CHEO

CHEO Research Ethics Board

Research Ethics Guidance

Revised 2025-December

Contents

Introduction to research ethics

What is research?

The Tri-Council Policy Statement (TCPS2) defines research as an undertaking intended to extend knowledge through a disciplined inquiry or systematic investigation.

What is a Research Ethics Board?

The Research Ethics Board (REB) is an independent, multidisciplinary board of CHEO. The REB's purpose is to protect the rights and welfare of human participants participating in research. The REB reviews and oversees research to ensure that it meets ethical principles and that it complies with all applicable regulations and guidelines pertaining to human participant protection.

These include, but are not limited to, the Food and Drugs Act and applicable Regulations, the International Council on Harmonization Good Clinical Practice Guidelines, the Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects, the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, and where applicable, US Federal Regulations.

The REB has the authority to approve, require modifications to, or disapprove, any research activity that falls within its jurisdiction.

Governing principles:

The REB is guided by the ethical principles regarding all research involving human participants including:

Respect for persons

- Recognize the intrinsic value of human beings and the respect and consideration they are due,
- Incorporate moral obligations to respect autonomy and to protect those with developing, impaired or diminished autonomy.

Concern for welfare

- Aim to protect the welfare of participants, and, in some circumstances, to promote that welfare in view of any foreseeable risks.
- Provide participants with enough information to be able to adequately assess risks and potential benefits associated with their participation.
- Ensure that participants are not exposed to unnecessary risks.

Justice

- Obligation to treat people fairly with equal respect and concern.
- Vulnerable or marginalized people may need to be afforded special attention.

REB Composition

The REB membership includes at least five members represented by the following categories:

- At least two members who have expertise in relevant research disciplines, field and methodologies covered by the REB (for biomedical clinical trials, this will include at least one member who practices medicine or dentistry and who is in good standing with their regulatory body),
- At least one member who is primarily experienced in non-scientific disciplines
- At least one member who is knowledgeable in ethics,
- At least one member who is knowledgeable in the relevant law. This is mandatory for biomedical research and is advisable, but not mandatory, for other areas of research, and
- At least one community member who has no affiliation with the organization or the sponsor, and who is not part of the immediate family of a person who is affiliated with the organization.

What activities require REB review and approval?

Research involving:

- living human participants [this includes data of living human participants];
- biological materials as well as human embryos, fetuses, fetal tissue, reproductive materials, and stem cells. This applies to materials derived from living and deceased individuals.

How to determine the level of risk involved in research:

Minimal Risk:

The research involves no more than minimal risk. This means that the potential risk(s) from research activities to the participant are not greater than what the participant is exposed to in their day-to-day activities and life.

Greater than Minimal Risk:

Potential risks from the research-related activities to the participant are greater than what the participant is exposed to in their day-to-day activities and life.

Types of REB reviews

Full Board review

Research involving greater than minimal risk is reviewed by the Full Board.

The REB meets once a month to review the submissions except for August. The CHEO Site Investigator and their research coordinator(s)/assistants will be invited to attend a board meeting of the REB to discuss their project.

Delegated review

Research involving less than minimal risk is reviewed in the delegated review stream by the REB Chair and/or designee(s). Additional REB members with relevant scientific expertise may be asked to review, in addition to the Chair and research ethics office staff.

There is no submission deadline for delegated research.

For assistance with determining the review stream, request a consultation with the CHEO REB office.

What research is exempt from REB review?

Certain types of research are exempt from REB review (TCPS2). Research does not require REB review when it relies exclusively on information that is:

- publicly available through a mechanism set out by legislation or regulation and that is protected by law; or
- in the public domain and the individuals to whom the information refers have no reasonable expectation of privacy.

REB review is not required for research involving the observation of people in public places where:

- It does not involve any intervention staged by the Researcher, or direct interaction with the individuals or groups,
- Individuals or groups targeted for observation have no reasonable expectation of privacy, and
- Any dissemination of research results does not allow identification of specific individuals.

REB review is not required for research that relies exclusively on secondary use of anonymous information, or anonymous human biological materials, so long as the process of data linkage or recording or dissemination of results does not generate identifiable information.

The opinion of the REB should be sought whenever there is any doubt about the applicability of the guidelines and regulations.

Quality assurance and improvement activities

Quality assurance and quality improvement studies, program evaluation activities, and performance reviews, or testing within normal educational requirements when used exclusively for assessment, management or improvement purposes, do not constitute research, and do not fall within the scope of REB review.

The Distinction between Quality Assurance and Research

The REB overseas all human research conducted at or through the hospital. In defining its scope, the REB adheres to Tri-Council definition of research as an undertaking intended to extend knowledge through a disciplined inquiry or systematic investigation. This is distinct from quality assurance activities that are intended to assess the performance of an organization or its staff, within the mandate of the organization.

