The Ontario Cancer Research Ethics Board
Overview

Research Ethics

Research ethics review is vital to the advancement of ethically sound research. Before individuals can be enrolled in a research study, the study must be approved by a research ethics board (REB). REBs are independent, multi-disciplinary committees that review the ethical acceptability of research involving humans. REBs that review biomedical research generally include doctors and other members of the scientific community, as well as non-scientific members with specific expertise, including ethicists, lawyers, privacy experts and community members. The REB's role is to safeguard the rights and welfare of the individuals who volunteer to participate in research, by ensuring that the study sponsors and the researchers have adequately considered and applied the required ethical principles into the design and conduct of the research.

The Ontario Cancer Research Ethics Board

The Ontario Cancer Research Ethics Board (OCREB) was established in 2004 as an arms-length program of the Ontario Institute for Cancer Research (OICR), accountable to the Board of Directors of OICR through an OCREB Governance Committee. OCREB is a central, expert oncology REB serving the hospitals/cancer centres in Ontario that conduct oncology clinical trials. OCREB's centralized model means that once a study has been approved by OCREB, participating study sites receive OCREB approval within days. This model not only provides a robust ethical focus on oncology research, but also streamlines the review process, minimizes redundancies, promotes consistency, and saves the time and cost of having the study reviewed by an REB at every participating institution/study site. Since its first meeting in January 2004, OCREB has been working with researchers, institutions and sponsors to safeguard the rights and welfare of research participants in Ontario, while advancing ethically sound cancer research.

For the purposes of its current mandate, multi-centre is defined as more than one participating Ontario centre, and clinical trial is defined as any research that prospectively assigns human participants to one or more health-related interventions to evaluate the effects on health outcomes. Interventions are restricted to drugs and other biological products, surgical procedures, radiological procedures and devices. OCREB will accept a new study with only one confirmed participating centre providing the sponsor is actively looking for and is confident that a second centre will agree to participate.

Because cooperative group studies generally include more than one centre in Ontario, OCREB will accept the submission of all cooperative group (e.g., CCTG, NRG) multi-centre clinical trials even if a second centre has not been identified by the Provincial Applicant (PA) at the time of initial submission.

Beginning in May 2015, OCREB began accepting non-phase 1, multi-centre Children's Oncology Group pediatric clinical trials, as the first pediatric trials reviewed by OCREB. "The Children's Oncology Group (COG), a National Cancer Institute supported clinical trials group, is

the world's largest organization devoted exclusively to childhood and adolescent cancer research."

Studies that meet OCREB's mandate may be sponsored by academia, by co-operative groups or by industry/pharmaceutical companies. Approximately 50% of the submissions received by OCREB are industry-sponsored and 50% are sponsored by academia or cooperative groups, including investigator-initiated trials.

OCREB Membership

OCREB operates in compliance with, and is constituted in accordance with, the requirements of: Canadian Institutes of Health Research; Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, TCPS2 (2014) - Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans; the International Conference on Harmonization of Good Clinical Practices; Part C Division 5 of the Food and Drug Regulations of Health Canada; and the provisions of the Ontario Personal Health Information Protection Act 2004 and its applicable Regulations. OCREB is registered with the U.S. Department of Health & Human Service under the IRB registration number IRB00003960.

OCREB members are drawn from the oncology communities from which clinical trial submissions are received. Members collectively have the qualifications and experience to review and evaluate the science, the medical aspects, and the ethics of the proposed research for both adult and pediatric oncology trials. OCREB membership includes: medical, surgical and radiation oncologists and hematologists; nurses with clinical and/or research experience in oncology; informed community members including people with cancer and family members of people with cancer; and members with expertise in research ethics, relevant law, privacy legislation and other related disciplines such as pharmacy, pathology, and statistics. OCREB is comprised of members from across Ontario representing many of the institutions affiliated with OCREB.

