to the MML legal counsel prior to the external study being considered for independent ethics review.

## 2.4 After approval

### 2.4.1 Updated safety information

- The principles of ICH GCP state: *"Amendments, safety and other reports may be reviewed and approved, actioned or noted by the Chairperson between meetings. Substantial amendments or serious safety issues may require full Committee review and / or subsequent ratification".*
- The MML HREC acts in accordance with the NHMRC Framework for Monitoring: Guidance for the national approach to single ethical review of multi-centre research, January 2012, Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods, November 2016, Mater policies and other external guidance.
- Amendments or safety reports requiring an urgent review to identify, reduce, expose or eliminate a real or potential risk or burden to participant safety or wellbeing are reviewed in accordance with this Procedure section 2.1.6 Exceptional Circumstances.
- *National Statement* section 3.3.22 directs that the researcher/s *"(e) informs the HREC as soon as possible of any new safety information from other published or unpublished studies that may have an impact on the continued ethical acceptability of the trial or may indicate the need for amendments to the trial protocol; and (f) informs the HREC, giving reasons, if the trial is discontinued before the expected date of completion".*

### 2.4.2 Amendments to research studies – single site and multi-centre

- Investigators are required to obtain ethical approval and research governance authorisation of amendments before they may be implemented to a previously approved study.
- Investigators should submit one hard copy of all documents and also email to the MML HREC Office.
- The majority of amendments may be reviewed and approved by the MML HREC Chairperson between meetings and will be noted or ratified at the next HREC meeting.
- If further information is required the MML HREC Office will email the investigator/s and after satisfactory response, approval may then be granted.
- Documents to include are:
    - Covering letter explaining the rationale for the amendment;
    - Documents that have been changed must be submitted in both tracked change and clean copies including new version numbers and dates in the footer of these documents;
    - Progress report if one has not been submitted in the previous 12 months; and
    - Confirmation of invoicing details if the research is sponsored by a pharmaceutical company.

### 2.4.3 Expansion of approval

**Multi-centre amendment to include another site**

Required documents:

- Covering letter briefly outlining the expansion to additional site/s and reasons for expansion;
- CPI advice to the HREC that no other changes have been made to the NEAF except for adding the new investigator/s and site/s;
- Updated online NEAF to include new site/s and investigator details with new submission code (a hard copy of the updated NEAF is not required however the new submission code should be included in the covering letter); and
- CV/s for additional investigator/s if not submitted to the MML HREC within the previous two years.

### 2.4.4 Substantial amendments

- Substantial amendments will be carefully considered by the HREC Chairperson for validity.
- If an amendment will fundamentally alter the nature of the research e.g. change in the primary purpose, and the extent of the involvement of, or risk to, existing and / or potential participants, the HREC may recommend the amendment not be approved and a new application be submitted.
- Substantial amendments that can be validated may be added to the next available HREC agenda for full Committee consideration and / or ratification of the HREC Chairperson's recommendation.

### 2.4.5 Urgent safety amendments

- Refer to sections 2.4.1 and 2.1.6

## 2.5 Other types of applications

### 2.5.1 Authorised prescriber

The HREC may review 'other' applications in accordance with the Therapeutic Goods Administration (TGA) Guidelines, *Human Research Ethics Committees and the Therapeutic Goods Legislation June 2001.* The following categories of 'other' application include but are not limited to:

- Submission to Access Unapproved Products;
- Requests to become Authorised Prescriber; and

- Request for ethics review of Special Access Scheme applications.

## 2.6 Monitoring research (*National Statement* Chapter 5.5)

### 2.6.1 Reporting

Where the MML HREC is the reviewing (lead) Committee, the CPI or site PI is required to conform to conditions set out in the formal approval letter as outlined below:

**Study commencement**

- Research should commence within 12 months of HREC approval. Researchers are responsible for notifying the HREC of their commencement date (post research governance authorisation) e.g. advertising or screening for participants, commence data collection.
    - If the research has not commenced within 12 months the CPI/PI should provide the HREC with a written explanation for the delay. The HREC may decide to extend the approval period, or not.

**Progress**

- At a minimum, researchers must submit an annual progress report or more frequently as directed by the HREC.
- The progress report is due on the anniversary date of the HREC approval, and not 12 months after commencement of the study at any of the sites.
- In investigator initiated research the role of the CPI is to submit a collated annual report including information from all sites listed in the HREC approval letter.

