SickKids Research Ethics Board: Research Ethics Handbook

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The purpose of this document to provide some background on fundamental topics in Research Ethics and essentially outline the purpose for conducing a research ethics review of a research study.

An Introduction to Research Ethics

Research ethics guides standards on how to conduct research involving human participants. Researchers are expected to conduct research with the highest ethical standards.

There are many guidelines that inform research ethics. In Canada, the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS 2) is followed to ensure ethical standards of research is met. TCPS 2 is updated as ethical considerations are needed to address science and medicine advancements as well as ensures ethical compliance. The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2) defines research as "any scientific undertaking intended to extend knowledge through a disciplined inquiry or systematic investigation."

Research ethics oversight is needed because the purpose of research is to understand something not yet understood or known, and therefore there are risks to participants. History contains many examples of research participants being harmed, in some cases significantly. Research ethics and the REB support the advancement of knowledge while protecting and respecting the rights of research participants.

Three core principles

The underlying core principle that guides research ethics review is respect for human dignity. Respect for human dignity is expressed through three core principles - *Respect for Persons*, *Concern for Welfare*, and *Justice*.

Respect for persons

- Autonomy allowing the potential participants to make an informed decision about whether they want to participate in a research study.
- Participants must provide their free, informed and ongoing consent to be in the research study without any interference or coercion.
    - Protects those with developing, impaired or diminished autonomy. Inadequate information, lack of transparency, influences, coercion, insufficient time to make a decision are some of the many factors that diminish a person's ability to exercise their autonomy.
- Recognizes the intrinsic value of human beings and the respect and consideration that they are due;
- Considers how persons of all ages are treated as research participants; and
- Incorporates the moral obligations to respect autonomy.

Concern for welfare

- Welfare is defined as the quality of a person's experience of life in all its aspects.
- Physical and mental health, socio-economic circumstances, privacy and control of their health information are all factors that affect a person's welfare.

- The aim of the REB and researchers is to protect the welfare of participants in the presence of any foreseeable risks associated with the research. The researchers and REBs must also always aim to minimize the risks associated with any given research activity and achieve the most favourable balance of risks and potential benefits in a research study.
- Considers the impact on persons of factors including physical, mental and spiritual health, as well as their physical, economic and social circumstances;
- Encompasses factors including privacy and control of information about the person and the assessment of foreseeable risks and benefits; and
- The treatment of data and human biological materials according to the free, informed and ongoing consent of the person who was the source of the information and materials.

Justice

- Justice is the obligation to treat persons fairly and equitably. This does not mean treating everyone the same, because every person has different needs.
- Inclusion criteria are justified by the research question and not designed to purposely exclude certain populations unrelated to the research question
- A threat to justice is the imbalance of power that may exist between researcher(s) and the potential participant(s). This is because, in general, potential participant(s) and/or participants do not comprehend research in the same way as the research team.
- Historically vulnerable populations in research includes children, the elderly, students, women, prisoners, those with mental health issues and those with diminished capacity for self-determination. Justice ensures those who were exposed to the risks during a clinical trial continue receive the study drug if the study drug has proven efficacy.

Research Ethics Board

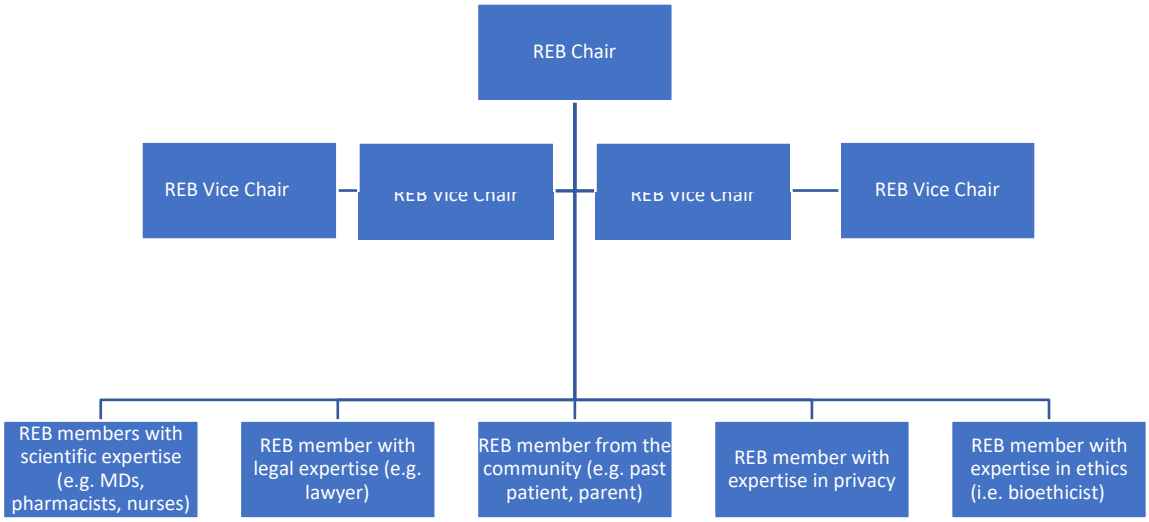
The Research Ethics Board (REB) is an independent body established by the SickKids Board of Directors to protect the rights and welfare of human research participants. The REB ensures that all research involving humans meets current ethical and scientific standards and is in compliance with national and international regulations, guidelines and policies, including the Tri-Council Policy Statement on Ethical Conduct of Research Involving Humans (TCPS 2, 2018).

Research ethics review is guided by respect for human dignity, which encompasses three core principles: Respect for Persons, Concern for Welfare, and Justice.

The SickKids REB is composed of an interdisciplinary and community representative group that brings their perspectives and expertise to the review, discussion, deliberation and approval of research studies. The REB is comprised of three panels (A, B, and C), and includes physicians, clinical staff, members of the community, lawyers, and individuals knowledgeable in ethics and privacy.

Panel C meets exclusively to review Artificial Intelligence and Machine Learning research studies.

To ensure REB decisions are independent, no one from the institution’s senior executive administrative will serve as an REB.



All decisions about a research study application are made by the REB. The Research Ethics Office carries out the REB requirements and decisions.

What types of Research requires REB review and approval

All research involving humans, including data and biospecimens (either directly or indirectly), require REB approval.

Below are examples of research studies requiring REB review and approval prior to commencement:

- Research involving living human participants.
- Research involving human remains, cadavers, tissues, biological fluids, embryos, or foetuses.
- Research involving secondary use of data (use of data initially collected for another purpose) - health records, employee records, student records, computer listings, banked tissue - if any form of identifier is involved and/or if private information pertaining to persons is involved.
- Research about a living person in the public arena if s/he is to be interviewed and/or private papers accessed.
- Quality improvement/assurance studies and program evaluations which address a research question. Program Evaluation: REB review is required only if a QI or PE meets the TCPS2 definition of research or serves as a component of a research project.

Who must submit Research project for REB review?

All SickKids staff conducting research involving humans must submit their research project to the REB for review.

If SickKids patients, family members of patients and/or SickKids staff are going to be approached for research participation, the research project requires REB review and approval.

If staff outside SickKids would like to conduct research at SickKids, they must collaborate with a SickKids researcher and submit the research project for REB review and approval prior to commencing research.

Similarly, if a SickKids staff would like to conduct research at another site, they would have to obtain REB at the external site, as well as submit the research project for proportionate review at SickKids REB.

Determining Research Risk Level

TCPS 2 Chapter 2, section B discusses the types of risk that are assigned to research studies.

Minimal Risk: the potential risk(s) from research-related activities to the participant is **not greater** than what the participant is exposed to in their day-to-day activities and life.

Above Minimal Risk: the potential risks from the research-related activities to the participant **is greater** than what the participant is exposed to in their day–to-day activities and life.