The Chair and Vice-Chair(s) of OCREB are appointed based on the process outlined in their Terms of Reference. The Chair's responsibilities includes the appointment of OCREB members, who may serve up to two terms (2 to 3 years per term). New members are provided with orientation and education prior to the assumption of their responsibilities, and also must complete the TCPS2 online tutorial. An evaluation of the OCREB Chair & Vice-Chair(s) is conducted annually. Evaluation of OCREB members is currently in development.

OCREB appoints "regular" and "alternate" members. Regular members are expected to attend 75% of the meetings. Substitute or alternate members are expected to attend a minimum of two meetings per year, and to attend meetings when/if the regular member is not available. When a regular member's term ends, an alternate member generally replaces the regular member; however, this is not a requirement. Members receive a modest honorarium for serving on OCREB, and are reimbursed for reasonable travel costs to attend the meetings.

OCREB Reviews

The OCREB meetings are held in Toronto on the second Friday of every month. Each OCREB member with their unique and informed perspective is expected to review all of the submissions on the agenda, and to provide their reviews prior to the meeting. Studies are assigned to a primary and a secondary reviewer who conduct in-depth reviews of one or more of the new

studies, in addition to any other assigned reviews (e.g., amendments). Due to the nature of the studies reviewed by OCREB, primary and secondary reviewers generally are oncologists and study nurses/trial coordinators, respectively.

In addition to submissions that are reviewed by the full Board, there are submissions that meet the criteria for expedited or delegated review (e.g., some amendments, provincial and centre reportable events, centre initial applications, investigator responses to OCREB review letters). For those submissions, the Chair or one of the Vice-Chairs and other OCREB members, as applicable, conducts the review on behalf of the Board. Submissions that are approved under expedited/delegated review procedures are appended to the agenda of a full Board meeting.

Establishing an Affiliation with OCREB through CTO

In February 2017, the Ontario Institute for Cancer Research (OICR) entered into a Participation Agreement with Clinical Trials Ontario (CTO). Under this agreement and as a CTO Qualified REB, OCREB continues to serve as an expert oncology central REB for multi-centre cancer trials. Applications for OCREB review are submitted in CTO Stream, which is a secure, web-based system developed and administered by CTO for province-wide health research submissions. OICR's participation agreement with CTO supports the initiative to have one online system with the same application forms for multi-centre health research review in Ontario, using a single review model, and facilitates these REB submissions for research teams, institutions and study sponsors.

Despite the change in the online submission system, all OCREB requirements as found in its policies, procedures and consent templates remain in effect. This includes the pre-approval of all centre-specific consent forms without the requirement for OCREB review. For any questions related to OCREB's policies, procedures, please contact the OCREB Research Ethics Officer.

In order to submit studies to OCREB, institutions must enter into a Participation Agreement with CTO. Each institution also must maintain a Federal Wide Assurance (FWA) with the US Office for Human Research Protection (OHRP) and designate OCREB as an REB responsible to the institution under the institution's FWA. The institution may authorize the use of OCREB as their REB of Record on a study-by-study basis by executing a CTO REB of Record Agreement. This Agreement defines the roles and responsibilities of the REB, of the institution and of the Principal Investigator (PI). In this REB of Record capacity, OCREB serves as the REB for the institution on the delegated study. Twenty-eight of the 29 institutions in Ontario have authorized OCREB to act as the REB of Record for designated multi-centre oncology trials.

Institutional roles/responsibilities

Given that ethics review is only one of the reviews that is required before research studies can be initiated at the centre-level, when OCREB is the REB of Record, the institution continues to be responsible for all ancillary reviews, (e.g., resource analyses, institutional/departmental impact assessments, grants and contracts, etc.). If these traditionally have been coordinated or conducted by the local REB, the institution must establish new processes for ancillary reviews.

Although OCREB will consider the PI's training and experience in its review, the institution is responsible for ensuring that the researcher and the research teams are qualified and adequately trained, and have appropriate resources to conduct the research. Institutions also are responsible

for internal audits of the studies, although the OCREB Research Ethics Officer (REO) will work closely with the institution's Quality Assurance (QA) department if requested.

