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THE UNIVERSITY OF BRITISH COLUMBIA

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UBC Clinical Research Ethics Board

Guidance Notes

These Guidance Notes (GNs) provide the most up-to-date overview of the UBC clinical Research Ethics Boards' policies and guidance concerning clinical research ethics at UBC. They are applicable to all UBC affiliated clinical Research Ethics Boards (REBs) [the Clinical Research Ethics Board (CREB), Providence Health Care REB, Children and Women's REB, and BC Cancer Agency REB]. However, each board may have separate Application Guidance Notes (AGNs) that are based on each individual board's practices and should be read together with the overarching clinical Guidance Notes.

Please refer to the separate Post-Approval Activity Guidance Notes on the Office of Research Ethics website for information pertaining to:

- Annual Renewals
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Guidance Note #1

Authority of the UBC-Affiliated REBs

The UBC REBs are established and empowered under the authority of the Board of Governors, through the Vice-President Research. They operate under the authority of UBC Policy #89 on "Research and Other Studies Involving Human Subjects". UBC administration, under the direction of the Vice-President Research, is ultimately responsible for overseeing the protection of human participants involved in research programs conducted by the University. University administration is responsible for ensuring that sufficient resources are allocated to the UBC Research Ethics Boards to allow them to perform their review, record-keeping and monitoring functions.

Purpose of the REBs: UBC's Research Ethics Boards are autonomous entities whose primary responsibility is to protect the rights and welfare of human participants taking part in research conducted under the auspices of UBC. The UBC REBs review and oversee such research to assure that it meets ethical principles and that it complies with all applicable regulations and standards pertaining to human participant protection. These include but are not limited to:

The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans
Health Canada's Food and Drugs Act
The International Conference on Harmonization Good Clinical Practice: Consolidated Guidelines
The Declaration of Helsinki
The U.S. Common Rule (for studies funded by the U.S. Government or regulated by the US Food and Drug Administration)

UBCs REBs have the authority to approve, require modifications in, or disapprove any research activity that falls within their jurisdiction.

UBC's REBs are required to conduct continuing ethical review of every approved study. Continuing review activities include, but are not limited to:

- Review of regular progress reports including renewals
- Review of changes in the design or conduct of the study prior to implementation
- Review of serious adverse events and other unanticipated events, including protocol deviations
- Monitoring to determine that the study is conducted as approved

- Monitoring of the informed consent process
- Suspension or termination of the approval of a study
- Placing restrictions on a study
- Any other review procedure deemed necessary to protect the rights and welfare of human participants.

Guidance Note #2

Jurisdiction of the UBC-Affiliated REBs

All research on human participants conducted at UBC facilities, (including UBC's affiliated hospitals) or undertaken by individuals connected to the University must be reviewed and approved by a UBC sanctioned Research Ethics Board *prior* to it commencing. [1]

In some cases, a research project may need to be reviewed by more than one Board or Committee. For example, research that involves human blood may require review by both the Biosafety Committee and the Clinical REB.

Important Note: None of UBC's Affiliated REBs will review or acknowledge research that has already been conducted. Requests for such review to satisfy, for example, publication **or graduation** requirements, will not be entertained.

One Board of Record: The UBC Research Ethics Boards that review research involving human participants have signed a one board of record agreement allowing approvals by one UBC-affiliated REB to be recognized by the other UBC-affiliated REBs. Research conducted by the same researcher at multiple UBC sites needs ethical approval from one UBC-affiliated REB only. **Most sites will, however, require separate approval for resource allocation purposes, e.g. hospitals.** Although there is one REB of Record, in order to ensure that institutional specific ethics requirements are being met, the Chair and the Manager of each UBC REB for the institution(s) involved in the research have the ability to view the application approved by the REB of Record. If the REB Chair of any institution involved in the research has questions or concerns, these will be directed to the REB Chair of the REB of Record for resolution. The REB Chair of any institution involved as a research site may refer a question or concern to the REB of Record at any time. The UBC-affiliated REB that initially reviews a research study will normally be the REB of Record. All activity involving the study that occurs subsequent to the initial approval (such as amendments, annual renewals, requests for acknowledgement) should be submitted to the REB that is the REB Board of Record.

[1] See UBC Policy 89, Article 7.8.1. " Where such research is conducted by members or associated members of the University acting in their University capacity".

Six REBs: UBC currently has six Research Ethics Boards that review and approve research studies involving human participants that are conducted under the auspices of UBC. Each individual Board has varying operational practices, and researchers are advised to familiarize themselves with the processes of the Boards that they submit applications to. Each Board has its own web-site to assist researchers with information concerning submission deadlines, meeting dates etc.

The **Behavioural REBs** (Panel A and Panel B) review research on humans that is behavioural or social scientific in nature or involves humanities research and that may involve the study of patients or health care providers. Behavioural studies are not clinical in nature and do not involve any invasive procedures. These types of studies include research involving interviews, administration of questionnaires, tests and/or observations. They can include the use of medical records but with consent.

The **Okanagan REB** reviews research that would otherwise be reviewed by the Behavioural REBs, which is being conducted by individuals affiliated with UBC-Okanagan.

The **BC Cancer Agency REB,** the **Children & Women's REB** and the **Providence Health Care REB** review research being conducted at these sites. If a UBC-affiliated researcher wishes to conduct research at ONLY one of these sites, they must submit their application to that site. If a UBC Researcher wishes to conduct research at other non-UBC affiliated sites, but not at a UBC-affiliated site, he or she should submit their research to the REB where they hold their primary appointment. UBC researchers who wish to conduct research at MULTIPLE UBC-affiliated sites have the option of having their study reviewed by any UBC-affiliated REB. It is recommended that they utilize the Board associated with the institution where they hold their primary appointment.

The **Clinical REB** reviews research that involves clinical interventions such as surgery, the administration or testing of drugs, medical devices, medical imaging or diagnostic techniques, taking of blood or other specimens, exercise programs, the analysis of clinical –e.g. laboratory, physiological or biological - data obtained from medical records or studies of a clinical nature involving the linkage of data from existing databases, or any invasive procedure involving an element of risk. The CREB reviews research being conducted at the UBC Hospital (Point Grey) site, and the Vancouver Coastal Health Authority Sites.

At the discretion of the Chairs and Managers of the UBC REBs, a submission may be re-directed to a more appropriate REB.

Please consult with the administrative REB staff if you are not sure which REB you should apply to.

