

**UNIVERSITY OF WATERLOO
CLINICAL RESEARCH ETHICS BOARD**

TERMS OF REFERENCE

A. Statement of Institutional Authority for Research Ethics Boards

The University of Waterloo has two Research Ethics Boards (REBs): the Clinical Research Ethics Board and the Human Research Ethics Board. As constituted sub-committees of the University of Waterloo's Senate Graduate and Research Council, both University of Waterloo's REBs are established and empowered under the authority of the University of Waterloo Senate.

B. Mandate and Accountability of the Research Ethics Boards

The REBs' mandate, on behalf of the University, is to protect the rights and welfare of human participants who take part in research conducted under the auspices of the University. The University of Waterloo's REBs review such research to ensure that it meets ethical principles and that it complies with all applicable regulations, guidelines and standards pertaining to human participant protection. These include but are not limited to the University of Waterloo's Statement on Human Research; its Guidelines for Research with Human Participants (Guidelines) and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, 2nd edition (TCPS 2). For clinical trials, the REBs follow Health Canada's Food and Drugs regulations (Part C, Division 5), Natural Health Products Regulations (Part 4), Medical Devices regulations (Part 3), International Conference for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidance: Good Clinical Practice, International Organization for Standardization of Good Clinical Practices (GCP) as set out by ISO 14155 – Clinical Investigation of medical devices for human subjects, and international regulations, including U.S. federal regulations for research involving human participants. The University of Waterloo's REBs also operate under applicable laws and regulations of the Province of Ontario and of Canada.

The University of Waterloo requires that all research involving humans or human biological materials conducted in its jurisdiction or under its auspices, undergo ethics review and clearance by one of its two REBs prior to initiation of any research related activities, including recruitment and screening activities.

The Clinical Research Ethics Board (CREB) has jurisdiction over clinical trials research (i.e., involving a drug or natural health product or is medical device testing) conducted under the auspices of the University of Waterloo, research involving a "controlled act" as defined under the Regulated Health Professionals Act of Ontario, 1991, and other research activities as defined under approved standard operating procedures. The Human Research Ethics Board (HREB) has jurisdiction over all other research involving humans with which the University is affiliated.

C. Membership of the CREB

Membership shall be consistent with the requirements for REB composition specified in Article 6.4. of the TCPS 2 and ICH Good Clinical Practice: Consolidated Guideline. All Board members shall be competent to judge the ethical acceptability of research ethics applications they review. In accordance with Article 6.3 and Chapter 8 of the TCPS 2, in the interest of fostering a collaborative spirit and appropriate levels of information sharing between both REBs, and to facilitate timely and effective reviews for researchers, members of CREB may be required to serve as reviewers, in either a delegated or ad-hoc sub-committee capacity, for applications

made to HREB if, in the judgment of the Chair of HREB, the application requires expertise which the CREB member has been judged to possess.

To fulfill the mandate of the Board, the membership will be comprised of both voting and non-voting members.

The CREB shall consist of a minimum of 11 voting members:

- three faculty members including
 - one faculty member with expertise in vision science from Optometry
 - one faculty member with expertise in Pharmacology or Immunology/Toxicology from Pharmacy
 - one faculty member with expertise in the science of human movement from Kinesiology
- two clinical physicians knowledgeable about clinical trials research
- one lawyer preferably knowledgeable about clinical trials research and privacy
- one member knowledgeable in ethics/bioethics
- two community members who have no affiliation with the institution
- one member that is a student or post-doctoral fellow preferably with experience in the conduct of research with humans
- one member with expertise in statistical methodologies

The Board must reflect gender diversity and therefore, will seek a membership including a mix of men and women, and where possible other gender minorities.

To ensure that research is open, accessible, and inclusive to all, the Board will always strive for the membership to represent diverse perspectives that go beyond gender including but not limited to race, cultural backgrounds, disability, lived experiences, and different ways of knowing and being. The Board's membership is to have the perspectives and capacity to review all forms of research, including studies with, for, and about people from diverse backgrounds, including but not limited to Black, Indigenous, and racialized peoples¹. The Board upholds the Ontario Human Rights Code prohibiting actions that discriminates against a person becoming a Board member based on a protected ground in a protected social area².

Non-voting members of the Board act as resource support, offer expertise and assistance on matters under consideration by the Board, and share information as needed³. The following additional members are ex-officio (non-voting):

- Director, Research Ethics
- Senior Manager / Manager, Research Ethics
- Research Ethics Advisor

An alternate community member and an alternate student member may be sought to ensure these positions are represented on the Board at each meeting, whenever possible.

D. Terms of Office for the CREB

¹ CREB uses the terminology Black, Indigenous, and racialized peoples but recognize that other terms may be used to encapsulate these identities. Language is regularly evolving, and CREB approaches this with the utmost respect, and with acknowledgement that as we move forward, there will be different perspectives.

