

Guidance Note #18
Special Categories of Research
Research Involving Human Biological Materials

Article 1: Research Involving Collection and Storage of Human Biological Materials

The TCPS2 defines research involving human biological materials (HBM) as well as human embryos, fetuses, fetal tissue, reproductive materials and stem cells as research requiring REB review [[TCPS2 Article 2.1\(b\)](#)] An individual whose data and/or biological materials 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 organs or their body after death. Researchers may seek access to human biological materials for secondary use in research, or they may intend to create a human biological materials repository to store tissue for use in future research. Secondary use means the use in research of bio-specimens originally collected for a purpose other than the current research purpose. [See Article 6 below]

The TCPS 2 states that REB review is not required for research involving anonymous (materials that never had identifiers attached to them) bio-specimens so long as any process of data linkage or recording or dissemination of results does not generate identifiable information. UBC Policy 89 provides that **genetic material may not be considered anonymous unless an REB determines otherwise**. Accordingly all research involving bio-specimens at UBC requires REB review, even if it is solely to make a determination of anonymity.

As noted in the TCPS2:2014, due to continuing technological developments in genetics, individuals with access to stored human biological materials are increasingly able to use genetic markers to link a non-identifiable sample with an identified sample and as such has made it increasingly more difficult to categorize human biological materials as anonymous or anonymized (see definitions in Article 2)

Article 2: Scope, Definitions and Categories of Human Biological Materials (HBM)

The provisions of this guidance apply to biological materials related to human reproduction and to human genetic research however, such studies are also subject to the provisions of the

guidance notes specifically dealing with those special categories of research. (Currently in development).

Human biological materials (HBMs) are materials obtained from participants and include tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva and other body fluids. Other terms for HBMs in common use or often used in consent forms are 'bio-specimens' and 'tissues, fluids, blood'. Bio-specimens are HBMs and include all of the materials noted. This guidance note will use the term bio-specimens throughout, rather than the TCPS2:2014 term, HBM.

Biobank (also known as a bio-repository) is a structured resource that collects, receives and stores and distributes human biological materials and associated data for use in subsequent research. Biobanks can be of any size.

IDENTIFIED human biological materials are materials that are labelled with a direct identifier (e.g. name, personal health number). Materials and any associated information are directly traceable back to a specific individual.

DE-IDENTIFIED / CODED human biological materials are materials with 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 human biological materials are materials that are irrevocably stripped of identifiers and a code is not kept to allow for future re-linkage.

ANONYMOUS human biological materials are materials that never had identifiers attached to them and the risk of identification of individuals is low or very low.

Article 3: Collection of Bio-specimens for a specific research purpose in specific research studies.

This Article applies prospectively, i.e. prior to the collection of human bio-specimens for research studies and applies to situations:

- in which researchers propose to collect bio-specimens from prospective participants
- in which consent to access previously collected and stored bio-specimens is obtained in instances either where the bio-specimen collection is a requirement of the study, or where it is an optional procedure or for a sub-study that has been developed as an

adjunct to the primary study. (i.e. is not a requirement of the primary research study being reviewed).

See Article 6 for applications for the secondary use of previously collected tissue. See Article 7 for applications involving the creation and maintenance of biobanks.

Article 3a) If collection of bio-specimens or use of bio-specimens previously collected as part of clinical care is a requirement of the primary study, the normal provisions concerning consent to research apply. The risks and benefits pertaining to the bio-specimen collection must be defined in the context of the informed consent for the primary study, and the provisions specific to collection of bio-specimens (see Article 5) must be contained within the primary study informed consent form.

Article 3b) Optional Consent is the default requirement

If collection of bio-specimens or use of bio-specimens 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, the default requirement is that participants are required to execute a separate, and optional informed consent form.

Article 4: Mandatory Tissue Banking:

Pursuant to UBC's [Policy on Mandatory Tissue Banking](#) mandatory banking of tissue samples (includes all bio-specimens) is only permitted if the banking is necessary for the study at hand; that is, the banking must be for purposes integral to the study. It is unethical to require that participants agree to the banking of their bio-specimens for future undefined research or for research unrelated to the study at hand as a condition for entry into a trial that offers the potential participant the prospect of some direct benefit. Such practice constitutes a coercive method of obtaining tissue samples by making access to a potentially therapeutic opportunity contingent upon the donation of the sample to the bank.

