Clinical Trials Ontario

Streamlined Research Ethics Review System

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CLINICAL TRIALS ONTARIO

CLINICAL TRIALS ONTARIO

- Independent non-profit, established in June 2012 and funded by the Government of Ontario
- Established to address the decline in clinical trials in Ontario and leverage Ontario's clinical research capabilities to attract more investment

THE VISION OF CLINICAL TRIALS ONTARIO (CTO) IS BEING ADVANCED UPON THREE STRATEGIC PILLARS:

1. Improving the speed and reducing the costs of multi-centre clinical trials by streamlining the research ethics approval process and harmonizing other administrative processes and platforms;
2. Attracting clinical trial investments to Ontario based on CTO's success in streamlining activities and by leveraging strategic partnerships with investigators, industry and government to access global decision makers; and
3. Improving participant recruitment and retention through education, and by engaging participants and the public in recognizing the benefits of clinical trials.

CTO STREAMLINED RESEARCH ETHICS REVIEW SYSTEM

- Supports a single REB in providing research ethics review and oversight to multiple research sites; relies on a “REB of Record Model”
- REB oversight responsibilities delegated by participating institutions to the REB of Record
- Can be used for any multi-site clinical research, i.e. industry sponsored or investigator initiated
- Currently can accept multi-site clinical trials; in future multi-site health research will be accepted as well
- Ensures that all REB reviews done through the CTO system are conducted by REBs that have achieved Qualification status
- Primary components:
  - ❖ **CTO REB Qualification Program**
  - ❖ **CTO Stream: Web-based Research Ethics Review System**

CTO REB QUALIFICATION PROGRAM

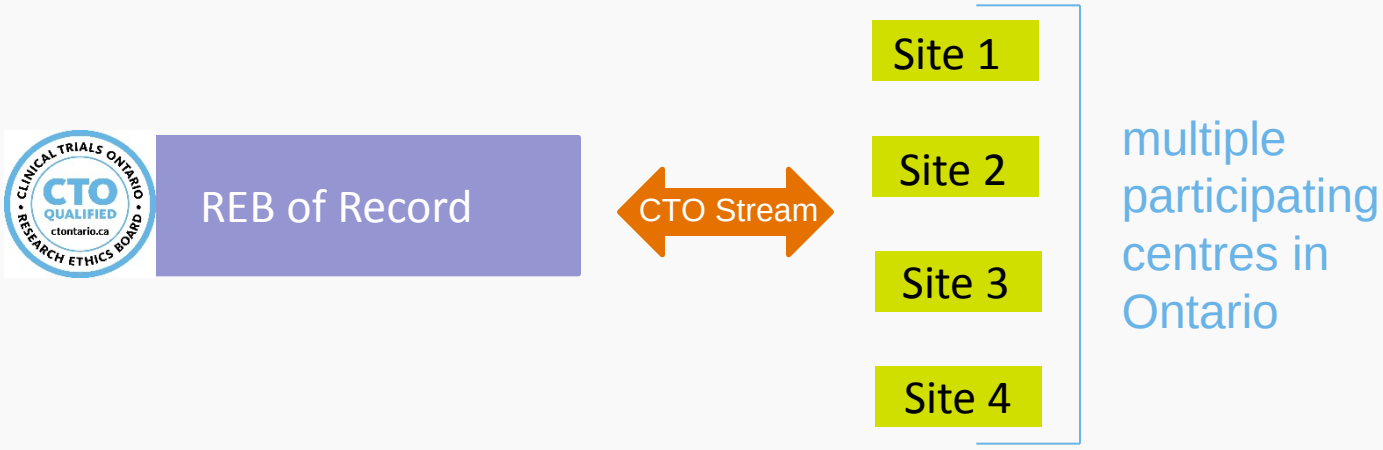
- Provides REBs planning to participate in the CTO Streamlined Research Ethics Review System with an external review of their governance, membership, operations and review procedures
- Based on the Toronto Academic Health Sciences Network (TAHSN) qualification process
- REBs are reviewed against a transparent standard, the CTO REB Qualification Checklist, that is informed by the applicable regulations, policies and guidelines. REB Qualification Manual available at www.ctontario.ca
- CTO REB Qualification checklist aligned with the N2/CAREB REB SOPS
- Each full visit is conducted by a Qualification Team composed of:
  - Auditor with specific training relating to review of REBs
  - CTO Program Coordinator
  - Two experienced members from the research ethics community (e.g., REB Chair/Vice-Chair and REB Director/ Manager/ Coordinator) selected from the CTO College of Reviewers.

WHICH STUDIES CAN USE THE STREAMLINED SYSTEM?

