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) which is an independent committee composed of medical and scientific experts, ethicists, researchers, and healthcare professionals, as well as non-scientific members, including legal and privacy experts, and community representatives. The REB's role, in collaboration with the investigator and the institution, is to ensure that the rights, safety and well-being of the research participants are protected.

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. Since January 2004, the OCREB has filled a unique role in Ontario as the single, expert, centralized oncology REB acting as the REB of record for institutions in which oncology clinical trials are conducted. During this time, OCREB has provided rigorous ethics reviews and oversight for multi-centre cancer trials, while streamlining the ethics review process.

OCREB's current mandate is limited to multi-centre oncology clinical trials**.** 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. Research submissions that meet the established mandate are accepted from academia, co-operative groups, and from industry sponsors; approximately 50% of the submissions are from industry and 50% from academic or cooperative group sponsors, 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 community 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 and/or cancer survivors; and members with expertise in research ethics, relevant law, privacy legislation and other related disciplines such as pharmacy 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 include the selection and 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 prior to conducting reviews.

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 terms ends, a substitute 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.

An evaluation of the OCREB Chair & Vice-Chair(s) is conducted annually. Evaluation of OCREB members is currently in development.

OCREB Meetings & Member Roles

The OCREB meeting schedules and submission deadlines for the monthly meetings that are held in Toronto on the second Friday of every month are posted publicly. Each OCREB member with their unique and informed perspective is expected to review all of the submissions scheduled for review, and to provide their reviews prior to the meeting. Each study also is assigned to a primary and a secondary reviewer who are delegated to 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, PI responses to OCREB review letters, etc.). For those submissions, the Chair, or one of the Vice-Chairs and/or one of the OCREB members conducts the review on behalf of the Board. Submissions that are approved under expedited/delegated review procedures are appended to the agenda of the next available full Board meeting, with a live link to the submission and reviews.

Establishing a Board of Record Affiliation with OCREB

In order to submit research studies to OCREB, institutions must first establish an affiliation with OCREB through a non-binding Letter of Intent. Each institution also must maintain a Federal Wide Assurance (FWA) with the US Office for Human Research Protection (OHRP) in which OCREB is designated as an REB responsible to the institution under the institution's FWA. Once this is established, the institution may authorize the use of OCREB as their REB ("Board") of Record on a study-by-study basis by executing a Board of Record Study Agreement. This

Agreement includes a division of responsibilities to define the roles and responsibilities for OCREB, for the institution and for the Principal Investigator (PI). In this Board of Record capacity, OCREB serves as the REB for the institution on the delegated study. Twenty-eight of the 30 cancer institutions (including pediatrics) in Ontario have established affiliations with OCREB as the Board 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 any ancillary reviews, (e.g., resource analyses, institutional/departmental impact assessments, grants and contracts, etc.). If these reviews traditionally have been coordinated or conducted by the local REB, the institution must establish new processes for ancillary reviews/approvals.

As an example of the division of responsibilities between OCREB and the institution, during the review of a centre initial application, OCREB will consider the PI's CV and other information about the PI's training and experience. However, the institution will be responsible for ensuring that the researcher and the research team are qualified and adequately trained, and have appropriate resources for the conduct of 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, where, if there are local policies to be considered, this information is brought to OCREB for consideration, prior to the submission of the initial centre-application.

