
WOMEN'S COLLEGE HOSPITAL Research Ethics Board Terms of Reference

INTRODUCTION

The Research Ethics Board (REB) of Women's College Hospital exists to ensure that all research activities involving human participants or human materials (hereafter referred to as "Research"), being conducted within or on behalf of Women's College Hospital, meet current scientific, regulatory and ethical standards for the protection of human research participants in accordance with the Tri-Council Policy Statement: Guidelines on Research Involving Human Subjects (TCPS2)ⁱ.

Ethics are principles of right conduct that guide 'what ought to be done'. In the context of the Tri-Council Policy Statement, Women's College Hospital REB subscribes to the following ethical principles that are commonly held, valued by diverse research disciplines and express common standards, values and aspirations of our research community:

Respect for human dignity	Respect for privacy and confidentiality
Respect for free and informed consent	Respect for justice and inclusiveness
Respect for vulnerable persons	Balancing harms and benefits

TERMS OF REFERENCE

The Women's College Hospital REB is responsible for:

- Ensuring that all Research proposals involving human participants or human materials being conducted at or under the auspices of Women's College Hospital meets the highest ethical and scientific standards,
- Ensuring that all protocols have a favorable risk/benefit ratio for research participants and respect a person's right for self-determination and autonomy.
- Ensuring equitable distribution of the benefits and burdens of Research,
- Monitoring on-going research activities at Women's College Hospital to ensure that ethical standards as outlined in the Tri-Council Policy Statement (TCPS2, 2014) are maintained throughout the course of investigations,
- Recommending policies and procedures governing ethical conduct of research at Women's College Hospital,
- Acting as a resource on matters of research ethics for Women's College Hospital.

As a general definition, Research to be considered by the REB includes all systematic collection of data from human participants that is intended to extend knowledge. Such Research includes not only intervention studies of possible therapeutic benefit but also minimal risk studies involving questionnaires, chart reviews, use of tissue and blood samples, and use of confidential information. Included in the jurisdiction of the REB is research carried out by staff, physicians, students and

trainees of Women's College Hospital, and investigators from other institutions who wish to carry out Research on Women's College Hospital premises or with Women's College Hospital patients.

AUTHORITY

From a research ethics perspective, the Women's College Hospital REB is invested with the authority and responsibility to independently approve, reject, propose modifications to, put on hold or terminate any proposed or ongoing Research involving human participants being carried out within, or on behalf of Women's College Hospital. The REB also has authority over investigators from other institutions who wish to carry out Research on Women's College Hospital premises or with Women's College Hospital patients.

The Hospital's Board of Directors has delegated decision-making authority to the REB. In accordance with current TCPS2 standards, the REB operates effectively and independently in their decision making.

The Board of Directors, MAC, or other administrative bodies within Women's College Hospital may not override a decision of the REB. That said, Women's College Hospital retains the authority to deny the implementation of REB-approved research protocols for reasons other than research ethics; such reasons may be administrative, programmatic, or resource-based in nature. As an entity that draws its authority and resources from Women's College Hospital, the REB remains accountable to the Hospital for the integrity of its processes.

If a protocol is rejected by the REB, the principal investigator may request a hearing by an Appeal Committee to review the decision process and documentation that formed the basis of the decision.

REPORTING RELATIONSHIP

The REB reports to the Board of Directors, through the Medical Advisory Committee (MAC). The Chair of the REB reports administratively to the CEO or delegate and has the additional responsibility to liaise with the University of Toronto on research ethics matters as specified under the current affiliation agreement between Women's College Hospital and the University of Toronto.

ACCOUNTABILITY

The REB reports to and is ultimately accountable to the Board of Directors, through the MAC. The REB is also accountable to the President of U of T regarding research ethics matters for staff holding university appointments.

RESEARCH ETHICS BOARD

Women's College Hospital has two research ethics boards of record as well as a third option for provincial studies. The boards of record are the Women's College Hospital REB, which is the primary Board of Record, and the Ontario Cancer Research Ethics Board (OCREB) for multi-centre oncology trials. Clinical Trials Ontario (CTO) has developed a review process to qualify REB's to oversee provincial multi-site trials and Women's College Hospital may delegate to a CTO-qualified REB. Women's College Hospital has a formal relationship with OCREB and CTO and has registered OCREB as an additional REB on the Institution's existing Federal Wide Assurance. (Note, CTO is not listed on WCH's Federal Wide Assurance because CTO itself does not have an REB.) The Institution may delegate OCREB or a CTO-qualified REB as the REB of record on a study-by-study basis by executing a Board of Record Study Agreement or similar documentation, which includes the division of responsibilities between OCREB or the CTO-qualified REB and participating institutions.

The Women's College Hospital REB has undergone a review process and has been designated as a CTO-Qualified REB. This means the Women's College Hospital REB is eligible to serve as the REB of Record for any site designated as a CTO Participating site across the province.

