Introduction to CTO Stream for Research Teams

Clinical Trials Ontario Streamlined Research Ethics Review System

What you will find here:

1. What is CTO Stream?
    a) How does CTO Stream work?
    b) When can you use the system?
    c) Why would you use CTO Stream?
2. Getting Started with CTO Stream
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6. Resources
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CTO Stream – what is it?

CTO Stream is a secure, web-based ethics application system for multi-site research (clinical trials or observational health studies) in Ontario

- ❑ 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

Note: CTO Stream is strictly for obtaining ethics approvals. All other institutional approvals and authorizations are managed through the local site and must be in place before you can begin the research.

How does CTO Stream work?

- The Provincial (lead) study team submits a research ethics application through CTO Stream
- The application is reviewed by one of our Qualified REBs meaning there is *one* ***full ethics review for multiple research sites in Ontario***
- Once the study is Provincially approved by the REB, sites can apply for their site ethics approval through CTO Stream

When can you use CTO Stream?

Any time ethics approval is needed for a multi-site health research study that will be performed at 2 or more CTO Participating sites, you can use CTO Stream

Who can use CTO Stream?

- A full list of sites (who have signed on as Participating Sites and can use CTO Stream) is available on the CTO website:

  www.ctontario.ca/streamlined-research-ethics-review-system/participating-sites

We have over 130 Participating Sites in Ontario and growing!

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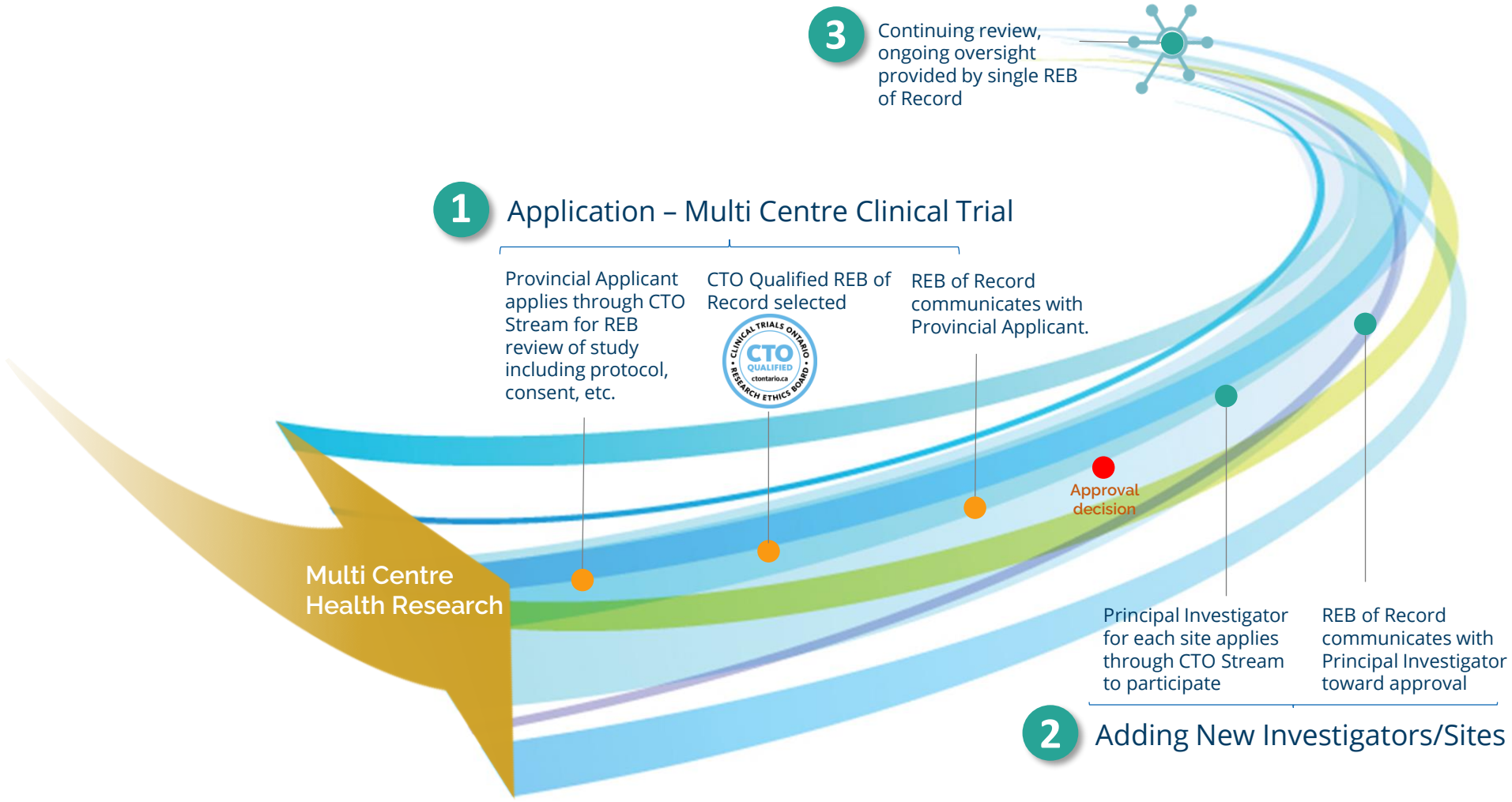
Why would you use CTO Stream?

