Guidelines for secondary use studies and case reports/series

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General Guidelines
What is a secondary use study?
Secondary use studies use data that already exists, i.e., the raw data to be included in the study does not result from the study’s research activity. Various forms of secondary data exist. Examples of secondary data include:

- data collected as part of clinical care and that exists in the patient’s health record
- data previously collected as part of a clinical or research database
- tissue samples that were previously collected as part of clinical care or for a biobank

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• previously completed surveys as part of a different study protocol or for educational/quality improvement purposes
• genetic data previously collected or analyzed for clinical or research purposes
• education materials
• etc.

Retrospective vs prospective secondary data studies

Retrospective secondary data studies evaluate data that already exists at the time the project is submitted for initial REB review (e.g., a chart review that uses clinical data that is already in the participant’s medical record). By comparison, a prospective secondary data study evaluates secondary data that does not yet exist at the time the project is submitted for initial REB review (e.g., a registry that will collect data from a participant’s medical record into the future). Some secondary data studies can have both a retrospective and prospective component (e.g., a study that collects chart data from the past 5 years and the next 5 years). If a secondary use study has a prospective component, the REB considers these studies to be prospective observational.

Case Reports and Case Series

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.

Does my secondary use study require REB review?

Most secondary use research studies require REB approval. Possible exceptions include:

- The data to be included in the study is already publically available (TCPS2 Article 2.2) and:
  - The information is legally accessible to the public and appropriately protected by law
  - The information is publicly accessible and there is no reasonable expectation of privacy
- The research 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 (TCPS2 article 2.4)
- Case reports of 2 or less individuals
  - Note that a case report of 2 or less individuals that is being contributed to a case series still requires REB review. See the SickKids Policy regarding Disclosure of Personal Health Information, and the REO’s Case Reports/Series guidance document (available on the REB website).

If you think your study may not require REB review, please contact the REB to confirm.

Does my case report or case series require REB review?

Case reports involving one or two patients do not require REB review since these do not meet the TCPS definition of research. However, consent for case reports is still required; see the SickKids Policy on Disclosure of Personal Health Information for further guidance.
If you are contributing a single case report to a multi-centre case series, then this case report requires REB review.

Case series do require REB review.

If you are unsure if your case report/series requires REB review, please contact the REB before submitting an application.

Do I need to get consent from participants for my secondary use study?
Consent from participants should always be sought. However, a consent waiver may be obtained for secondary use studies if researchers satisfy the REB that all of the following apply (TCPS2 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 individuals to whom the information relates;

c. the researchers will take appropriate measures to protect the privacy of individuals, and to safeguard the identifiable information/human biological material(s);

d. the researchers will comply with any known preferences previously expressed by individuals about any use of their information;

e. it is impossible or impracticable to seek consent from individuals 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.

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.

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” (TCPS2 article 5.5B).

If researchers wish to contact individuals for whom a consent waiver was previously provided, REB approval is required prior to making contact (TCPS2 articles 5.6).

Note: Any waiver of consent excludes any record where the patient or patient’s family has previously requested that the information be kept private.
Privacy and Confidentiality

For secondary use studies, privacy and confidentiality are among the biggest ethical concerns. Researchers have an ethical duty 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 TCPS2 (Chapter 5) and the Personal Health Information Act (PHIPA).

What is personal health information?
PHIPA defines personal health information (PHI) as identifying information about an individual in either an oral or in a recorded form if the information:

- relates to the individual’s physical or mental health, including family health history,
- relates to the provision of health care, including the identification of persons providing care,
- is a plan of service for an individual 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 individual’s Provincial health number; or
- identifies an individual’s substitute decision-maker.

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

What is identifiable information?
According to the TCPS2 (Chapter 5), information is identifiable if it may reasonably be expected to identify an individual, when used alone or combined with other available information. Information is non-identifiable if it does not identify an individual, 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 an individual:

- **Directly identifying information** – the information identifies a specific individual through direct identifiers (e.g., name, social insurance number, personal health 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).
- **Coded (de-identified) 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 name so data can be re-linked if necessary).
• **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.

• **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.

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

**Collection of identifying information**

The collection of any identifying information (direct or indirect) must be justified to the REB (e.g., date of birth is justified when it is required to determine the age of participants). Where possible, the amount of information collected should be the minimum required to answer the research question (e.g., date of birth will be collected in mm/dd/yy format only when age in days is required).

**Protecting information 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 **Legal Services** 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:

• **Physical safeguards** – includes locked office, locked storage unit, biometric authentication, cipher/coded locks, access cards, etc.

• **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 individual responsible for controlling who has access to data, etc.)

• **Technical safeguards** – includes use of computer passwords, firewalls, anti-virus software, network drive, encrypted computer, encrypted USB etc.

Data from secondary use studies must be stored by researchers for a minimum of 7 years post publication or study closure.

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 IS help desk, and old CDs, DVDs, videos, USB keys, external hard drives and other technology can be sent to the repair centre for destruction.

**Secondary Use Study Document Guide**

**Required Documents**

*Note that all study documents must contain the study’s title and a version date.*

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The following documents **must** be included with a secondary use study application:

- Study Protocol
- Data collection form/Case report form, or a list of data points/variables to be collected if using external data management system (e.g. ICES)
  - If you are using Excel, RedCap or other software to collect data the actual Excel spreadsheet, a copy of the RedCap PDF, or other PDFs/screenshots should be provided to the REB
- Code breaking file/Master linking log

The following documents **may** need to be included with a secondary use study application:

- Scientific peer review (for retrospective studies involving biological samples)
- Study budget, if funding is required
- Consent/assent forms, when there is no waiver of consent

See below for guidance RE mandatory components of these documents.

**Study Protocol**

Study protocols should contain, at minimum, background information, the research objectives, study population, inclusion/exclusion dates, date range for access, methods, and analysis.

**Data collection form**

Data collection forms or case report forms must list all data points/variables that will be collected as part of the study. Only data points that are required to answer the research question should appear on the data collection form. Moreover, the amount of information collected should be the minimum required to answer the research question (e.g., data such as date of birth or date of treatment should be collected in the mm/yy format where possible, unless data in days is required).

The collection of any indirectly identifying information must be scientifically justified. 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 (see below).

**Code breaking/master linking log**

Code breaking forms should be used to link individual ID with study ID. It should contain the minimum amount of identifying information (e.g., MRN, name) required to link the individual to their study ID. It must also contain a confidentiality disclaimer (e.g., “Confidential Information – Keep Separate from Study Data”).

See the REB website’s template section for a code breaking/master linking log template.

**ICES Studies**

A formal study protocol is not required if your study involves the use of data from ICES only. You must submit the ICES application form and list of data variables from ICES in place of the study protocol and data collection form. The approval letter from ICES must also be included in your REB main application.