Guidance Note #3

Principal Investigator Responsibilities

Article 3.1: Principal Investigators

All Principal Investigators must have a faculty appointment at UBC or if permitted by the applicable board, a staff appointment at an affiliated institution. Principal Investigators bear the overall responsibility for the conduct of the study, including the activities of co-investigators and others on the study team. **As the individual responsible for the implementation of the research, the principal investigator bears direct responsibility for ensuring the protection of every research participant.** All Principal Investigators are required to meet the responsibilities assigned to them in UBC Policy #89, Procedures. These responsibilities include, but are not limited to:

- Read and be aware of all *UBC* policies related to research, including without limitation this *Policy #89* (which includes procedures, and any other enactments under the *Policy* or procedures).
- Bring to the attention of the Head of his/her department any research or other study proposed by him or her, or proposed by a student working under his or her direction, that could be defined as a study involving human participants.
- Present sufficient information to the Head to enable a judgment to be made by him or her as to whether the project comes within the definition of research involving human participants.
- Submit *Research* for *REB* review in the form and with the content specified in the *UBC Human Ethics Application*
- Include as part of each *REB* application a process for continuing review appropriate to the project.
- Promptly inform the *REB* that is considering, or will consider, an application by the researcher for any similar or equivalent proposal to:
    - other *REBs*;
    - funding agencies or regulatory bodies; or
    - research ethics boards, or the like, of other institutions.
- Maintain any issued *Certificate of Approval* in good standing during the research project.

- Promptly notify the *REB* that issued a *Certificate of Approval* of any change in the research involving human participants as proposed and when the project concludes.
- Ensure that informed consent, when required, is obtained from research participants prior to their enrolment into the research project in a form and manner prescribed by *TCPS2, UBC Ethical Directives* and other relevant national and international standards or condition of funding, where applicable.
- Report all serious and unexpected study related events to the applicable REB in accordance with applicable regulations and guidelines.
- Ensure that any amendments to the study personnel, funding, protocol, consent form or any recruitment procedures are approved by the applicable REB prior to implementation, except where necessary to eliminate apparent immediate hazards to human participants.
- Promptly notify the applicable REB of any unexpected incident, experience or outcome, or any new research knowledge that could impact the conduct of the study or alter the REB's approval or favourable opinion to continue the study.

Article 3.2: Investigators Conducting Clinical Trials

Investigators conducting clinical trials for either drugs/radiopharmaceuticals, devices or natural health products used for therapeutic purposes have special obligations that are defined in the Food and Drugs Act Regulations that govern each type of experimental therapy. If the study is investigator-initiated, the Investigator bears additional regulatory responsibilities as a study Sponsor. Application Guidance Note #7.11 outlines REB requirements pertaining to regulatory approvals and registration of clinical trials. Investigators conducting clinical trials must also ensure that they comply with the provisions of the TCPS 2 and the International Conference on Clinical Trials Good Clinical Practice: Consolidated Guidelines.

Article 3.3: Investigators Conducting Research Funded or Supported by the United States Federal Government or Regulated by the U.S. Food and Drug Administration.

3.1. Investigators (and their institutions) that receive funding or support for studies from the U.S. Federal Government or its agencies are subject to the requirements of the Department of Health and Human Services, found at 45CFR46 (for a list of the applicable agencies click **here**).

3.2. Investigators (and their institutions) that conduct studies that are regulated by the U.S. Food and Drug Administration (including but not limited to most privately funded clinical trials)

are subject to the requirements of the U.S. Food and Drug Administration, most of which are found at 21CFR50 and 21CFR56.

3.3. Investigators conducting studies that are subject to the U.S. regulations are responsible for ensuring that they comply with these additional requirements, and in particular, the requirements for reporting unanticipated problems to the Research Ethics Board and if necessary to the applicable regulatory agency. Click **here** to link to the DHHS Regulations, 45CFR46. Click **here** to link to the U.S. Food & Drug Administration Regulations, 21CFR50 and 56.

Guidance Note #4

Types of Research that Require Review

Article 4.1: Scope of REB Review Requirements

All research involving human participants and all other activities that even in part involve such research, regardless of sponsorship, must be reviewed and approved by a UBC-affiliated REB. No intervention or interaction with human participants in research, including the use of their data, tissue, or the initiation of recruitment, may begin until a UBC REB has reviewed and approved the research protocol, consent documents, and recruitment materials and has issued a certificate of approval. Specific determinations as to the definition of "research" or "human participants", and their implications for the jurisdiction of the REB under University of British Columbia policy are determined by the REBs. Determination of exemption from REB review must be based on regulatory and institutional criteria.

Article 4.2: Definition of Research and activities that require REB Review

Research involving human participants is defined as an undertaking intended to extend knowledge through a disciplined inquiry or systematic investigation that includes the following:

a) Living human participants; and/or
b) Human biological materials, as well as human embryos, fetuses, fetal tissue, reproductive materials and stem cells. This applies to materials derived from living and deceased individuals.[2]

Human Participants are those individuals whose data, or responses to the interventions, stimuli or questions by the researcher, are relevant to answering the research question.

Human biological material include tissues, organs, blood, plasma, serum, DNA, RNA, proteins, cells, skin, hair, nail clippings, urine, saliva and other body fluids.

The following are *examples* of types of research involving human participants:

[2] TCPS 2, Article 2.1

- administering a drug, taking a blood sample, doing a test or performing a procedure, clinical, therapeutic or otherwise, upon a person, for research rather than treatment;
- asking people for information whether by telephone, letter, e-mail, internet, survey, questionnaire or face to face interview;
- using non-public records that contain identifying information previously gathered about anyone, either directly or indirectly;
- using identifiable information previously gathered about anyone, (e.g., secondary data analysis. See definition of "identifiable");
- observing anyone's responses or behaviour, either directly or indirectly.

All research involving living human participants (faculty, patients, staff, students or members of the community), all research involving tissues, fluids, biological fluids, embryos or fetuses, or cadaveric remains, all research in which access to human participants involves any records maintained by UBC or any of its affiliated Hospitals, and all research involving data collected from human participants which is to be carried out by faculty, staff or students of the University of British Columbia, shall be reviewed and approved in advance by the REB.

Please note that if your study is funded or supported by the U.S. Federal Government or subject to U.S. Food & Drug Administration oversight and regulations, somewhat different definitions apply. Research funded or supported by the U.S. government is any activity that either: 1) meets the HHS definition of "research" and involves "human participants" as defined by the HHS regulations 45CFR46 102(d)(f) or 2) meets the FDA definition of "clinical investigation" and involves "human participants" as defined by the FDA regulation 21CFR50.3(c)(g).