OCREB works with each affiliated institution to ensure that the local context and relevant institutional policies are respected. To date, this has been reflected mainly in consent form language. If there are local policies to be considered, this information is brought to OCREB for consideration prior to the submission of the centre initial application.

Submission and Review Processes

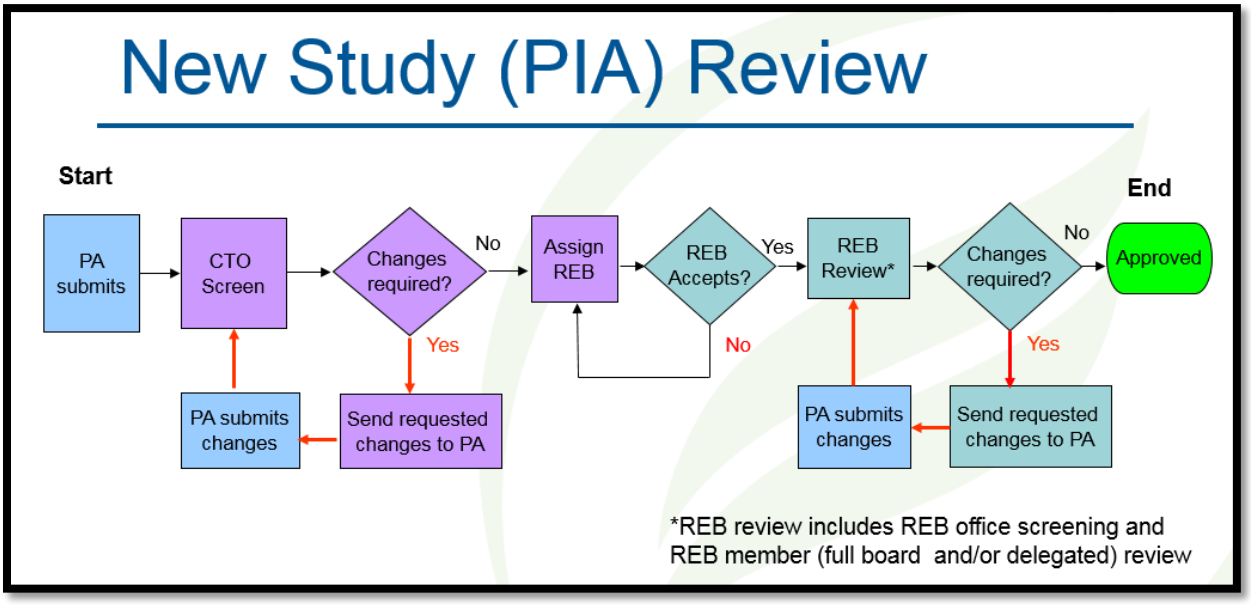
Applications to OCREB must be prepared and submitted in CTO Stream - CTO's online submission system - using the CTO Stream clinical trial application forms. To access information about CTO Stream, including user manuals, go to www.ctontario.ca/streamlined-research-ethics-review-system/cto-stream/cto-stream-overview/. For questions related to CTO Stream, contact CTO Support at 1-877-715-2700 or streamline@ctontario.ca.

NOTE. All OCREB requirements as found in its policies, procedures and consent form templates remain in effect.

Provincial or Study-Wide Submissions

A Principle Investigator (PI) at one of the participating centres assumes the role of lead or "Provincial Applicant" (PA) and as such, assumes responsibility for submitting all study-related (provincial) materials to the REB on behalf of the participating centres. This includes the provincial initial application (PIA), and all provincial post-approval applications. To facilitate submissions, representatives of the sponsor or the CRO may create and complete applications; however, the submitting PI is responsible for the content and quality of the submissions.

Before assigning a PIA to an REB, CTO screens the initial submission of the PIA to ensure that the study meets the CTO mandate, that the appropriate institutional representative is listed in the application, and to confirm that the PA/PI has signed the application.