UBC's position in relation to this issue is consistent with the prohibitions on this practice established by (among others) the US Department of Health and Human Services Common Rule ([45 CFR 46](#)), the U.S. Health Insurance Portability and Accountability Act ([HIPAA](#)), as well as the principles for free and informed consent as outlined in key ethical guidelines including the TCPS2 (for example, [Article 3.1](#)).

By way of clarification, this policy does not apply to the mandatory collection of bio-specimens where this is necessary to answer questions integral to the defined and specific goals of the research study, or to verify eligibility of a participant to be enrolled in a particular study. In

addition, this policy does not address the issues associated with requiring trial participants to undergo a biopsy for evaluation of scientific end points related to the clinical trial in question.

Article 5: Informed Consent – Templates for Optional Bio-specimen Acquisition and for Optional Bio-specimen Banking are available. ([CREB templates](#) and [C&W templates](#))

Informed consent must be obtained from:

- a) The participant who will donate the human bio-specimens materials; 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 accordance with the provisions of [Article 12.2](#) of the TCPS2, in addition to the standard elements of consent, when researchers are seeking participant consent for use of bio-specimens in research, the following additional details must be included in the Informed Consent:

- (a) The type and amount of bio-specimens to be taken
- (b) The manner in which the bio-specimens will be taken and the safety and invasiveness of the procedures for acquisition;
- (c) The intended uses of the bio-specimens, **including any commercial use**;
- (d) The measures employed to protect the privacy of and minimize risks to participants;
- (e) The length of time the bio-specimens will be kept, how they will be preserved, location of storage (e.g. in Canada, outside Canada*) and process for disposal, if applicable
- (f) Any anticipated linkage of bio-specimens with information about the participant;
- (g) The researchers plan for handling results and findings, including clinically relevant information and incidental findings;
- (h) The right to withdraw the bio-specimens (or not) and what will happen to data already obtained or aggregated into the existing analysis;
- (i) If the bio-specimens are going to be transferred outside of the institution, a description of how that will occur and what safeguards will be in place;
- (j) Any anticipated future use of the bio-specimens for other research objectives. Refer to Article 5, below and to [Chapter 12 C](#) for a description of specific conditions related to secondary use of bio-specimens.

*If tissue is to be transferred and stored outside of Canada, special provisions apply. See for example the provisions in Article 15 of the CREB optional tissue informed consent template [here](#)

Article 6: Secondary Use of Previously Collected Tissue

This article applies to situations where researchers propose to use tissue that has been collected previously for another purpose, i.e. either for medical or diagnostic purposes with no initial intent to be used in research or for a different research study or for medical or diagnostic purposes with some expectation that they may or may not 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 Article 3 above).

6.1. The default requirement is that secondary use of **identifiable** bio-specimens requires informed consent from the donor (participant). If the researcher did not obtain informed consent from the donor an application may be made to the REB for a waiver of the default informed consent requirement. In accordance with the provisions of the TCPS2, ([Article 12.3](#)) the REB may grant a waiver of informed consent if the REB is satisfied that **all** of the following requirements have been met:

- (a) Identifiable human biological materials are essential to the research;
- (b) The use of identifiable human biological materials without the participant's consent is unlikely to adversely affect the welfare of individuals from whom the materials were collected;
- (c) The researchers will take appropriate measures to protect the privacy of individuals and to safeguard the identifiable human biological materials;
- (d) The researchers will comply with any known preferences expressed by individuals about any use of their biological materials;
- (e) It is impossible or impracticable to seek consent from individuals from whom the materials were collected; and
- (f) The researchers have obtained any other necessary permission for secondary use of human biological materials for research purposes. (For example, approval from the relevant clinical department or from pathology.)