Article 4.3: Research Exempt from REB Review

Research situations that are exempt from the REB review include the following. Note that the opinion of the appropriate REB should be sought if there is any doubt about the applicability of any of the below criteria.

4.3.1: REB review is not required for research that relies *exclusively* on publicly available information that is legally accessible to the public and appropriately protected by law or is publicly accessible and there is no reasonable expectation of privacy.[3]

See the TCPS2 Article 2.2 for examples of and additional information pertaining to the concepts of publicly available information, legally accessible information, and reasonable expectation of privacy.

[3] TCPS, Article 2.2

4.3.2: REB review is not required for research involving the observation of people in public places where there is no intervention or interaction on the part of the researcher, the targeted individuals or groups have no reasonable expectation of privacy, and the dissemination of research results would not allow for the identification of individuals.[4]

4.3.3: REB review is not required for research that relies exclusively on secondary use of anonymous information or anonymous human biological materials, provided that the results do not generate identifiable information. Refer to CREB Guidance Notes for Tissue Collection and Banking

Secondary use refers to the use in research of information originally collected for a purpose other than the current research purpose.[5] When this information was collected anonymously**,** it can be used for research purposes without REB review. (See GN #5 for a discussion on secondary use of data and biological information where REB review is required). Examples of anonymous secondary use data may include datasets from a QA/QI survey or questionnaire where the participant's identity was never known.

Important Note: In accordance with Article 7 of UBC Policy #89 , genetic material shall not be considered anonymous unless a REB determines otherwise.

Article 4.4: Activities Not Requiring REB Review

4.4.1 Quality Assurance and Quality Improvement: Quality assurance and quality improvement (QA/QI) studies, program evaluation activities, and performance reviews, or testing within normal educational requirements, when used exclusively for assessment, management or improvement purposes, do not constitute research under the TCPS 2 and do not fall under the scope of REB review.[6] However, QA/QI projects that contain an element of research do require review and a determination of whether a project requires review is often difficult to make. Researchers who are unclear as to whether a project is solely QA/QI should complete the jointly created VCHRI-UBC tool designed to assist researchers to decide whether or not their project constitutes research requiring review or whether it is quality assurance and does not. Click here to

[4] TCPS, Article 2.3

[5] TCPS, Article 2.4

[6] TCPS, Article 2.5

access the tool. If after completion of the QA/QI tool you are still unsure as to whether or not your project constitutes research, please consult with the applicable REB administration.

An intention to publish QA/QI results does not necessarily mean that the project needs REB review. If an academic journal requires REB oversight or review for publication, consult with the appropriate UBC REB **prior** to commencing the project. Each REB has different administrative processes in this regard. Note that many journals do not directly ask for REB approval but rather whether the activity meets the ethical requirements of the country. In these cases, if the project was truly QA/QI then an appropriate answer would be the following: Yes, under article 2.5 of the TCPS2, the overarching ethical framework for research involving human participants in Canada, QA/QI activities are exempt from Research Ethics Board review.

4.4.2 Case Reports: Individual case reports do not meet the definition of research, they are considered to be a medical / educational activity. UBC's REBs expect that patients will be made aware that the author / investigator plans to create a report about their case which may be published. Case reports for REB purposes are a retrospective analysis of one or two clinical cases. If more than two cases are involved in the analytical activity, the activity will normally constitute "research" and be subject to review.

Individual Board practices vary, but generally, Investigators may apply to a UBC REB for an acknowledgement of the fact that a specific case report does not constitute research and does not require ethical review. Investigators should inform the applicable REB if the journal does not accept the REBs decision.

The opinion of the REB should be sought whenever there is any doubt about the applicability of the TCPS2 and UBC Policy #89 to a particular research project, particularly since no UBC REB will retroactively review research or any other proposed activity.

Guidance Note # 5
Proportionate Review and Minimal Risk Studies

Article 5.1: The Principle of Proportionate Review

UBC's REBs use a proportionate approach to review research involving human participants. They review applications in accordance with the level of risk that the proposed study poses to the research participants: the lower the level of risk, the lower the level of scrutiny; the higher the level of risk, the higher the level of scrutiny. In accordance with the TCPS2, full review by a fully convened REB is the default requirement, unless the REB has determined that the research is of minimal risk and that delegated review by one or more experienced reviewers appointed by the REB is appropriate. UBC's REBs have different procedures for delegated review, in accordance with individual Board policies. UBC REBs retain the right to decide to put any application submitted for minimal risk review forward for full board review.

UBC also strives to use a proportionate approach for multi-jurisdictional studies, i.e. research studies that require review and approval by more than one Canadian research ethics board as a result of the requirements of the TCPS2[7] or due to UBC's institutional policies. UBC is implementing a variety of processes and entering into agreements with other Canadian Institutions in an effort to avoid duplicate ethical reviews of research; in particular, duplication of review by a fully convened UBC REB in circumstances where a research study has previously been reviewed by a fully convened REB at another Canadian institution.

Article 5.2: Definition of Minimal Risk

Minimal risk is defined in the TCPS2 as follows: if potential participants can reasonably be expected to regard the probability and magnitude of possible harms implied by participation in the research to be no greater than those encountered by the participants in those aspects of their everyday life that relate to the research. UBC currently recognizes the following categories of clinical research as meeting the criteria for minimal risk and being eligible for delegated review.

[7] TCPS2, Article 2.1.

Note: If a study is funded or supported by the US Federal government or is subject to the US Food and Drug Administration regulations, ONLY studies that meet the U.S. definition of minimal risk AND that are listed in the U.S. Federal Register may be considered as qualifying for delegated / expedited review.

Article 5.3: Types of Minimal Risk Research Studies that may qualify for Delegated Review

5.3.1 Studies relying exclusively on secondary use of data, e.g. previously collected / existing clinical data, medical records, or other personal records

1. Studies using existing database / registries or linking information between databases]
2. Studies using previously collected data from existing documents, records or charts (generally "retrospective chart reviews"). Case reports involving 1 or 2 clinical cases do not require REB review (refer to Article 4.2), **however, reviewing more than 2 cases is considered research and requires REB review.**
3. Studies using *previously* collected clinical specimens where there is no current or future clinical need for the specimens

5.3.2 Studies intending to collect and analyze specific types of data

1. Studies that will involve only the collection 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. Studies that involve only the collection of placenta or amniotic fluid as a consequence of childbirth, or fetal tissue collected as a consequence of therapeutic abortion or miscarriage.
3. Studies that involve only the collection of blood samples by venipuncture, or a central line already present as part of clinical care that was installed as part of clinical care.
4. Studies that involve clinical data collected prospectively as part of clinical care.