- Any clinical trial with 2 or more CTO participating sites in Ontario
  - List of CTO participating sites can be found at: http://www.ctontario.ca/streamlined-research-ethics-review-system/participating-sites/
- In general, academic hospitals, community hospitals, and academic organizations are eligible to be a CTO participating site
  - At present, private sites (e.g., those that would normally use a private REB) are not considered CTO participating sites
- Some non-clinical trials are currently going through the system, and we're hoping to fully implement our non-clinical trial application forms in the near future

THE STREAMLINED SYSTEM

- Facilitates a streamlined approach to research ethics review
- Supports any single CTO Qualified Research Ethics Board (REB) in providing ethics review and oversight for multiple research sites



CTO STREAM

CTO Stream is a standalone web-based electronic platform:

- Enables research ethics review, document management, and communication between multiple institutions and REB of Record
- Common application forms – all REBs use the same form
- Designed and built by Infonetica (UK), CTO and the research community
- Supports any file type for uploads (i.e., word documents, excel documents, pdfs and text files)
- Built using smart questions and smart forms; applications can be drafted by Sponsors/Coordinating Groups
- Electronic signatures for all applications; User friendly

REB OF RECORD MODEL

Initial Application Process

Step 1
Applying for a New Multi-Centre Clinical Trial

REB application submitted by any registered investigator/site, i.e. “Provincial Applicant”

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CTO assigns REB of Record **(any Qualified REB in Ontario)** and advances application

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REB of Record reviews application and resolves any issues with applicant

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Once issues are resolved REB of Record approves study

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Sites wishing to participate are notified and given access to REB materials in CTO system

Step 2
Adding New Investigators / Research Sites

Recruiting Institution signs REB of Record Agreement, delegating ethics review and oversight to REB of Record; Local PI adopts approved consent form and submits site application focused on site specific information

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Site application advances to REB of Record

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REB of Record Host Institution signs REB of Record Agreement and REB reviews application **(usually expedited)** and resolves any issues with site applicant

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REB of Record issues approval for site to participate

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REB OF RECORD MODEL

Continuing Oversight and Approval

New overall (study-level) event, e.g. amendment, Data Safety Monitoring Board report, safety update

Documentation submitted by “Provincial Applicant”

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REB of Record reviews submission and resolves issues with provincial applicant

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Once issues are resolved, approval or acknowledgement is issued by REB of Record and sent **simultaneously to all approved participating sites**

New site level event, e.g. continuing (annual) review, local Serious Adverse Event, protocol deviation

Documentation submitted by research site

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REB of Record reviews submission and resolves issues with research site

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Approval or acknowledgement issued by REB of Record

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RESPONSIBILITIES OF THE PROVINCIAL APPLICANT

- The Provincial Applicant is the individual responsible for submitting all study-specific information that applies to the overall research project to the REB of Record

- Provincial Applicant:
  - Investigator initiated studies – typically the investigator who holds the grant/funding
  - Industry sponsored trials – sponsor chooses

- This information includes:
  - Amendments
  - Continuing Review
  - Reportable Events (e.g., DSMC reports, Unanticipated Problems that result in a change to the protocol)
  - Study Completion/Termination/Suspension

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RESPONSIBILITIES OF THE PROVINCIAL APPLICANT

- The Provincial Applicant is required to review and sign the provincial submissions to the REB of Record
    - Preparation of the forms and material can be delegated to others, as applicable.
- Post-approval forms (e.g., amendments) that are being re-submitted to the REB of Record (e.g., following an REB's request for changes) can be signed by a delegate

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INFORMED CONSENT FORM-PROVINCIAL

- The Provincial Applicant team will create the study-wide consent form(s) that will be used as a basis for all local consent forms
    - This will be developed using the CTO Consent Form Template
- If there is an amendment that requires participant re-consent, a Consent Form Update format will be used
    - This is a short form that only contains the new/updated information, and is provided to previously enrolled participants

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RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

- The Principal Investigator is the lead investigator at each research site, who is responsible for submitting all centre-specific information to the REB of Record
- This information includes:
  - Centre Amendments
  - Centre Continuing Review
  - Centre Reportable Events
  - Centre Study Completion/Termination/Suspension

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RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

- The Principal Investigator is responsible for complying (and ensuring the research team complies) with the determinations of the REB of Record, and ensuring that approval from the REB of Record and all other institutional authorizations are in place prior to beginning the research

CLINICAL TRIALS ONTARIO

RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

- The Principal Investigator is required to review and sign the centre submissions to the REB of Record
  - Preparation of the forms and material can be delegated to others, as applicable
  - Post-approval forms (e.g., amendments) that are being re-submitted to the REB of Record (e.g., following an REB's request for changes) can be signed by a delegate

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RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

- The Principal Investigator is also required to:
  - review applications submitted by the provincial applicant (e.g., after they are approved by the REB of Record),
  - ensure all REB approved provincial changes are implemented at the centre when relevant,
  - promptly report to the REB all centre-specific information/changes to previously provided information.

