THE UNIVERSITY OF BRITISH COLUMBIA	**Guidance Note No.:** **#18**

Title:

Research Involving Human Biospecimens

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1. Research Involving Collection and/or Storage of Human Biospecimens

The TCPS2 defines research involving human biospecimens as research requiring research ethics board (REB) review [TCPS2 Article 2.1(b)]. An individual whose biospecimens and/or data are used in research becomes a research participant. Individuals may become research participants for example, by agreeing to provide a blood sample for use in a particular study or by choosing to donate leftover surgical tissue or their body after death. Researchers may seek access to biospecimens for immediate use in research, or they may intend to create a biobank to store biospecimens for use in future research.

The TCPS2 states that REB review is not required for research involving anonymous biospecimens (materials that never had identifiers attached to them) so long as any process of data linkage or recording or dissemination of results does not generate identifiable information [TCPS2 Article 2.4].

The TCPS2 also states that REB review is not required for research that relies exclusively on the re-use of de-identified human somatic cell lines where the original consent terms are respected, and researchers do not have access or will not attempt to access participant identifiers [TCPS2 Article 12.21]. Further, it states that research that relies exclusively on the re-use of identified somatic cell lines that are already available and identified in the public domain are exempt from REB review [TCPS 2 Article 12.22].

However, due to rapid technological advances, it is becoming increasingly possible to re-identify individuals from de-identified biospecimens, which makes it harder to achieve anonymity. **Accordingly, as per UBC Policy LR9 all research involving biospecimens (including human somatic cell lines) at UBC requires REB consultation/review, even if it is solely to make a determination of anonymity.**

2. New Collection of Biospecimens for a Specific Research Study

This section applies to situations in which researchers propose to collect biospecimens prospectively from participants with their consent.

** See Section 3 for applications for the secondary use of previously collected biospecimen. See Section 4 for applications involving the creation and maintenance of biobanks.*

The risks and benefits pertaining to the biospecimen collection must be defined in the informed consent for the specific research study, and the provisions specific to collection of biospecimens (see Section 5) must be contained within the specific research study's informed consent form. The biospecimen testing should be limited to research directly related to the specific research study's objectives and not future unknown research.

According to UBC's Policy on Mandatory Biobanking, mandatory collection for banking of biospecimens is only permitted if it is necessary for the study at hand for purposes integral to the study. It is unethical to require that participants agree to the banking of their biospecimens for future undefined research or for research unrelated to the study at hand as a condition for entry into a study. Such practice constitutes a coercive method of obtaining biospecimens.

If the collection of biospecimens or use of biospecimens previously collected as part of clinical care is **desired** for the purpose of a **sub-study** that is linked to but not a required part of the primary study, researchers must execute a separate and optional informed consent form.

3. Secondary Use of Previously Collected Biospecimen

This section applies to situations where researchers propose to use biospecimens that were collected previously for another purpose. Examples include but are not limited to situations where the collections were for:

- medical or diagnostic purposes with no initial intent to be used in research.
- medical or diagnostic purposes with some expectation that they may be used in future research, although the precise research project(s) may not have been known at the time of initial collection, and where the research is not linked to a concurrently conducted primary study (see Section 2).
- a different research study.

REB review is required in **all** cases involving human biospecimens (See Section 1). Consenting requirements are dependent on whether the biospecimens are classified as identifiable or non-identifiable as determined by the REB.

Specific considerations for the secondary use of biospecimens identifiable as originating from a specific First Nations, Inuit or Métis community, or a segment of the Indigenous Community at large, are addressed in TCPS2 Articles 9.20 to 9.22.

3.A Secondary use of previously collected (i.e., archival) identifiable biospecimens with participant's consent or with waiver of consent.

For biospecimens previously collected as part of clinical care that researchers are now requesting to use for research, standard requirements concerning consent to research apply, or researchers may apply for a waiver of consent.

