

## **Human Tissue Banks and their Use for Research Purposes: Guidance to UBC-Affiliated Custodians of Human Tissues**

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### **Introduction:**

This guidance document was generated by the UBC Research Ethics Policy Advisory Board (REPAB) in 2004 and the draft version has been found to be useful. It is endorsed by the UBC Research Ethics Boards. REPAB has decided to circulate it more widely. It should be particularly helpful for researchers with existing tissue banks which were collected prior to current ethical requirements.

### **Objectives:**

The objectives of this guidance document are:

- To educate custodians about the Tri-Council Policy Statement (TCPS) requirements for obtaining human tissue and the conditions on its use.
- To assist custodians, who have a human tissue bank of previously-collected tissue, in determining whether the conditions under which the tissue was obtained meet TCPS requirements.
- To encourage custodians in possession of tissue obtained without TCPS-compliant consent to come forward by providing them with guidance on remedying ethical deficiencies so that TCPS requirements can be met and, where ethically possible, the tissue can be utilized in worthwhile research.

### **Definitions:**

**Tissue:** a collection of human cells with or without the intercellular substances surrounding them. This includes blood.

**Custodian:** any person who is responsible for collection, storage, and/or regulating access to human tissues for research purposes.

**Identifiable/Traceable tissues:** tissues where the possibility of linking the specimen to its donor's identity exists, regardless of how difficult it may be to do so.

**Anonymized/Anonymous tissues:** tissues where the link between the specimen and the identity of the donor never existed (following donation) or has been obliterated such that it would be impossible under any circumstances to re-link it.

**Bank:** any collection of human tissues which are being stored for planned or unplanned future research uses.

**Double or multiple codes:** (also called "reversibly anonymized") Two or more codes are assigned to the same participant's data held in different datasets (e.g. health administrative data, clinical data, genetic samples and data). The key connecting codes and providing the link back to participants' direct identifiers is held by a third party and is not available to investigators. If the data recipient is not permitted to request a re-linking of data to identifiers, double-coded data may be considered by the data recipient to have the status of "anonymized data".

**Impracticable:** For the purposes of this document, "impracticable" means a degree of difficulty in doing something under present conditions, where the degree of difficulty is greater than would arise if something is merely inconvenient to do but may be less than if something is impossible. Seeking consent from individuals for the use of their personal data may be considered impracticable when there are difficulties in contacting or notifying individuals due, for example, to:

- the size of the population being researched; or
- the proportion of prospective participants likely to have relocated or died since the time the personal information was originally collected; or
- lack of an existing or continuing relationship between prospective participants and the data holder who would need to contact them (e.g. a patient registry that does not have a regular follow-up program to maintain a complete and accurate record of changes in registrants' contact information over time);

**Tri-Council Policy Statement Tissue Categories [TCPS Section 10(A)]:**

- “Identifiable tissue can be immediately linked to a specific individual (e.g., by way of an identifying tag or patient number).”
- “Traceable tissue is potentially traceable to a specific donor provided there is access to further information such as a patient record or a database.”
- “Anonymous tissue is anonymous due either to the absence of tags and records or the passage of time (e.g., tissue recovered from archaeological sites).”
- “Anonymized tissue was originally identified but has been permanently stripped of identifiers.”

**Tri-Council Policy Statement Guidance on Human Tissues:**

Some applicable Articles from the TCPS are extracted below. Custodians are referred for the full discussion of these issues to the primary document at <http://pre.ethics.gc.ca/english/policystatement/policystatement.cfm>

**Article 8.6 “Banking of Genetic Material”**

*“Though the banking of genetic material is expected to yield benefits, it may also pose potential harms to individuals, their families and the groups to which they may belong. Accordingly, researchers who propose research involving the banking of genetic material have a duty to satisfy the REB and prospective research subjects that they have addressed the associated ethical issues, including confidentiality, privacy, storage, use of the data and results, withdrawal by the subject, and future contact of subjects, families and groups.”*