If the research is sponsored it is the role of the sponsor or CRO to collate the progress from each site and submit to the CPI for review by the HREC.

**SAE / SUSAR / Safety**

**The NHMRC advises in Safety monitoring and reporting in clinical trials involving therapeutic goods:**

*The sponsor, through their independent safety monitoring arrangements, has the primary responsibility for monitoring the ongoing safety of the investigational medicinal product. The HREC should be satisfied that the sponsor's arrangements are sufficiently independent and commensurate with the risk, size and complexity of the trial.*

*The HREC should:*

*a. assess the safety of proposed trials, including whether the evaluation of the anticipated benefits and risks is satisfactory and ensure that the sponsor has proportionate systems in place to mitigate and manage any identified risks*

*b. satisfy itself that the sponsor's ongoing safety monitoring arrangements are adequate, including the justification for appointing/not appointing a Data Safety Monitoring Board and any 'stopping rules' or criteria for withdrawing individual participants from the trial*

*c. keep under review the adequacy and completeness of the informed consent process and documentation in the light of new information about risks and benefits*

*d. assess whether changes to the risk-benefit ratio that are reported by the sponsor are compatible with continued ethical approval*

*e. advise the TGA, investigators and their institutions of any decision to withdraw approval*

*Note: While HRECs must keep approvals under review in light of safety information it receives, the responsibility for proactively monitoring the ongoing risk-benefit ratio of the trial remains with the sponsor at all times.*

*Investigators should assess all local safety events and should act on any events as clinical care dictates. The role of the investigator with regard to safety reporting is to provide the sponsor with all relevant information so that an appropriate safety analysis can be performed.*

*The Principal Investigator should:*

a. *capture and assess all AEs that occur at the site as required and in accordance with the protocol*
b. *report to the sponsor **within 24 hours of becoming aware of the event**:*
    - *all SAEs, except those that are identified in the protocol as not needing immediate reporting*
    - *any occurrences of congenital anomaly/birth defect arising from any pregnancy of a participant (or partner)*
    - *all urgent safety measure instigated by the site*
c. *report to the sponsor as specified in the protocol:*
    - *all safety critical events*
    - *any additional requested information relating to reported deaths*
d. *report to the institution **within 72 hours** of becoming aware of the event:*
    - *all significant safety issues*
    - *SUSARs20 arising from the local site.*

*An institution's responsibilities and oversight of safety information in clinical trials will differ depending on whether they are hosting externally sponsored clinical trials or sponsoring locally led non-commercial trials. In both cases they should help ensure that their site(s) understands and complies with sponsor requirements. Institutions should have oversight of any issues that may require management, such as disputes or litigation resulting from trials. Where the institution is also named as the trial sponsor, the institution will also assume the sponsor responsibilities set out in this document.*

*The Institution should:*

a. *assess whether any safety reports received impact on medico-legal risk, the responsible conduct of research, adherence to contractual obligations or the trial's continued site authorisation and, where applicable, facilitate the implementation of corrective and preventative action*
b. *develop clear guidance for investigators detailing the requirements for safety reporting and monitoring in clinical trials. This document(s) should cover the requirements for both externally sponsored clinical trials and, if applicable, internally sponsored investigator/initiated or collaborative group trials.*

**Investigator initiated trials where MML will take responsibility as the Sponsor:**

The NHMRC guidance on Safety Monitoring indicates that '*The sponsor, through their independent safety monitoring arrangements, has the primary responsibility for monitoring the ongoing safety of the investigational medicinal product.'*

**Before the HREC provides ethical approval of a clinical trial it must be assured that '***the sponsor* **(MML)** *has proportionate systems in place to mitigate and manage any identified risks'* **and** "*assess the safety of proposed trials, including whether the evaluation of the anticipated benefits and risks is satisfactory" and "ensure that satisfy itself that the sponsor's ongoing safety monitoring arrangements are adequate, including the justification for appointing/not appointing a Data Safety Monitoring Board and any 'stopping rules' or criteria for withdrawing individual participants from the trial"* **are in place. (3. Responsibilities of the HREC). This information should be included in the HREC application.**