When you use CTO Stream:

- ❑ Only one REB reviews the study (i.e., one full-board review)
  - Applications are reviewed by a CTO Qualified REB from leading institutions across Ontario
- ❑ There is one consent template used for all sites
- ❑ 50% of centre applications are approved within 1 week
- ❑ CTO Stream system **improves transparency** between all parties
- ❑ Enhanced collaboration features
  - Sponsor and CRO users can work on applications with sites
  - Coordinators can help fill out applications for other sites

CTO Streamlined Research Ethics Review System



Getting Started

with CTO Stream

Getting Started with CTO Stream

Are you ready to get started? Here are some simple but important steps:

1. Sign up for a CTO Stream account to access the system
2. Go to *apply.ctostream.ca* and click on 

3. Attend CTO Stream training – check the CTO website for dates of upcoming webinars www.ctontario.ca/cto-programs/streamlined-research-ethics-review/webinars-and-training/#WebinarTraining
4. Make sure your Investigator and Department Head have their own CTO Stream accounts as they will need to electronically sign-off on applications.

Related resources:

- ❑ Video Tutorials: Getting Started for New Users (1:49)
- ❑ User guides: Getting Started, CTO Online Helpdesk

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Provincial Initial Application (PIA)

- Research teams first submit an initial application called the Provincial Initial Application (PIA)
- Includes **study-wide** information such as risks, benefits, protocol, IBs, and the study consent form template(s)
- Submitted by the Provincial study team through CTO Stream for REB review

Provincial Applicant

- The Provincial Applicant (PA) is the investigator responsible for all ethics submissions that apply to the overall study (including the PIA)
- The PA is usually the overall study lead/recipient of grant funding (investigator-initiated studies) or determined with input the sponsor (industry-sponsored studies)
- The PA must be an investigator affiliated with one of CTO`s participating sites.
  - A list of all participating sites can be found on the CTO website:

www.ctontario.ca/streamlined-research-ethics-review-system/participating-sites

Provincial Informed Consent Form

- The Provincial research team will create the study-wide consent form template that will later be used as the basis for all site-specific consent forms
- This Provincial ICF template is uploaded into the PIA and should not have any site-specific information, contact details, logos/letterhead etc.
- Researchers **MUST** use the applicable CTO consent form template to create their Provincial ICF*. This template can be found on the CTO website:
  www.ctontario.ca/streamlined-research-ethics-review-system/tools-and-resources/
- Be sure to follow the instructions for using the template; mandatory language and sections should not be altered, and yellow-highlighted text must remain in the Provincial template (will be replaced by sites later)

***Exception – studies being submitted for review by OCREB must use the OCREB consent template available on the OCREB website**

Related resources:

- Video Tutorials: Creating the Centre-Specific ICF (5:35)
- User guides: Getting Started, CTO Online Helpdesk

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Informed Consent Form Template Example

CTO Clinical Trial Informed Consent Form Template

Instructions:

This Clinical Trial Informed Consent Form (ICF) Template has been designed to meet current regulatory and ethical standards.

The study-wide (provincial) ICF template uploaded into the Provincial Initial Application must follow the prescribed structure and format as set out in this template. Consent forms will be screened by CTO for concordance with this template. Consents that do not meet these requirements will be sent back to the study team for revision before the study is assigned to a REB of Record.*

*This screening is not applicable to studies reviewed by the Ontario Cancer Research Ethics Board (OCREB). OCREB studies will continue to use the applicable OCREB ICF templates.

The Summary of Informed Consent Form on page 3 of the template must only be included for studies funded or supported by a US federal funding agency. **DO NOT include for studies not meeting this criterion.