Potential risk of research studies include:

- Physical risk: harm that could be done to the body from research procedures/intervention. E.g. needle poke becoming a bruise, device insertion
- Emotional/psychological risk: harms associated with feeling uncomfortable, embarrassed
- Social risk: harm of losing job, insurance, privacy

Vulnerability of the research population or the disease can also determine the type of review. The vulnerability factors such as power relations, age, socio-economic status, participant capacity that is affected by diagnosis, cognitively and emotionally, communities with unique needs, along with the research design can influence the risk level of the research study.

Example: Research study that is conducting qualitative interview questions in a group setting of patients diagnosed with HIV will be considered a group that is highly vulnerable.

Example: Medical students asked to participate in a research study to evaluate their professor's teaching skill in an interview would be considered a group that is with low vulnerability because the power relation of teacher to student and the potential threat and fear of receiving a failing grade.

The risk level of a research study determines the type of review that will be conducted on the research study.

Vulnerability	**Research Risk**			
		Low	**Medium**	**High**
	High	Full Board	Full Board	Full Board
	Medium	Delegated review	Full board	Full Board
	Low	Delegated review	Delegated review	Full Board

In accordance with the Tri Council Policy Statement 2 (TCPS2) guidelines, SickKids REB review is based on the general principle of proportionate review (i.e., the higher level of risk, the higher the level of scrutiny in the review).

Types of REB reviews

Full Board Review

Full board applications are assigned to a primary and secondary reviewer. In the primary/secondary reviewer system, two board members are responsible for an in-depth review of the study application. The research ethics coordinator, in consultation with the REB Chair, assigns primary and secondary (and occasionally tertiary) reviewers based on the expertise required for each submission.

- Each full board study is assigned at least 2 reviewers.
- The primary reviewer is the person with the most applicable scientific expertise in the area of research.
- Secondary reviewer is a REB member whose expertise would enhance the review.
- Tertiary reviewers are also sometimes assigned to research studies when the research study is complex and or requires review by a bioethicist, community member or another member with a certain scientific expertise the review can benefit from.
- If it is determined that appropriate expertise is not available within the REB membership, an internal or external consultant may be sought for a review.
- All members during the meeting also provide their comments/concerns with the study.

Delegated Review

- The research study application and all submitted study documents are reviewed by the REB Chair/Vice-chair and a REB coordinator (who is considered a non-voting member of the REB).
- Sometimes REB members with the relevant scientific expertise are asked to review or provide feedback on a specific of a research study.

Secondary Use Review

If a study has been deemed to be minimal risk *and* involves the use of secondary data/tissues only, the study will undergo a secondary use review process, which is an expedited delegated review process. Although the review process is the same, the requirements for a secondary use study are different than for a prospective study – see the Secondary Use Guidelines here for further information.

Other types of Review

If a research study does not fall under one of the above categories, then a required proportionate review will be done.

International Research/Research outside SickKids:

If a SickKids staff is conducting research outside SickKids and or outside Canada, REB approval is required from the site where research activities will take place.

The PI is required to submit the research project to the SickKids REB, and a proportionate review will be conducted on the submission.

REB review Exemption

Case Reports

Case reports are a description of some or all of the diagnosis, treatment, and follow-up of an individual patient. They are normally based off of information found in the individual's health record and contain personal health information; consequently, case reports are subject to the provisions of PHIPA (Personal Health Information Protection Act).

Case series involve case reports of 3 or more patients.

Case reports are not be confused with case series, which may be conducted by several sites, and where SickKids contributes three or fewer cases to a case series requires consent from the participants, REB review and approval prior to data collection and sharing.

Please refer to the Guidance document for secondary use studies and case reports series.

Research versus Quality Improvement

Quality improvement projects have many things in common as research, such as a detailed methodology, data collection, data analysis and date interpretation. The aim to publish results does not determine if the project is research or quality improvement. The chart below was taken from the SickKids Quality Improvement Team.

	Research	Quality Improvement
Purpose	to develop or contribute to generalizable knowledge	to implement knowledge, assess a process or program as judged by established or accepted standards
Rationale	knowledge-seeking independent routine care and intended to answer a question or test a hypothesis	knowledge-seeking integral to the ongoing process of health care delivery
Design	follows a rigid protocol that will remain unchanged throughout the study	adaptive, iterative design; flexible and responsive to change throughout project lifecycle
Benefits	might or might not benefit current subjects; intended to benefit future patients	directly benefits a process, system or program; might or might not benefit patients
Risks	may put subjects at risk	does not increase risk or cause excessive burden to patients or staff
Participant Obligation	no obligation of individuals to participate	participation typically occurs as component of care or work
Endpoint	answer a research question and contributes to generalizable knowledge	improve a program, process or system

Analysis	statistically prove or disprove hypothesis	compare program, process or system to an already established or accepted standard
Adoption of Results	little urgency to disseminate results	results rapidly adopted into local setting

For more information about Quality Improvement projects, please visit the Quality Improvement Project Review Process site.

Privacy and Confidentiality

When it comes to collecting health specific information about patients, the manner in which Personal Health Information (PHI) is collected and stored must satisfy the Personal Health Information Act (PHIPA) law.

Researchers have an ethical duty and professional code of conduct to treat personal information in a confidential manner so as to protect the privacy of participants. Privacy risks may arise at all stages of the research life cycle, from initial collection of information, to data analysis, dissemination of findings, storage and retention of information, and disposal of records or devices on which information is stored.

- As a result, researchers must develop a plan to ensure the confidentiality of all personal information throughout the research life cycle; this is in accordance with both TCPS 2 and the Personal Health Information Act (PHIPA).

Personal Health Information

PHIPA defines **personal health information (PHI)** as identifying information about a person in either an oral or in a recorded form if the information:

- relates to the person's physical or mental health, including family health history,
- relates to the provision of health care, including the identification of persons providing care and the institution at which care is provided
- is a plan of service for a person requiring long-term care;
- relates to payment or eligibility for health care;
- relates to the donation of body parts or bodily substances or is derived from the testing, or examination of such parts or substances,
- is the person's Provincial Health Number; or
- identifies a person's substitute decision-maker.

Any other information about a person that is included in a record containing PHI is also included in this definition. This definition does not include information about a person if the information could not reasonably be used to identify the person.

What Is Identifiable Information?

According to the TCPS2 (Chapter 5), information is identifiable if it may reasonably be expected to identify a person, when used alone or combined with other available information. Information is non-identifiable if it does not identify a person, for all practical purposes, when used alone or combined with other available information.

The following categories provide guidance for assessing the extent to which information could be used to identify a person:

Directly identifying information

The information identifies a specific person through direct identifiers (e.g., name, health card number, hospital MRN, social insurance number).

Although with appropriate consent and REB approval directly identifying information can be collected from research participants for research purposes, there needs to be strong justification for wanting to collect and store directly identifying information about the participants.

Indirectly identifying information

The information can reasonably be expected to identify a person through a combination of indirect identifiers (e.g., date of birth, full address, full postal code or unique personal characteristics including a person's voice, unique body markings or features that are either inborn, the result of the disease, or artificially added such as tattoos).

Coded (de-identified) information

Direct identifiers are removed from the information and replaced with a unique code. Depending on access to the master code breaking file, or inclusion of strong indirect identifiers, 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 name so data can be re-linked if necessary).

Anonymized information

The information is irrevocably stripped of any information that can directly or indirectly link research information to the participant. The master code breaking file is destroyed to prevent any future re-linkage. The risk of re-identification of persons from remaining indirect identifiers is low or very low.

Anonymous information

The information never had identifiers associated with it (e.g., anonymous surveys) and risk of identification of persons is low or very low.

Ethical concerns regarding privacy decrease as it becomes more difficult (or impossible) to associate information with a particular person. These concerns also vary with the sensitivity of the information and the extent to which access, use or disclosure may harm a person or group.

Collection of Initials of First name Last name

Initials are considered as an identifier under PHIPA and does not add scientific value to research. Initials are also not a unique identifier. For example Jane Doe and John Doe have the same initials, hence collecting initials not permitted.

Protection and Storage of Data

The Sponsor, Sponsor/Investigator, Qualified Investigator or PI is responsible for ensuring data and privacy protections are in place. This includes both physical (premises and equipment) and logical (access control) security of research data.