**Protocol violations (*NHMRC Framework for Monitoring, January 2012*)**

*'The distinction between protocol violations and protocol deviations is neither clearly understood nor consistently applied amongst Australian HRECs, but, for the purposes of this document, protocol violations are those variations to a protocol that implicate participant consent, participant safety or data integrity that compromises the ethical acceptability of the project, and, thus, require retrospective notification to or review by a HREC, whereas protocol deviations relate to other matters and do not require notification to or review by a HREC. This definition is consistent with ICH/GCP taxonomy.'*

- The definition of protocol violation applicable to this Procedure is consistent with the extract above and with ICH GCP taxonomy which emphasises the potential for safety or efficacy implications, rather than a requirement for them to eventuate.
- The CPI/PI is responsible for reporting all protocol violations to the reviewing HREC.
- The MML HREC should consider these violations at the next HREC meeting and determine whether any further action is required in regard to participant safety or research misconduct and consider if further action is required.

### 2.6.2 Study discontinuation

- Where a research project is terminated or suspended by the Principal Investigator prematurely, the MML HREC must be promptly informed and provided with a detailed written explanation of the circumstances, having regard to the ongoing safety and welfare of any research participants who may be receiving study treatment.
- Notification of early termination of a study should be included on the next HREC agenda for noting and / or recommendation.

### 2.6.3 Suspension of approval

- The MML HREC may suspend 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 MML HREC 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 MML Group CEO.
- The CEO must instruct the CPI (or site PI for single site studies) to:
    - Immediately cease all study related activities;
    - Ensure the health and wellbeing of participants are not compromised;
    - Notify any study sponsor of the MML HREC's decision and
    - Notify the authorising RGO.

## 2.7 Storage and retention of records

- MML HREC hard copy records are stored in Room 293, Level 2, Aubigny Place, Mater Misericordiae Ltd, South Brisbane.
- Hard copy files for completed studies are stored off site at GRACE Records Management.
- In accordance with *The Code* and TGA requirements clinical trial records to be stored for a minimum of 15 years. In the case of paediatric research records are stored for up to 33 years (participant reaching the age of 18 years plus 15 years for a clinical trial). In addition, if legal action has been taken the files are stored for 10 years after the legal action has been completed. Further information can be found at Queensland State Archives.

## 2.8 Schedule of fees

- The MML HREC schedule of fees is publicly available on the MML HREC website.

## 2.9 HREC management

### 2.9.1 Appointing members (*National Statement* section 5.1.34 – 5.1.36)

- Prospective members should forward an Expression of Interest (EOI) to the HREC Office at MR. Vacancies may be filled from the persons who have submitted an EOI or by advertisement in local, state, and national newspapers.

- Membership must reflect the *National Statement* minimum membership requirements as listed in section 5.1.29.
- Members are appointed as individuals for their knowledge, qualities, expertise and relevant experience, and not as representatives of any organisation, group or opinion (*National Statement* Section 5.1.35).
- Members are not to be appointed in more than one of the categories listed in 5.1.30 of the *National Statement*.
- Before appointment, members acknowledge in writing their acceptance of the terms of reference and relevant policies of the MML HREC and any requirements for confidentiality and conflict of interest required by MML.
- Members will be provided a letter of appointment including the date of appointment, length of tenure, assurance that indemnity will be provided by MML in respect of the conduct of their duties as a HREC member, HREC meeting attendance responsibilities and general responsibilities as a HREC member.
- Membership appointments to the MML HREC will be considered for review every three years (*National Statement* Section 5.1.34).
- A member may be re-appointed for further three year periods.
- Members are appointed by the MML Board of Directors. All changes to the MML HREC membership are communicated to the NHMRC and other official research regulatory bodies as required.
- Members should inform the Chairperson if leave of absence is required. If unable to attend three or more consecutive meetings, members should consider their availability to remain on the Committee.

### 2.9.2 Conditions of appointment

- Membership of the MML HREC is publicly available on the website.
- All essential and necessary expenses incurred by members in carrying out their MML HREC duties will be paid for or reimbursed by MML on production of original receipts.
- Parking and refreshments will be provided at MML South Brisbane to facilitate members' attendance at meetings.