5.3.3 Studies that involve only questionnaires or surveys

1. Studies that involve only questionnaires or surveys should generally be sent to the Behavioural Research Ethics Board, unless they are clinical in nature. If the questionnaires involve sensitive information from vulnerable populations or significant nuisance or inconvenience they will generally not qualify for delegated review.

5.3.4 Exercise Studies

1. Studies that will involve the collection of output data obtained as a result of moderate exercise undertaken by healthy volunteers
2. Studies that will involve the collection of output data obtained as a result of maximal exercise by healthy volunteers who are less than 40 years old. In these cases, the REB must receive and approve a safety protocol.

Note: Exercise in a patient population will generally be referred to the full board unless the exercise being observed is part of standard care.

5.3.5 Scans

1. Studies using data recorded using non-invasive procedures such as EEG, EKG, MRI, ultrasound or x-rays will generally meet the criteria for minimal risk.

Note: X-rays will not be expedited if the radiation exposure is in excess of 0.01 mSv (the approximately equivalent of one return transcontinental airline flight). For additional guidance on X-ray exposure and PET scans, please refer to GN #17.

5.3.6 Stem Cell Research

1. Stem cell research qualifies for delegated review with the exception of any research that concerns 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.
2. Research that uses permanent stable cell lines in laboratory research (i.e. in vitro) does not require ethical review.

5.3.7 Observational research on Standard Treatment(s)

1. Observational research on standard treatment(s) where the treatment(s) is (are) determined clinically and not assigned by research methodology (e.g. randomization).

Article 5.4: Types of Minimal Risk Studies That Require Full Board Review

The following types of studies **may** require full board review depending upon board specific policy.

1. Studies whose purpose it is to collect or use tissue/DNA for the purpose of creating a tissue/DNA bank or adding new sources of tissue to a tissue/DNA bank.
2. Studies whose purpose it is to collect or use tissue/DNA for genetic research related to determining susceptibility of acquiring a disease; or studies whose purpose it is to collect or use tissue/DNA for genetic research the results of which could be potentially harmful to participants if disclosed.
3. 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.
4. Minimal risk studies where a waiver of consent or alteration of the required elements of informed consent is being requested.

The following types of studies do ***not*** require full board review when a waiver of consent or an alteration of the required elements of informed consent is being requested.

a. retrospective chart reviews,
b. studies using data obtained from previously banked anonymized tissue that is not linked to other sources of data,
c. studies using data from provincially regulated databases/registries (e.g Medical Services Plan, BC Centre for Disease Control) or from disease specific registries with data collected from participants who have already consented to its use for the sort of research being done.
d. Prospective chart or medical record reviews where the data has been de-identified through an acceptable privacy guardian program or anonymized (i.e., there is no way to link the data to the participant), and there is no potential harm to the participant.
e. Prospective chart or medical record reviews where members of the research team are not in contact with participants during the data collection and where the researcher has provided an appropriate justification for why contacting the participants to obtain consent would be impracticable.

Important Note: For guidance pertaining to informed consent requirements for Minimal Risk studies please see Guidance Notes 13 and 14.

Guidance Note #6

Governing Principles and Criteria for Review and Approval

Article 6.1: Governing Principles

UBCs REBs are guided by the ethical principles regarding all research involving human participants as set forth in the Tri-Council Policy Statement 2: Ethical Conduct for Research Involving Humans (TCPS2). The TCPS2's core principles are based in the underlying value of respect for human dignity and are as follows:

- Respect for Persons
- Concern for Welfare
- Justice[8]

For a thorough discussion of the TCPS2's core principles, see Chapter 1 of the TCPS2**.**

Article 6.2: Minimal criteria for approval of research

In order for a research project to be approved, the REB must find that:

A. The Investigator (and his/her team) has the credentials to conduct the research.
B. There are no conflicts of interest which will compromise the safety or well-being of participants.
C. The research will generate knowledge that could lead to improvements in health or welfare.
D. The methodology must be scientifically sound and capable of answering the research question.
E. Risks to participants are minimized:
   (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk, and
   (ii) Whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.
F. Risks to participants are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, the REB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies those participants would receive even if not participating in the research).

[8] TCPS2, pg 7.

G. Selection of participants is equitable. In making this assessment, the REB will take into account the purposes of the research and the setting in which the research will be conducted and will be particularly cognizant of the special problems of research involving vulnerable circumstances, which have historically included children, elderly, prisoners, pregnant women, those with mental health issues, and those with diminished capacity for self-determination. .
H. Recruitment methods which respect the privacy of individual participants must be followed. Except under unusual circumstances, only members of the participant's/patient's healthcare team may approach the participant/patient regarding participation in the study.
I. Informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with and to the extent required by appropriate local, provincial or national guidelines or regulations.
J. Informed consent will be appropriately documented as required by local, provincial and federal regulations.
K. Any waiver or alteration of the informed process will be properly justified and documented.
L. Where appropriate, the research plan makes adequate provision for on-going monitoring of the data collected to ensure the safety of participants.
M. Where appropriate, there is adequate provision to protect the privacy of participants and to maintain the confidentiality of data.
N. When some or all of the participants, such as children, prisoners, elderly, pregnant women, those with mental health issues, and those with diminished capacity for self-determination, are likely to be vulnerable to coercion or undue influence or international sites are used, additional safeguards have been included in the study, and in the REB review process to protect the rights and welfare of these participants.
O. The resources required for successful completion of the study are committed (e.g., funding, space, personnel, etc.).

Article 6.3: Other Requirements

6.3.1: Other Criteria

UBC REBs may require verification of information submitted by an investigator. The need to verify any information will be determined by the REB at a convened meeting. The purpose of the verification will be to provide necessary protection to participants when deemed appropriate by the REB.

6.3.2: Cooperative Research Arrangements

The Vice-President Research & International may enter into ethics review agreements that provide for alternative models of ethical review and approval. Where necessary the Institutional FWA will be appropriately modified.

6.3.3 US Federally Funded Research

For research that is subject to the provisions of 45CFR 46 or 21CFR56, the researcher should ensure that they include the listed criteria in the applicable regulations, to the extent that they differ from or vary the criteria noted in 6.1 and 6.2 above

Guidance Note #7

REB Decisions and Term of Approval

Article 7.1: REB Determinations

The REB may make one of the four following determinations as a result of its review of research submitted for initial or continuing review: Approval, Proviso, Deferral, or Rejected.