The Interagency Advisory Panel on Research Ethics (PRE) has provided guidance on the distinction between quality assurance and research. The Panel states that quality assurance studies may share characteristics with research and in fact, may use scientific methods. In quality assurance, however, the data are used to advance the needs and functioning of the organization. By contrast, in research, data are used to answer a scientific question. The primary distinction between research and quality assurance is therefore, in their respective objectives, rather than the methods used.

Research

- Data is used to answer a scientific questions
- Intended to extend knowledge through disciplined inquiry

Quality Assurance

- Data is used to advance the needs and functions of the organization.
- Intended to assess organizational or staff performances

Recognizing that there can be overlap between these two concepts, the REB should be consulted to determine whether a specific activity constitutes research.

Case Report Form vs. Case series

It is common to report unique and interesting clinical cases through publication in medical journals or presentation at medical or scientific meetings. This gives rise to questions regarding when a case report or case series becomes research requiring REB review and approval.

What is the distinction between a case report and a case series?

Case report: A detailed report on an individual patient (e.g., presentation, diagnosis, treatment, response and follow-up) arising from routine clinical practice. The report describes the course of medical treatment of one or more patients that has a unique outcome or the handling of a unique clinical case.

Case series: A presentation of information or a collection of case reports on more than three patients. It is important to note that direct consent from patients for publication is always required when conducting a case report or case series.

When is REB review and approval required?

A case report or **a case series** requires REB review and approval when it meets the definition of research as "an undertaking intended to extend knowledge through a disciplined inquiry or systematic investigation."

A case report with three or fewer patients does not require REB review and approval. This is because it generally does not meet the definition of research on the basis that there is:

- A limited number of ‚'unique,' patient/cases from a single physician or clinic (≤3)
- No research intent at the time of the intervention (i.e., no prospective plan to systematically evaluate the outcomes for purposes other than treatment)
- No systematic data collection (e.g., chart reviews)
- No intention to test or compare various therapies/outcomes/data
- No descriptive or comparison statistics between cases
- Not considered to be generalizable information

Conversely, if anything was done in the course of treatment with a research intent or that aims to answer a specific research question, the case report becomes research that requires REB review and approval.

A case report with more than three patients becomes a case series that is considered research because it necessarily meets at least one of the criteria above and requires REB review and approval.

In accordance with TCPS2 Article 6.11, researchers must submit their application prior to the start of any research activity. REBs do not grant "retroactive" approval after research is complete.

Clinicians/researchers are advised to consult with the REB when there is uncertainty as to whether an activity constitutes human subjects research that requires REB review and approval.

Conduct of research

Personal Health Information Protection Act (PHIPA) Requirements for the Collection of Personal Information (PI) and Personal Health Information (PHI) in Research

The Personal Health Information Protection Act, 2004 (PHIPA) governs the collection, use, and disclosure of personal health information (PHI) by health information custodians in Ontario. It aims to protect individuals' privacy while enabling effective health care and research.

Personal Information (PI): Any information about an identifiable individual, including name, address, and identification numbers.

Personal Health Information (PHI): Identifiable information about an individual's health or health care history, including medical records, lab results, and health card numbers.

Consent is required for the collection, use, and disclosure of PHI unless an exception applies.

Under PHIPA, PHI may be collected, used, or disclosed for research without consent only if:

- The research plan is approved by a Research Ethics Board (REB).
- The REB has determined that:
  - The research cannot be conducted without the PHI.
  - The PHI is necessary for the research.
  - The researcher will take steps to protect the PHI and limit its use and disclosure.
  - The public interest in conducting the research outweighs the privacy intrusion.

De-identification and Data Minimization

Researchers should use de-identified data whenever possible.

Only the minimum necessary PHI should be collected to meet research objectives.

Types of Data

Researchers may seek to collect, use, share and access different types of information about participants to meet a research objective with Research Ethics Board approval. Such information may include personal characteristics or other information about which an individual has a reasonable expectation of privacy (e.g., age, ethnicity, educational background, employment history, health history, life experience, religion, social status).

This document describes identifiable and non-identifiable information as defined in TCPS2:

Identifiable Information:

Directly identifying information

The information identifies a specific individual through direct identifiers (e.g., name, social insurance number, personal health number).

If datasets or other data sources accessed for this study will contain identifiable information and for the purpose of data analysis the following should be included in the data management plan.

- Data captured on data collection tools will include direct and indirect identifiers. These include e.g., name, email, address, phone number, date of birth, partial date of birth, medical record number, pathology number, full postal code, social insurance number.