### 2.9.3 Education and training

- New members are provided induction material and mentoring via the Chairperson or other members of the HREC (*National Statement* Section 5.1.28(b)).
- Throughout their tenure, members are given the opportunity to attend conferences and workshops, supported by MML, that are relevant to the roles and responsibilities of the HREC (*National Statement* section 5.1.28(b)).
- Members and HREC Office staff are asked to report back to the Committee on any course or conference attended.
- The MML HREC Coordinator or Administrator will record education training records in members' contact details in AU RED.

### 2.9.4 Essential reading for HREC members

- Mater Misericordiae Ltd Human Research Ethics Committee (MML HREC) (EC00332) Terms Of Reference
- National Statement on Ethical Conduct in Human Research, National Health & Medical Research Council, 2007 (Updated 2015) (herein referred to as the *National Statement*)
- The Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects, World Medical Association, 2013.
- Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) – Annotated with TGA Comments. Therapeutic Goods Administration, 2000

- Human Research Ethics Committees and the Therapeutic Goods Legislation June 2001
- NHMRC guidance for multi-centre research
- Safety monitoring and reporting in clinical trials involving therapeutic goods
- Catholic Health Australia Code of Ethical Standards for Catholic Health and Aged Care Services in Australia, 2001
- Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research, 2003
- Australian Code for the Responsible Conduct of Research 2007 (the Code)
- Privacy Act, 1988; *Guidelines approved under Section 95 of the Privacy Act, 1988*; *Guidelines approved under Section 95A of the Privacy Act, 1988*; Guidelines approved under Section 95AA of the Privacy Act, 1988 (Cth); Australian Privacy Principles;
- Coroners' Act 2003, Section 53.

## 2.10 NHMRC HREC certification and compliance

- The MML HREC has current certification from the NHMRC as a lead HREC under the National Approach to Single Ethical Review of Multi-Centre Research. The Committee is certified for single ethical review of studies in clinical trials of drugs and devices – Phase 0, I, II, III, IV; Clinical Interventional Research other than Clinical Trials; Qualitative Health Research; Mental Health; Paediatrics; Population Health and / or Public Health Research.
- The MML HREC reports to the NHMRC under registration requirements (NHMRC Registration No: EC00332). The MML HREC Coordinator submits an Annual Certification and Compliance Report to the NHMRC.

## 2.11 Complaints (*National Statement* Chapter 5.6)

- Research complaints can be about the conduct of research including the conduct of researcher/s and / or about the conduct of the HREC or Office.
- The process for receiving and resolving allegations of research misconduct at MML / MR is described in the Research Misconduct Policy (see Section 4 Documents related to this procedure).
- Participant Information Sheets must include contact details for the MML HREC Office for complaints to be made.
- Complaints should be made in writing however may be sent by email or by telephone.
- All complaints will be dealt with by the MML HREC Chairperson with assistance from the MML HREC Coordinator.
- The Chairperson will notify the MML Group CEO as soon as possible.
- The Chairperson will investigate the complaint and its validity, and make a recommendation to the MML HREC / MML Group CEO on the appropriate course of action.
- The Institutional Research Governance Officer should also be informed by the Coordinating or site Principal Investigator.
- All complaints will be acknowledged within 7 days.
- The complaint and the proposed action will be reported to the next meeting of the MML HREC.
- Complainants will be advised of an outcome within 30 days.
- The MML HREC Office may contact the MML Patient Representative if considered helpful for the purpose of the investigation.
- If the complaint refers to care provided to a patient of Mater Health the Director of that Service and the Patient Representative should be advised as soon as details become available.
- If the complainant does not accept the decision of the MML HREC the complaint may be forwarded to the MML Group CEO.
- The MML Group CEO will consider the need for further investigation.
- If it is decided there is to be a further investigation, the MML Group CEO will convene an investigating committee to review the complaint, ensuring that both the complainant and the MML HREC are afforded the opportunity to make submissions. In conducting its review, the panel shall

be concerned with ascertaining whether the MML HREC acted in accordance with the *National Statement*, Terms of Reference and Standard Operating Procedures.

- In situations where a conflict of interest is suspected the Conflict of Interest Policy is applied.