Data safeguarding procedures may be delegated in writing on a study task delegation log to appropriately trained research team members, however, the ultimate responsibility for ensuring data confidentiality rests with the Sponsor, Sponsor/Investigator, QI or PI.

Protection during data collection and analysis

The collection of any identifying information (direct or indirect) must be justified to the REB. Where possible, the amount of information collected should be the minimum required to answer the research question (e.g., you should not collect full date of birth in dd/mmm/yyyy format when only age in years is required). If a study team is required to collect identifying information, the team must provide a scientific justification to the REB why this data must be collected, and how it will be safeguarded. This may also be required to be stated in the participant consent documents.

If your study sponsor provides data collection forms or case report forms that include identifying data fields (e.g., full DOB without justification), research teams should use 'dummy dates' in order to complete the required fields. For example, if study CRFs require full DOB, study teams can use the '1st' or '15th' of the month for all participants. This ensures that exact DOB is not sent off site.

The SickKids REB, however, may exercise the right to consider the use of other identifiers (i.e. partial DOB with month and year) whereby potential harms of using additional identifiers are well understood in relation to the risks of not using them. When this is the case, the collection, use, transfer and storage of PHI must be disclosed in the ICF.

- A unique study identifier (e.g. unique study number/code) should be used to collect and store data (electronic or hard copy) pertaining to research participants.
- Any information leaving SickKids (case report forms, data collection forms, other study documents), including electronically captured data, should only be identified with a unique study identifier.
- Videotapes, photographs, and other identifying images of research participants must be securely stored in locked cabinets or on a secure server separate from the research participants' study data.
- Electronic data files with unique study identifiers must be stored on a secure server. If this is not possible, data are to be encrypted (i.e. laptop, USB key) and where applicable, hard copy data files with unique study identifiers securely stored in locked cabinets.

No directly identifying information (e.g., MRN, participant name) should appear on the data collection form. A master linking log/code breaking form can be used to link the participant's identifier to a study ID. Only the minimum amount of information required to identify a participant (e.g., MRN) should appear on the master linking log. The study ID must NOT contain any identifier or derivative of an identifier (e.g., partial MRN, year of birth, year of admission). The master linking log must contain 1) the study's title, 2) a version date), and 3) a confidentiality disclaimer (e.g., "Confidential information – keep separate from study data"). Access to the master linking log should be limited and it must always be kept separate from study data.

Use of linking logs

The use of a unique study identifier or code only as the unique identifier is considered best practice. Unique study identifier/study code **must not** include any Personal Health Information (PHI) of research participants, such as name, initials, full date of birth (DOB), and medical record number (MRN).

Protection during data / materials transfer

If data or materials are being transferred to or from SickKids, details on how they will be adequately protected and safeguarded during the transfer with external sites should be described to the REB. No identifying information should ever leave SickKids. If you are exchanging data or materials with another site, you may require a data or materials transfer agreement. Please consult with the Research Contracts Management Office (RCMO) regarding the requirements for a transfer agreement.

Data Storage and Destruction

SickKids policy requires that all study data be stored behind two of each of the following types of safeguards:

a) **Physical safeguards –** includes locked office, locked storage unit, biometric authentication, cipher/coded locks, access cards, etc.
b) **Administrative safeguards** - includes the development and enforcement of organizational rules about who has access to personal information about participants (e.g., computer passwords only with study team, designated person responsible for controlling who has access to data, etc.)
c) **Technical safeguards** – includes use of computer passwords, firewalls, anti-virus software, network drive, encrypted computer, encrypted USB, etc.

Data must be stored by researchers for a **minimum of 7 years post publication or study closure**, or **25 years** from end of study in the case of **Health Canada regulated studies**.

Details of how data will be destroyed should also be provided to the REB. Paper records can be disposed of in SickKids confidential disposal bins, electronic records can be destroyed by contacting SickKids Research IT help desk, and old CDs, DVDs, videos, USB keys, external hard drives and other technology can be sent to the repair centre for destruction.

Participant Recruitment

Participant recruitment is the seeking out of individuals, groups or communities that meet the inclusion criteria of a study. It involves the identification of potential participants, initial contact with potential participants to introduce them to the study, and actual recruitment of participants (e.g. screening and informed consent.

Ethical Considerations

According to TCPS 2 (Article 3.1), the approach to recruitment is an important element in assuring the voluntariness of participation. In particular, how, when and where participants are approached and who recruits them are important elements in assuring (or undermining) voluntariness. Study teams should consider how their recruitment process may affect potential participant's privacy, as well as the potential for undue influence in the recruitment process.

Identification of Potential Participants

Depending on the study population, potential participants may be identified via a review of medical records, staff records, student/trainee records, or they may self-identify (e.g., community members, healthy controls after learning about the study).

Via Medical Records

Medical records include clinic and hospital patient records (e.g., EPIC) as well as clinic databases. In general, accessing medical records for research activities requires prior written consent.

Pre-screening of medical records

The REB may grant a waiver of consent when medical records are being pre-screened to identify potential participants. Study teams must request this waiver and provide justification in the REB application. This pre-screening process involves access of minimal information (e.g., age, medical condition) to identify potential participants; no information should be recorded as part of this process. Details of who will pre-screen medical records and when should be provided in the eREB application. A delegation log should be maintained throughout the study to maintain list of research team members who access medical records.

Eligibility screening

The pre-screening process differs from the more in-depth screening process (e.g. eligibility determination) which typically involves a detailed review of patient records and requires patient consent prior to accessing the records or asking participants to do assessments or lab tests to confirm eligibility.

Via Staff Records or Student/Trainee records

Access to staff/student lists and other information related to a potential participant's employment/education is restricted to persons who are directly involved in the individual's work/education. Access to staff/student data for research purposes requires documented permission from the custodian of the information.

Via Self-Identification

Potential study participants may self-identify or express interest to be part of a study as controls after hearing about the study through various promotional materials (e.g., poster advertisements). Some may also be identified via secondary recruitment through family members and friends.

Initial Contact

Initial contact involves informing the potential participant about the study and gaining consent for further contact from the study team. The methods used to contact a potential participant should not intrude on the individual's life or privacy, and the potential for undue influence should be mitigated. The following general rules should be followed when establishing initial contact:

1. Initial contact of a potential participant should be made by someone who the participant expects to have relevant information about them.
    - **Patient/Parent Participants:** A person who is part of the individual's circle of care or someone the patient/parents know should make the initial contact. A person's circle care includes any member of the health care team which provides direct care to the patient or assists with providing the care required.
        i. For high risk studies such as clinical drug trials or new device trials, initial contact will need to be done by a member of the potential participant's treating team such as the treating physician or nurse involved in the patient's care. For low risk studies, such as those which do not involve new drug treatments or devices (i.e. surveys, questionnaires, interviews), study staff may be introduced by any of the members of the potential participant's circle of care, including admitting staff, reception, etc.
    - **Staff Participants:** The potential participant's work supervisor should issue information about the research study (e.g., through communications/announcements or materials distributed during staff meetings) to potential participants on behalf of the study team.
    - **Student/Trainee Participants:** The institution's training division or course instructor should make the initial contact with the potential student/trainee participants using study information provided by the study team.
    - **Members of a Health Professional Society:** The head or a known representative of the society should issue communications on behalf of the study team.
    - **Community Members/Healthy Controls:** Community members/healthy controls will contact study teams based on advertisements/media that inform them about the study. They consent to be contacted by informing a study team member that they are interested in the study.
2. Initial contact should **not** be conducted in open/public areas where there is no expectation of privacy (e.g., clinic waiting rooms)
3. If a potential participant has previously participated in a research study, they may be contacted directly by a member of the research staff only if they previously consented to be contacted for future research.
4. If the contact information of a potential participants is available through another organization (e.g., government or non-government officials, business leaders, organizational staff, etc.), the researcher should first seek institutional, organizational or agency approval prior to contacting these individuals.