In acting as the REB of record, the Women's College Hospital REB shall be responsible for reviewing all Research protocols. It shall also act in compliance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2); the International Conference on Harmonization (ICH), Good Clinical Practice (GCP) Consolidated Guideline; Part C Division 5 of the Food and Drug Regulations of Health Canada; the provisions of the Ontario Personal Health Information Act (PHIPA) 2004 and its applicable regulations; and the US Code of Federal Regulations (CFR) Title 21 Parts 50 and 56, and CFR Title 45 Part 46.

To ensure that research proposals requiring ethics review are reviewed in a timely manner, an appropriate meeting schedule shall be organized by the Chair of the REB. The Research Ethics Office will coordinate the ethics review process and all related activities of the REB. Where necessary, subcommittees of the REB may be established. A Vice-Chair for the REB may be appointed following the same appointment process outlined in the Women's College Hospital Research Ethics Board Chair Terms of Reference.

Every person involved in the research ethics process at Women's College Hospital should have training and expertise to make sound judgments on the ethics of research proposals involving human participants. As a pre-requisite for involvement, the Chair, the Research Ethics Coordinator and all Research Ethics Board Members are required to complete the following web-based training (through the CITI Program, University of Miami):

1. Good Clinical practice (GCP)
2. Responsible Conduct of Research (RCR)
3. Basic Biomedical Research Ethics

4. Health Canada Division 5

CHAIR OF THE RESEARCH ETHICS BOARD

The Chair of the REB is an administrative position within Women's College Hospital appointed by the hospital CEO in consultation with the Chair of the MAC of the Women's College Hospital Board of Directors. The Chair reports administratively to the hospital CEO or delegate and liaises with the University of Toronto on research ethics matters, as specified under the current affiliation agreement between Women's College Hospital and University of Toronto.

REB MEMBERSHIP

The REB will have a majority of members who are Canadian citizens or permanent residents under the Immigration and Refugee Protection Act and consistent with minimum TCPS2 guidelines. The REB will consist of at least 5 members, of whom:

- At least two members have expertise in relevant research disciplines, fields and scientific methodologies covered by the REB,
- At least one member is knowledgeable in ethics,
- At least one member is knowledgeable in Canadian laws relevant to biomedical research,
- At least one member is knowledgeable in privacy issues;
- At least one member is knowledgeable in complementary or alternative health care (where applicable)
- At least one community member has no affiliation with the sponsor, institution, investigator, and who is not part of the immediate family of a person who is affiliated with the institution
- at least one community member whose primary area of expertise/interest is in a non-scientific area

To ensure the independence of REB decision making, institutional senior administrators shall not serve on the REB.

Potential members of the REB will be nominated by the relevant Hospital leaders (usually Department/Division Chairs) to the MAC. It shall be the responsibility of Department/Division Chairs to nominate members as needed and to replace members as required. Members may serve in more than one capacity such as representing both a Department/Division and a profession.

New members will be selected from the Hospital and from the community by the Chair of the REB and a delegate of the President/CEO in consultation with the Chair of the MAC.

At its discretion, the REB may invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the Board. These individuals may not participate in the REB's final deliberations.

TERMS OF SERVICE

The Chair of the REB will serve at the discretion of the Women's College Hospital CEO or delegate in consultation with the MAC. Chairs shall normally be appointed for a two (2) –year term, subject to an annual review, and may be renewed at the discretion of the Women's College Hospital CEO or delegate in consultation with the Chair of the MAC.

The Chair must not occupy any administrative position or committee membership or other professional activity over the course of his or her term that may compromise the independence of the ethics review process at WCH.

The Members of the REB will normally serve for a term of two years. By mutual consent between Members and the Chair of the REB, Members may be appointed for additional terms. The terms of service will be staggered to ensure continuity.

MEETINGS AND ATTENDANCE

A schedule of REB review meetings will be regularly updated and communicated to Women's College Hospital researchers via the REB website so that Research can be planned in an orderly manner. Typically, these shall be monthly, though the Chair may call additional meetings if the need arises.

A quorum shall consist of at least 5 members of the REB representing the full range of membership and expertise as defined in the TCPS2 and should include at least one physician and one non-physician. Members will be assigned protocols to review in an equitable fashion. Protocols will only be approved by the REB if those present afford sufficient and appropriate expertise to review the ethical acceptability of that research.

Attendance at REB meetings is crucial to the success of the review procedure. REB Members are expected to attend every REB meeting. Failure to attend a minimum of seventy five percent (75%) or 9 out of 12 scheduled meetings per year without explanation (i.e. sabbatical, maternity or parental leave) may result in a loss of membership to the REB. In the event that a REB member fails to meet these criteria, the appropriate Hospital leader will be notified by the Chair of the REB so that a replacement can be obtained.