6.2. **Informed consent** for secondary use of non-identifiable (de-identified, coded with the researcher having no access to the code, anonymous or anonymized) bio-specimens is not required, however, if practical the REB may direct that it be obtained. Due to the provisions of

UBC's Policy 89, REB **review** is required in all cases involving human bio-specimens. (See Article 1 above.)

6.3. The TCPS2 considers the term "impracticable" to refer to situations that go beyond mere inconvenience and extend to undue hardship or onerousness that jeopardizes the conduct of the research.

6.4. If secondary use of human bio-specimens without informed consent has been approved by the REB, researchers may not contact donors (participants) for additional samples or information without REB approval. ([TCPS2 Article 12.4](#))

Article 7: Biobanks

These articles apply to situations where a researcher is

- creating a new biobank, or
- is seeking REB approval of an existing biobank where the material is intended to be accessed by the researcher and/or other researchers for future use over an extended period of time and where the researcher intends to be the steward or guardian of the information.

These articles do not apply to:

- i) Human bio-specimens that are collected for the sole purpose of analysis for a specific research study and consumed by this study so that no residual material remains in storage after the completion of the study;
- ii) instances where the sponsor will be the steward or guardian of the bio-specimens for future research;
- iii) secondary use of existing bio-specimens which have already been collected clinically or under a previous research project.

7.A. New Biobanks.

This article applies to situations where researchers are creating a new repository (bank) of tissue that is specifically intended to be used for research, either entirely for future projects, or for a specific study and subsequently for future research. The protocol elements listed below can be developed most effectively by completing CTRNet registration and/or certification. UBC's REBs strongly encourage all researchers who are creating a biobank to register with [CTRNet](#)

7. A.1. When the intended purpose of a tissue repository includes research (even in part), collecting, storing, sharing and using the tissue / specimens is considered research involving human participants which requires review and oversight by a UBC affiliated REB. Informed consent is usually required as well (See Article 5).

7. A. 2. Researchers intending to create tissue repositories for research should develop a repository protocol that provides detailed information concerning the implementation, operation and maintenance of the biorepository, including governance and privacy and confidentiality standards. Researchers are required to complete [View C](#) of the clinical research ethics application form. The protocol for the repository should include at least the following information:

- Scope and purpose of the biorepository
- Anticipated public and scientific benefits of the biorepository
- Period of time over which the tissue will be collected
- An indication of the sources of the bio-specimens
- Whether the bio-specimens will be linked to personally identifiable information
- If the bio-specimens will be linked, how long will they remain identifiable and who will have access to them
- Will participants be consenting to have their specimens included?
- An explanation of whether the consent will be pre-procedure or post-procedure (see for example, the CTRNet certification program SOP 02.001, participant recruitment into a Tumour Bank Program found [here](#))
- Describe the process for participant's rights to access and/or withdraw their samples and any limitations on when that may no longer be feasible
- Describe the governance developed for the bio-repository, for example who is the person/ who are the people responsible for overseeing the management and use of the biorepository, what are the main rules governing use and access, which organization is the custodian accountable to for the proper management of the bio-specimens, including for example who will become the steward in the event of the named custodian's death or disability
- The location of the biorepository procedural, technical and physical measures planned for maintaining the confidentiality and security of the bio-specimens
- Provisions for transfer of the bio-specimens outside of the institution
- Whether the bio-specimens are going to be linked to another data source, how the linkage will occur and to what data items/ what other specimens.
- If a linkage will occur, identify what personal information will be used to link them and how confidentiality will be preserved
- Length of time the specimens will be retained, how they will be destroyed (if needed)
- A description of anticipated future uses
- Full description of the bio-specimen stewardship process including whether the database repository will have formalized standard operating procedures
- Whether a privacy impact assessment will be conducted (this will vary depending upon the requirements of the institution in which the bio-specimens are being held)

- Any anticipated commercial uses for which the bio-specimens may be used
- Peer review of the biorepository protocol if available
- Whether the biobank has undergone registration, certification, or accreditation
- What relevant training the staff/researchers have taken

7.A.3 Informed Consent for Optional Tissue Banking ([CREB templates](#) and [C&W templates](#))

For a detailed example of an informed consent for Optional Tissue Banking, see the above links to the CREB Optional consent for DNA biobanking for future research studies, or the BCCA REB template for Optional Sample or Tissue Collection and Banking

The Informed Consent for Optional Tissue / Biobanking must include the following but will also need to meet the requirements of the UBC affiliated REB that is reviewing and approving the biobank.

