Review of Research Projects at Melbourne Health
How the Process Works

Submission of New Research Projects for Review

The Human Research Ethics Committee (HREC) meets on a Wednesday each month (usually the 2nd Wednesday). There is no meeting in January. Proposals for new research projects must be lodged with the Office for Research no later than 11.00 am on the Wednesday – 14 calendar days before the meeting. Researchers are encouraged to submit proposals as early as possible. This will enable the Office for Research staff to validate submissions and identify any problems that may delay approval. Detailed submission guidelines are available on our website at http://research.mh.org.au.

New research project applications must be submitted using the Human Research Ethics Application (HREA). One single sided original and one electronic copy submitted to hrecsubmissions@mh.org.au are required.

Submission of a new research project by the 11:00 am deadline is not a guarantee that a project will be accepted for review by the HREC at its next meeting. Following the submission deadline each month, all projects received are carefully checked against the Ethics Cover Letter and Checklist to ensure that projects meet the criteria required to allow a thorough review of the project. Any project not meeting these criteria in full will not be accepted for review and will be returned to the principal researcher for attention.

Ideally, all research projects to be conducted at Melbourne Health or using Melbourne Health resources will include a Melbourne Health staff member as a member of the research team. If this is not possible, a member of the senior medical staff must be appointed as 'sponsor' of the project and must sign a Statement of Approval Form in this regard.

Review Processes

New research project applications are “triaged” within the Office for Research upon submission and allocated to review by the full HREC or by a low risk review process. There is one set of application procedures and submission deadlines for all levels of review.

1. Low Risk Research

In accordance with the NHMRC National Statement on Ethical Conduct in Human Research (2007), the Melbourne Health HREC has established a process for the review of research involving no more than low risk – review by a Low Risk Research Sub-Committee.

The Low Risk Research Sub-Committee is a “sub-committee” of the HREC which meets in the week prior to the monthly meeting of the full HREC. The membership of the Low Risk Research Sub-Committee is fluid but is required to comprise a minimum of two “scientific/clinical spokespersons” and two “ethics spokespersons” from amongst the membership of the HREC. At least one of the scientific/clinical spokespersons attending each “low risk” meeting must be a medically qualified clinician/researcher. The HREC Manager or Assistant Manager Research Governance and Ethics also attend these meetings.

Each month, different members of the HREC attend the meeting of the Low Risk Research Sub-Committee. This “rotation” of service to the Low Risk Research Sub-Committee ensures that all HREC members have an opportunity to contribute to the review of research determined to be of low or negligible risk.

The minutes of the meetings of the Low Risk Research Sub-Committee are incorporated into the agenda and then the minutes of the next scheduled meeting of the HREC and the decisions of the Low Risk Research Sub-Committee are endorsed and adopted by the HREC before any correspondence is forwarded to the researchers involved.

The application procedures and submission deadlines for the Low Risk Research Sub-Committee are the same as those for the HREC. New projects are "triaged" as being suitable for review by the Low Risk Research Sub-Committee by the HREC Manager and Assistant Manager Research Governance and Ethics after each monthly new research project submission deadline.

The main purpose of the low risk research review process is to free up time during meetings of the full HREC to discuss more complex projects in greater depth. The endorsement of the minutes of the Low Risk Research Sub-Committee by the HREC at its monthly meetings means that correspondence concerning low risk research projects can be forwarded to the researchers concerned, usually without delay, the day after the full HREC meetings.

2. Full HREC Review

Expert Scientific Review

The membership of the HREC is constituted so that the scientific/clinical expertise needed to review the research projects presented to the HREC is almost always available from within the membership. In the event that the scientific expertise required to review a particular project cannot be provided by an existing HREC member, Melbourne Health has established an independent Expert Scientific Review Panel whose members may be called upon to provide any expert scientific advice that the HREC may require to assist with its deliberations. Panel members provide written advice to the HREC and may also attend HREC meetings, if requested to do so.

First time in Human Clinical Trials

In the event that the HREC is presented with a first time in humans phase 1 clinical trial to be reviewed under the CTN scheme, the HREC follows the *Scientific Expert Review Toolkit – Early Phase Clinical Trials* developed by the Department of Health and Human Services. This protocol is designed to assist HRECs to meet their obligations under the *National Statement (2007)* and the Therapeutic Goods Administration's Guidelines, Access to Unapproved Therapeutic Goods – Clinical Trials in Australia (2004), by providing a rigorous, standardised protocol for the review of first time in humans trials, which includes access to a comprehensive database of independent experts with extensive expertise in evaluating preclinical data.