DECISION PROCESS

For protocols that do not qualify for a delegated review process carried out by the Chair and/or a qualified member of the REB, a fully detailed review will occur and the REB will meet in a face-to-face forum to review such proposals.

Decisions will be made by consensus. Only in exceptional circumstances will decisions be made by majority vote at the discretion of the Chair. All documentation and communication will flow through the Chair and Research Ethics Office to investigators. Decisions by the REB will be communicated in

writing to the investigator by the Research Ethics Office based on the documentation and deliberations at the REB meeting.

On behalf of the full REB, the Chair:

- Is mandated to review, modify and approve/reject delegated protocols.
- Is delegated the authority to review and approve amendments and monitor reports of serious adverse events.
- Is delegated to assess responses from investigators regarding concerns raised by the REB and issue approval of further requests for modification to the investigators.
- The Chair shall report all such actions to the full REB at the next available opportunity.

Submissions to the REB may receive (i) approval, (ii) approval pending revision or clarification, (iii) deferral to obtain further information or consultation, or (iv) rejection (as submitted). If a submission is initially rejected, the REB will provide the investigator with a detailed list of the deficiencies so that any resubmission addresses and these issues prior to re-submission.

Applicants will be notified of the REB decision as soon as possible after the meeting. The approval of a research submission will be valid for no more than 12 months (unless otherwise stipulated).

CONFLICTS OF INTEREST

Members of the REB must disclose any real or apparent conflicts of interest regarding a proposal under review. Members may not be present for any REB discussion regarding a proposal in which they have any vested interest and may not participate in the decision process for such a proposal.

APPEALS PROCESS

In the event that the REB rejects a submission, an appeal of the decision may be made to the TAHSN Appeal Committee. The Appeal Committee will decide whether or not to hear the appeal. If the Appeal Committee decides to hear the appeal, it will review the REB process and documentation that supports the original decision. The Appeal Committee may dismiss the appeal or may direct the REB to reconsider its decision based on the findings of the appeal. The Appeal Committee will provide the REB and the principal investigator with a written decision documenting the reasons for its decision.

RECORDS AND DOCUMENTATION

All records for submissions will be maintained by the Research Ethics Office. In order for a protocol submission to be approved, all documentation must be complete including but not limited to, the most current Investigator's Brochure for clinical trials, the budget for the proposed research and evidence of the qualifications of the investigator to carry out the proposed research. All correspondence with the investigator will go through the Chair and the Research Ethics Office.

Minutes of each REB meeting shall be prepared by the Research Ethics Office and these minutes will document relevant discussions and decisions by the REB.

Submissions that are either reviewed through the delegated process or approved based on an adequate response by the investigator to REB concerns will be reported at the next REB meeting.

REVIEW PROCEDURES FOR ONGOING RESEARCH

The approval of any study will remain in force for a 12-month period unless otherwise stipulated. The investigator must seek a renewed approval for a further 12 months prior to the expiration of the current approval. At the very least, a continuing review should consist of a succinct annual status report to the REB. The investigator cannot continue with the study after the initial approval period without applying for a renewal of REB approval.

Depending on the nature of the research, the REB may require more frequent reporting and more rigorous monitoring. As well, the REB may, at any time, audit an ongoing study to ensure compliance with ethical standards. If the REB becomes aware of any new information that alters the risk/benefit ratio in the study, it may suspend previous approval of the study until the REB can assess the safety implications of this new information.

Ongoing research is subject to continuing ethics review. In keeping with a proportionate approach to research ethics review as mandated by the Tri Council Policy Statement 2 (TCPS2, 2014), the selection of the level of REB review shall be determined by the level of foreseeable risks to participants. In addition to the annual review, continuing review of Research that exceeds the threshold of minimal risk may include a:

- Formal review/random audit of the process of free and informed consent
- Establishment of a safety monitoring committee
- Periodic review by a third party of the documents generated by the study
- Review of reports of adverse events
- Random audit

REFERENCE GUIDELINES OF WOMEN'S COLLEGE HOSPITAL REB

The REB is guided in its decisions on research protocols by a number of key documents at the local, national and international level. As the Tri-Council Policy Statement 2 – Ethical Conduct for Research Involving Humans (2014) has been adopted as a national standard, at a minimum the REB will be in compliance with the standards set forth in this document.

The REB is responsive to changing best practices in research ethics and will attend to developments at the local, national and international levels, including the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); The Ontario Personal Health Information Protection Act, 2004; Food and Drug Administration Policy and interpretations; the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protection (OHRP) and the Office of Research Integrity directives and international declarations such as the Helsinki Declarationⁱⁱ on research ethics.

To the extent that such guidelines enhance the protection of research participants, the REB will adopt such practices.

ⁱ Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, 2014.

ⁱⁱ 64th WMA General Assembly, Fortaleza, Brazil, October 2013