² The Ontario Human Rights Code protected grounds and protected social areas can be found at <https://www.ohrc.on.ca/en/ontario-human-rights-code>.

³ TCPS 2, Article 6.4 stipulates "where research ethics administration staff have the requisite experience, expertise, and knowledge comparable to what is expected of REB members, institutions may appoint them (based on written policies and procedures of the institution) to serve as non-voting members on the REB.

1. Following consultation with the respective Faculty Deans and Department Chairs/School Directors and the CREB Chair, the Director will nominate members of the CREB.
2. The Senate Graduate and Research Council shall appoint members of CREB.
3. The Vice-President Research and International will nominate the Chair and Vice Chair from the CREB membership. The Chair will have a minimum of one-year prior experience as a member of the CREB. An additional member may be appointed from the same area of expertise as the Chair. The Vice Chair may discharge the responsibilities of the Chair when the Chair is unable to do so, discharge responsibilities assigned by the Chair and assist in the overall operation of the REB, as requested,
4. Members of the CREB, except the ex-officio members, will serve for a three-year term, when possible, normally renewable once. Terms will be overlapping to preserve experience and continuity of function.

E. Meetings of the CREB

1. The CREB normally will meet face to face eleven times per year. In the absence of any business, meetings may be cancelled by the Manager (or delegate) in consultation with the Chair.
2. Additional meetings of the CREB, or of a sub-committee of its members, may be called by the Manager in consultation with the Chair, as necessary.
3. Each meeting will require the involvement of a quorum defined as half the total voting membership plus one. Quorum must also meet membership criteria specified by relevant research ethics guidelines and regulations. Every effort will be made to ensure that each meeting includes a community member.
4. Members shall normally attend CREB meetings with at least 70% attendance per year. When unexpected circumstances arise that prevent a regular member from attending a CREB meeting in person, arrangements will be made where feasible with the member to participate through use of technology (e.g., telephone or video link). In cases where a regular member cannot attend CREB meetings for a protracted period (e.g., during a 6 month's sabbatical), a substitute member from the same discipline may be appointed to serve during the regular member's absence.
5. Members shall notify the Manager of an anticipated absence at least one day prior to a meeting. Members who cannot attend a meeting are expected to provide written comments on each of the protocols under review at the respective meeting. This information is provided to other members of the CREB and becomes part of the discussion and meeting minutes.
6. At the outset of each meeting, members shall declare any real, perceived, or potential conflict(s) of interest related to the applications under review. Examples of conflicts of interest include but are not limited to applications on which they are listed as Principal Investigator (PI) or co-investigator; current or past research collaborations with investigators listed on the application; applications on which students they supervise are listed. Other members of the CREB will decide whether the member with the conflict of interest should recuse themselves from related discussions.
7. The CREB will reach its decisions concerning the ethical acceptability of research that is undergoing ethics review through a process of open discussion and consensus. When members are unable to reach consensus, a vote of the quorum present may be taken

and recorded.

8. The CREB's deliberations and decisions will be documented in comprehensive, confidential minutes that are securely maintained. The Research Ethics Advisor shall serve as secretary to the CREB.
9. Detailed written feedback from the CREB including its decision on the ethical acceptability of the research shall be communicated to the researcher(s) by the Manager following consultation with the Chair, CREB, in an efficient and timely manner according to standard operating procedures. Feedback is based on minutes of discussion of the research project.
10. The CREB may, where appropriate, request that the PI or his/her designate attend a meeting to provide further information about and/or to discuss his/her research. The CREB will also accommodate reasonable requests from a PI to attend a meeting to participate in discussions about their research.
11. The CREB may seek the confidential opinion or advice of an ad hoc advisor/reviewer from among University of Waterloo faculty or from a confidential external consultant on a particular application to ensure it has the necessary background information and knowledge to review the ethical acceptability of the application.

F. Responsibilities and Mandates of the CREB

1. To ensure that all research under CREB jurisdiction, involving human participants conducted by students, staff and faculty affiliated with the University of Waterloo, and all clinical trials research conducted at Waterloo by unaffiliated students, staff, and faculty researchers, undergo ethics review and clearance prior to being conducted. This research may be conducted on- or off-campus and may be funded or unfunded.
2. To review the ethical acceptability of all research projects, under CREB jurisdiction, involving human participants on behalf of the institution including, but not limited to, those that:
 - may pose greater than minimal risk to participants (i.e., physiological, psychological, economic, social, or other);
 - involve recruitment of persons who may be vulnerable as research participants in the context of a specific study, and/or cannot legally give free and informed consent
 - include ethically sensitive issues, topics and/or procedures; and
 - stipulate full REB review as required by certain granting agencies

The CREB may grant clearance, propose modifications, disapprove, or terminate proposed or ongoing research conducted within the jurisdiction of the University or under its auspices to ensure that a proportionate review of risks and benefits has occurred in accordance with the ethical framework proposed under the TCPS 2.