Indirectly identifying information

The information can reasonably be expected to identify an individual through a combination of indirect identifiers (e.g., date of birth, place of residence or unique personal characteristic).

If datasets or other data sources accessed for this study will contain identifiable information and will be de-identified for the purpose of data analysis the following should be included in the data management plan.

- Data captured on data collection tools will include indirect identifiers. These include e.g., date of birth, partial date of birth, full postal code.

De-identified/Coded information

Direct identifiers are removed from the information and replaced with a code. Depending on access to the code, it may be possible to re-identify specific participants (e.g., the principal investigator retains a list that links the participants' code names with their actual names so data can be re-linked if necessary).

If datasets accessed will include direct identifiers but the information will be de-identified, include the following in the data management plan.

Datasets accessed for this study will contain indirect identifiers. These include e.g., date of birth, partial date of birth, medical record number, pathology number, full postal code. No direct identifiers will be included in datasets.

Non-identifiable information:

Anonymized information

The information is irrevocably stripped of direct identifiers, a code is not kept to allow future re-linkage, and risk of re-identification of individuals from remaining indirect identifiers is low or very low. If datasets accessed will include anonymized data, include the following in the data management plan.

- Datasets accessed for this study will contain indirect identifiers. These include [e.g., date of birth, partial date of birth, sex, gender, partial postal code]. No direct identifiers will be accessed or collected for this study.

Anonymous information

The information never had identifiers associated with it (e.g., anonymous surveys) and risk of identification of individuals is low or very low. If datasets accessed will include anonymous information, include the following in the data management plan.

- All data collected will be anonymous. No direct or indirect identifiers will be accessed or collected for this study.

Participant recruitment

Participant recruitment refers to the process by which researchers identify, approach, and invite individuals to take part in a research study. It is the initial phase of engaging potential participants and is a critical component of the informed consent process.

Recruitment involves:

- Determining eligibility criteria for participation.
- Selecting appropriate recruitment methods (e.g., advertisements, referrals, direct contact).
- Communicating study information in a clear, ethical, and respectful manner.
- Ensuring voluntariness, meaning individuals feel free to choose whether to participate without pressure or undue influence.

Ethical considerations

The Tri-Council Policy Statement 2 (TCPS2) article 3.1, consent must be voluntary, meaning participants freely choose to participate based on their own values and preferences Recruitment is the first step in the consent process and plays a critical role in ensuring voluntariness.

Ethical Recruitment Practices

Researchers must ensure that recruitment methods:

- Respect autonomy and avoid undue influence or coercion.
- Are transparent, providing clear and accurate information.
- Are inclusive, avoiding discrimination or exclusion without justification.
- Are approved by the REB before implementation.

Identification of Potential Participants

There are numerous ways to identify potential participants, such as a review of medical records (patient-participants), research records, or eligible participants can self-identify.

Pre-screening of medical records

The REB may grant a waiver of consent when medical records are pre-screened to identify potential participants. Study teams must request this waiver in the protocol or site-specific protocol addendum for multi-site studies. This pre-screening process involves access of minimal information to identify potential participants; no information should be recorded as part of this process.

Recruitment for research under PHIPA

Recruitment must be consistent with PHIPA, according to which a patient's circle of care must first obtain consent to share personal health information and/or personal information with a member of the research team for the purposes of recruitment into a research study.

Recruitment by a member of the circle of care who is also the researcher (dual-role)

A dual role researcher is an individual who holds both a research role and another professional role (e.g., clinician, teacher, supervisor, service provider) in relation to potential participants. This duality can create ethical complexities, particularly during recruitment, due to the potential for perceived or actual power imbalances, conflicts of interest, and undue influence, including research benefit misconception (or therapeutic misconception) when inviting their own patients, students, employees, colleagues or subordinates to participate in research. Strategies to mitigate undue influence and research benefit misconception must be clearly delineated withing the submission to the REB.

Acceptable Recruitment methods at CHEO:

In person/Over the phone

Initial contact must be made by a member of the circle of care. Permission to share the potential participant's contact information with the research team is obtained and then the research team may contact the potential participant and provide them with further information regarding the study, conduct consent discussion and obtain informed consent (if eligible). Relevant recruitment scripts should be included in the submission to the REB.

Recruitment Letters/emails

Recruitment letters provide potential participants with information about a study and the contact information for the research team to indicate interest or to decline being contacted further. It should be sent by within the circle of care who would have access to their personal information.

Research Connection

Research Connection is a program that links families to research opportunities at CHEO. It enables CHEO Research teams to contact families, children and youth directly who might qualify to participate in a specific research study. Starting on February 1, 2025, any child or youth who receives services at CHEO is automatically included in the Research Connection program, unless they choose to withdraw from the program. For more information on the program and whether a study will qualify, please visit the CHEO Research Institute's website for more information.