A. Approval: The protocol and accompanying documents are approved as submitted. Research may begin as soon as the Principal Investigator receives a Certificate of Approval to proceed from the REB Chair or designate via the RISe system. Once the Certificate of Approval has been issued, the research may begin, provided that all other Institutional requirements have been met, and that approval to proceed is not withdrawn by the Vice-President Research, the Board of Governors or the President. The period of approval will commence on the day the study is approved by an action of the convened REB or the REB Chair or his/her designate and expire within one (1) year of the meeting date in which the study was approved.

B. Provisos: The Board may decide that a Protocol may be approved provided that certain conditions are met or required changes are made. A written explanation of the conditions and/or modifications is sent to the Investigator by the Chair of the REB through the REB administrative staff, via RISe. When appropriate the provisos will include written reasons for the required modifications. When the Investigator provides the Research Ethics Board with proof that the conditions have been met and the documents have been amended, (as confirmed by Research Ethics Administrative Staff or the REB Chair), the Certificate of Approval will be sent to the Investigator.

C. Deferral: The REB may defer a decision on any submitted research application if it does not have sufficient information to arrive at a determination, or if the REB requires extensive revisions to any part of the research. The application will be brought back before the full Board for consideration after the additional information or revisions are received.

D. Rejection: The REB may reject any protocol which does not meet its standards for ethical or scientific review and where revision is unlikely to enable the REB to reach a positive determination. No other UBC REB or Institutional official may approve a study which has been previously rejected by a UBC REB. A researcher may request reconsideration of a

decision made by the REB and has the right to appeal the REB's decision pursuant to the provisions of UBC Policy #89, Articles 29 and 30.

Article 7.2: Appeals

In accordance with the provisions of the TCPS2 and UBC Policy #89, the REB will reconsider its decision if it is requested to do so in writing. A researcher may submit additional information and/or attend an REB meeting in person to present information. If after the completion of the REBs reconsideration a researcher is still not satisfied with an REB decision a written appeal may be submitted to the Vice-President Research in accordance with the provisions of UBC Policy #89, Procedures, Article 6.

Article 7.3: Term of REB Approval

In accordance with the TCPS2, UBC Policy #89 and the US Federal Regulations, all research studies must be reviewed by the REB at least annually, if not more frequently. UBC's REBs will not issue certificates of approval for terms longer than one year. The determination of what constitutes a one year term varies slightly, depending upon whether or not the study was reviewed by the full board process, by a delegated review process or whether or not it is a renewal of a previously approved study. Full Board Approvals are effective one year from the meeting date at which the application was reviewed and approved. Delegated review approvals are effective one year from the date that the delegated reviewer issued his or her approval of the study and the certificate was issued. Annual renewal approvals will be effective one year from the date of issuing of the certificate of approval, unless the annual renewal was required to be reviewed by the Full Board. If the annual renewal is required to be reviewed and approved in a full board meeting, the one year period will be effective from the date of the meeting in which the renewal application was reviewed and approved.

Please note that approval of study amendments does not affect the expiry date of the original certificate of approval or annual renewal.

UBC's REBs may issue certificates of approval for terms of less than one year. The Board's determinations will be based upon the design of the study in question, and the perceived level of risk to participants.

Guidance Note #8

Required Information

Article 8.1: Requirement for a Research Protocol or Proposal

All of UBC's REBs mandate that a research protocol MUST be submitted for all research applications regardless of the type of study. These must be submitted as separate documents attached to box 9.1 of the RISe application form. Research proposals submitted to granting agencies may be used to meet this requirement. Protocols must include the following components although some variation is allowed in the discretion of the reviewing REB.

1. A background literature review (with accompanying references) that includes an explanation of the need/justification for the study.
2. The study purpose
3. Hypotheses
4. Objectives
5. Specification of endpoints/outcomes (if applicable)
6. Research design including statistical analysis plan (if applicable) and
7. Detailed research procedures

Important Note: The requirement for a research protocol is a UBC-wide REB policy. **Your application will be sent back, and approval delayed, if a protocol is not submitted with your application.** Ensure that ethical issues as implicated by the research design are addressed within in the protocol.

Article 8.2: Peer Review

For all research, UBCs REBs must be satisfied that the value and the scientific validity of the study warrant it being conducted such that study participant's time and effort regardless of level of risk of the study, is not being expended with no corresponding benefit to either society or to the participants.

Peer review (sometimes referred to as scholarly or scientific review) is generally understood by UBC's REBs as a review of the importance of the research question and the validity of the methodology. Traditions for scholarly review vary between disciplines or fields of research.

Minimal Risk Research: Clinical Research that poses no more than minimal risk may not require peer review. The REB must be satisfied about both the value and scientific validity of the study. Research in the humanities and social sciences that poses no more than minimal risk does not normally require peer review.[9]

More-than-minimal-risk research: Clinical Research posing more than minimal risk must have undergone some prior peer review, for example, review by a funding sponsor, or by some other peer review mechanism. UBC's REBs must be satisfied about both the value and the scientific validity of the study. If clinical research which is more than minimal risk has not undergone some level of peer review, the REB must be provided with an explanation concerning why such a review has not be undertaken/is not possible to obtain. UBC's REBs may conduct peer review of studies, if there is no other available mechanism and they have the appropriate scholarly expertise. If the REB does not have the appropriate scholarly expertise, it can establish an ad hoc peer review committee to conduct such a review. The ultimate responsibility to provide some level of review in more than minimal risk clinical studies, however, lies with the Principal Investigator.

Independent peer review: Scholarly review by an independent group of experts who are not affiliated with the institutional department conducting the research, or with the company sponsoring the clinical drug/device trial is preferable to peer review by experts who are not independent.

UBC's REBs Requirements: All more than minimal risk studies submitted to UBC REBs require a peer review or scholarly review, or an accepted argument about why one has not been obtained. Your application will be sent back to you, if you do not provide appropriate peer review information on page 4 of the RISe application. If you make an argument that one is not necessary and the REB does not agree, you may be asked to submit one as a condition of study approval.

Article 8.3: Other Required Information

Depending upon the nature of the study, the REB will require additional documentation to be submitted with the application for its review. Required documentation includes:

[9] TCPS, Article 2.7

- A draft informed consent form (unless waiver of consent is being requested)
- Where applicable, assent forms, tissue consent forms, letters of initial contact recruitment letters or brochures or flyers, telephone scripts, radio or TV ad scripts, and advertisements
- Where applicable all study materials including, questionnaires, interview scripts, patient diaries, patient wallet cards, tests or patient information or instruction pamphlets
- Where applicable, the Investigator's Brochure, proof of appropriate agency authority or regulatory approval such as Health Canada no objection letters, school board approvals, agreements or contracts with aboriginal communities, etc.