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INFORMED CONSENT FORM - LOCAL

- Each participating centre will create their local consent form(s) that will be provided to participants at their centre
    - This will be developed using the Provincial Consent Form
- Changes should only include local administrative information – letterhead, investigator name and contact information – and any documented institutional ethics requirements (if applicable)
- This is submitted to the REB of Record as part of the Centre Initial Application, and also if it is amended during the study

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ONGOING SUBMISSIONS TO THE REB OF RECORD

Provincial Information	Centre Information
Initial Application (study-wide information)	**Initial Application** (centre-specific information)
Amendments: • Changes to protocol • Changes to consent/assent form(s) • Changes in other participant materials • Updated IB/PM • Translation of Provincial Materials • Other changes in previously submitted information	**Amendments:** • Changes to local consent/assent form(s) • Translation of centre-specific material • Changes in other centre-specific participant materials • Other changes in previously submitted centre-information
Continuing Review (study-wide information)	**Continuing Review** (centre-specific information)
Reportable Events • DSMB/C Report • Interim Analysis Results • Safety Notice/Update (e.g., Action Letter), Periodic External (non-local) AE/SUSAR Summary Report, Single External (non-local) Adverse Event meeting reporting definition	**Reportable Events** • Local (internal) Serious Adverse Event meeting reporting definition • Protocol Deviation/Violation • Privacy Breach • Audit/Inspection Report • Participant Complaint
Study Completion/Termination (all centres)	**Study Completion/Termination** (centre-specific information)

HOW DO I KNOW IF A STUDY IS USING CTO?

- Ask CTO (we're here to help!)
- Ask the Sponsor/Lead Investigator
- If you are the Sponsor/Lead Investigator, check to see if there are two or more CTO Participating Sites from which you intend to recruit

CTO can liaise with the Sponsor and other sites, but we may need you to act as a conduit for the introduction.

SELECTION OF THE REB OF RECORD

- The REB of Record will provide ethics review and oversight on behalf of multiple research sites
- The REB of Record is selected by CTO once the initial application is submitted for the study
- The REB of Record must be *CTO Qualified*
- Should an REB indicate that they do not have the capacity to review certain types of research, CTO will not assign such studies to that REB

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SELECTION OF THE REB OF RECORD

STUDIES INITIATED AND FUNDED BY INDUSTRY

If the research study could benefit from specific REB expertise, CTO will attempt to match the study with an REB with such expertise

Balance the distribution of research studies amongst CTO Qualified REBs

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SELECTION OF THE REB OF RECORD

INVESTIGATOR-INITIATED STUDIES

Consider the REB at the institution of the Lead Investigator/ Provincial Applicant

If the research study could benefit from specific REB expertise, CTO will attempt to match the study with an REB with such expertise

Balance the distribution of research studies amongst CTO Qualified REBs

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REB OF RECORD STUDY AGREEMENT

- Study-specific agreement signed by the host institution of the REB of Record, the recruiting site's signatory authority, and PI at the recruiting site
- Included as a Schedule E within the Participation Agreement
- This template agreement formally delegates REB review and oversight responsibilities to the REB of Record and must be executed prior to the start of the study at each recruiting site
- Administered by CTO

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FEES

- There are no fees for investigator-initiated, grant funded research (e.g., the research you do not currently pay fees for)
- Fees are charged for industry-sponsored research according to the schedule posted on the CTO website at: http://www.ctontario.ca/cms/media/Fees-Structure-for-industry-sponsored-clinical-trials-February-3-2015.pdf
- Fees are collected and distributed by CTO; there is no additional/separate billing by the institution for research ethics review

CTO STREAM – ADDITIONAL DETAILS

- Designed to facilitate collaboration and transparency
  - Applications can be shared with other users, with corresponding degrees of permissions
  - Centres can see and are notified of things that happen on a study-wide (provincial) basis
  - Document management system allows all users to see their current approved materials
  - Information can be accessed in multiple ways, with ability to sort, search, etc., for the entire trial or by centre

- Signatures are electronic

- Email notifications for key items
  - When you've been asked to sign a form
  - When a decision is made on provincial-level submissions*
  - Continuing ethics review reminders, expiry and lapse notifications*

  *based on role in study

- Training provided free of charge by CTO, along with user manuals and other guidance materials
  - Typically use a just-in-time model, so that users are trained close to when they will be completing an application

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