Study advertisements

These include recruitment posters/flyers, brochures media advertisements on websites or social media. Recruitment poster templates should comply with Institutional requirements.

At minimum, the CHEO REB requires the following information:

- Statement that participation is voluntary
- Statement that CHEO REB has approved the study
- Version date
- Contact information for further questions

Passive recruitment at CHEO:

Passive recruitment for research conducted at external institutions entails informing potential participants about studies taking place outside of CHEO/CHEO RI, without any direct involvement from CHEO/CHEO RI. This process is limited to providing general information, whereby interested individuals independently initiate contact with the external research teams. Importantly, there is no exchange, collection, or transfer of personal or study-related data between CHEO/CHEO RI and the external sites.

Passive recruitment in research involves strategies where potential participants are provided recruitment materials (e.g., posters, information handouts). Of note, if any of the study will be explained by the research team at CHEO/CHEO RI this would not constitute passive recruitment.

Where research activities at CHEO are limited to **passive recruitment,** this activity may **not** require CHEO REB review and approval.

Will you:

- pre-screen medical records?
- collect, transfer and/or store eligible participant contact information?
- Explain what the study procedures are or other aspects of the study?

Yes

These research activities require CHEO REB review.

Please submit the main site protocol, CHEO protocol addendum (refer to the CHEO REB minimal risk protocol template) and recruitment materials for REB review.

- Romeo: Prospective Minimal Risk application
- CTO: Participating site application

No

If CHEO/CHEO RI involvement is limited to providing eligible participants with recruitment material and participants will self-refer/reach out directly to the external research site, this passive recruitment does not require REB review at CHEO.

Consent and capacity

Consent is a process through which a participant's agreement to participate in research is confirmed. Consent must be free, informed and ongoing. It must be obtained and documented prior to the start of any research activities for the participant.

Capacity to consent refers to a potential participant's ability to understand relevant information about a research study, appreciate its implications, and make an informed, voluntary decision.

In Ontario, consent is based on capacity, not on age (as in some jurisdictions). Assent is based on the ability of a child to assent to participation in research, also not on age. To respect participant autonomy and a child's developing capacity, participants should thus be consented or assented using a consent or assent process appropriate to their capacity or ability, not based on their age or the requirement for parental consent if they are deemed capable. Participants with capacity (generally 12 years or older) must be given the opportunity to consent on their own behalf.

- If the potential participant has the capacity to consent on their own behalf, they must be consented.
- If the participant lacks the capacity to consent, they should be assented to participate in the study and their substitute-decision maker (parent/caregiver/guardian) must consent to their participation in the study. Potential participants should not be excluded from research solely because they lack capacity.

Assessing capacity/ability

The Principal Investigator (PI) holds primary responsibility for assessing and monitoring participants' capacity to consent. This includes:

- Evaluating capacity at the outset of the study.
- Monitoring for changes in capacity throughout the study.
- Describing the assessment process in the ethics application

Other members of the research team can also assess capacity if they are appropriately trained and designated by the PI.

If a participant initially lacks capacity to consent on their own behalf at the time of enrollment, but gains (or re-gains) capacity throughout the study period, their consent should be sought for their ongoing participation in the study.

Assent

Potential participants who lack the capacity to consent must still be informed of the research at a level appropriate to their understanding. Assent is the agreement to participate in research.

Assent should be obtained when the potential participant has some ability to understand the significance of the research (TCPS 2 Article 3.10).

The assent process should involve taking the time to explain, at whatever age they can understand:

- what is occurring in the research;
- purpose of the research;
- research procedures

In accordance with TCPS 2, a participant's expression of dissent—whether verbal, written, or behavioural—must be respected and precludes their participation in research. Researchers must not proceed with involving any individual who has refused or withdrawn consent. Respect for Persons requires that participation be voluntary, informed, and ongoing. Therefore, any indication that a participant does not wish to participate, including non-verbal cues or passive resistance, must be interpreted as a withdrawal or refusal of consent and honored immediately

Consent/assent models

Written consent

Is obtained in person and is documented using a hard copy informed consent form.

Remote consent

A signature or an attestation of consent may be obtained using different methods: via an electronic system designed to verify digital signatures (e.g., REDCap,Docu-Sign); a picture of a signed and dated written statement may be sent via email or text; or participant replies by email. Other options may be considered with appropriate justification.

If it is impossible to obtain a signature, to ensure equity of participation, consent may be obtained verbally. (See template for verbal consent). This means that the content of the written consent form remains the same and participants provide consent verbally.