- Location of the biobank/repository
- Type and amount of materials to be stored
- Research scope for the stored biological materials
- Overview of what a biobank is, the scientific relevance of biobanks and their importance to human well-being
- Specific health and personal data also to be collected if applicable
- Nature of the research activities in the field of biological materials
- The participant's options for handling new findings, including clinically relevant information and incidental findings if applicable
- Risks related to the collection of the sample
- Voluntary character of the donation
- Right to withdraw material and restrictions on that right e.g. if samples are anonymized
- Duration of storage
- Identifiability of biological materials, privacy confidentiality and security measures in place
- The physical, administrative and technical safeguards which will protect the human biological materials. This should include information about the governance structure of the biobank or repository and access to and management of the samples.
- Information about the potential for commercial use(s) if any, of the samples, including any disclaimers concerning participant remuneration for such use.

7.B. "Existing Non-Compliant" Tissue banks

This article applies to situations where there is an existing human tissue bank and some or all of the samples were collected without appropriate *research* consent. This article only applies to tissue that was collected for a legitimate, authorized purpose in the first place, for example tissue that was collected for clinical purposes, tissue that was collected for research authorized by an REB prior to the 1998 implementation of the TCPS consent requirements, or research already approved by an REB.

Note: The guidance below is based upon guidance that was initially developed by the UBC Research Ethics Policy Advisory Board in 2004 in response to the requirements of the August 1998 promulgation of the first version of the Tri-Council Policy Statement. It is expected that by the date of this guidance that all UBC Investigators who are custodians of tissue and who are utilizing the stored tissue for research (i.e. operating a biobank as defined above) will be doing so having already obtained appropriate REB approval and in compliance with the current consent requirements as set out in [Article 12.2](#) of the TCPS2: 2014 and Article 5 of this Guidance. The following is being retained in this guidance for the sake of completeness in the event that there may be a limited number of small repositories that have been operating in contravention of current requirements and professional standards.

7.B.1 When Investigators identify that they may be in possession of tissues that were not obtained under the circumstances dictated by the TCPS, the following staged approach to remedying this should be followed.

1. Investigators (custodians) must inform the appropriate UBC REB of full circumstances (insofar as they are discoverable) of the initial tissue collection including the purpose of the collection, whether consent was obtained and in what form, and whether consent is documented. The UBC REB will provide oversight in the process of remedying the situation in the context of the TCPS guidance. The investigator is responsible for ensuring that the REB is informed of all actions taken in relation to the tissue and for ensuring that the REB approves of these actions.
2. Investigator (custodians) should pursue the following options in the order given:

Option 1: Seek Informed consent from tissue donors

The ethically preferred method for remedying deficiencies in the original consent process under which tissues were obtained is to contact the donors (or their descendants) to seek their properly informed consent. 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 person at the patient's last known address.

Option 2: Anonymize the tissues

The TCPS requirements for obtaining consent from donors for tissue banking apply to identifiable tissue. [See the current [TCPS2:2014 Article 12.3.B](#)]. If the tissue is anonymized donor consent is not required. It is up to the researcher/custodian to establish to the satisfaction of the REB that the tissue has been effectively anonymized.

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

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

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

- i) 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
- ii) The privacy guardian may need to be independent of the tissue custodian. Assessment of whether this is required would take into consideration the proportionate risk to donors, if there were disclosure of their personally identifiable information
- iii) 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
- iv) The privacy guardian must not fulfill any request by an investigator to link tissue 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.

Best practices can be accessed at:

CTRNet.ca [CTRNet](#)

ISBER <http://www.isber.org/>

UBC Office of Biobank Education and Research (OBER) <http://pathology.ubc.ca/education-resource/ober/>