Initial Contact Involving Dual-Role Researchers

Dual-role researchers should be aware of the potential for undue influence and research benefit misconception (or therapeutic misconception) when inviting their own patients, students, employees, colleagues or subordinates to participate in research. The trust and dependency inherent in clinician-

patient, teacher-student, and supervisor-employee relationships may unduly influence voluntariness to consent to research. Strategies to mitigate undue influence and research benefit misconception should be developed.

Acceptable Recruitment Methods

The following is a list of the recruitment methods that are accepted by the SickKids REB.

Direct Contact

In person

Recruitment to a study may occur in person. In this case, initial contact should be made by a member of the circle of care or someone the potential participant is familiar with. At this point, permission to share the potential participant's contact information with the study team is obtained. Once consent to be contacted by a research team is obtained and documented, study teams may follow up with potential participants to provide them with further information regarding the study, conduct consent discussion and obtain informed consent.

Over the phone

Potential participants may be recruited to a study over the phone. Prior to calling potential participants, they should be introduced to the study via an introductory letter (see below).
A recruitment script is required to standardize information provided to potential participants. The recruitment script and all follow-up contact scripts should be submitted to the REB for review and approval.

Introductory Letters

Introductory letters inform potential participants about a study and provide them with a way to contact the study team for more information, to indicate interest or to decline being contacted. It should be sent by someone the potential participant is familiar with, such as someone involved in their care or who would have access to their personal information.

Introductory recruitment letters should include the following:

1. **The method that the study team will use for follow-up contact:** this includes when potential participants can expect to be contacted, and who will contact them. A period of 2-3 weeks after the letter is sent is a reasonable time frame for follow-up. A maximum of 3 follow-ups with the potential participant are permitted; after this, if no contact has been established, then a potential participant is deemed as having refused to be part of the study.
2. **How to opt-out of the follow-up:** provide the name and contact information of a study team member who can be contacted to opt out of being followed up. A self-addressed stamped envelope that can be mailed back to the study team or an opt-out card can also be used. If an opt-out card is used, it should not contain any personal health information.
3. **Instructions for next steps**, such as contacting the study team to indicate interest, meeting with the study team member at the next clinic visit, etc.

The introductory letter, recruitment script, and all follow-up contact scripts should be submitted to the REB for review and approval. Please see the 'Forms, Templates and Guidelines' section of the Clinical Research services website for introductory letter templates that can be used.

Mailed out introductory letters

A mailed-out letter is considered a secure form of communication. For this reason, a limited amount of personal health information (PHI) can be included in the letter, as long as it is sent from an individual the potential participant would recognize as having access to their personal information.

Recruitment Email

Indirect recruitment: Listing a study-related email address in recruitment flyers, pamphlets or study information sheets for potential participants to contact the research team if they are interested in potentially participating.

Direct recruitment: obtaining potential participants' email addresses (with permission) and emailing them REB approved recruitment materials about a research study. Potential participants can be sent email directly from mailer lists they are part of.

Email is considered a non-secure form of communication as it may be accessed by unauthorized third parties. As a result, consent to be contacted about a research study should be obtained prior to sending out study information in an email. When consenting to contact, the potential participant should be informed that email communications are not secure, and that personal information may be included in the email. This consent should be documented in the study files.

When using email for recruitment of study participants, the following guidelines need to be followed:

1. The sender's SickKids email account should be used;
2. Do not use mass emails;
3. Avoid sending emails with sensitive personal health information;
4. Forms containing personal health information (e.g., consent forms that describespecific disease conditions) must not be sent without prior consent

The SickKids REB requires the following information and documents be submitted with the application:

1. Information about the source of the email list and whether consent has been provided to be contacted by email;
2. A copy of the proposed email text, subject line and any graphic used in the email;
3. A copy of any follow-up emails and frequency with which these are to be sent. A maximum of 3 follow-up emails are permitted; after this, if no contact has been established, then a potential participant is deemed as having refused to be part of the study.

Please refer to the Use of Email in Research Guidance document for further guidance and details.

Study advertisements

Study advertisements include study posters/flyers, study brochures, direct media advertisements, and internet/social media web posts. In general, study advertisements should include the following basic information:

1. Study title, PI, Whom to contact with questions, Full version date (DDMMMYYYY)
2. What is the study about?
    a. "We are doing this research study to …"
3. Who can participate?
    a. "We are looking for …"
4. A brief summary of what participants will have to do as part of the research study in an easy-to-read format, preferably a bulleted format
5. A statement that participation is voluntary
    a. "Participation is any research study is voluntary."
6. Compensation information may be included but should be stated in a manner which should not influence the decision to participate
    a. "Participants will get a gift card in appreciation of their time" but not state the amount.
7. What are the benefits of the research study?
    a. "There are no direct benefits to you for participating, but will help researchers to X, Y."

All study advertisements must comply with institutional guidelines for formatting and content and should be submitted for review and approval by the SickKids Communications and Public Affairs Office after the content is reviewed and approved by REB.

Although the Communications and Public Affairs Office can make visual formatting and SickKids branding suggestions, the wording/content of the final document must be exactly as how REB approved it, otherwise the revised content will need to be submitted via an amendment application for REB review.

Study Posters and Flyers

Study posters and flyers are used to recruit potential participants internally. They are site-specific.

Study Brochures

Study brochures contain basic information about the study and may be distributed in clinic and other public areas.

Direct media advertisements

Direct media advertisements include newspaper ads, radio and TV announcements, and bulletin board ads. If you are using radio or TV ads, the REB must view the recording. All other ads are also subject to REB review.

Social Media or Other Web Posts

Messages posted on social media (e.g. Twitter, Facebook, discussion forums) should contain basic information about the study, subject to character and space limits.

Posting study information on other websites (e.g., professional website, foundations, or support groups sites) requires proof of sign-off from the organization or group that own the website. Content posted should contain the basic information required for recruitment materials, subject to space and character limits.

Third Party Recruitment and Snowball Sampling

Third party recruitment involves asking research participants to identify other potential participants. In most cases, the SickKids REB will not allow third party recruitment because it places an additional burden on research participants, it may generate undue influence to participate in the study, and it may violate privacy laws. However, the REB may allow third party recruitment in some cases with appropriate justification (e.g., research on genetic or hereditary conditions which may run in families).

In these cases, the REB will require information on how third-party recruitment will be operationalized. All materials distributed to third parties will need to be submitted for review and approval.

Unacceptable Recruitment Methods

The following recruitment methods are not accepted by the REB:

- **Finder's Fees / Recruitment Incentives:** The SickKids REB prohibits the acceptance or use of finder's fees, direct recruitment incentives, or bonuses of any type to recruit and enroll study participants.
- **Cold Calling:** Unless the potential participant has previously consented to be contacted for future research, the use of "cold calls" to recruit participants to research studies is not allowed. An introductory letter or other informational material must be sent first or given directly to participants prior to telephone contact.
- **Recruitment materials that describe more than one research study:** Recruitment materials that describe more than one research study are called general advertisements. The SickKids REB prohibits the use of general advertisements because it is difficult to keep the information up to date due to modifications made over the life cycle of several studies. Advertisements must be study-specific.

Capacity

In the pediatric context, it is common that participants may not be able to consent.
To be able to consent, an individual must have **decision-making capacity**.
Decision-making capacity is commonly described as involving the following elements:

1) **Understanding -** know the meaning of the information
2) **Appreciation** - able to recognize how the facts are relevant
3) **Reasoning -** able to compare options, infer consequences, apply values and beliefs

Developing an appropriate plan for capacity assessment is integral to designing the research and upholding the principle of **respect for persons.**

With research involving children, potential participants may or may not have the capacity to consent to the study.

