CREB Guidance Notes Related to Tissue Collection and Banking

2.1 MINIMAL RISK RESEARCH STUDIES

2.1.2 Types of Minimal Risk Research Studies Qualifying for Expedited Review

It is difficult to identify what does and does not fall within the boundaries of minimal risk research. The TCPS definition of minimal risk itself represents a controversial standard (it is not currently in use as a definition of minimal risk in any other English-speaking country). In these circumstances, rather than apply on a case-by-case basis an open-ended and not clearly defined standard, the CREB has decided to list categories of research that it has identified as sufficiently low risk to undergo a process of Expedited Review. This helps to ensure openness and accountability in ethically reviewing a category of research that is not well-defined and whose limits are controversial. Researchers are invited to propose amendments to the listed categories of minimal risk research qualifying for Expedited Review.

Studies that may meet the criterion for minimal risk include research that is *limited* to the following sources of data (GN #2.1.2.1 and GN #2.1.2.2) and, as such, may undergo expedited review by the CREB Chair (or designate). See GN #2.1.4 for exceptions.

2.1.2.1 Primary Sources of Data Obtained For Prospective Research (03 Jul 2008)

2.1.2.1.1 Sources of Data

1. Collections of hair, nail clippings, deciduous teeth, excreta, salivary secretions, additional swabs, or other external secretions that have been collected in a non-invasive manner and that may also be collected as part of routine clinical care.;
2. Placenta or amniotic fluid collected as a consequence of childbirth, or fetal tissue collected as a consequence of therapeutic abortion or miscarriage;
3. Data recorded using non-invasive procedures(e.g. EEG, EKG, MRI, ultrasound, or x-rays not exceeding radiation exposure equivalent to one return transcontinental air flight) , but not including questionnaires requesting sensitive information from vulnerable populations or involving significant nuisance or inconvenience.;
4. Blood samples collected by venipuncture or a central line installed as part of clinical care;
5. Output data obtained as a result of moderate exercise undertaken by healthy volunteers;
6. Output data obtained as a result of maximal exercise undertaken by healthy volunteers who are less than 40 years old, and the CREB has approved a safety protocol.
7. Certain types of pluripotent stem cell research as described under GN 2.1.2.4.3.
8. Clinical data collected prospectively as part of clinical care.
9. Observational research on standard treatment(s) where the treatment(s) is (are) determined clinically and not assigned by research methodology (e.g. randomization).

2.1.2.1.2 Consent Requirements

Consent must be obtained from subjects for the use of data derived from the preceding sources. For further information, see GN 2.1.3.

2.1.3 Requirement for Consent Forms for Minimal Risk Applications

2.1.3.1 Circumstances Where Consent Is Required for Minimal Risk Studies

Subject consent IS required for collecting prospective subject data as described above in GN 2.1.2.1 .

For further clarification, consent IS normally required in all situations where researchers prospectively gather data from individuals under a research protocol, even though that data is also collected as part of clinical care and the research is minimal risk. Obtaining consent in these circumstances ensures transparency in the relationship between researchers who are also clinicians and those who are their patients/subjects, and it is normally practicable as well.

The CREB does not accept the argument that because prospectively collected clinical data could be obtained retrospectively from a chart review at a later date, standards for retrospective research of medical records, including waiver of consent, should apply. If one adopts as a guiding presumption that any information that could be gathered retrospectively does not require consent, then it makes perfect sense not to require consent for prospectively gathered clinical data that could in principle be gathered later, retrospectively. However, this presumption is incorrect. The correct ethical presumption in research is that consent is required for the use in research of any personal medical information. If one starts with this presumption, then the implied standard is that consent must be obtained wherever it is practicable to do so. In prospective research, it is normally practicable to obtain consent. Retrospective chart reviews are different. They represent a recognized exception to this presumption, since research ethics boards have recognized that it would typically be impracticable, for many reasons, to obtain consent in those circumstances. But it is not so evidently impracticable for prospective data gathering, since the subject is actually present during the data gathering. As well, during the time her/his care and treatment is administered, the patient is also a known and identifiable subject of research, and the patient is presumptively entitled to know this (in addition to knowing that her/his personal information will be used for research purposes). Finally, researchers know that their patients are also subjects of research in those circumstances, and they need to disclose this non-clinical relationship to them. These considerations identify a number of ethically significant disanalogies with retrospective chart reviews.

In summary, if the researcher is gathering clinical information prospectively from subjects and entering it into, say, a research data base, it can admittedly be inconvenient to obtain consent, but the presumption in favour of obtaining consent stands as do the other ethical considerations mentioned. It is possible that these ethical considerations can be outweighed by other ethical considerations, as per TCPS Article 2.1(c) . However, the argument that the data could have been gathered differently is a

red herring. It is not being gathered that way, and thus different ethical reasoning applies, at least presumptively.