- If consent is obtained verbally, read the consent form to prospective participants.
- Consider providing a copy of the consent form in advance of the consent discussion.

Verbal consent

Verbal consent is obtained by reading the informed consent that has been approved by the REB to prospective participants. Participants then provide their consent verbally. This method is typically used in remote interactions, such as telephone conversations, and is not permitted for in-person consent processes.

When verbal consent is used, the individual obtaining consent must document the interaction in writing. This documentation serves as a formal record of the participant's consent and must be retained in accordance with institutional and REB guidelines.

For studies using a verbal consent model, please adapt (or revise) consent/assent forms to include text that allows participants to ask questions throughout the consent/assent process to ensure that they understand and appreciate all the information in each section of the consent/assent form. Please refer to the CHEO REB templates for specific required changes.

Electronic consent

Electronic informed consent means that the traditional written informed consent form is reproduced by electronic means. It refers to the use of electronic systems and processes to communicate information related to the study and to obtain and document informed consent. It includes traditional (written) informed consent as well as other formats and media (e.g., online forms (such as REDCap), text, graphics, audio, video, interactive websites).

Electronic written informed consent necessarily means that participants sign a consent form. Written consent is often understood to mean a handwritten ('wet ink') signature on a paper document. According to Canadian law, an electronic signature (also referred to as a digital signature) obtained and documented in compliance with the Canada Evidence Act and the Personal Information Protection and Electronic Documents Act (PIPEDA) is equal to a handwritten signature.

Requirements for electronic written informed consent (eIC)

1. EIC can take place in-person or remotely;
2. The investigator is responsible for verifying the identity of the person giving their consent.
3. EIC forms must include all information generally required for informed consent in accordance with TCPS2 Chapter 3, section 3.2 (a)-(i).
4. Potential participants must always have an opportunity to ask questions before they give their consent.
5. A signed (electronic or hard) copy of the consent form must be provided to participants. The content of the original and signed forms must be identical.
6. All REB-approved versions of the eIC must be archived and retained for the auditing purposes.

Additional requirements for regulated clinical trials: Electronic signatures (eSIG)

1. It is mandatory to obtain an electronic signature for regulated clinical trials as prescribed by Health Canada and the Food and Drug Administration.
2. The electronic system used for obtaining a digital signature (eSIG) must be compliant with the US Code of federal regulations Title 21, Part 11 (e.g., Docu-Sign). This includes that it must
    i) be secure with restricted access,
    ii) include a method to verify the authenticity of the participant's signature (e.g., by using a password, verification question specific to that individual),
    iii) maintain confidentiality and privacy regarding the participant's identity, study participation, and personal information after consent has been obtained,
    iv) encrypt the participant's name and personal information, and
    v) capture and record the date that the participant or legal representative provides an eSIG.
3. A completed, authorized eSIG is defined as a "secure electronic signature" as defined in the Canada Evidence Act, Secure Electronic signature regulations and PIPEDA, Part 2.

In accordance with Health Canada guidance for the management of clinical trials during the COVID-19 pandemic, when consent cannot be obtained in person, other methods for obtaining consent may be used, such as over the phone or via a virtual platform. Consider the following:

- ensure participants always have an opportunity to ask questions before they give their consent
- accepting a text or email of a picture of a signed and dated written statement for participants who enroll remotely
    - this statement should indicate they are voluntarily accepting participation in the trial
- if consent is given verbally, read the consent to the prospective participant and provide an opportunity for the person to ask questions
    - consider providing the document to the person ahead of time
- ensure that in cases of verbal consent, a witness (can be a family member) is present and signs an attestation
    - it must be clear that the witness was present during the process regardless of the method of communication (for example, can be on a conference call)
    - a scanned copy of the attestation may be forwarded to the investigator by email or a picture of the signed attestation may be sent by email or text
    - the conversation should be recorded if it isn't possible to have a witness (this recording becomes part of the trial records)
- ensure the method used meets local privacy requirements

Study documentation

Include the following information in the protocol (or CHEO-specific protocol addendum):

1. Specify the procedures that will be used to obtain electronic consent or assent (e.g., via email only, via email and supported by a discussion on a virtual platform or by telephone) and method to verify a participant's identity.

    If it includes an electronic signature, specify the method to verify the authenticity of the participant's signature.

2. Describe the consent and assent process (in accordance with TCPS2 Chapter 3), including the process to 1) address participants' questions, 2) obtain an attestation of consent (electronic signature, signed statement, or replying via email), and 3) provide a signed (electronic or hard) copy of the consent form to participants. See template below if participant replying by email (point #4b).
3. Describe the archival process.