How to use this template:

- Suggested text/examples in blue font may be omitted if they are not relevant to the specific protocol
- Headings in UPPERCASE, UNDERLINED BLACK FONT denote sections which should not be altered or removed from the template All text included in the study-wide ICF must be applicable/appropriate for that specific clinical trial
- Instructions are indicated in *italics/grey background*
- Turquoise highlighting provides a prompt to adapt text to the research study (e.g., to select from the available options highlighted)
- Text with yellow highlighting reflects instructions for participating centres to follow when creating their site-specific ICF. This text, INCLUDING THE HIGHLIGHTING, should not be altered or removed from the ICF that is uploaded into the Provincial Initial Application through CTO Stream
- When developing their site-specific ICF, participating centres should follow the instructions and insert the applicable site-specific content. The instructions and highlighting should be deleted from the local consent form submitted to the REB of Record

Informed Consent Form for Participation in a Research Study

Study Title: *insert study title as written on the protocol*

Sponsor's Study ID: *Insert sponsor's study ID if applicable*

Study Doctor: *insert name, department and telephone or pager number*

Sponsor/Funder(s): *Insert the name of the Sponsor or, if applicable, the funder(s) of the research*

Emergency Contact Number (24 hours / 7 days a week):

Non-Emergency contact numbers are noted at the end of this document under the section heading "Contacts".

INTRODUCTION

For studies where consent is sought through a substitute decision maker, include the following paragraph:
As a Substitute Decision Maker, you are being asked to provide informed consent on behalf of a person who is unable to provide consent for him/herself. If the participant gains the capacity to consent for him/herself, your consent for them will end. Throughout this form, "you" means the person you are representing.

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Submitting the PIA

- Provincial research team submits the completed PIA
  - When the application is complete, navigate to the last section of the PIA and request the required signatures; application will automatically submit when all signatures have been applied
  - Signatories must match the individuals named in section 1.0
- CTO performs a brief initial screen to ensure the application meets CTO's mandate, the required signatures are in place and the Provincial ICF template follows the CTO ICF template format*
  - Applications that do not pass the screening requirements will be returned to the research team for correction
  - New users can contact CTO to request a "pre-screen" of the PIA to check if it will meet the screening requirements before they request signatures

***N/A for studies submitted to OCREB which must use the OCREB consent template**

Submitting the PIA (cont'd)

- ❑ A CTO Qualified REB will be selected to oversee the ethical conduct of the study
- ❑ Any future communication occurs directly between the REB of Record and the Provincial Applicant team

Teams can use the Correspondence feature in CTO Stream to send a direct message or question to the REB regarding their application

Note: the Correspondence feature within CTO Stream should not be used to communicate with CTO.

Related resources:

- ❑ Video Tutorials: Creating a New Project (5:01), The Project Tree Page (5:13), Navigating the Application Form (5:26), Sending a Correspondence Message to the REB of Record (2:49)
- ❑ User guides: Submitting a New Study, Submitting a New Observational Study, Correspondence,
- ❑ Tip sheets: Provincial Initial Application (PIA) Submission

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What is the REB of Record?

- CTO will select the REB of Record (the single REB who will provide ethics review and continuing oversight on behalf of multiple centres)
- This REB is responsible for overseeing the ethical conduct of the study at all participating centres being submitted through CTO Stream
- Selection of the REB of Record depends on whether the study is Investigator- Initiated or Industry Sponsored

REB of Record Selection

1) **Industry Sponsored/Supported**

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

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Balance the distribution of research studies amongst CTO Qualified REBs

2) **Investigator-Initiated**

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

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

↓

Balance the distribution of research studies amongst CTO Qualified REBs

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REB Fees for using CTO Stream

- REB Fee Structure and Distribution is available on the CTO website
  www.ctontario.ca/cto-programs/streamlined-research-ethics-review/tools-and-resources/
- Fees are applicable to Industry Sponsored/Supported studies
- Fees are managed by CTO; CTO will bill sponsor/payee on behalf of participating institutions
- Application Fees:
  - $3,000 for each participating site for the first 5 sites
  - $2,000 for each of the next 5 sites (6-10)
  - $1,500 for each additional site after 10
- Major Amendment Fees:
  - No charge for the first 3 major amendments (e.g., requiring Health Canada approval); $500 for each major amendment after the first 3
- Continuing Review, Reportable Event, Study Completion
  - No additional fees

Centre Initial Application (CIA)

- ❑ Once the PIA is approved, each participating site (including the Provincial Applicant's own site) will submit a CIA
- ❑ CIA is an abbreviated ethics application containing site-specific information describing exactly how the study will occur at that site (local PI, main study contact, conflict of interest, site-specific consent forms, etc.)