The researcher's argument at this point may be that the low risk of gathering and entering the data justifies overriding the presumptions because of the potential health benefits of the research. But this requires showing that consenting subjects would in fact undermine the ability to carry out the research and that there is a substantial research-related health benefit to be gained that could only reasonably be obtained by waving nor altering consent requirements. The CREB has accepted this argument in some cases, but the argument has to be made.

2.1.3.2 Circumstances Where Consent Is Not Ethically Required for Minimal Risk Studies (03 Jul 2008)

Subject consent is NOT ethically required for the use of data obtained from previously banked anonymized tissue that is NOT linked to other sources of data. Subject consent is NOT ethically required for the use of data obtained from the following sources and where subjects are not being contacted for any research related purpose:

1. retrospective chart or medical record reviews ;
2. provincially regulated databases/registries (e.g. Medical Services Plan, BC Centre for Disease Control);
3. disease specific registries with data collected from subjects who have already consented to its use for the sort of research being done.
4. Tissue collected previously for clinical purposes that is no longer needed for any clinical purpose and that has been anonymized (i.e., there is no way to link the tissue to the subject), and there is no potential for harm to subject.(03 Jul 2008)

2.1.3.3 Legal Requirements for Consent (Updated 30 March 2007)

The requirements for seeking consent are subject to federal and provincial privacy laws and investigators are responsible for compliance with these laws that relate to their research. The CREB does not have the authority to authorize any procedure that contravenes these laws, and any CREB approval of a waiver of the ethical requirement to obtain consent for Minimal Risk Studies does not entail a waiver of the investigator's legal responsibility to comply with the law on consent. See GN #39.7.1 for further detail on the privacy legislation requirements as they pertain to information that must be included in consent forms. **(24 September 2004)**

2.1.3.4 Use of Data Obtained from Non-UBC Affiliated Sites (24 September 2004)

Studies that involve the analysis of data obtained from non-UBC investigators working at non-UBC affiliated institutions must also include the consent form used to obtain permission for collection of the data/tissue OR a statement that explains the confidentiality provisions under which consent was initially obtained.

2.1.4 Minimal Risk Studies That Require Full Board Review (03 Jul 2008)

The following types of studies must be submitted for full board review.

1. Studies whose purpose is to collect tissue/DNA for the purpose of creating or adding to a tissue/DNA bank or for genetic research. See GN 39.6.1 for further details on consent form requirements.
2. Studies whose purpose is the derivation of stem cell lines from human somatic tissue, umbilical cord or placenta OR research involving the grafting of stem cell lines into humans must be submitted for Full Board Review
3. Any minimal risk studies where researchers request waiver or alteration of informed consent.
4. Minimal risk studies that recruit residents as subjects.

29.4 USE OF TISSUE AND/OR DATA OBTAINED FROM TISSUE AND DATA BANKS (24 September 2004)

29.4.1 Use of tissue or data that has been previously collected must receive authorization from the custodian of that bank or registry for its use, regardless of whether the tissue/data is anonymized. Evidence of this authorization must be submitted with the application to the CREB.

29.4.2 If the tissue/data is not anonymized, evidence that consent was obtained at the time of collection for use of the tissue/data must also be submitted. This may include the original consent form or an assurance from the investigator that appropriate protections were undertaken to ensure confidentiality and privacy.

Guidance Note #29 Reference:

- **TCPS Section 3 re: Privacy and Confidentiality, Secondary Use of Data**

30.3 LINKABLE DATA/TISSUE OBTAINED FROM DATABANKS OR BIOBANKS (24 September 2004)

Identify who (i.e. data/biobank custodian) has authorized access to the stored data/tissue. Identify who retains the key for linking coded tissue or data to a register of human subjects. Explain who will perform the necessary data linkage. It is preferable if the custodian of the bank holds the key to linking the data and performs the data linkage so that identifying information is not released to investigators.

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30.4 STORAGE OF DATA

UBC Policy #85 states, *"A factor in many cases of alleged scholarly/scientific misconduct has been the absence of a complete set of verifiable data. The retention by the University of accurately recorded and retrievable results is of utmost importance. Wherever possible, all primary data should be recorded in clear, adequate, original and chronological form. In scientific departments, a record of the primary data must be maintained in the laboratory and cannot be removed. Original data for a given study should be retained in the unit of origin for at least five years after the work is published or otherwise presented (if the form of the data permits this, and if assurances have not been given that data would be destroyed to assure anonymity)".*

This means data should be stored for at least 5 years, but it may be retained for a longer period provided that it is stored securely. UBC has no explicit requirement for the shredding of data at the end of this period; however destruction of the data is the best way of ensuring that confidentiality will not be breached. Please note that the responsibility for the security of the data rests with the PI.