(See Application Guidance Notes on Required Regulatory Approvals and Registration of Clinical Trials)

Note that all additional documentation should be attached as separate documents, (e.g. not in the appendix of the protocol), to the appropriate box on page 9 of the RISe application. The certificate of approval populates from the boxes on page 9 of the application and failure to do this will result in a document not being listed on the certificate of approval.

Guidance Note #9

Inclusion and Exclusion Criteria

Article 9.1: Requirement for Equitable Selection of Participants

In accordance with the provisions of the TCPS2's principle of justice, the selection of participants must be equitable. In assessing this aspect of the research proposal, the REB will take into account the purposes of the research and the setting in which the research will be conducted and will be particularly cognizant of the special problems of research involving vulnerable circumstances. Vulnerability is often caused by limited capacity, or limited access to social goods, rights, opportunities and power. Individuals or groups in vulnerable circumstances have historically included children, women, prisoners, those with mental health issues and those with diminished capacity for self-determination. Special consideration will be given to the potential for inclusion of participants in vulnerable circumstances. The research proposal must never intentionally or inadvertently increase or exploit this vulnerability, nor should these types of populations be excluded from research, which is potentially beneficial to them as individuals or to the group that they represent.

Article 9.2: Participants who lack capacity to consent

Individuals who lack capacity to consent to participate in research shall not be inappropriately excluded from research.[10] However, the inclusion of participants who lack the capacity of consent must meet the requirements of the TCPS2, Article 4.6, which outlines the following criteria:

- the research can be addressed only with participants within the identified group; and
- the research does not expose the participants to more than minimal risk without the prospect of direct benefit for them; or
- where the research entails only minimal risk, it should at least have the prospect of providing benefits to the participants or to a group that is the focus of the research and to which the participants belong.

[10] TCPS2, Article 4.6

Important Note: U.S. Federal Regulations differ in their approach to allowing individuals who are legally incompetent to consent to participate in research that is more than minimal risk and not of direct benefit to them. UBC's REBs are governed by the TCPS2 and will not approve such research unless the TCPS2 criteria are met.

Article 9.3: Exclusion Criteria

Researchers must not exclude individuals from participation in research on the basis of attributes such as culture, language, religion, race, disability, sexual orientation, ethnicity, gender, reproductive capacity, or age unless there is a valid reason for the exclusion, which is explained to the REB in the application.[11] Individuals who are not proficient in the language used by UBC Researchers should not be automatically excluded from the opportunity to participate in the research. Researchers should consider appropriate measures to allow such individuals to participate.

See TCPS2, Chapter 4, Fairness and Equity in Research Participation, for further information on inclusion and exclusion criteria in research.

See AGN #5.4 for tips on filling in your application appropriately**.**

[11] TCPS2, Article 4.1 . Also, see TCPS2, Chapter 4, Section B, Inappropriate Exclusions, for further discussion, in particular article 4.3 on reproductive capacity.

Guidance Note #10

Recruitment A

Article 10.1: Recruitment

As stated in the TCPS2, "the approach to recruitment is an important element in assuring voluntariness. In particular, how, when and where participants are approached, and who recruits them are important elements in assuring (or undermining) voluntariness."[12] It is the researchers' responsibility to demonstrate to the REB that their research methodology adheres to the principle of voluntariness.

10.1.1: Information Required by the REB

The UBC REBs require information concerning how potential study participants are identified and initially contacted. In particular, this information should include a description of the following:

a. The source (i.e. its original purpose, if relevant) of the contact information, and how the researcher gained access to it;

b. Who will collect the contact information;

c. Who will make the initial contact with the prospective participant(s);

d. How the prospective participant will be initially contacted;

e. When the prospective participant will be initially contacted;

f. The relationship, if any, of the study team members to the participants (e.g. treating physician, teacher); and

g. All recruitment materials such as letters, advertisements, flyers, television or radio scripts, internet/e-mail messages

10.1.2: Ensuring Recruitment is Free from Undue Influence

The REB prefers that initial contact of prospective participants be by someone who is within their circle of clinical care (this is not a defined term, but for assistance in assessing its meaning, researchers may review a document prepared by the Ontario

[12] TCPS 2, Article 3.1.

Privacy Commissioner called "Circle of Care: Sharing of Information for Health Care Purposes". However, UBC's REBs also recommend that a treating physician/care provider, who is also an Investigator in a study, not be the person making the initial contact with the potential participants unless this is necessary due to the requirements of the study design or because of limited resources. It is preferable to have initial contact by someone who is not in a relationship of power and/or authority over the potential participants, due to the potential for undue influence (e.g. when the investigator is also providing medical care to a prospective participant or when there is a relationship of investigator-teacher and participant-student).

Whenever possible, when inviting potential participants a method free of the potential for undue influence should be used. These might include posting notices to invite volunteers from the entire group concerned, for example, in the waiting room of the medical clinic, or for the entire school rather than one particular class. The notices, in these cases, would ask the interested individual to contact the research team for further information. At that point, the PI and/or study team can follow-up to explain the study, answer questions, and take consent, if necessary.

10.1.3: Exclusion of Remuneration from Recruitment Materials

Recruitment materials that are used for the purpose of recruiting participants, such as letters, advertisements, flyers, radio or television scripts, or internet messages, should not include any information about the value of the remuneration for participation. This mitigates the possibility of inducing participants to accept potential risks for financial gain. Prospective participants may not realize that participation can only occur if they meet the conditions of the study's inclusion and exclusion criteria. The promise of remuneration in the recruitment materials may unintentionally mislead some prospective participants into thinking that they will automatically be enrolled into the study. There may be circumstances specific to the study where this general principle should not apply. In such cases, applicants should explain the rationale for needing to include remuneration information in the recruitment materials and the REB may allow an exception to the general rule.

10.1.4: Allowing Sufficient Time for Prospective Participants to Consider Participation

Recruitment should be done in such a way that prospective participants have adequate time between the time of initial contact to the actual consent phase to consider whether or not they wish to participate. For example, for non-minimal risk studies, prospective participants who are attending a clinic for elective or scheduled procedures should not normally be approached and asked to consent to participate in a study at that time. They may be invited to participate in the study and if interested, given the consent form, which they can return, should they decide to participate.

For studies involving more than minimal risk, twenty four hours is often considered an appropriate amount of time to give participants to think about participating in a study.