# 3 Definitions

| Term | Definition |
|---|---|
| Adverse Event (AE) | Any untoward medical occurrence in a research participant using an investigational product which does not necessarily have a causal relationship with the product.<br>Therefore, an adverse event (AE) can be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. |
| Amendment | A change to the Human Research Ethics Committee (HREC) approved application including the protocol or supporting documentation. |
| Applicant | For multi-centre studies the Coordinating Principal Investigator (CPI).<br>For single site studies the Site Principal Investigator (PI). |
| Associate Investigator (AI) | Another term used for Sub-Investigator. |
| AU RED | Australian Research Ethics Database. A secure web-based research ethics database used by HREC Administrators to store ethics documents, applications and correspondence in relation to studies submitted to the MML HREC. |
| (The Code) | The *Australian Code of for the Responsible Conduct of Research* (2007) (The *Code*).<br>This guides institutions and researchers in responsible research practices and promotes integrity in research. It shows how to manage breaches of The Code and allegations of research misconduct, how to manage research data and materials, how to publish and disseminate research findings, including proper attribution of authorship, how to conduct effective peer review and how to manage conflicts of interest. It also explains the responsibilities and rights of researchers if they witness research misconduct. |
| Certified HREC | An HREC which has had its processes assessed and certified under the National Health and Medical Research Council (NHMRC) National Certification Scheme. NHMRC certification lasts for three years and may be renewed depending on review by the NHMRC.<br>• Go to NHMRC Certification Scheme, for further information.<br>• List of certified HRECs |
| Clinical Audit | Quality assurance programmes may use planned clinical audits along with other monitoring tools to assure that standards are being met. A clinical audit is not research.<br>• Clinical audit tells us whether we are doing what we should be doing and how well we are doing it. Clinical audit is about quality and finding out if best practice is being practised.<br>• Research is about obtaining new knowledge and finding out what treatments are the most effective. Research tells us what we should be doing.<br>There is a clear distinction between clinical audit and research and clinical |

| Term | Definition |
|---|---|
| | audit does not need approval from a research ethics committee. Even if an ethical opinion is sought for a clinical audit and even if the project is to disclose non-identifiable confidential information without consent, clinical audits do not require research authorisation as they are not research activities. |
| Clinical Research Coordinator (CRC) | The CRC is the person designated by the CPI to be responsible for coordinating the conduct of the research project, including scheduling of participant visits, liaison with Sponsor management personnel and the HREC / Research Governance Office(r) (RGO). May also be known as the Site Coordinator or Contact Person. |
| Contact Person | The person designated by the Principal Investigator (PI) to be responsible for liaising with the HREC / RGO. May also be known as the Site Coordinator or Clinical Research Coordinator. |
| Clinical Research Associate (CRA) | The CRA is a representative of the Sponsor or Contract Research Organisation (CRO) employed to monitor clinical trials. The CRA ensures compliance with the clinical trial protocol, checks site activities, reviews Case Report Forms (CRFs) and acts as a communication conduit between sites and the sponsor organisation. |
| Confidential Information | Confidential information means any information that— is about a person who is receiving or has received health care and could identify the person. |
| Contract Research Organisation (CRO) | The CRO is an organisation (commercial, academic or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties or functions. |
| Coordinating Principal Investigator (CPI) | The CPI the investigator responsible for coordinating a multi-centre research study, and the submission and communication of all subsequent requests and notifications to the site PIs.<br><br>The CPI and their team are responsible for coordinating the HREC applications and correspondence throughout a multi-centre study, on behalf of the Accepting PIs for which the CPI is responsible.<br><br>For single site studies the terms CPI, Coordinating<br>Principal Researcher, Site Principal Investigator and Principal Investigator are all synonymous. |
| Good Clinical Practice (GCP) | GCP is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. May also be referred to as ICH GCP (International Conference on Harmonisation). |
| Human Research Ethics Application (HREA) | *"As part of the initiative to streamline ethics approval, NHMRC has developed the Human Research Ethics Application (HREA) as a replacement for the National Ethics Application Form (NEAF). The aim of the HREA is to be a concise application to facilitate efficient and effective ethics review for research involving humans. The application will assist researchers to consider the ethical principles of the National Statement on Ethical Conduct in Human Research (2007) in relation to their research, rather than focus on requirements for approval."*<br><br>The HREA when available at the Online Forms website will replace both the NEAF and LNR. The HREC office will determine the level of review when the |