The default requirement is that secondary use of identifiable biospecimens requires informed consent from the participant. If the researcher did not obtain informed consent from the participant, they may apply to the REB for a waiver of this requirement. In accordance with the provisions of the TCPS2 [Article 12.3], the REB may grant a waiver of informed consent if **all** the following requirements have been met:

(a) Identifiable biospecimens are essential to the research;

(b) The use of identifiable biospecimens without the participant's consent is unlikely to adversely affect the welfare of individuals from whom the biospecimens were collected;

(c) The researchers will take appropriate measures to protect the privacy of individuals and

to safeguard the identifiable biospecimens;

(d) The researchers will comply with any known preferences expressed by individuals about any use of their biospecimens;

(e) It is impossible or impracticable to seek consent from individuals from whom the biospecimens were collected; and

(f) The researchers have obtained any other necessary permission for secondary use of biospecimens for research purposes. (E.g., approval from the relevant clinical department or from pathology.)

3.B Secondary Use of Non-identifiable Biospecimens

Informed consent for secondary use of non-identifiable biospecimens (de-identified, anonymous, or anonymized) is not required.

The onus will be on the researcher to establish to the satisfaction of the REB that, in the context of the proposed research, the biospecimens to be used can be considered non-identifiable for all practical purposes.

If a waiver of consent for the secondary use of human biospecimens has been approved by the REB, researchers may **not** contact donors (participants) for additional samples or information without REB approval [TCPS2 Article 12.4].

4. New & Existing Biobanks

This section applies to situations where a researcher is seeking REB approval for:

- the creation of a new biobank, or
- an existing biobank where UBC (and UBC-affiliated institutions) is being added as a new site

This section does not apply to instances where:

- biospecimens are collected for the sole purpose of analysis for a specific research study and entirely consumed, leaving no residual material in storage;
- for-profit sponsors will be the steward of the biobank;
- secondary use of existing biospecimens as mentioned in Section 3.

UBC's REBs strongly encourage all individuals creating a biobank to **register** with CTRNet Biobank Registration Program. In some cases, researchers/biobankers may also want to consider **certifying** the biobank. Certification requirements include education for all members of the biobank and review of essential documents.

4.1. When the intended purpose of biospecimen collection is for one or more specific or future unspecified research purposes, it is considered biobanking involving human participants and therefore requires review and oversight by a UBC-affiliated REB. Informed consent is usually required as well (See Section 5).

When seeking consent for a specific research project at the same time as seeking consent for biobanking for future unspecified research, prospective participants must be provided with an option to consent to each separately, either through separate consent forms or separate sections on the same form [TCPS2 Article 3.13].

4.2 Researchers intending to create a biobank for research should develop a protocol that addresses the governance, operation, maintenance, and sustainability of the biobank (A biobank protocol template created by BC Cancer's Biobanking and Biospecimen Research Services can be found here).

5. Informed Consent for Collection of Biospecimens for Research and/or Biobanking Purposes

When collecting human biospecimens for use in research, informed consent must be obtained from [TCPS 2 Article 12.1]:

(a) The participant who will donate the biospecimens; or

(b) In the case of a participant who lacks capacity, consent shall be given by a legally authorized representative who must take into account any research directive of the proposed participant; or

(c) In the case of a deceased participant, consent may be given through a donation decision made prior to death by the deceased, or by a legally authorized third party (e.g. next-of- kin).