However, the time given to consent should be based on the nature of the study in question. The TCPS2 states that the time required for initial consent should "depend on such factors as the magnitude and probability of harms, the complexity of the information conveyed, and the setting where the information is given." [13]

10.1.5: Third Party Recruitment and Snowball Sampling

In most cases, the REB will not permit third party recruitment or snowball sampling techniques in clinical research. Research participants should not be asked to identify potential participants as this may put both the participant and the people they contact into a variety of uncomfortable situations, e.g. undue influence over the participant to recruit from the research team or over the recruited from the participant recruiter.

In some situations the REB may allow this type of recruitment when justified, e.g. research on a genetic condition that may run in a family. In these cases, the researcher should outline the process to reduce potential undue influence on the person being recruited. For example, the third party may distribute an introductory letter describing the study with details on how to contact the researcher, if they are interested in participating. Details of how third party recruitment will be accomplished and copies of any letters sent to either the third party or to the participant via the third party must be provided for review by the REB.

10.1.6: Initial Contact by Telephone

The UBC clinical REBs generally do not permit that researchers make initial contact with potential research participants by telephone unless they have previously consented to be contacted about participating in research. A letter of initial contact should be mailed to the potential participants that outlines when the telephone call will occur, by whom, and give participants the option to opt-out of receiving the telephone call, e.g. list a number they can call or email address they can write to request that they not be contacted further. See Article 10.3.1 below for specific inclusions for the letter of initial contact.

See Article 14.6.1 for information regarding initial contact by telephone in emergency situations.

Article 10.2: Examples of Recruitment Methods

10.2.1: Study Nurses or Research Coordinators

A study nurse or research co-ordinator who co-ordinates studies out of a specialized medical clinic can make direct initial contact with a prospective participant who is attending the clinic for patient care or for research purposes. This avoids any potential

[13] TCPS 2, Application Section of Article 3.2, p.31.

undue influence from a physician/researcher and eliminates the need to extract contact information from medical charts. The study nurse/co-ordinator must identify him/herself and explain his/her relationship to the clinic/medical department at the time of contact with the prospective participant.

10.2.2: Initial Contact by a Personal Care Physician who is also a Principal Investigator

Prospective participants under a Principal Investigator's care may also be contacted by mail, using an REB approved initial contact letter. The letter can be followed up by a telephone call after a reasonable length of time. The letter should stipulate who will make the follow-up phone call and when this will occur. While the PI should be the signatory on the letter of initial contact, it is preferable to have a study nurse/co-ordinator make the follow up telephone contact, for the reasons outlined in Article 10.1.2. See Article 10.3.1 below for a detailed list of what should be included in the letter of contact.

Important Note: Principal Investigator's should become involved in the consent process whenever explanations are required or questions are asked which the person making the initial contact is unable to provide.

10.2.3: Recruitment from School Populations

British Columbia's school districts vary in their requirements for conducting research involving teachers, staff or students. School Boards can be contacted concerning their specific policies. It is the responsibility of the investigator to know and comply with the local school board policy. Documentation of school approval should be provided to the REB. If required by local policy, the REB may issue their approval of the research, conditional upon school board approval, so that the Researcher may supply the UBC REB approval to the school board for its consideration.

10.2.4: Contact with Prospective Participants through Sponsors' Call Centres

Sometimes prospective participants provide their contact information to sponsors' call centres. This information is then sent to a local study centre for follow up. This practice is permissible; however, researchers must describe the procedure to the REB in the REB application, including providing the REB with the script used by the call centre to receive calls, and all screening scripts. Investigators contacting potential participants under these circumstances must provide the prospective participants with an explanation of how they obtained their contact information. The REB must also be provided with written information pertaining to the sponsors subsequent use and disposition of all personal information obtained by the sponsor in this manner.

Article 10.3: Recruitment Material

All recruitment material used must be approved by the REB in the form it will be used in before recruitment begins, e.g. a newspaper ad and a poster should be submitted separately even if the text is only slightly different. Recruitment materials should give potential participants a basic understanding of the research, what would be expected of them (including time commitment), and their potential eligibility for the study. Include directions for the potential participant to contact the research team, if they believe they are interested in the study. All recruitment material should be labeled with a version date. Do not include any payment or remuneration value for participation on the recruitment material; however, you may mention an honorarium, gift, or small token of appreciation etc. will be given (See Article 10.1.3 above)

10.3.1 Letter of Initial Contact

A letter of initial contact should be used when initially contacting any person whose contact information was obtained from medical records, databases, or registries as per GN #11.Note that although the PI should sign the letter, the REBs prefer that any follow-up phone call be done by a research nurse or coordinator. The letter of Initial contact should include the following:

a) The full study title and name of the PI.

b) Why the potential participant is being invited to take part in the study;

c) How the research team obtained their contact information. This should include the relationship of the researcher to the department/clinic/ unit where the information was housed (if applicable);

d) Brief overview of the study;

e) If a telephone call will occur, a statement of when it will occur and by who should be included. The participants should be given an option to opt-out of being further contacted and a process for opting out should be described;

f) The letter should be signed by the PI.

Guidance Note #11

Recruitment B: Use of Contact information obtained from Medical Records, Databases, and Registries

Article 11.1: Identifying and contacting Prospective Participants from Primary Health Care Provider Records

In some situations, the prospective participant's primary care (i.e. family doctor) physician (or other primary health care provider) holds the participant's personal contact information. In these situations, permission to release the contact information must be obtained from the participant by the primary care physician before the researcher can use the information for recruitment purposes. The primary care physician must either verbally ask the prospective participants' permission to release their names to the Investigator, or distribute an introductory letter describing the study to the prospective participants, with details on how to contact the Investigator if they are interested in participating. Private practice physicians fall under the provisions of the British Columbia Personal Information Act (PIPA). PIPA section 21SECTION 21 regulates the disclosure by physicians of personal information for research or statistical purposes.

Article 11.2: Identification and Initial Contact of Prospective Participants from Personal Data Obtained from Public Bodies

The BC Freedom of Information and Protection of Privacy Act (FOIPPA) applies to public sector institutions. These include some health care (e.g. hospitals), public (e.g. government Ministries, WCB), and educational (e.g. School boards, universities) bodies. Special rules apply to Health Ministry databases and to designated health information banks under Part 2, Division 1, Sections 3 and 4 of the E-Health (Personal Health Information Access and Protection of Privacy) Act.