| Term | Definition |
|---|---|
| | HREA is submitted. |
| Human Research Ethics Committee (HREC) | The HREC review research proposals that involve humans or their tissue or data. HRECs are established by organisations which register their HREC with the NHMRC. It may also be referred to as the Reviewing HREC in multi-centre research studies.<br><br>"HREC" in this document means the Mater Misericordiae Ltd Human Research Ethics Committee established under the MML HREC (EC00332) Terms of Reference. |
| HREC Coordinator | An employee of MML who provides administrative support and advice on the MML / MR process of ethics review of research studies. The Coordinator reports to the Manager, Mater Research Office and consults with the Chairperson of the HREC in matters related to the activities of the HREC. |
| Individually Identifiable Data | Where the identity of a specific individual can reasonably be ascertained. Examples of identifiers include the individual's name, image, date of birth, or address. |
| HREC Checklist | The HREC checklist is available on the MML HREC website. This checklist provides a guide to researchers on the types of attachments that may be included with a new research application, and the number of copies required. |
| Low and Negligible Risk (LNR) | Low and Negligible Risk Research is described in section 2.1.6 of the *National Statement as low risk where the only foreseeable risk is one of discomfort. Where the risk, even if unlikely, is more serious than discomfort, the research is not low risk*. Negligible risk is described in the *National Statement* as *research in which there is no foreseeable risk of harm or discomfort; and any foreseeable risk is no more than inconvenience.* |
| LNR Application | An application form used for research which is defined as low or negligible risk. The form is available on the Online Forms website. |
| Mater Misericordiae Ltd (MML) | "MML" means Mater Misericordiae Health Services Brisbane Ltd ACN 096708922 owner and operator of the Mater Hospitals South Brisbane, and other sites notified to the HREC. |
| Mater Research (MR) | "MR" means Mater Medical Research Institute Ltd ACN 109834719 owner and operator of Mater Research and Mater Medical Research Institute. |
| Members' Portal | The online portal for HREC members to access meeting documents and upload reviews. |
| Multi-Centre Research | Includes research conducted through the collaboration of at least two unique institutions that may be situated in more than one state or territory or within a single jurisdiction. It does not refer to research being conducted at several sites or locations of a single institution e.g. Mater Hospital Brisbane and Mater Private Hospital. |
| *National Statement* | The *National Statement on Ethical Conduct in Human Research (2007) Updated 2015 (and subsequent revisions)*. A guidance document developed by the NHMRC, the Australian Research Council and the Australian Vice-Chancellors' Committee to provide guidelines for researchers, HRECs and others conducting ethical review of research. It also states institutions' responsibilities for the quality, safety and ethical acceptability of research |

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| | that they sponsor or permit to be carried out under their auspices. |
| NEAF | National Ethics Application Form |
| Non-Identifiable Data | The *National Statement* advises non-identifiable data as *data that have never been labelled with individual identifiers or from which identifiers have been permanently removed, and by means of which no specific individual can be identified. A subset of non-identifiable data are those that can be linked with other data so it can be known they are about the same data subject, although the person's identity remains unknown*. |
| Online Forms | The Online Forms website is an online system that enables users to complete their applications for research ethics review electronically. The website hosts a licensed copy of the NHMRC's NEAF and the LNR form. |
| Personal Information | Information or an opinion, including information or an opinion forming part of a database, whether true or not and whether recorded in a material form or not, about an individual whose identity is apparent, or can reasonably be ascertained, from the information or opinion. |
| Principal Investigator (PI) | The PI is the investigator responsible for the overall conduct of the research study at an individual site.<br>• For multi-centre studies the PI may be known as the Accepting PI if they do not have CPI responsibilities.<br>For single site studies the terms CPI, Coordinating Principal Researcher, Site Principal Investigator and Principal Investigator are used interchangeably. |
| Protocol | The protocol is the study working document. It is the formal design or specific plan for the research. It provides detail for the conduct of the research consistent with the scope of the template available on the MML HREC website. If the study is amended after approval, a revised tracked protocol must be submitted and approved. The protocol should include document identifier, version number and date.. |
| Quality Assurance Activity (QA) | A clinical governance activity that is a requirement of the compulsory National Safety and Quality Health Service Standards and an associated Australian Health Service and Quality Accreditation (AHSSQA) Scheme.<br>This includes patient satisfaction surveys, surveillance and monitoring and clinical audits. If there are research elements then it will be reviewed under the research review process. Ethical considerations apply to such work. |
| Re-Identifiable Data | Data from which identifiers have been removed and replaced by a code, but it remains possible to re-identify a specific individual by, for example, using the code or linking different data sets. |
| Research Governance Authorisation | Authorisation is issued by the Research Governance Office or delegate to conduct research at a site within their jurisdiction. Authorisation is contingent upon receiving HREC approval and completion of governance requirements which may include an SSA form. |
| Research Governance Office (RGO) | The Research Governance Office is the Office(r) or coordinated function within MML whose responsibilities are:<br>• assessing the site-specific aspects of research applications,<br>• making recommendations to the CEO or delegate as to whether a |