Additional requirements for regulated clinical trials

4. Describe the method for documentation of consent.
    a. Documentation of consent by way of electronic signature must comply the requirements outlined above.
    b. If not obtaining an electronic signature for clinical trials during the COVID-19 pandemic, describe the methods used to obtain an attestation of consent. (See Health Canada guidance).
    c. Documentation of consent by way of email:
        - Include a method to verify the identity of the participant replying (consenting) by email (e.g., using a password, verification question specific to that individual).
        - The reply email from the participant must include the following information:
            - Study title
            - Version date of consent form
            - Attestation of consent (below)

Implied consent

Implied consent refers to a form of participant agreement that is not explicitly documented through a signed consent form but is reasonably inferred from a participant‚Äôs actions or circumstances. Participants must still be provided with information about the study although a consent form will not be used. Implied consent may be acceptable in specific contexts where obtaining written or verbal consent is impracticable or inappropriate, provided that ethical safeguards are in place.

Implied consent may be appropriate in some scenarios, such as:

- **Anonymous surveys** where participants voluntarily complete and submit a questionnaire after being informed of the study purpose, risks, and benefits.
- **Online research** where participants proceed past an information screen to engage with the study (e.g., clicking "Next" after reading a consent statement).

The protocol or protocol addendum must clearly delineate the rationale and use of an implied consent model.

Alterations and waivers of consent

In general, researchers must obtain informed consent from potential participants before initiating any study. However, certain types of research may necessitate alternative approaches to consent, and in specific circumstances, a waiver of consent may be ethically acceptable.

Alterations to Consent in Prospective Studies

Some research questions cannot be adequately addressed without modifying the standard consent process. The REB may approve such modifications if the study team demonstrates that all the following conditions, as outlined in TCPS 2 Article 3.7A, are met:

a. The research poses no more than minimal risk to participants;
b. The modification is unlikely to negatively impact participant welfare;
c. The research cannot be conducted, nor the research question properly addressed, without the alteration to consent;
d. The nature and scope of the proposed alteration are clearly defined; and
e. A debriefing plan (if applicable) is in place, which may include options for participants to refuse consent, withdraw their data, and/or biological materials, in accordance with TCPS 2 Article 3.7B.

Waivers of Consent for Secondary Use Data or Samples (Retrospective Studies)

For studies involving the secondary use of identifiable information (e.g., medical records, previously collected biological specimens), researchers must seek consent unless they can demonstrate to the REB that all of the following criteria, as per TCPS 2 Articles 5.5A and 12.3A, are satisfied:

a. The use of identifiable information or biological materials is essential to the research;
b. The use without consent is unlikely to harm the individuals to whom the data or materials pertain;
c. Adequate measures are in place to protect privacy and safeguard the data/materials;
d. The researchers will respect any known preferences previously expressed by individuals regarding the use of their information;
e. It is impossible or impracticable to obtain consent from the individuals concerned; and
f. All other necessary permissions for secondary use have been obtained.

Understanding Impracticability in Consent

TCPS 2 defines impracticable as a situation where obtaining consent would involve a level of hardship or burden that jeopardizes the feasibility of the research. This does not include inconvenience.

Examples of impracticability include:

- Extremely large participant groups;
- Participant groups where a large proportion are deceased or difficult to locate;
- Resource constraints that would impose undue hardship on the research team.

For the REB to consider a request for a waiver of consent, researchers must provide sufficient justification to the REB demonstrating that obtaining consent is truly impracticable.

Research Consent form(s) in the medical record

To ensure that research participants privacy and confidentiality are maintained, research consent forms should only be included in participant medical records or electronic medical record (EMR) under certain circumstances (i.e., the study is clinically relevant or involves procedures that could impact the participant's clinical care).

Research consent form(s) must be included in the medical record only if it is clinically relevant, meaning the study involves activities (i.e., investigational drugs, devices, biologics, or procedures) that could impact the participant's treatment. If the research consent form will be included in the medical record, this information must also be delineated in the research consent form.

If the study does not meet this threshold, the research consent form should not be included in the medical record.

For studies involving minimal risk and where there are no clinical interventions, such as surveys, interviews, or use of de-identified data consent forms are should not be included in the medical record.

Studies that will register a participant in a research study in EPIC, this must be described in the consent form.

Refer to the CHEO REB Documented Institutional Ethics Requirements (DIER), or changes required to Clinical Trials Ontario (CTO) consent form template for consent form language.

If there is uncertainty as to whether the consent form should be included in the medical record, please reach out to the REB (reb@cheo.on.ca) for further guidance.

Post-initiation of study activities

Ongoing Review

Modifications to an approved study are categorized as either major or minor based on the impact on participant risk. Requests for changes to approved research may receive delegated or full REB review depending on the level of risk to participants that the changes represent (TCPS2 Article 6.16).