In addition to the standard elements of consent, when researchers are seeking participant consent for use of biospecimens in research, the following additional details must be included in the Informed Consent [TCPS 2 Article 3.13 and Article 12.2]:

(a) The type and amount of biospecimens to be taken;

(b) The manner in which the biospecimens will be taken including the safety and invasiveness of the procedures for acquisition;

(c) The intended/potential uses of the biospecimens, **including any commercial use**;

(d) The measures employed to protect the privacy of and minimize risks to participants;

(e) The storage duration, location (e.g. in Canada, outside Canada), preservation method of the biospecimens, and process for disposal, if applicable;

(f) Any anticipated linkage of biospecimens and related data with information about the participant either contained in public or personal records;

(g) The researchers' plan for handling results and findings, including clinically relevant information and incidental findings;

(h) The feasibility and right to withdraw the biospecimens and/or associated data (or not) and what will happen to data already obtained or aggregated into the existing analysis;

(i) Planned/Potential transfer of biospecimens outside of the institution, a description of and what safeguards will be in place;

(j) Any anticipated future use of the biospecimens for other research objectives. Refer to Section 3 and to the TCPS2 [Chapter 12, Section C] for a description of specific conditions related to secondary use of biospecimens;

(k) The identifiability of the biospecimens and/or data and whether the research will (if known) or might include whole genome sequencing or similar technologies that may pose a substantial risk of re-identification of the participant;

In addition to standard elements of consent and above points, the following points must be included in the Informed Consent for **biobanking**:

(l) Access to a general description of the biobank and its governance;

(m) Specific restrictions: For example, the consent may be restricted to a particular field of study, to a specific disease, or may prevent use by private industry [TCPS2 Chapter 3, Section E].

6. "Non-Compliant" Biobanks

This section applies to situations where:

- biospecimens were collected without appropriate *research* consent.
- the biobank was authorized by an REB prior to the 1998 implementation of the TCPS consent requirements.

When a researcher/custodian identifies that they may be in possession of biospecimens that were not obtained under the circumstances dictated by the TCPS, they must:

- inform the appropriate UBC REB of full circumstances (insofar as they are discoverable) of the collection including the purpose of the initial collection,
- disclose whether research consent was obtained and in what form, and whether consent is documented,
- ensure that the REB is informed of all actions taken in relation to the biospecimens and for ensuring that the REB approves of these actions.

The UBC REB will provide oversight in the process of remedying the situation in the context of the TCPS guidance.

There are several options for the researcher (custodian) including the three options below:

Option 1: Seek informed consent from donors

The ethically preferred method for remedying deficiencies in the original consent process under which biospecimens were obtained is to contact the donors (or their descendants) to seek their informed consent for research. Consideration should be given to contacting donors through their last known health contact (e.g. attending physician, hospital of record, etc.).

Care should be taken to avoid inadvertent breach of patient confidentiality by, for example, revealing confidential information to other people at the donor's last known address.

Option 2: Anonymize the biospecimens

The TCPS2 requirements for obtaining consent from donors for biobanking apply to identifiable biospecimens [TCPS2 Article 12.3.B]. If the biospecimens are anonymized, donor consent is not required. It is up to the researcher/custodian to establish to the satisfaction of the REB that the biospecimens have been effectively anonymized.

Option 3: Implement systems which make the biospecimens non-identifiable to the researcher/custodian

This option involves creating systems which make it extremely difficult for researchers using the biospecimens to determine the identity of the donor while at the same time allowing them to link the biospecimens with relevant clinical information about the donor.

An acceptable method of rendering the biospecimens non-identifiable would require that a third party with training in the importance and methods of maintaining confidentiality be inserted between the researcher and the source of the identifiable information to function as a *privacy guardian.* In such cases:

- The measures used by the privacy guardian to protect privacy and confidentiality of the information they access and disclose must be documented and should be part of the REB's consideration of acceptability of any proposed linkages.
- The privacy guardian may need to be independent of the biobank custodian. Assessment of whether this is required would consider the proportionate risk to donors if their personally identifiable information was disclosed.
- The inquiry to be answered by recourse to the privacy guardian must be pre-approved by the REB as part of the ethics review for the study or approved subsequently as part of an independent submission.
- The privacy guardian must not fulfill any request by a researcher to link the biospecimens with personal information without the investigator providing evidence of ethical approval of the specific linkage proposed.