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| | research study should be granted authorisation at the site; and monitoring authorised research at the site to ensure it meets appropriate standards. |
| Reviewing HREC | The certified HREC that reviews multi-centre research studies. |
| 60-day clock | The period of 60 review days allowed for the deliberation of an ethical decision on an application. For research not requiring review at a full HREC meeting, the clock starts on receipt of a valid application. For research requiring review at a full HREC meeting the clock starts on the relevant HREC meeting closing date. The 60-day time limit excludes stop clock days. May also be called 60 Review Days. |
| Serious Adverse Event (SAE) | The definition of an SAE will be defined by the Sponsor and included in the protocol. Generally, an SAE in human drug trials is defined as any untoward medical occurrence that at any dose, results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage.<br><br>Suspected Unexpected Serious Adverse Reactions (SUSARs) are considered a subset of SAEs. |
| Single Ethical Review Process | The mechanism to allow ethical review of multi-centre research by one NHMRC Certified HREC rather than submitting a study to multiple HRECs for review. |
| Single Site Research | Research to be conducted at one site only. |
| Site Coordinator | The person designated by the (PI) to be responsible for liaising with the HREC / RGO. May also be known as the Clinical Research Coordinator, Contact Person or Study Liaison Officer. |
| Site-Specific Governance Amendment | An amendment request for an authorised research study that may be submitted by the applicant to the RGO only (for studies approved by an HREC other than MML). Examples would be changes to site contracts and changes to participating site staff other than the PI. |
| Site-Specific Assessment (SSA) | The SSA Form is a tool to assist RGOs in the research governance process to document the level of support and suitability of a research study to be conducted at a site, irrespective of whether the study is multi-centre or single site. |
| Site Start Date | The site start date refers to either the anticipated first point of recruitment (i.e. the date when the advertising or screening for participants begins) or start of data collection. |
| State Specific Modules | Victoria, Western Australia and the Australian Capital Territory have developed additional modules for HREC review that must be completed and submitted as part of the HREC review of clinical trials, when sites from those States / Territories are participating in multi-centre research. For further information go to:<br><br>VIC: http://www.health.vic.gov.au/clinicaltrials/application-instructions.htm#vsm<br>WA: http://www.health.wa.gov.au/researchdevelopment/home/hrec.cfm#ethics |

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| | ACT: http://healthresearch.anu.edu.au/human-research-ethics-committee.html |
| Stop Clock Facility | For HREC applications, the time when the 60-day clock is stopped while awaiting a satisfactory response from the applicant to a written request from the HREC for further information or clarification. The clock will re-start automatically when a response from the applicant is logged in to AU RED. |
| Study Site | The location(s) under the control of the Institution where the study is actually conducted. |
| Sub Investigator | May also be called Associate Investigator (AI) or Associate Researcher. ICH GCP defines a sub-investigator as "any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial related procedures and/or to make important trial related decisions". |
| Submission Code | The final step in completing an Online Forms NEAF or LNR is to generate a submission code. This alpha numeric code appears in the bottom right of the footer. The "draft" watermark disappears after the submission code has been generated. |
| Therapeutic Goods Administration (TGA) | The TGA is the agency responsible for regulating therapeutic goods: Follow this link for further information. |
| Validation | An administrative check carried out by an HREC Administrator or RGO to verify that all applicable application documentation is submitted prior to review. Decisions on validation should be made within one week of receipt. |
| Validation Date | • For research not requiring review at a full HREC meeting, the date on which a valid application is received by the HREC Coordinator.<br>• For research requiring review at a full HREC meeting, the relevant HREC meeting closing date. |