- If the **child has capacity**, then they must be consented to participate in the study and their parent/guardian **may** need to consent to their participation, and this will be assessed on a study by study basis.
    - Example of when a parent/SDM may also need to consent is when the research study is complex and the child cannot participate without the parent's assistance with research activities.
- If the **child lacks capacity**, then they should be assented to participate in the study and their parent/guardian **must** consent to their participation. Potential participants should not be excluded from research on the basis that they lack capacity as this goes against principles of justice.
- In Ontario, there is no age to consent or assent. Rather, capability to consent is based on capacity; capacity varies between persons and may vary according to the complexity of the choice being made, the circumstances surrounding the decisions, or the point in time at which consent is sought.

It is important to note that decision-dependent nature of capacity, for example a child can have capacity for one type of decision but not for another.

For example, a child may not have the capacity to determine how often they should have ice cream, however, they do have the capacity to make the decision on what type to enjoy. In the context of research, a child will likely not have the capacity to consent to participate in an interventional clinical trial, but if the child doesn't want the blood drawn for optional components of the research study, then that wish needs to be respected. If the assenting child says 'no' to optional needle poke, that should be considered over parent's consent into the overall study.

NOTE: Lack of decision-making capacity is not a reason to exclude participants from research nor should it be used to inappropriately include participants in research.

Who should assess capacity?

According to the Health Care Consent Act, a health care practitioner belonging to the regulated health profession can assess capacity. Examples of regulated health professions include a member from the following: College of Nurses of Ontario, College of Physicians and Surgeons of Ontario, College of Audiologists and Speech-Language Pathologists of Ontario, College of Dietitians of Ontario, College of Occupational Therapists of Ontario, College of Physiotherapists of Ontario, College of Psychologists of Ontario. For an up to date complete list, please check with the ministry of health and long-term care.

In research studies with no health care practitioners on the research team, the research team can request and provide rationale for requesting a non-health care practitioner to conduct the capacity assessment. This will be evaluated on a case by case by the REB.

Why should capacity be assessed?

In Ontario it is the law to assess capacity of a patient regardless of age.

The law, Health Care Consent Act, states "a person is capable with respect to a treatment, admission to a care facility or a personal assistance service if the person is able to understand the information that is relevant to making a decision about the treatment, admission or personal assistance service, as

the case may be, and able to appreciate the reasonably foreseeable consequences of a decision or lack of decision."

Similarly, in research capacity assessment must be done to ensure participant has the capacity to understand the requirements of the research study, potential risks and benefits.

In ongoing research studies such as long-term observational research studies, initial capacity assessment ensures that potential participants are capable of consenting and that they know what they are consenting to. It also helps to ensure that all potential participants are given an opportunity to consent to research.

Capacity should also be regularly assessed. There should always be a plan to assess capacity at regular intervals, especially for longitudinal research studies.

- As children grow and develop, they may gain capacity to consent to the study. See below for guidance on ongoing consent.

Other factors may modulate decision-making capacity and should be considered in capacity assessments:

- the complexity of the study/procedure/decision
- the individual child's context
- the child's experience with different procedures, their illness (acute/sudden vs chronic), and the healthcare system
- support systems

Assent

Patients who lack the capacity to provide consent must still be informed of the research study at a comprehension level they are able to understand.

In paediatric research, assent is always accompanied by the parent(s)/legal guardian/SDM's consent.

Assent is a child's 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).
    - If assent was not obtained from the child, there should still be a brief documentation as to why assent was not obtained.
- Like the informed consent process, the assent process is intended to be an ongoing, interactive conversation between the research team and the child or adolescent lacking the capacity to give informed consent.

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

- what is going on in the proposed study;
- why the study is being done; and
- what will be done to them
- if they object, the research will be terminated, and they will not be punished.

- prospective participants' dissent precludes their participation; expression of dissent or signs suggesting they do not wish to participate must be respected.

Consent

Age does not determine whether a potential participant can consent to be in the research nor does being under the age of majority automatically imply that consent must be obtained from parent(s)/SDM.

In all longitudinal research studies such as registry or biobanks, capacity assessment should be done at regular intervals. If an assenting child is able to provide informed consent for themselves at a later time, then the informed consent should be obtained at that time.

The assent process also involves providing the child with information that when they become able to consent, they will be asked if they still want to be part of the study. If they do, they will be asked to provide their own consent.

A re-consent process is required for all longitudinal studies and studies which require the collection, storage and future use data and samples.

Documenting Capacity

The research team should document capacity in the research file in a private and secure manner. It should be accessible to determine when a participant should be assessed for capacity again. When storing/documenting in the research file, the capacity assessment will have to be de-identified, i.e. only the master code breaking file can link the capacity assessment with the name.

Capacity could also be documented in the patient's medical chart as assessed by their primary physician/circle of care at SickKids. Research teams can refer to the assessment done by the clinical team to determine capacity of potential participants.

For research purposes, it is best practice to document capacity assessment on a research study document (e.g., an enrolment log) so that children who had previously assented can be consented to participate later during the study.

Comprehension

Comprehension is not the same as capacity. Capacity assessment is done to determine the decision making capacity of a participant, while comprehension is specific to the research study to ensure participant understands the research procedures, risks, of the study.

Assessing Participant's Understanding

Researchers must ensure that participants genuinely understand the research; they should not rely solely on the potential participant to ask questions about the research. Prior to obtaining consent, researchers should prepare questions to ask potential participants to assess their comprehension of what participating in the study entails.

- Asking questions can further the discussion, elicit questions from the potential participant, prompt the potential participant to think more carefully about the project, and help the researcher decide whether the potential participant has adequately understood the project.

Useful questions will be open-ended and non-directive; they should not be yes/no questions. Open-ended questions often start with "what," "where," "how often," "when," and "please describe."

Examples of open-ended questions to be used to assess potential participant's understanding (not assessing capacity) of the research study are:

About the Study

1. Can you explain to me what you will have to do if you are in the study?
2. Who is this study for?
3. What do the researchers want to learn?
4. Can you please describe the alternatives to participation in this study?
5. What more would you like to know about the study?
6. Where will the study take place?
7. Who do you contact if you have questions or side-effects during the study?

Risks and Benefits

1. What are some good things that might happen in this study?
2. What are some bad things might happen in this study?

Privacy and Confidentiality

1. Who will know what you say during the study?

Voluntary

2. Do you have to be in this study? Why or why not?
3. What should you do if you are not sure about participating?

Questions

1. If you have any questions about the study, who can you ask?

Examples of close-ended questions that are **not** helpful in assessing comprehension of the study:

1. Do you understand what we are asking you to do?
2. Do you have any questions for me?
3. Do you understand that there are risks to participating in this study?
4. Do you need any more information before you make your decision to participate?

An example to illustrate Capacity versus Comprehension:

In a study looking at which of two drug regimens is superior, one can understand that they will be taking either of the drug regimens and having blood tests done. However, one may not appreciate the impact of the research study on their health, their home life or family should they choose (or refuse) to participate.

Consent Discussion

Privacy Considerations:

- Ensure the area is private and the conversation will not be overheard by others

Essential elements of the consent process

An effective informed consent process involves the following elements:

- Consent discussion happens in a manner and location that ensures participant privacy
- Potential participant is given all relevant and necessary information about the study in and at a language level that is understandable to the participant
- Potential participants are informed of the purpose of the research study, the risks and the potential benefits
- Potential participants are informed of what procedures are necessary and optional for the research study
- Appropriate individuals with relevant expertise are available at the time of consent to answer any and all questions posed by potential participants
- Potential participants are given adequate time to consider all their options before they make a decision regarding the research study
- Potential undue influence and coercion is mitigated
- Potential participants are informed that clinical care will not be affected by their decision to participate or not in the research study
- The possibility and meaning of incidental findings as a result of research participation is discussed, if applicable
- Potential participants are informed of the extent to which anonymity and confidentiality can be assured in publication and dissemination of results, and of the potential re-use of data.
- The dialogue between the research team and participants is ongoing; participants are updated, informed, and re-consented at appropriate times and as new information become available

Study teams must both inform participants and ensure their understanding of the above.

Remote consent discussion

Remote consent discussion is permitted when in-person consent discussion is not possible. The ethical requirements of remote consent discussion does not differ from when in-person consent discussion takes place.