Creating the Site-Specific Consent Form(s):

- ❑ Sites will download the approved Provincial ICF template(s) and insert their local, site-specific details (letterhead, investigator name and contact details) PLUS any wording required by your institution as outlined in the Documented Institutional Ethics Requirements Form **(DIER)***
- ❑ Upload the site-specific ICFs into the CIA (tracked and clean versions)

Note: Not all sites have a DIER Form. If your site has DIERs, these must be addressed in the CIA and/or site-specific ICF. DIER forms are available through the CTO Website on the Participating Sites page (see slide 5).

Centre Initial Application (CIA) Cont'd

Research team submits the completed CIA

- When the application is complete, navigate to the last section of the CIA and request the required signatures; the application will lock and automatically submit once the final signature is applied (submission process may take up to ~10 minutes)
- All signatures can be requested in parallel (no need to wait for someone to sign before requesting the next signature)
- Signatories must match the individuals named in section 1.0

Related resources:

- ❑ Video Tutorials: Creating a Centre Initial Application (5:41), Requesting Signatures (3:18)
- ❑ User guides: Creating a Sub-form, Creating a Centre Initial Application (CIA)
- ❑ Tip sheets: Centre Initial Application (CIA) Submission

Centre Initial Application (CIA) Cont'd

- CTO performs a brief initial screen to ensure the Institution Representatives are listed correctly, the required signatures are in place, the DIERs (if applicable) have been addressed and the Site-specific ICF follows the CTO ICF template format
  - Applications that do not pass the screening requirements will be returned to the research team for revision before they can be sent to the REB
  - New users can contact CTO to request a "pre-screen" of the CIA to check if it will meet the screening requirements before they request signatures
- Sites are not required to submit non-consent, participant facing materials (such as wallet cards, recruitment posters etc.) when the only change to the Provincially approved version is the insertion of site-specific contact information and/or letterhead
- CIAs will be reviewed by the REB of Record and typically undergo delegated review

Documents for Translation

- Translation of study documents (such as the site-specific consent form or other participant materials, as required) usually occurs at the Centre-level, after the documents have been approved with the CIA
- Once approved, the documents can be translated and submitted for review and approval at the site using the Centre Amendment Form in CTO Stream

Managing User Access and Notifications Using Roles

- Access to individual Projects (studies) is controlled by members of the research study team using the 'Roles' feature in CTO Stream
- To gain access to a Project, users will contact the Project Owner or a member of the Provincial Applicant site or Centre Study team

Granting or Removing Study Access for Other Users:

- When someone joins or leaves a study, it is the study team's responsibility to manage that user's access by adding/removing their Role
- This is done using the 'Roles' button on the Provincial and/or Centre Initial Applications (as applicable)
- Assigning the correct Role ensures an individual receives the appropriate email notifications
- Removing their Role when they leave will ensure they no longer receive email notifications and removes their study access

Adding or removing an individual's contact information within the application forms does not control access to the study and system notifications.

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Ongoing (Post-Approval) Ethics Submissions

- During the course of the research project/study, the Provincial Applicant (PA) is responsible for all study-wide submissions in CTO Stream (see next slide for examples)
  - Centres are notified whenever the PA submits an application in the system, and when the REB approves/acknowledges a Provincial application
  - Each centre has Read access to the Provincial Applications so they can view and download the relevant materials and REB letters as needed
- Each centre is responsible for their site-specific submissions in CTO Stream (see next slide for examples)

Collaboration features in CTO Stream enable Industry/Academic sponsors (or Provincial Teams) to assist sites with their site-specific submissions in CTO Stream if they wish to do so

Types of Submissions in CTO Stream

Provincial/Study-Wide Submissions	Centre/Site-Specific Submissions
Provincial Initial Application	**Centre Initial Application**
Provincial 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	**Centre 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 • Changes in local PI
Provincial Continuing Review (annual)	**Centre Continuing Review (annual)**
Provincial 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	**Centre Reportable Events:** • Local (internal) Serious Adverse Event meeting reporting definition • Protocol Deviation/Violation • Privacy Breach • Audit/Inspection Report • Participant Complaint
Provincial Study Closure: Can only be submitted after each centre in CTO Stream has submitted their own Centre Study Closure form	**Centre Study Closure:** Submit once research activities at the site are complete and ethics approval is no longer required at the site