**Article 8.7 “Commercial Use of Genetic Data”**

*“At the outset of a research project, the researcher shall discuss with the REB and the research subject the possibility and/or probability that the genetic material and the information derived from its use may have potential commercial uses.”*

**Section 10(B) “Free and Informed Consent”**

**Article 10.1**

*“Research proposing the collection and use of human tissues requires ethics review by an REB. Amongst other things, the researcher shall demonstrate the following to the REB:*

- (a) That the collection and use of human tissues for research purposes shall be undertaken with the free and informed consent of competent donors;*
- (b) In the case of incompetent donors, free and informed consent shall be by an authorized third party;*
- (c) In the case of deceased donors, free and informed consent shall be expressed in a prior directive or through the exercise of free and informed consent by an authorized third party.”*

**Article 10.2**

*“For the purpose of obtaining free and informed consent, researchers who seek to collect human tissue for research shall, as a minimum, provide potential donors or authorized third parties information about:*

- (a) The purpose of the research;*
- (b) The type and amount of tissue to be taken, as well as the location where the tissue is to be taken;*
- (c) The manner in which tissue will be taken, the safety and invasiveness of acquisition, and the duration and conditions of preservation;*
- (d) The potential uses for the tissue including any commercial uses;*
- (e) The safeguards to protect the individual’s privacy and confidentiality;*
- (f) Identifying information attached to specific tissue, and its potential traceability; and*
- (g) How the use of the tissue could affect privacy.”*

**Section 10(C) “Previously Collected Tissue”**

**Article 10.3**

*“(a) When identification is possible, researchers shall seek to obtain free and informed consent from individuals, or from their authorized third parties, for the use of their previously collected tissue. The provisions of article 10.2 also apply here.*

*(b) When collected tissue has been provided by persons who are not individually identifiable (anonymous and anonymized tissue), and when there are no potential harms to them, there is no need to seek donors’ permission to use their tissue for research purposes, unless applicable law so requires.”*

**Managing Identified Ethical Deficiencies in Consent for Human Tissue Banking:**

Potential ethical deficiencies span the spectrum from no consent for banking being obtained at all, through to one or two minor omissions from the TCPS requirements in the consent process for banking. Added complexity results from uncertainty about how important particular aspects of consent really are to the subjects, and it is understood that this may be context-dependent. For example, healthy volunteers donating blood for research uses may be much more or less interested, for example, in potential commercial uses of their tissue than terminally ill cancer patients donating tissue obtained during the course of routine tumor biopsy.

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.

**It is critical to recognize that that the options presented below apply only to tissue that was collected for a legitimate, authorized purpose in the first place. Examples of this would include tissue 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. Tissue collected under other circumstances may not be ethically salvageable using the remedies listed in this document.**

The most appropriate remedy would depend on the specific nature of the ethical deficiencies identified, and oversight of the process of remedying the situation must be provided by the relevant REB in the context of the guidance provided in this document.

First, investigators must inform the 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 most appropriate of the UBC Clinical REB, UBC/Providence REB, or UBC/BCCA REB should be chosen. The UBC REB should provide oversight in the process of remedying the situation in the context of the guidance given above. The custodian 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.

***Custodians/Researchers should pursue the following options in the order given:***

**Option 1: Seek consent from tissue donors**

(a) 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 persons at the patient’s last known address.

(b) A challenging ethical issue is whether non-response from the individual with whom contact is attempted

can be interpreted as assent, consent, lack of dissent, or any other sort of permission to use their tissue for research purposes. Except under extraordinary circumstances, lack of response from attempted contacts **cannot** be interpreted as consent or assent to use their tissues for research purposes. A compelling argument that options 2 and 3 are inappropriate would be required for the REB to consider approving such a procedure.

If such a procedure was approved, the contact letter (e.g., or other suitable form of communication) would have to convey (1) the ethical deficiencies identified; (2) any known research uses their tissue has been put to already; (3) all the TCPS-required elements of informed consent; (3) the option of having their tissue destroyed if they do not consent; and (4) the timeframe for interpreting non-response (eg. 3 months) and what will happen to their tissue if they do not respond.