A video platform is preferred for remote consent discussion because this will allow the research team members to assess virtual cues of potential participants, ensure comprehension of the study and what is required of the participants.

All research teams will be expected to use PHIPA compliant video platform to conduct the consent discussion. A teleconference platform may be approved on a per participant basis for consent discussion.

Please refer to the REB guidance for Remote Recruitment and Consent Process on the CRS website.

Responsibility for Obtaining Consent

The Principal Investigator (PI) is responsible for ensuring that the consent process is followed, and for the actions of any member of the research team involved in the consent process (TCPS 2 Ch. 3).

In general, the PI should not obtain consent from study participants. The PI can introduce the study to potential participants and answer questions regarding the study, but consent should ideally be obtained from another member of the study team who is not directly involved in the patient's clinical care. This minimizes any potential form of coercion or undue influence. Individuals who obtain consent must be delegated by the PI to do so, and they must be trained and qualified for the consent process. Formal delegation of this role should be documented in a delegation log.

In rare circumstances, it may be appropriate for the PI to obtain consent (e.g., study population only available for consent during off-hours when no other study team staff are available). These are considered on a case-by-case basis; contact the REO if your study requires the PI to obtain consent.

Timing for Obtaining Consent

Sometimes the research information to be imparted to potential participants is complex or possibly distressful. Time to absorb and appreciate the information may be necessary. In these circumstances, the researcher should present the information and discuss the issues with potential participants on more than one occasion or allow a period of time to elapse between imparting the information and requesting a signature on the consent form. During this waiting period, potential participants should be encouraged to discuss their possible participation with family members, close friends, or trusted advisors. With REB approval, other approaches to communicating complex information can be used, including the use of audio-visual materials and brochures.

Topics requiring consideration

Pregnancy

In addition to the guidance provided in the REB informed consent templates, consider the following during consent discussion:

1. Pregnancy language in the consent form and in consent discussion will likely not be relevant for children providing assent.
2. The PI/study doctor should explain importance of not becoming pregnant and/or fathering a baby during an interventional clinical trial and explaining birth control to the patient participants in a clinical trial, discussing complex or permanent birth control methods such as vasectomy or sterilization and is not appropriate with a younger population.

Paternity through genetic research

Researchers need to submit the plan for what will happen in the event of paternity contradictions results emerge from genetic research.

1. Consent discussion and consent forms should be clear about requiring ‘biological’ relatives
2. Clearly state paternity will not be investigated and reported

Consent Documentation

Consent may be obtained in writing (in person or via mail/email), verbally (over the phone), or be implied. In all methods of obtaining consent, the consent process must be documented (TCPS 2 Article 3.12, GCP 4.8).

Templates for different consent processes (i.e., consent form, introductory letter, telephone script etc.) are available in the Forms, Templates, and Guidelines section of the Clinical Research Services website.

NOTE: All consent forms used for SickKids studies should conform to these templates.

Obtaining written consent in person

Most often, written consent is obtained in person. When obtaining consent in person, consent should be documented using an informed consent form.

In addition to signing a consent form, study teams should always ensure that they document the time that a participant consented to a study. This can be done on the consent form, on a consent tracking document, or in the patient chart. Documenting the time consent is obtained ensures that research activities do not occur prior to consent being obtained.

The following is an example of how consent may be obtained in person:

1. The PI or a person known to the participant (e.g., person in circle of care) introduces the study to the potential participant and asks if they are interested in learning more about it.
2. The PI, research nurse, or research coordinator (as appropriate) explains the study in a private area with a consent form.
3. Sufficient time for questions and consideration is provided.
4. A person outside of the circle of care (e.g. research coordinator) obtains consent. Both the participant and person obtaining consent sign and date the consent form.

Obtaining written consent remotely/electronically

Obtaining written consent remotely may be permitted when obtaining in-person consent is not possible and or affects the safety of the participants and research team members. Remotely means that written consent is not obtained in-person, but consent will have to be signed by the participant and the research team member obtaining consent.

Remote and electronic methods of documenting informed consent should be considered where physical signing of the informed consent document is not possible, and after a consent discussion with potential participants.
The following are examples of how to obtain written consent electronically:

1. Email
    a. A copy of REB approved consent form is emailed to participant with password protection and participants emails back a signed and dated consent form back with their preferences documented for any optional research activities.

2. REDCap
    a. Email potential participants link to the REB approved consent form replicated in REDCap.

    REDCap Electronic Consent Template

    The REDCap Electronic Consent Template was created by Research IT in collaboration with Clinical Research Services for Clinical Study Teams to collect and store participant consent information remotely. For additional information pertaining to the REDCap Electronic Consent Template please visit the CRS website.
3. Secure File Transfer Protocol (FTP)
    a. Sending consent form to potential participants via FTP and participants send back signed consent form their preferred method.

Please refer to the REB Guidance for Remote Recruitment and Consent and Email Guidance for detailed information.

Obtaining verbal consent over the phone

Verbal consent is not the same as obtaining remote consent. Use of verbal consent is only appropriate in selective minimal risk in research studies.

Verbal consent involves reading an REB approved verbal consent script to participants who then give their verbal consent. Verbal consent is generally obtained over the phone, and it is not acceptable to use when obtaining consent in person.

- When obtaining verbal consent, consent must be documented in writing by the person obtaining consent.

Consent over the phone typically considered when the **study is minimal risk** and it is the only feasible method of obtaining consent from participants (e.g., when recruiting participants and completing surveys over the phone).

The following is an example of how verbal consent may be obtained over the phone:

1. An introduction/information letter from member(s) of the potential participant's circle of care is sent to the family. The information letter should briefly explain the purpose of the study, why the participant is being contacted, and what the participant can do if they do not wish to be called.
2. A member of the study team (not the PI) calls the potential participant and explains the study using a verbal consent script.
3. The person obtaining consent provides opportunity for questions and verifies the potential participant's understanding of the study.
4. The verbal consent is sought and recorded on the Verbal Consent Script document by the approved research team member.
5. The approved research team member obtaining consent signs and date the verbal consent document.
6. The person obtaining consent documents all the conversation, including all questions asked by the potential participant and whether or not the potential participant consented to the study.
    i. For certain instances, an independent witness may be required to attest to how consent was obtained over phone.

If the research study is obtaining verbal consent, the following information and documents should be

submitted to the REB for review:

1. Introduction/information letter to the potential participants from member(s) oftheir circle of care.
2. A written script of verbal consent.

3. Details about who will obtain verbal consent and how.
4. Where and how verbal consent will be documented.
5. All other study documents that may be communicated to the participants such as:
    a. Study recruitment advertisements, posters
    b. Any email templates
    c. Scripts to follow-up phone calls.

Implied consent

In implied consent, participants indicate that they knowingly agree to participate in the study by completing a research activity (e.g., by completing a survey, interview etc.). It does not require a signed consent form, but it does require provision of information to research participants.

Implied consent is acceptable for some minimal risk studies. It is most commonly used in research that involves surveys, where completion and return of the survey indicates consent.

The following is an example of how implied consent may be obtained:

i. Along with the research activity (e.g., survey), potential participants are provided with a written study information summary/letter or presented with this information verbally. Information regarding the purpose of the research, the time commitment involved, statement regarding risks and benefits to potential participants, contact information for questions about the research, and contact information for questions about rights as a research participant should be provided to potential participants.
ii. Participants complete the study activity and return any relevant documents to the study team, implying their consent.

If the research study is using implied consent, the following information and documents should be submitted to the REB for review:

1. An explanation as to why implied consent is appropriate
2. The written study information summary/letter OR script for verbal explanation of study
3. Implied consent statement must appear on the relevant study documents (e.g., survey).

If you are unsure whether or not your study qualifies for implied consent, please contact the **Research Ethics and Regulatory Compliance (RERC)** to discuss prior to submitting to the REB because consent is a crucial part of the research methodology.