Ongoing Ethics Submissions - Amendments

- **Provincial Amendment (PAM)**
  - Required for any change in study-wide material/information
  - REB Approval/acknowledgment applies to all participating sites
    - **Note: extra step is required when a new/revised Provincial ICF template is approved → sites must submit a Centre Amendment Form with their revised ICF template***
  - This is created as a sub-form of the Provincial Initial Application
- **Centre Amendment (CAM)**
  - Required for any change to local site-specific information e.g., PI change, changes to the site-specific consent form for example, in response to a change in the approved Provincial ICF template(s)
  - This is created as a sub-form of the Centre Initial Application

N/A for studies reviewed by OCREB

Ongoing Ethics Submissions - Continuing Review

- Studies in CTO Stream have a **single ethics expiry date** for the entire study and all participating sites → expiry date is set at the Provincial level
- Email reminders are sent out at 45, 30, and 15 days prior to the *expiry* date
- Provincial Continuing Review (PCR) form must be submitted by the Provincial Applicant (PA) team, and each research site **(including the PA site)** must submit a Centre Continuing Review (CCR) form by the deadline for the full-board meeting which occurs prior to the expiry date
- A lapse in ethics approval occurs if the continuing review is not approved prior to the ethics approval expiry date

If provincial ethics approval expires, ethics approval for all research sites is automatically considered to have expired as well

Signature Requirements in CTO Stream

- CTO Stream uses electronic signatures. Applications must be signed by the appropriate signatories before they can be submitted for review – signatories must have their own CTO Stream account to access the system and sign-off
  - On the initial submission of any application form, the Provincial Applicant/Principal Investigator (and Co-Applicant/Co-Investigator if listed in the form) must sign-off in CTO Stream*
  - The re-submission of any form can be signed by a member of the study team in CTO Stream
  - The signature delegation is optional and the REB of Record may require that the PA/PI sign-off when a re-submitted application contains significant changes

Exception: A study team member may sign the initial submission of Amendment forms where the only change is to the contact details for the PA/PI/Co-Applicant or Co-I or to the name/contact details for the main contact/institutional representative

Resources

- Video tutorials, user manuals, and tip sheets are available on the CTO Website at the following link: https://www.ctontario.ca/cto-programs/streamlined-research-ethics-review/webinars-and-training/

We recommend all new users review the following resources:

- Video tutorial: Creating a New Project (5:01), Creating a Centre Initial Application (5:41)
- Applicant Tip Sheets - Provincial Initial Application Submission, Centre Initial Application Submission
- Quick Guides – Submitting a New Study, Creating a Centre Initial Application (CIA)

Questions?

We are here to help!

If you have questions about the Streamlined Research Ethics Review System or need technical support you can reach us through the CTO Online Helpdesk system

- **Submit a support ticket at:** https://support.ctostream.ca
- **CTO Mandatory Consent form template (in French and English) and MS Word versions of the application forms are available here:**

  https://www.ctontario.ca/cto-programs/streamlined-research-ethics-review/tools-and-resources/

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10th Anniversary

Vision

Make Ontario a preferred location for global clinical trials, while maintaining the highest ethical standards.

Mission

Strengthen, promote and capitalize on Ontario's competitive advantages to conduct high-quality clinical trials.

Strategic Priorities

Streamline

Streamline processes to help make high-quality clinical trials more timely, efficient and cost-effective.

Engage

Engage with patients and the public to increase awareness, foster collaboration and improve how clinical trials are conducted.

Promote

Promote Ontario's competitive advantages and clinical trial capacities to attract more trials and industry investment to the province.

Canada is a globally competitive trials jurisdiction

Ranked 1st
in active clinical trials per capita among G7 nations

Ranked 3rd
among G7 nations for total number of clinical trials

2nd lowest cost
among G7 nations for managing clinical trials – with the US ranked 10th

Ontario is Canada's leading clinical trials sector

4,600+
active clinical trials in Ontario – the highest in Canada

2x more
more active clinical trials per capita compared to the US

160% increase
in clinical trials over the past decade

Ontario's World Class Clinical Trials Environment

Canada's largest concentration of clinical trial sites

19 of Canada's top 40 research hospitals

140 hospitals with over 200 unique sites
14 acute academic hospitals
46 community hospitals
13 complex continuing care & rehabilitation hospitals
62 small hospitals
5 mental health & addiction hospitals

$1.73 billion
invested in health research at Ontario hospitals

A hub for health research talent

22,000+
employed researchers and staff in academic hospitals

30,000+
Jobs in drugs and pharmaceuticals

26,000+
Jobs in medical devices

63,500
Annual STEM graduates

18
Clinical research programs at Ontario Colleges and Universities