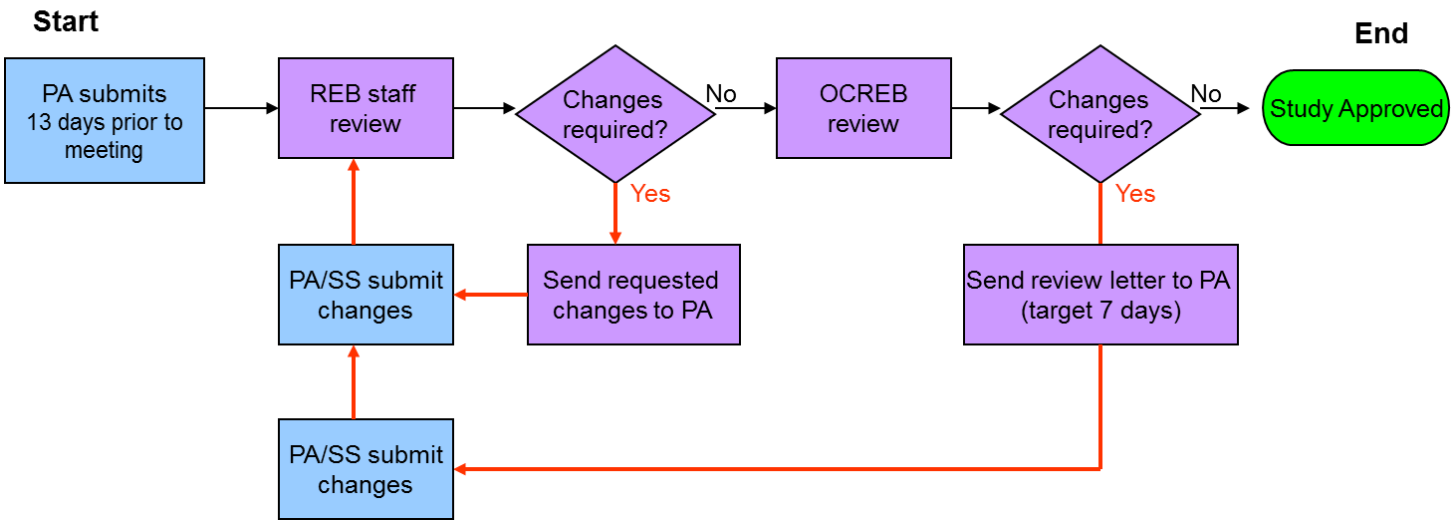
Submissions to OCREB

Provincial Submissions

For research studies submitted to OCREB, a designated lead or "Provincial Applicant" assumes responsibility for the study submission. For most new studies and all industry sponsored studies, a Principle Investigator at one of the participating centres assumes the role of the Provincial Applicant (PA). Alternatively, a representative from one of the academic or cooperative group sponsors (e.g., OCOG, PMHC) may serve as the PA. The PA assumes overall responsibility for submitting all study- related materials to OCREB on behalf of the participating centres. This includes the initial submission/new study, as well as any study- related amendments, reportable events, and continuing reviews (annual renewals).

The provincial initial submission includes the provincial initial OCREB application form as well as all of the supporting study documents provided by the sponsor. Supporting documents may include, but are not limited to: the protocol; the sponsor's proposed budget; the Investigator Brochure(s) and/ or product monograph(s); the generic consent form(s); any other study participant materials such as questionnaires and diaries; the demographic page(s) of the CRF; and the Health Canada authorization letter (e.g., NOL), as applicable. The sponsor also provides the PA with a list of the Ontario PIs who potentially will conduct the study at their centres. The provincial initial approval of the study applies to all subsequent centre initial submissions.

Provincial Initial Application



The PA is responsible for all ongoing/post-approval, study- related submissions on behalf of all participating centres, such as: amendments to the protocol, to the consent forms, and to the investigator brochures; DSMB reports or interim analysis reports; external serious adverse event reports that meet the OCREB reporting criteria; etc. Provincial amendments are approved simultaneously for all approved participating centres. The PA also is expected to obtain information from the sponsor on the overall study status and global enrolment at the time of the continuing review submission (usually annually).

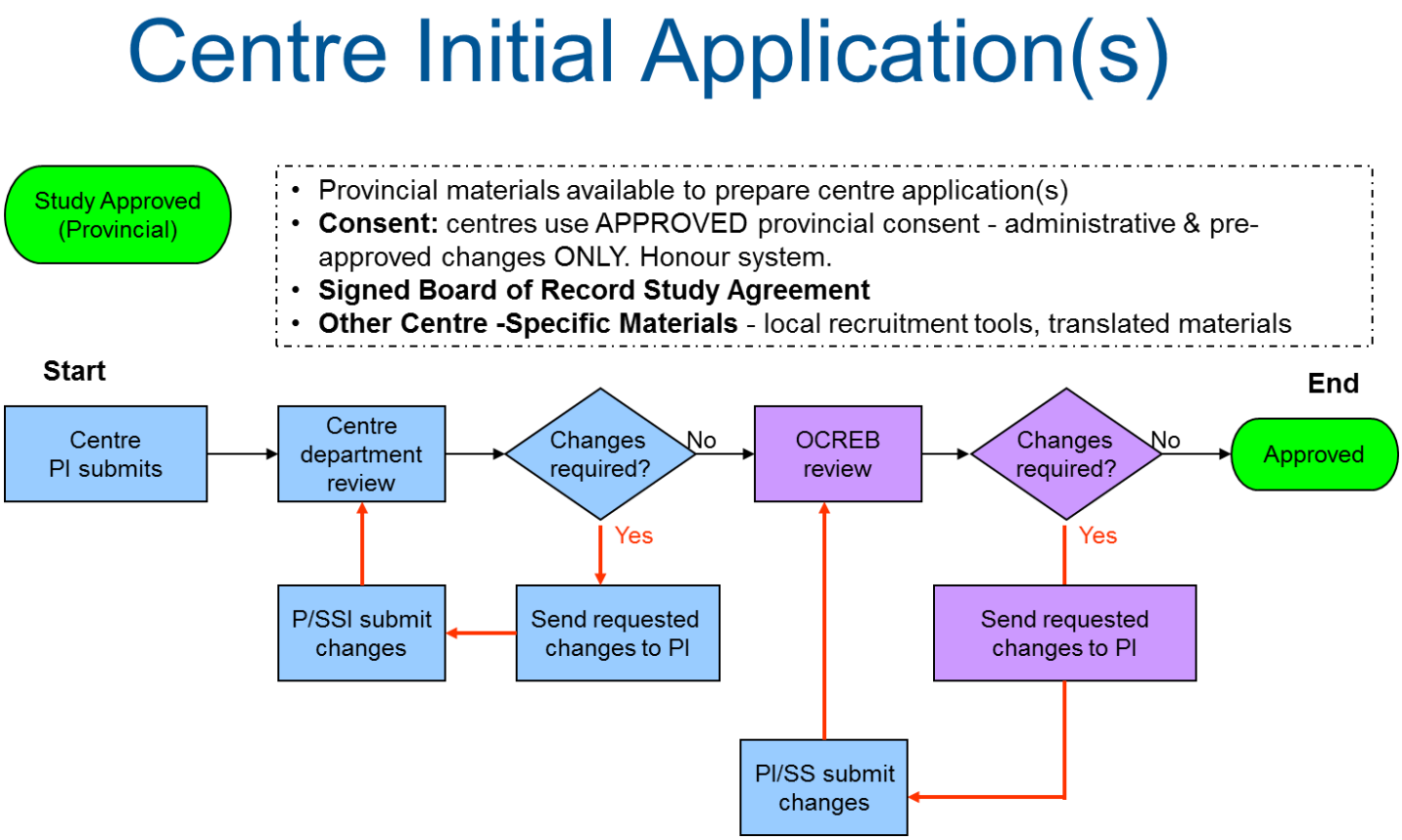
Notes:

- The PA is not expected to play a coordinating role for the centres conducting the study.
- To facilitate the submission process, representatives of the sponsor and/or the CRO may be provided with access to the OCREB materials. The PA must send a request to OCREB Online (O2) Support to obtain O2 accounts for each sponsor/CRO representative. Once the accounts are created, the PA can grant the individual(s) access to view the OCREB materials. In addition, if the sponsor/CRO is in agreement, after creating a provincial application, the PA may send the submission to one sponsor/CRO representative for completion; the representative must route the submission back to the PA for final review and submission to OCREB.

The combined initial provincial and initial centre applications are similar to a single initial application typically submitted by a researcher to a local REB. However, in the OCREB model, the submission is divided into two parts – a provincial initial (generic) application followed by a centre initial (centre-specific) application. Using the OCREB centre-review model, only the PA submits both the provincial (on behalf of all the participating centres) and a centre-specific application. All other applicants submit only a centre initial application.

Centre Submissions

Once OCREB issues approval of the new study (i.e., the provincial initial approval), the PI at each participating centre must submit an abbreviated centre-specific application for approval to conduct the study. The study cannot be initiated at the centre-level until the centre initial application is approved. An authorized department approver (DA) must sign-off on the centre initial application as part of the submission to OCREB. The DA attests to the following: 1) the feasibility and appropriateness of the study; 2) the PI's qualifications; 3) adequate space and resources to conduct the study; and, 4) that all institutional requirements will be met.



In order to present a consistent consent form(s) to all study participants in Ontario, each centre is expected to adopt the OCREB approved provincial consent form(s) for implementation at the centre-level. Centres may apply centre-specific administrative changes to the consent documents without further OCREB approval. Administrative changes include, for example, the addition to the document of centre contact information, a centre letterhead, the correction of spelling errors, and any pre-approved, centre-specific changes that have been authorized by OCREB and which are listed in the centre approval letter. The version date of the centre-specific consent form(s) retains the version date(s) of the already-approved provincial consent form(s).

At the time of a provincial amendment, all provincially approved study documents (including amended or new participant materials such as wallet cards and consent forms), are approved for use by all of the participating centres that have received approval from OCREB to conduct the study.

Each centre PI is responsible for the conduct of the study at his/her centre, and for the submission to OCREB of all centre-specific reportable events, (e.g., local adverse events, privacy breaches, protocol deviations that meet OCREB's reporting criteria, etc.), and of continuing review applications. Infrequently, centres may need to submit centre-specific amendments (e.g., to change the centre PI, to obtain OCREB approval for centre-specific recruitment materials or translated documents, etc.).

OCREB Office & Operations

The OCREB program is staffed by an Executive Director (ED), a Research Ethics Officer (REO) and three 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. In addition, the ED is the business lead on the development, implementation and ongoing operation and enhancement of the OCREB Online (O2) system, which was rolled out in 2011.

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.

Supplementing the OCREB support staff are an O2 Client Coordinator and an O2 Business Analyst. The Client Coordinator provides support to all users on the online system. The Business Analyst ensures continuity of O2 by providing the planning, technical leadership, and project coordination necessary to implement software improvements and upgrades and to resolve technical problems.

O2 is a secure, web-based system designed to simplify and streamline the ethics submission and review processes. With O2, OCREB processes, including meetings, are virtually paperless. Enhancements are made periodically to meet the user requirements. O2 provides important transparency and operational efficiency.

Education

OCREB hosts monthly 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 and https://ocrebonline.ca