Major Modifications

These changes have a substantial impact on the research, potentially affecting the study's overall design, participant population, or risk assessment.

These are changes that:

- Increase the level of risk or discomfort to participants.
- Substantially change the study's objectives, design, or procedures.
- Adding a new drug, device, or invasive procedure.
- Revising the inclusion/exclusion criteria.
- Changes to the study intervention (i.e., dosing)
- Restarting a study after a safety-related hold.
- For Health Canada Regulated trials, major modifications require that a Clinical Trials Application Amendments (CTA-A) is submitted, for which a new Health Canada No Objection Letter (NOL) is issued. The REB will only approve major modifications of this type after the NOL has been received.

Under limited circumstances, the REB can waive the requirement for the Amendment Health Canada Non-Objection letter prior to activation of the protocol modification. The waiver is based on section C.050.008 of the Division 5 Food and Drugs Act, which allows **safety-based** protocol modifications to be activated immediately providing that the sponsor notifies Health Canada of such changes.

Major modifications require full board review at a convened meeting.

Major modifications to minimal risk protocols are reviewed in the delegated stream and do not require full board review.

Minor Modifications

These are changes that:

- Do not significantly increase risk to participants.
- Do not substantially alter the study's aims, design, or methodology.
- Examples include:
  - Minor updates to recruitment materials (e.g., phone number changes).
  - Revisions to surveys or interview questions.
  - Minor changes in participant compensation or schedule.
  - Change in local Principal Investigator.

Minor modifications are reviewed in the delegated review stream.

Additional Co-Investigators &/or Research Staff

The addition of a co-investigator and/or research staff that does not modify any study specific documents **(i.e., consent forms contact section)**, does not require submission to the REB office. Please send an email to romeo@cheo.on.ca that indicates the CHEO REB study number, the name of the individual, their role on the study and indicate that there are no changes to study documents. Please ensure that the additional staff has the appropriate training certificates as well as a ROMEO account; if they do not, the staff will not be added to the study.

Deviations to previously approved research

Researchers must report to the REB any deviations that meet the following reporting criteria (CHEO REB SOP 404):

- Deviations that in the opinion of the Researcher jeopardize the safety of research participants, or that jeopardize the research efficacy or data integrity
- Any sponsor-approved waivers to the participant eligibility criteria,
- Any change in the approved process for obtaining consent (e.g., improper translation, current ICF not implemented)
- Any deviations that lead to an SAE

Serious Adverse Event(s)

The Researcher is required to report to the REB only those local serious adverse events (AE)/ adverse drug reactions (ADR) that are deemed to be unanticipated problems (unexpected, related/possibly related and involving greater risk) (CHEO REB SOP 413 & 414).

The following local AEs/ADRs should NOT be reported to the REB:

- SAEs/SADRs that are considered expected; defined by the protocol and/or IB/PM;
- SAEs/SADRs that are considered not related to the investigational product or research procedures, whether the event is expected or not;
- AEs/ADRs that are non-serious, whether expected or not, or related or not.

The researcher should only report external (non-local) serious AEs/ADRs or unanticipated problems in the form of periodic safety update reports accompanied by information that is meaningful and useful to the REB. The content of the safety report should include at a minimum a sponsor analysis of the significance of the event or an analysis from the DSMB, with (where appropriate) a discussion of previous similar events, and a position statement as to whether any changes are required to the approved documents.

The CHEO REB requires that researcher(s) clearly identify AEs/ADRs that involve children. These periodic reports should be submitted to the REB no later than fifteen days after receipt by the researcher.

In accordance with articles 11.8 and 11.9 of the Tri-Council Policy Statement (TCPS 2) and ICH E6, researchers are required to promptly report new information that may affect the welfare and ongoing consent of participants to the REB.

Examples of new information to be reported include, but are not limited to the following:

- Changes to research design;
- Evidence of any new risks;
- Unanticipated Problems (see definition);
- Study results that clearly show the benefits of one intervention exceed the other;
- New research findings, including publications in the literature or other relevant non-study findings that could influence the decision of participants to continue in the study;
- Lack of efficacy, recruitment issues, closures of other sites that may be relevant to the welfare or consent of participants in an ongoing trial(s), or other matters determined to be serious enough to warrant disclosure;
- Safety Alerts;
- Updated Investigator's Brochures;
- Notification of Sponsor suspension or termination of the study;
- Changes in the Health Canada or Food and Drug Administration (FDA) labelling or withdrawal from marketing of an investigational product used in a research protocol;
- Serious or continuing non-compliance with organizational policy or REB requirements; and
- Protocol deviations that jeopardize research participants' safety or data integrity.