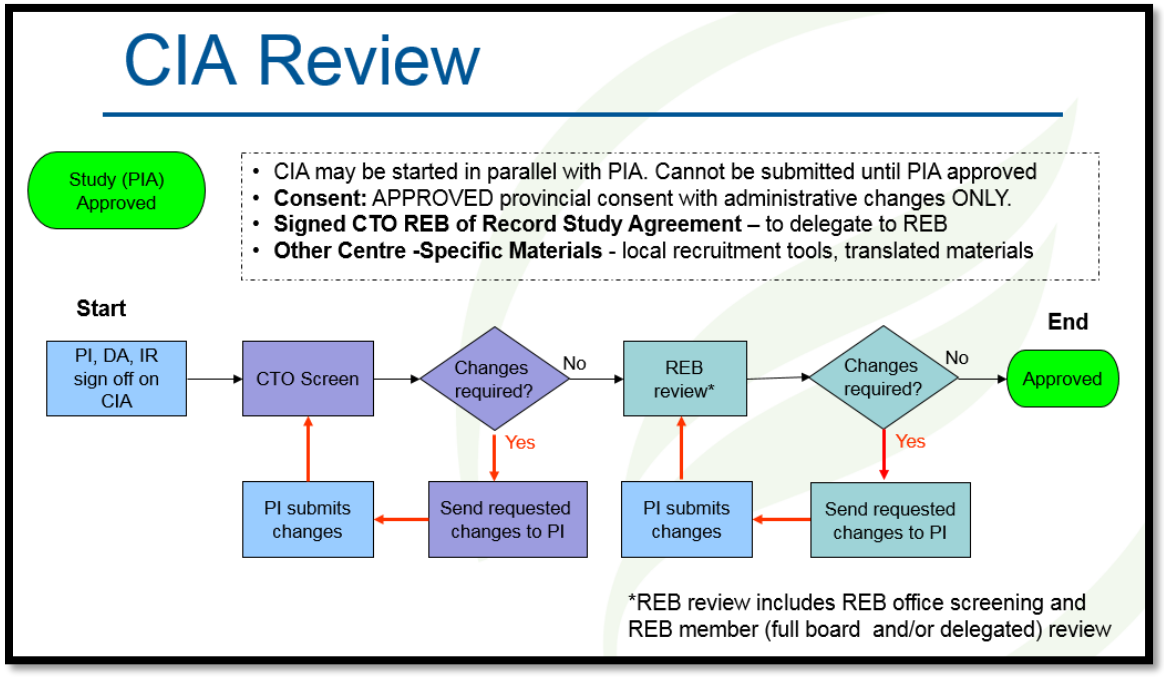
The PA is responsible for all post-approval, study-wide submissions on behalf of all participating centres: provincial amendments (PAMs) - e.g., protocol, consent forms, investigator brochures; provincial reportable events (PREs) - e.g., DSMB reports, interim analysis reports; and provincial continuing review (PCR) applications. OCREB approves PAMs simultaneously for all approved participating centres.

If combined, the provincial initial and centre initial applications would be similar to a single initial application typically submitted by a researcher to a local REB. However, in the multi-centre, single review model, the submission is divided into two parts – a generic PIA followed by a CIA. In this single REB review model, only the PA submits both the provincial and their own centre-specific applications. All other applicants submit only their own centre-specific applications.

A member of the Provincial Applicant research team (which may include the sponsor) usually creates the CIA for each participating centre, and then add a member of that centre's study team to the application by giving them a 'role' on the study. This user subsequently can add other centre users as needed and complete the CIA.

Centre Submissions

The CIA may be drafted in parallel with the PIA; however, the application cannot be submitted until the PIA is approved. Once OCREB issues approval of the PIA, the PI at each participating centre is able to submit an abbreviated centre initial application (CIA) for approval to conduct the study. The study cannot be initiated at the centre-level until the CIA is approved. CTO screens the initial submission of the CIA to ensure that the PI, a department approver (DA) and an Institutional Representative (IR) have signed-off on the CIA.