The privacy guardian must maintain processes and records that allow full auditing of inquiries, permitting verification of the protection of confidentiality and continued oversight by the REB and any other regulatory body's audit processes.

7. Useful links

- CTRNet Biobank Registration/Certification: https://biobanking.org
- Biobanking Best Practices-International Society for Biological and Environmental Repositories (ISBER)Best Practices: http://www.isber.org/
- BBRS Contact for CTRNet Biospecimen and Biobanking Research Services biobanking.org: info@biobanking.com
- ISO biobanking standards 20387: https://www.iso.org/standard/67888.html
- TCPS 2 – Chapter 12 on **Human Biological Materials Including Materials Related to Human Reproduction**: https://ethics.gc.ca/eng/tcps2-eptc2_2022_chapter12-chapitre12.html
- TCPS 2 – Chapter 13, Section E on **Broad Consent for the Storage of Data and Human Biological Materials for Future Unspecified Research**: https://ethics.gc.ca/eng/tcps2-eptc2_2022_chapter3-chapitre3.html#e

8. Glossary of Definitions

Research: an undertaking intended to extend knowledge through a disciplined inquiry and/or systemic investigation.

Research ethics board (REB): a body of researchers, community members, and other with specific expertise (e.g., in ethics, in relevant research disciplines) established by an institution to review the ethical acceptability of all research involving humans conducted within the institution's jurisdiction or under its auspices.

Biobank (also known as *biorepository*)**:** An organized collection of searchable biospecimens stored for one or more specific or future unspecified research purposes. It may also include associated information about individuals from whom the biospecimens were collected.

Biospecimens (also known as *human biological materials*)**:** tissues, organs, blood, plasma, serum, DNA, RNA, proteins, cells, skin, hair, nail clippings, urine, saliva, and other body fluids. This term also includes materials related to human reproduction, including embryos, fetuses, fetal tissues, and human reproductive materials (Note: This guidance note uses the term biospecimens throughout, rather than the TCPS2 term, human biological material).

> **IDENTIFIED biospecimens** are labeled with a direct identifier (e.g., name, personal health number). Biospecimens and any associated information are directly traceable back to a specific individual.
>
> **DE-IDENTIFIED/CODED biospecimens** have direct identifiers removed and replaced with a code. Depending upon access to the code, it may be possible to re-identify specific individuals. For example, the holder of the code may be the principal investigator, or it may be an arms-length individual approved by the REB as an appropriate privacy guardian.
>
> **ANONYMIZED biospecimens** are irrevocably stripped of direct identifiers, and a code is not kept allowing for future re-linkage. The risk of re-identification of individuals from remaining indirect identifiers is low or very low.
>
> **ANONYMOUS biospecimens** never had identifiers attached to them, and the risk of identification of individuals is very low or impossible.

Cell line: the progeny of a primary culture, obtained from tissue and placed into culture to proliferate, when it is subcultured through transfer to a new culture that allows for continued growth.

Consent: an indication of voluntary agreement by an individual, or their authorized third party, to become a participant in a research project.

Broad consent: an indication of agreement by an individual, or their authorized third party, for

the storage and use of their data and/or biospecimens for all types of future unspecified research, subject to specific restrictions (permitted under TCPS2).

Practicable: possible and reasonable to be executed. For example, it is practicable to offer consent materials and task instructions in multiple languages when members of the desired participant population speak different languages, and there is no common language understood by all participants. An action is possible but not practicable when circumstances render a possible action unreasonably difficult to execute, or when the action will jeopardize the ability of the researcher to address the research question. For example, in a study examining the effect of two types of exit signage (alternated daily for two weeks) on crowd behaviour in a stadium, it would be impracticable to seek prior consent without affecting the behaviour under observation. It may be practicable to offer debriefing once the study is concluded, by advertising the availability of information about the study to the community that makes use of the stadium.

Impracticable: 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.

Secondary use: the use in research of information and/or biospecimens originally collected for a purpose other than the current research purpose.