Alterations and Waivers of Consent

Consent should always be obtained from potential participants prior to the conduct of research. However, certain types of research require alternate processes for seeking consent, and in some circumstances a waiver of consent may be appropriate.

Waivers and alterations for prospective studies

There are some research questions that cannot be answered without an alteration to consent requirements. The REB may approve research that involves an alteration to the requirements of consent if the study team demonstrates that all of the following apply (TCPS 2 article 3.7A):

a. The research involves no more than minimal risk to the participants;
b. The alteration to consent requirements is unlikely to adversely affect the welfare of participants;
c. It is impossible or impracticable to carry out the research and to address the research question(s) properly, given the research design, if the prior consent of participants is required;
d. In the case of a proposed alteration, the precise nature and extent of any proposed alteration is defined; and
e. The plan to provide a debriefing (if any) which may also offer participants the possibility of refusing consent and/or withdrawing data and/or human biological materials, shall be in accordance with TCPS 2 Article 3.7B.

Waivers for secondary use (aka Retrospective) studies

For studies which require secondary use of identifiable information (e.g., health charts, previously collected biological specimens) or secondary use of biological samples, researchers must obtain consent unless the researchers satisfy the REB that all of the following apply (TCPS 2 articles 5.5A and 12.3A):

a. Identifiable information/human biological material(s) is essential to the research;
b. The use of identifiable information/human biological material(s) without the participants' consent is unlikely to adversely affect the welfare of persons to whom the information relates;
c. The researchers will take appropriate measures to protect the privacy of persons, and to safeguard the identifiable information/human biological material(s);
d. The researchers will comply with any known preferences previously expressed by persons about any use of their information;
e. It is impossible or **impracticable** to seek consent from persons to whom the information relates or from whom the materials were collected; and
f. the researchers have obtained any other necessary permission for secondary use of information/human biological material(s) for research purposes.

Consent may be impossible or impracticable when the group is very large, when its members are likely to be deceased, or difficult to track down. Resources required to contact persons and seek consent may also impose undue hardship on the researcher.

- In these instances, a waiver of consent may be appropriate. In order to obtain a waiver of consent, study teams must provide sufficient information to the REB to demonstrate that obtaining consent is impracticable.

Note that the TCPS2 defines impracticable as "incapable of being put into practice due to a degree of hardship or onerousness that jeopardizes the conduct of the research; it does not mean mere inconvenience." Consent may be impossible or impracticable when the group is very large, when its members are likely to be deceased, or difficult to track down. Resources required to contact individuals and seek consent may also impose undue hardship on the researcher. In these instances, a waiver of consent may be appropriate. In order to obtain a waiver of consent, study teams must provide sufficient information to the REB to demonstrate that obtaining consent is impracticable.

The fact that it would be inconvenient for the PI and research team is not an acceptable rationale for why it is impracticable to obtain consent from participants.

For studies which require the **secondary use of non-identifiable information** (e.g., results from anonymous surveys), researchers **must seek REB review** but are **not required** to seek **participant consent**. Researchers must "establish to the satisfaction of the REB that, in the context of the research, the information to be used can be considered non-identifiable for all practical purposes" (TCPS 2 article 5.5B).

If researchers wish to contact persons for whom a consent waiver was previously provided, REB approval for the plan for making contact is required prior to making contact (TCPS 2 articles 5.6).

Ongoing Consent

All researchers, irrespective of risks and potential benefits of the research study, should maintain an ongoing consent process with participants. (TCPS 2 Article 3.3) The research team should engage participants in discussions throughout the research study. This does not mean that participants are asked to re-sign consent forms at regular intervals; however, re-consenting participants may be necessary in the following instances:

1. Participants who assented previously to the research study now have the capacity to consent for themselves (TCPS 2 Article 3.9);
2. Significant new findings were developed or discovered during the course of the research which may affect participants' willingness to continue participation in the research study (e.g., change to risk/benefit ratio);
3. Consent form is updated with changes in study procedures or other significant information;
4. The original consent was improperly obtained:
    - Consent was obtained using the wrong version of the consent form
    - Research procedures, risks and potential benefits of the research study were not discussed during the consent process
    - Consent was obtained by an unauthorized person;
5. Transfer of care of research participants from paediatric to adult care;
6. PI or one of the investigators have a conflict of interest to declare.

NOTE: If you have questions about when re-consent should occur, please contact the **Research Ethics and Regulatory Compliance (RERC) Office.**

Overview of Consent Do's and Don'ts

DOs	**DON'Ts**
DO use the SickKids consent templates available on the SickKids Clinical Research Services page.	DON’T use altered approved consent forms without REB approval.
DO update your consent form with changes of study procedures and/or identify new risks.	DON’T state that it is a ‘REB’ approved research study as it suggests a guarantee of safety and this is not true.

DO obtain REB approval before using a revised consent form before re-consenting participants.	DON'T confuse initials with checkmarks or "X"s. i.e. don't ask for "X" and accept initials or ask for initials and accept "X" as indication of consent.
DO verify that each participant is given a signed and dated copy of the consent form at the time of initial consent.	DON'T include consent instructions that you do not follow; it may be considered noncompliance.
DO keep all original signed consent forms with research study records.	DON'T omit signature or date signed by person obtaining consent.
DO verify that person obtaining consent has signed, when applicable.	DON'T enter dates for participants – they must write it themselves.
DO verify that the participant signs and dates the informed consent form/assent form, otherwise it is not valid and you will not be allowed to use the data.	DON'T correct errors for anyone other than yourself on the form itself.
DO train the research staff about the consent process before beginning a study.	

Witness

The witness is an observer to the consent discussion (i.e., they are not part of/do not contribute to the actual discussion), and must be able to complete the documentation requirements outlined below. The witness must be able to hear both the person conducting the consent discussion and the prospective participant/SDM. Researchers must identify who is permitted to act as a witness in their REB application.

Interpreter

Potential participants/SDM may be limited in English proficiency, and in such instances informed consent is only possible with the use of an interpreter. A translated consent form will be helpful, but the need to for discussion between the potential participant and research team is required. Interpreter is part of the verbal exchange between the potential participant and research team member(s).

The role of the interpreter is to interpret the communication between the research team member(s) and the potential participant. It should be clear that the interpreter didn't "translate" the conversation between the research team and potential participant, because "translation" refers to written rendering of a language. The interpreter should be given enough time to explain complex topics within the research study.

Ethical considerations for obtaining informed consent using an interpreter:

1. Respecting participant autonomy
2. Satisfying justice and fairness by not excluding those that have difficulty with English

When an interpreter is used during the consent process, their part in the consent discussion must be documented. Use of an interpreter must be documented and attested/signed by the interpreter also.

Informed consent is an ongoing process, hence, it is important to ensure an interpreter is used throughout the study for ongoing study related communication.

Even with the use of the interpreter, if the principal investigator and or the research team feel the potential participant does not have a comprehensive understanding of the research study, they should not be enrolled.

Translation/Translated documents

If the research study documents are translated into another language, a translation certificate needs to be submitted to the REB along with the translated document. The translation must be completed by a certified translator.

Principal Investigators

For the purposes of ethical review, there can be only one principal investigator that assumes responsibility for the conduct of the research study at one site. There can be many co-investigators. If the study consists of multiple sites, then each site can have a different principal investigator. All Principal investigators must have a research appointment from the Research Institute at SickKids.

The REB may review investigator qualifications to ensure that: (a) the investigator has the appropriate qualifications and/or licensure to carry out the procedures involving human subjects with an acceptable degree of potential risk, and (b) the investigator has adequate facilities and equipment to conduct the research with an acceptable degree of potential risk.

Qualified Investigator

When a Principal Investigator of a regulated research study is not a Medical Doctor, a Qualified Investigator may be required in addition to the Principal Investigator. Please discuss this during the regulatory review of the research study.

List of Investigators on Research Documents

The protocol should include the author(s) of the protocol and the study sponsor. Every time a staff member listed on the protocol leaves or is replaced, amendments to the REB required. For Health Canada regulated research studies, updated documents will have to be submitted to Health Canada as well.