**Option 2: Anonymize the tissues**

The TCPS requirements for obtaining consent for tissue banking apply to identifiable tissue. If the tissue is rendered completely unidentifiable (i.e., anonymized), TCPS requirement 10.3(b) is satisfied.

The primary ethical issue here is that the utility of the tissues can be diminished by anonymizing them. Hence, the seriousness of the ethical deficiencies in how the tissue was obtained must be weighed against the potential value of the tissue for research purposes in deciding whether to exercise this option. In all such situations, help of the applicable REB should be sought.

**Option 3: Implement systems which make the tissue *reversibly anonymized***

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.

An acceptable method of accomplishing this is given below:

A third party functioning as a “*privacy guardian*” can be inserted between the investigator and the source of identifiable information. This entity would have the ability to link the tissue specimens with personal information about the donor. The investigator in possession of anonymized specimens (e.g. colon cancer biopsies) could request from the privacy guardian additional information (e.g. five year survival) that could only be derived by inquiry to the subject’s identifiable information (e.g. the medical record). The privacy guardian would then abstract the requested information (e.g. five year survival) related to that specimen (e.g. colon cancer biopsy), strip the data of all identifying information (e.g. name, identification number, etc), attach the now anonymized information to the specimen and return that information to the investigator. Certain characteristics must be built in to such a system so that privacy, confidentiality, respect for individuals and specimens derived from them and ethical oversight are guaranteed. These include, but are not limited to the following:

- (a) The privacy guardian must be a professional with training in the importance and methods of maintaining confidentiality.
- (b) 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 proposed linkages.
- (c) The privacy guardian may need to be independent of the tissue custodian. The REB should evaluate the risks and benefits of the of having the privacy guardian and the tissue custodian be independent. Because having them entirely separate increases the risks of errors and may complicate the process, the principle of proportionate risk should be followed. If the overall ethical risk to the subject is minimal (that is, similar to risks that reasonable individuals are willing to assume in ordinary day to day life) the privacy guardian and the tissue custodian need not be separate. On the other hand, if the ethical risk

is judged to be more than minimal by the REB the privacy guardian and the tissue custodian must be separate.

For example, if the type of information that the investigator wishes to obtain, e.g. a blood hemoglobin matching the date of collection of a lung biopsy specimen, the ethical risk to the subject is minimal and would not require separation of the privacy guardian and the tissue custodian. This situation is quite different from the case of a researcher requesting the syphilis serology of a subject from whom a blood specimen was taken during a criminal investigation. In the former, the risk to the subject even if the confidentiality protection were breached is very small; in the latter, the potential risk is obvious and the REB should insist on great rigor protecting the subject's confidentiality including complete separation of the privacy guardian and the tissue custodian.

- (d) The inquiry to be answered by recourse to the privacy guardian must be pre-approved by the REB as part of the original research project. The description of the research project must include justification for the type of information being requested.
- (e) Inquiries that were not pre-specified and approved by the REB when the original project was reviewed but are proposed later must be submitted to the REB for review and approval.
- (f) 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.
- (g) 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 (e.g. Health Canada, UBC Continuing Review Program).

#### **Option 4: Non-Individualized Attempts to Inform Tissue Donors**

In some unusual circumstances, the REB may approve of making a general "call to patients" who might have donated tissue, using public announcements in the lay press, public venues, hospital bulletins, using print and/or electronic media, describing a way they can have the tissue destroyed if they do not consent to its remaining in the tissue bank.

In considering this option, the REB may require that advice be sought from individuals or groups similar to those of the original donors. Similarity includes such factors as culture, religion, experience or situation. This advice is not a form of proxy consent, but it can provide the REB and investigators with significant insights about the situation in which tissue was collected and potential effects of continued or future utilization of the tissues in research. **This is the least ethically preferred option and the REB would demand robust arguments for discounting options 1 through 3 before considering it.**