Review by Spokespersons

Each new project reviewed by the full HREC is allocated two "spokespersons" from amongst suitably qualified members of the HREC. It is the spokespersons' responsibility to thoroughly review a project before a meeting and present the project to the rest of the HREC at the meeting. The "Scientific" spokesperson is a clinician or scientist, with relevant research expertise, who is responsible for assessing the scientific merit, safety and statistical aspects (where relevant) of a project. The "Ethics" Spokesperson is a member of the HREC with no clinical or scientific background. It is their responsibility to review the ethical aspects of the project – recruitment, consent process, participant information and consent form, questionnaires, etc.

Scientific and ethics spokespersons, and expert reviewers where required, are "assigned" to a project for the life of the project and ongoing project correspondence including amendments, safety reports and progress reports are referred to the appropriate reviewers as required to ensure timely and ongoing expert oversight of every research project.

In addition to the "scientific" and "ethical" review, projects are also subject to expert statistical review by the expert statistician members of the HREC. Where it is deemed necessary, the HREC also refers projects to internal/external statistical consultants who provide a comprehensive, written statistical evaluation of a project.

The spokespersons may contact the principal researcher prior to the meeting to clarify aspects of a project. As indicated above, the HREC may also seek independent expert scientific and/or ethical advice in relation to any given project, before or after a project has been considered at a HREC meeting, if this is deemed necessary. All independent experts are asked to sign a confidentiality and conflict of interest agreement before reviewing a protocol.

Decisions at HREC meetings are arrived at by consensus.

Written correspondence is sent to the Principal Researcher within 3-5 days of the meeting outlining the comments and any queries raised by the HREC. If the HREC recommends the attendance of a researcher at the next meeting to elaborate on a specific issue, this invitation is issued to the researchers in the HREC's formal written correspondence. Where applicable, researchers are asked to sign a confidentiality and conflict of interest agreement before attending the meeting. Following initial review of a new research project at a meeting of the full HREC, any replies to queries received by the Office for Research are sent directly to one or both of the spokespersons (depending upon the nature of the queries) or if delegated, are reviewed by the HREC Manager and Assistant Manager Research Governance and Ethics. The spokespersons review the correspondence and send back a written comment indicating approval or requesting further information.

If the correspondence is approved by the spokespersons, the matter is simply registered on the agenda of the next full meeting of the HREC for confirmation of approval. This entire process takes place daily, between HREC meetings, to ensure that new projects and other correspondence (e.g. amendments and serious adverse event reports) are approved and/or dealt with as quickly as possible.

3. Quality Assurance Projects

All Quality Assurance Projects (QA) that involve humans, or their information or tissue must be submitted to the Melbourne Health Office for Research for review. The review will assess whether the project is QA that does or does not require independent ethical review and whether it complies with all applicable legislation and codes of practice.

Projects that are assessed as requiring ethical review will be advised to submit an application to Melbourne Health Human Research Ethics Committee through the normal HREC review system described above. Projects that are deemed to not require ethical review will be approved as QA projects.

Melbourne Health's QA process is detailed on our website.

The Melbourne Health HREC has delegated the authority to review and assess QA applications to the Manager or Assistant Manager Research Governance and Ethics and the Chair of the Melbourne Health HREC

Monitoring

Melbourne Health's Guidelines for Monitoring and Reporting of Safety in Clinical Trials Involving Therapeutic Products and Other Clinical Research clearly set out the processes in place in relation to monitoring and reporting adverse events, including significant safety issues (SSI), Suspected Unexpected Serious Adverse Reaction (SUSAR) and Unanticipated Serious Adverse Device Effect (USADE) involving clinical trials for which MH, or a MH HREC, is responsible. These guidelines are available on our website.

Proposed monitoring of participants must be described in the research project protocol. The HREC may require additional monitoring depending on the risk to participants. More frequent reporting is required for higher risk projects. For example, for projects deemed by the HREC to be "high risks", reports may be requested after 2 patients have received study treatment, and then after the next 3 patients, etc. Reporting requirements in additional to annual progress reports and reporting described in the study protocol, will be requested and prescribed by the HREC, where deemed

necessary, on a case by case basis.

Approval

The Office for Research has a target for *Total Time to Approval* for new research projects of 60 calendar days. This includes the time for *both* HREC and Research Governance/Site Specific Assessment approval.

HREC approval of a project is ongoing provided a project progress report is submitted annually.

Requests for progress reports are sent out on the anniversary of ethical approval by the Office for Research.

When ethical approval for a project is withdrawn, all participants should be informed, wherever possible. Researchers are required to promptly suspend the research and make all necessary arrangements to meet the needs of participants. Researchers must advise the HREC of the consequences to the participants of the project ceasing and how this process will be managed to minimise any risk and inconvenience to the participants. All parties must comply with the requirements of the *National Statement* and *Guidelines for Good Clinical Practice* in relation to managing withdrawal of ethical approval for a research project.