Consent and Assent forms must list the Principal Investigator, SickKids co-investigators and at least one SickKids research contact and their contact information.

Potential Conflict of Interest

Participants must be informed of significant individual financial conflicts of interest in the consent form, including information concerning the possibility of commercialization of research findings, and

the presence of **any real, potential or perceived** conflicts of interest on the part of the researchers, their institutions or the research sponsors.

Conflict of Interest information is collected in the eREB application form. However, there needs to be explicit statements in the consent form stating the nature of any real, potential or perceived conflict of interest with principal investigators, co-investigators, overall research team and or if relatives of research team have conflict of interest to declare.

The REB may require further clarifications and or action of the researcher to minimize or abandon a conflict, require formal oversight procedures for the research.

The Canadian Medical Association Guidelines for Physicians in Interactions with Industry Article 12 states: "Because of the potential to influence judgment, remuneration to physicians for participating in research studies should not constitute enticement. It may cover reasonable time and expenses and should be approved by the relevant research ethics board. Research participants must be informed if their physician will receive a fee for their participation and by whom the fee will be paid."

Researchers should disclose any conflict of interest to SickKids as per the institutional Relationship Disclosure and Management (Conflict of Interest) Policy.

Data Collection Tools

All data collection tools (questionnaires, surveys, de-identified imaging) must be submitted to the REB for review. Research teams should review the data collection tools ensure that no direct PHI is being collected.

Validated questionnaires: validated questionnaires often have name, full DOB as part of the questionnaires, it is crucial for study teams to ensure participants are not completing these fields on the data collection forms.

Prior to submitting the validated questionnaires to the REB for review, do the following to confirm that directly identifiable information will not be collected on these questionnaires:

1. Blacking out the fields collecting the direct identifiers so that participants will not input the details
2. Details of how participants will be informed not to complete any identifiable information, and if they are accidently completed by study participants, how it will be redacted/removed.
3. Research team members can complete the fields by inputting study ID and in places where direct identifiers are collected

Case Report Forms: For interventional clinical trials, the sponsor of the trial, often pharmaceutical companies will provide the CRFs. These are often extensive data collection and REB requires confirmation from the research team that directly identifying PHI will not be collected and documented on the CRFs.

Types of Research requiring additional considerations

Research Involving Investigational Drugs/Medical Devices

Research involving an investigational drug and or medical devices requires Health Canada approval. Please contact the Clinical Research Ethics and Regulatory compliance office regarding regulatory review.

Research Involving Deception/Incomplete Information

Research with deception includes giving participants false/inaccurate information, events, social conditions or the purpose of the research.

Research involving deception must satisfy TCPS 2 Article 3.7A

1. No more than minimal risk to participants
2. Alteration to the consent requirement unlikely to adversely affect the participants
3. It is impossible/impracticable to conduct research without deception and alteration to consent
4. The proposed consent alteration is clearly defined
5. Participants have the ability to refuse consent and/or withdraw from the study

There needs to be a clear distinction between cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Focus group

When research is conducted in a focus group setting, it is difficult for research team alone to satisfy privacy and confidentiality of the research activities. The requirements of each focus group participant must be clearly explained prior to starting the focus group.

Research involving video recording

If the research activities involve the video recording of the participants, the following must be explained:

1. Is video recording a mandatory part of the research? If yes, why is it mandatory?
2. Will identifiable features (face, tattoos, birth marks, etc.) be blurred, i.e. will a form of de-identification take place prior to the video becoming part of the research data?
    a. How will it be de-identified
3. Who will have access to the video recording and for what purpose?
4. Where will the video recordings be stored, and when will it be destroyed?
5. How can participants request withdrawal of their video recording?

Research involving audio recording

If research activities include audio recording, the following must be explained:

1. Is audio recording a mandatory part of the research? If yes, why is it mandatory?
2. Who will have access to the audio recording and for what purpose
3. Where will the audio recordings be stored?
4. Will the audio recording be destroyed after transcription?
5. How can participants request withdrawal of their audio recording?

Research Involving Induced pluripotent stem cell

CIHR has a Stem Cell Oversight Committee (SCOC) to review research involving pluripotent stem cell to ensure TCPS 2 compliance and to compliment the REB review. https://cihr-irsc.gc.ca/e/15349.html

Genetic Research

Genetic research requires the following consideration:

Whole Genome Sequencing (WGS):

If WGS will be done as part for the research study, there must a detailed plan for the following items:

1. Participants are informed during the consent discussion and in the consent form what whole genome sequencing is and the purposes of doing WGS in the research study
2. What the primary findings will be and what the secondary (incidental) findings will be
3. What is the plan for informing participants with their secondary findings:
    a. Medically actionable secondary findings must be discussed with participants and appropriate referrals must be made.
    b. Clearly explain that medically non-actionable findings will not be 'searched' for during the research and even if it is discovered it will not be disclosed.
    c. Carrier status information
4. For genetic research with multiple options and complexities, it is expected that a genetic counsellor conducts the consent discussion and obtains informed consent
5. Explicit consent must be obtained from the participants to do the following:
    a. Share genetic biospecimen with for-profit commercial companies such as pharmaceutical companies
    b. Share de-identified genetic data and health information with for-profit commercial companies such as pharmaceutical companies
6. Clearly explain that National Institutes of Health (NIH) funded genetic research studies require the de-identified/anonymized genetic research data will have to be shared with National Human Genome Research Institute. This means their genetic data will be publicly available to anyone without restriction, and researchers requesting data to conduct research.
7. Discuss potential psychological and social risks of participating and receiving genomic information that are fully not known at this time.
8. Genetic research is constantly and quickly evolving, hence, the researchers themselves may not know the potential of genomic research

Biospecimen

Biological samples must be collected with participant's consent. In research, biospecimens can be collected for the following purpose:

1. Specific type(s) of biological sample collected to answer a specific research question
    a. Sometimes optional type(s) of biological samples are collected but the collected biospecimen will only be used to answer the objectives under the main protocol, it cannot be used for other purposes
2. Biobanking of specimens for future research
3. In potentially therapeutic clinical trials, banking of biological samples for future unspecified research or research unrelated to the study at hand must be optional.

Please refer to the Biobank Guidance for detailed guidance and content about how to start a research biobank.

The Right to Withdraw and its Modalities

Participants always have a right to withdraw from research at any time, even verbally, including the right to ask their data and or biospecimens be destroyed. Researchers should ensure that participants understand this right, and provide a simple way of exercising it, including control over future use and/or destruction of samples or data. This right, procedures for its exercise, and any limitations posed to it by data aggregation and anonymization or publication, should be clarified in the consent form.

Participants must be informed in the consent form:

1. How participants can withdraw samples
2. In what instances participants cannot withdraw samples, i.e. the samples have already been used for research purposes
3. Whether research data can be withdrawn

Although participants may have given/donated their biospecimen and data, the biospecimen and data still belongs to the participants. It is important to let participants know this information during the consent discussion and via the consent form.

Non-Compliance

While protocol and REB approved process violations may not be intentional, if situations arise where there has been non-compliance and or protocol violations the REB shall determine corrective actions that is required by the PI.

Examples of what might happen if non-compliance and or protocol violations are found:

1. Disallowance of data
2. Disallowance of publication, presentation or dissemination of the data in any form
3. Hold/Suspension of the research
4. Termination of the research
5. Request oversight for the study by another researcher
6. Imposing additional monitoring activities

References:

Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2018)
https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2018.html

SickKids Quality Improvement
: http://my.sickkids.ca/staff-support-resources/qrm/project-review-process/Pages/default.aspx

Relationship Disclosure and Management (Conflict of Interest)
http://policies.sickkids.ca/published/Published/CORP12/Main%20Document.pdf#search=conflict%20of%20interest

Regulated Health Professions
http://www.health.gov.on.ca/en/pro/programs/hhrsd/about/regulated_professions.aspx

Health Care Consent Act
https://www.ontario.ca/laws/statute/96h02