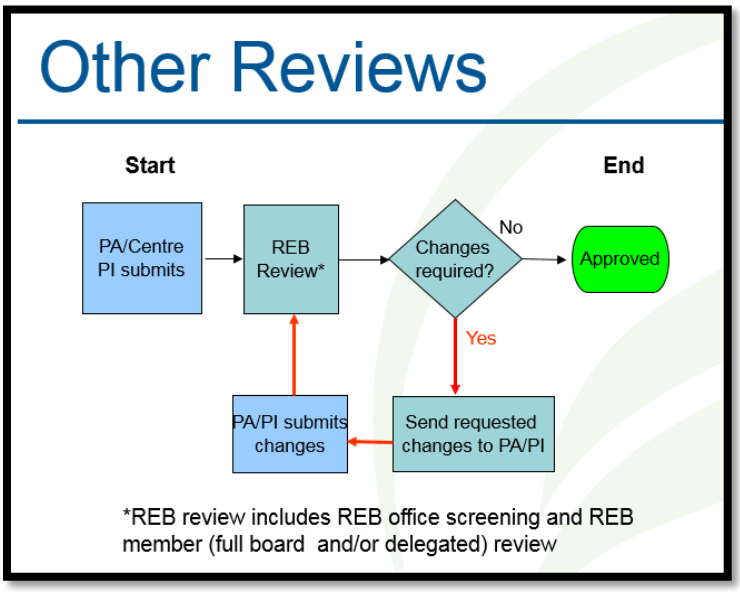


In order to present a consistent consent form(s) to all study participants in Ontario, each centre must adopt the OCREB approved provincial consent form(s) for implementation at the centre-level. Centres may apply pre-approved administrative changes to the consent documents without

further OCREB review and approval. Administrative changes include, for example, the addition to the document of centre contact information and letterhead, the correction of spelling errors, compensation information, and any pre-approved, centre-specific changes that have been authorized by OCREB. The version date of the centre-specific consent form(s) retains the version date(s) of the approved provincial consent form(s). Refer to OCREB's "*Guidance for pre-approved administrative changes*" for details.

At the time of a provincial amendment, all provincially approved study documents (including amended and new participant materials such as wallet cards and consent forms), are approved for use by all of the participating centres which have OCREB approval to conduct the study. Thus the centres do not have to submit a separate application to implement an approved PAM.

Each centre PI is responsible for the conduct of the study at his/her centre, and for the submission of all centre-specific post-approval applications such as: centre reportable events (CREs) - e.g., local adverse events, privacy breaches and protocol deviations that meet the reporting criteria; centre amendments (CAMs) – e.g., to change the centre PI; and, centre continuing review (CCR) applications.



NOTE. *The review process flowcharts displayed in this document assume a final REB decision of "approved". However, some submissions may not receive REB approval.*

OCREB Office & Operations

The OCREB program is staffed by an Executive Director (ED), a Research Ethics Officer (REO) and Research Ethics Coordinators (RECs). The RECs support the activities of OCREB on a day-to-day basis, working closely with the Chair & Vice-Chair(s), as well as other OCREB members when necessary.

The ED is responsible for the management of the overall operations of OCREB. In collaboration with the OCREB Chair, the ED also is responsible for stakeholder relations and quality management activities. The ED works closely with the Chair on setting the strategic direction and annual goals of the program.

The REO is responsible for developing, implementing and monitoring ethics review process standards. The REO contributes to OCREB's continuous quality improvement through education and communication on research ethics, and through quality control and quality assurance activities that promote conformity with applicable guidelines, standards, policies, and regulations associated with human research participant protections.

Education

OCREB hosts monthly web meetings/teleconferences to offer opportunities for OCREB staff, and for clinical trial staff at the affiliated centres to learn about participant protection responsibilities, and to stay up-to-date on current issues in the research ethics field and on current OCREB processes and procedures. Although not mandatory, centres are encouraged to attend. Additional ongoing education opportunities are provided for OCREB members and for OCREB office personnel.

For more information about OCREB, visit www.ocreb.ca.