39.2 EXCEPTIONS TO THE REQUIREMENT TO OBTAIN INFORMED CONSENT (03 Jul 2008)

Studies that do not require informed consent include those whose data is derived solely from:

a. secondary data obtained from medical records (i.e. chart reviews),

b. previously anonymized tissue (i.e., there is no way to link the tissue to the subject) from tissue banks

c. tissue previously collected for clinical purposes that is no longer needed for any clinical purpose and that has been anonymized (i.e., there is no way to link the tissue to the subject) ,and there is no potential for harm to subject; or.

d. anonymous questionnaires (i.e., where there is no way to link subjects to the questionnaire responses). No formal consent form is required for such questionnaires, although the CREB will require a letter of invitation describing the goals of the study, the confidentiality protections that that are in place, and other CREB requirements regarding questionnaires.

TCPS Article 10.3b states "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."

39.6.1 Tissue Banking Studies

The following TCPS requirements must be observed for obtaining free and informed consent for the purposes of banking tissue (including blood).

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.

d. 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 following CREB policies must be applied if relevant:

39.6.1.1. Mandatory Tissue Banking

UBC CREB Policy #9: Criterion for Permitting Mandatory Tissue Banking (25 March 2003)

Mandatory tissue banking is only permitted if the tissue is being banked for purposes **directly related** to the study at hand (i.e. the tissue banking must be integral to the study, such that there would be no study if the subject did not contribute the tissue).

It is unethical to *require* that subjects agree to allow their tissue to be banked for future use or experimentation that is unspecified or unrelated to the study at hand as a condition for entry into a therapeutic trial, as this could be perceived as a coercive method of obtaining tissue/blood samples through offering a perceived therapeutic opportunity.

39.6.1.2 Donation of Tissue For Unspecified Uses

UBC CREB Policy #10: Voluntary Donation Of Tissue For Unspecified Uses (25 March 2003)

Subjects *may* donate their tissue for future, unspecified uses provided:

1. this condition is made explicit in the main consent form for the study;

2. that such donation is optional, and;

3. that the Investigator discloses whether or not they plan to seek the subjects' consent for future projects involving their tissue.

39.6.1.3 Information Details Required In Consent Forms For Tissue/DNA Banking Purposes

The information described below must be included in either the subject consent form for the entire study, if tissue/DNA banking is part of the study, OR in a separate consent form, if consent to bank tissue/DNA is being requested in connection with a research study but is independent of the subject's participation in that study. Include the following information in the tissue/DNA banking consent form:

a. The research purpose, and the **specific** uses of the tissue;

b. The type and amount of tissue to be taken, as well as the location(s) 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 (i.e., address whether the tissue will be stored after the study is completed and, if so, why this is required);

d. The potential uses for the tissue, including any commercial uses, who the tissue might be sold to if this is known, and transfer to another institution;

e. The safeguards to protect the individual's privacy and confidentiality;

f. Access by other Investigators to banked tissue;

g. Identifying information attached to specific tissue, and its potential trace-ability;
h) How the use of the tissue could affect privacy;

h. Whether the subjects will be notified of the results, and if so, the provisions for counselling of subjects upon receipt of the results;

i. Whether tissue can be removed from the bank, if the subject later withdraws permission. In the case of a subject's withdrawal from a research study, TCPS Article 8.6 states that there may be a variety of options for dealing with the tissue or data, such as the "Actual destruction of genetic material or research data, or the removal of all identifiers." Any options must be discussed with the research subject and disclosed in the Consent Form.

39.11 USE OF "NEGATIVE CONSENT"/CHECK BOXES IN CONSENT AND ASSENT FORMS

UBC CREB Policy #14: Use of "Negative Consent" Check Boxes in Consent and Assent Forms (08 October 2002)

1. The use of "Yes/No" check boxes for consent is not allowed. Lack of signature on a consent form is taken as evidence of dissent, and no subject shall be required to declare in writing in any way that they do not consent to participate in a research project.

Exception to #1:
1a. Where a single consent form contains multiple optional sub-components, (e.g. tissue banking for genetic research) where subjects can choose which ones they wish to participate in, the optional SUB-COMPONENTS (but not the main question of consent to participate in the main project) may employ "Yes/No" indicators to signify willingness to participate.

Lack of indication of "Yes" (or equivalent) shall be taken as evidence of DISSENT and **no requirement to check "No" (or equivalent) is allowed.**

The CREB may require that *separate* consent forms fully describing a sub-component(s) of a project be required instead of allowing the procedure described in 1(a) where necessary.