Continuing Review

In accordance with TCPS2, REB approval can be granted for no more than 1 year at a time. Applications for re-approval must be filed with the Board on an annual basis or by the expiry date listed on the REB approval.

A research project involving human participants will require annual re-approval from the REB as long as the investigator conducting the research continues to collect data about the participants of the research; which includes, entering, collecting and verifying data.

Approval of an annual renewal event form must be obtained prior to the expiry date of approval. A lapse in approval requires that recruitment into the study and all study activities must be discontinued. Should the investigator wish to continue the research, the study must be re-activated. This requires both a protocol deviation event along with a duly completed annual renewal report.

The REB will close a study 30 days after the study expiry date. Under these circumstances, a notice will be sent to the investigator and the CHEO Research Institute Administration Office who will suspend access to the study funds.

The date of final approval of a protocol will be determined following the procedures outlined in CHEO REB SOP 408.

The REB follows a procedure for maintaining fixed anniversary dates for the expiration of annual REB approvals. This anniversary date appears on the final approval letter. The final approval letter also specifies the date at which investigators should submit to the Board an annual renewal report. The determination of the expiry (anniversary) dates follows the procedures outlined in the CHEO REB SOP 408.

A research project involving human participants no longer requires annual re-approval when the investigator:

- is no longer collecting data about the participants which includes entering, collecting and verifying data and;
- indicates there is no longer a need to obtain more data for the research project.

Study Closure

The REB must be advised if a study closes to accrual permanently or if accrual is temporarily suspended.

A study should be permanently closed, if:

- The study was never initiated and there are no plans to do so in the future.
- The research project is no longer collecting data about research participants, which includes entering, collecting and verifying data, and there is no longer a need to obtain more data for the research project.
- The study is interrupted unexpectedly (e.g., the sponsor withdraws support, the investigational agent is no longer available, etc.).

Data retention

All research records pertaining to studies that fall under Health Canada Division 5 regulations must be retained for a minimum of 15 years after closure. All other studies should retain records for a minimum of 7 years after the study closure, unless otherwise approved by the REB. The public hospital's act requires that health records be retained for a minimum of 10 years past the child's 18th birthday. For the most part, this requirement would not affect study records that would be retained separately from the health record.

Translated Documents

Informed consent forms must normally be available in both English and French for research conducted at CHEO. This requirement is based on the importance of free and informed consent in research, and the hospital's commitment to bilingual service for families and youth.

Under limited circumstances, the REB can waive the translation requirement. In order to obtain such a waiver, the investigator must demonstrate that it is either inappropriate or impracticable to require both French and English consent forms. In other words, the investigator would need to show that the additional financial, material, human, organizational and other resources needed to carry out a study in both languages are so burdensome as to render the research unfeasible. An investigator might argue, for example, that a study cannot be responsibly conducted in one or other official language because the outcome measures have not yet been translated and the resources needed to do so are prohibitive.

The decision to waive the requirement for consent forms in both official languages will be sensitive to the specific nature of the study. Projects are not likely to be given a waiver if they present more than minimal risk to subjects or if they offer innovative therapies to patients that would otherwise be unavailable.

For more information on translation service providers click here: Resources

Investigators must ensure that the French and English versions of the consent form are equivalent in every aspect. To do so, a professional translator should normally carry out the work.

Research studies requiring French translation cannot be approved until the French documentation has been submitted and approved, or confirmation provided to the REB that the documentation has been submitted for translation (a copy of the email or letter to the translator).

This policy requires that a French (or English) version of the consent form be made available within two to three months of the initial approval. However, if an investigator believes that it is impossible to meet this time line, the Board should be advised and a reasonable alternate timeline proposed.

External service providers

Travel Service Providers

What are travel service providers?

Travel service providers are third party companies used to assist research participants in scheduling travel/transportation for research study visits.

What documents need to be included in my REB submission from TSPs?

All travel consent forms must be included in the REB submission.

- Note that travel consent form refers to the document a participant must sign to access travel service provider services or supports but may be named something other than 'consent form'.

At a minimum, the consent forms must include the following information:

- What identifiable information will be collected
- Location where data will be stored (e.g., country) Risks associated with the use of this service.
- A statement that the sponsor will not receive any identifiable information.
- A statement that the use of Scout services is not required for study participation.
- Contact information for question regarding participant data (e.g., Data Protection Officer, Privacy Officer)

All other documents do not require REB review; however, they can be submitted for acknowledgement if mandated or requested by the sponsor. Examples of some of these documents are included below:

- Rideshare message template
- Welcome letter template
- Participant portal
- Message template
- Travel reference guide
- Travel contact card
- Cardholder FAQ
- Card graphic
- Dispute form