G. Delegation of CREB Authority Related to Ethics Review and Clearance

The CREB delegates to the Director, Senior Manager / Manager, and Research Ethics Advisor(s), by virtue of their membership on the CREB, and according to standard operating procedures, authority to conduct:

1. Initial ethics review and clearance of research under its jurisdiction that poses minimal risk to research participants and includes provision of comprehensive and timely written feedback.

2. Ethics review and clearance of modifications to ongoing research under its jurisdiction that poses minimal risk to research participants and includes provision of comprehensive and timely written feedback.
3. Annual ethics review and clearance of all research under its jurisdiction that continues beyond one year.
4. Ethics review and clearance of all revised materials and related documents associated with the ethics review feedback process involving minimal and greater than minimal risk research except for applications that have been categorized as requiring a review by a sub-committee of the CREB or the full CREB.

H. Delegation of CREB Responsibility for Record Keeping and Research Ethics Education

The CREB ensures with assistance of Research Ethics Staff that:

1. CREB members are provided with opportunities for research ethics education during their tenure on the CREB beginning with a new member orientation session.
2. Comprehensive, accurate records (i.e., paper, and electronic) of the initial and continuing (i.e., modifications, annual) ethics review and clearance processes are securely maintained for all research under its jurisdiction. This includes all revised materials associated with initial and continuing ethics review.
3. CREB meeting dates and submission deadlines are easily accessible by researchers through information posted on the Research Ethics website.
4. CREB members receive a monthly report is received on minimal risk research that has undergone ethics review and clearance through the delegated ethics review process by the Research Ethics staff.
5. Timely information and regular reports are received on any unanticipated issues (events) that have occurred in association with research under its jurisdiction.
6. University of Waterloo guidelines, procedures and sample materials related to the conduct of research with humans are reviewed and updated on a regular basis (e.g., annually) to ensure that they remain current in an evolving research ethics environment.
7. Educational activities (e.g., in-class presentations, seminars, and workshops) are provided to University of Waterloo students, faculty and staff involved in research with human participants.
8. Legal or other advice is sought, as required, on matters related to the protection of human participants in research.
9. Timely information on guidelines, procedures, and other matters related to the conduct of research with human participants is provided to the CREB as well as student, staff and faculty researchers who conduct research with humans.

G. Reconsideration and Appeal of CREB Decisions

1. Reconsideration Process

A Principal Investigator (PI) may make a written request for reconsideration of a CREB decision when ethics clearance is not granted, or when ethics clearance is conditional on revisions that the PI believes may jeopardize the feasibility or integrity of the research. In consultation with the Chair, the Director (or delegate) will refer such a request, including documentation and supporting materials received for reconsideration from the PI to other members of the CREB for discussion at its next meeting. The CREB will review the written documents, and where appropriate, will request an informal meeting with the PI (or their designate). Following consideration of all additional information (verbal and written), the CREB will reach a final decision with respect to its position on the original decision. Every attempt will be made, in consultation with the PI to reach a resolution by this informal route.

2. Appeal Process

In the event the matter cannot be resolved through a reconsideration or informal process, the institution shall provide the PI with prompt access to an established appeal process through which the PI may appeal the CREB's decision. An appeal can be requested for procedural or substantive reasons. An appeal committee shall be appointed through the same authority that established the REB, ensuring that members of the appeal committee will have expertise and knowledge to be able to competently judge the ethical acceptability of the research ethics application under review. Members of the CREB whose decision is under appeal shall not serve on the appeal committee. The appeal committee will act impartially in its review of documentation provided by the CREB and the PI (or designate), and will consult with others as required, including but not limited to, members of the CREB and the PI (or designate). The appeal committee will issue a written report with its decision on the matter with copies to the PI and CREB. It may approve, reject, or request modifications to the research proposal. The appeal committee's decision will be final.

*Approved Senate Graduate & Research Council, February 2009;
 Revised CREC Oct. 2011; approved Senate Graduate & Research Council, Nov. 14, 2011
 Revised CREC August 2012, approved Senate Graduate & Research Council, Sept. 10, 2012
 Revised ORE August 2013; approved Senate Graduate & Research Council, September 9, 2013;
 Revised ORE August 2016; approved Senate Graduate & Research Council, September 12, 2016
 Revised CREC December 2019; approved Senate Graduate & Research Council, February 10, 2020
 Revised CREB September 2022; approved Senate Graduate & Research Council, October 3, 2022
 Revised CREB April 2024; approved Senate Graduate & Research Council, May 6, 2024*