# 4 Documents related to this procedure

**Mater documents**

| Document type | Document ID | Document Title |
|---|---|---|
| Committee Terms of Reference | CT-RSH-300000 | Mater Misericordiae Ltd Human Research Ethics Committee (MML HREC) (EC00332) Terms Of Reference |
| Governance | CA-CEO-000001 | Mater Misericordiae Ltd By-Laws |
| | PY-PAL-060000 | Code of Conduct Policy |
| Policy | PY-RSH-300300 | Ownership, Storage and Retention of Human Research Materials and Data Policy |
| Policy | PY-RSH-300301 | Collection, Storage, Use and Disposal of Human Biospecimens in Research Policy |
| Policy | PY-RSH-300302 | Responsible Conduct of Research Policy |
| Policy | PY-RSH-300305 | Human Research Ethics Review Policy |
| Policy | PY-RSH-300309 | Conflict of Interest in Research Policy |
| Policy | PY-RSH-300310 | Research Misconduct Policy |
| Policy | PY-RSH-300304 | Human Research Governance Policy |

**External documents**

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| **1.** | National Statement on Ethical Conduct in Human Research, National Health and Medical Research Council, 2007 (Updated in March 2015) (herein referred to as the *National Statement*) |
| **2.** | The Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects, World Medical Association, 2013 |
| **3.** | Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) – Annotated with TGA Comments. Therapeutic Goods Administration, 2000 |
| **4.** | Human Research Ethics Committees and the Therapeutic Goods Legislation, June 2001 |
| **5.** | NHMRC Guidance for multi-centre research |
| **6.** | Catholic Health Australia Code of Ethical Standards for Catholic Health and Aged Care Services in Australia, 2001 |
| **7.** | Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research, 2003 |
| **8.** | Australian Code for the Responsible Conduct of Research 2007 (herein referred to as The Code) |
| **9.** | Public Health Act 2005, Hospital and Health Boards Act 2011 and other relevant requirements of Commonwealth and State/Territory laws |
| **10.** | Privacy Act, 1988<br><br>*Guidelines approved under Section 95 of the Privacy Act, 1988, (March 2014)*<br><br>*Guidelines approved under Section 95A of the Privacy Act, 1988, (March 2014)*<br><br>Guidelines approved under Section 95AA of the Privacy Act, 1988 (Cth), *(March 2014)*<br><br>Australian Privacy Principles, March 2014 |

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| **11.** | Sections 65, 68, 72 and 74 of the *Guardianship and Administration Act 2000* |
| **12.** | Memorandum of Understanding (MOU) between the State of Queensland and Mater Misericordiae Health Services and all Queensland Hospital and Health Services in relation to mutual acceptance of ethical and scientific review of multi-centre research studies, May 2013 |
| **13.** | Standard Operating Procedures (SOP) for Queensland Health (QH) HREC Administrators Version 4, November 2013 |
| **14.** | Ethical considerations in Quality Assurance and Evaluation Activities. |
| **15.** | Safety monitoring and reporting in clinical trials involving therapeutic goods |
| **16.** | Framework for Monitoring |

# 5 Document controls

## 5.1 Document revision history

| Version | Release date | Description | Risk-rated review date |
|---|---|---|---|
| 1. | July 2011 | Standard Operating Procedures (SOP) for Mater Health Services HREC Secretariat | July 2011 |
| 2. | 28 August 2013 | Standard Operating Procedures (SOP) for Mater Health Services HREC Secretariat | August 2013 |
| 3. | 1 Sept 2014 | Mater Health Services Human Research Ethics Committee (HREC) (EC00332) Office Standard Operating Procedure (SOP) | September 2014 |
| 4. | 3 March 2015 | Mater Misericordiae Ltd Human Research Ethics Committee (MML HREC) Office Standard Operating Procedure (SOP) | 3 March 2015 |
| 5. | 16 March 2017 | Procedure for Mater Misericordiae Ltd Human Research Ethics Committee (MML HREC) Office | |

## 5.2 Document review and approval

| **Name**<br>Person/committee | **Position**<br>If applicable | **Function**<br>Owner/author/review/approve |
|---|---|---|
| Odette Petersen | HREC Coordinator | Author |
| Dr Conor Brophy | HREC Chairperson | Review/Approve |
| Corporate Policy Governance Committee | | Approve |

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