Section 35 of FIOPPA (amended in March 2008) limits the disclosure of personal information collected by such bodies such that this information cannot be released by the public body for contact purposes, unless the research purpose, the use for contact and the manner of contact are approved by the Privacy Commissioner [Section 35(2)].Researchers should be aware that the REB must also review and approve the plan for initial contact and that it is within the REB's discretion to determine that such contact is not ethically acceptable notwithstanding the Privacy Commissioner's approval. [TCPS2 Article 5.6]

Article 11.3: Identification and Initial Contact of Prospective Participants from Information held by Ministry databases and by designated health information banks

Part 2, Division 3, Section14 of the E-Health Act limits the disclosure of personal information held by a Ministry database or by a designated health information bank. This information cannot be released by the bank or database for the purpose of contacting named individuals unless the request for disclosure has been approved by the Data Stewardship Committee created under the Act, **and** provided that the research purpose, the use for contact and the manner of contact are approved by the Privacy Commissioner (Part 2, Division 3, Section 14.2.1(c)).

Article 11.4: Information held by disease specific registries (that are not Ministry databases or designated health information banks)

Participants who have previously consented to be included in a registry for research purposes including consented to be contacted for future research studies, must first be contacted by mail using the contact information included in the registry. The contact letter must be approved by the REB and must explain to the prospective participant how their contact information was obtained, in addition to explaining the reason why they are being contacted. See Article 10.3.1, for specific inclusions for the letter of initial contact.

Article 11.5: Prospective Participants who are Patients of a Hospital Department / Unit or Specialized Medical Clinic

Ideally, prospective participants in clinical studies are approached for the purpose of recruitment into a research study by someone who is within their circle of clinical care (see "Circle of Care: Sharing of Information for Health Care Purposes" for further discussion). Investigators who are not acting as health care providers for prospective participants but who are attached to a hospital department/clinical/medical unit that offers clinical care and conducts research on the patient populations of the specific unit, may be able to obtain prospective participant names from the patient lists of their hospital's medical units for initial contact purposes, provided that the practice is agreed upon by the head of the unit, and the participating physicians. With REB approval, prospective participants may be contacted in writing with an explanation of how their personal contact information was obtained, and a description of the Investigator's relationship to the medical unit, department or clinic. See Article 10.3.1 for specific inclusions for the letter of initial contact.

Guidance Note #12

Risks and Benefits

Article 12.1: Risks and Benefits Related to Research:

The TCPS2 states that "the analysis, balance, and distribution of risks and potential benefits are critical to the ethics of research involving humans. The principle of Concern for Welfare imposes an ethical obligation to design, assess and conduct research in a way that protects participants from any unnecessary or avoidable risks. In their review, the REB should be concerned with an assessment that the potential research outcomes and potential benefits merit the risks."[14]

UBC's REBs are responsible for determining whether the research presents an ethically acceptable balance of risks and potential benefits. The decision to participate in approved research, however, is that of the potential participant, based upon his or her own appreciation of whether it serves their interests or welfare to do so. With this in mind, the general description of the research and the research risks and benefits should be disclosed in such a way as to avoid therapeutic misconception. It should be made abundantly clear that the primary purpose of the study is for research and not to produce therapeutic benefits for participants. Participants must clearly understand how a clinical trial design could potentially interfere with the healthcare options that are available to them in order to make an informed decision about participating.[15]

Article 12.2: Required Information

Information on risks in the application and the consent form must be consistent with the information provided in the protocol and the Investigator's Brochure/Product Monograph if applicable. If risk information/data is provided from another source, the source of the data should be identified in the application.

- **Minimize Harms:** Include an explanation of any strategies put in place to minimize and/or manage the harms for participants and others (e.g. reporting side effects, rescue medication, early withdrawal from the study)

[14] TCPS 2, Chapter 2, Balancing Risk and Potential Benefit, p. 24.

[15] See TCPS2, Chapter 11, Section A, *Therapeutic Misconception,* for further discussion, pg. 149.

- **Unknown Interactions With Other Drugs:** Disclose whether the research necessitates that certain medication or treatments not be administered during the study so that potential participants may evaluate this in the context of their current health.

- **Wash-Out Periods/ Requirements for Stopping Medication:** The consent form must explain the symptom/signs that participants could experience from being taken off any medication, and the potential impact on the participants health.

- **Risks to Pregnant Women and Others:** Potential harms to individuals other than the participant must be noted (e.g. unborn children, sexual partners, family members). The risk of any harms to pregnant women, to women who could become pregnant during the course of the research, or to men in relation to the reproductive capacity need to be disclosed in the consent form.

  Specific instructions concerning the prevention of pregnancy must be included in the consent form as follows:

  - Specific measures to take to prevent pregnancy (**note: Acceptable measures will vary depending upon the Research Ethics Board)**

  - How to notify the researcher if a participant suspects that she is pregnant; and

  - What would happen if a pregnancy should occur during the research.

For further information about standard disclosures around risks and discomforts, see the Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB, Section 10**.**

Article 12.3: Risks That May Require Special Counselling

Note that risks to the participants may also include social harms such as breach of confidentiality, social stigmatization, threats to reputation and psychological harm. Explain what strategies are in place to minimize and/or manage the risks for participants and other affected individuals.

It is the PI's responsibility to ensure that any harms such as psychological distress, arising from any knowledge that participants could obtain as a result of their participation in any type of research study, be eliminated if possible, and if elimination is not possible that such harms be minimized to the greatest extent possible.

In the course of research, there are tests that might have results that impact seriously on the research participant's health or have other serious implications (e.g. HIV, Hepatitis, some genetic tests, etc.) Appropriate pre- and post-test counselling services shall be made available to the participant and when appropriate, to his or her family.

Article 12.4: Genetic Testing

Some studies may provide results to participants which identify them as belonging to a high-risk group on the basis of the result (e.g. genetic status, biochemical test result). TCPS2 Article 13.2 specifies that in the case of research involving individuals, families, and groups in genetic research, the researchers must describe a plan to manage "the types of information that may be revealed through genetics research – and the implications of this information for participants and their biological relatives". TCPS2 Article 13.4 requires that "where researchers plan to share results of genetic research with participants, the research proposal should make genetic counselling available at that time, where appropriate." This will normally require making both pre- and post-testing counselling available. See Article 12.3 above.

In addition, some genetic testing may provide results to participants which identify them as belonging to a high-risk group on the basis of their genetic status. If this may be the case in the context of the specific study, the consent form must include a statement that informs participants that any knowledge gained from the research study that identifies the participants as belonging to a high-risk group, may reduce the ability of the participant to obtain health and/or life insurance.

Article 12.5: The Risk of Not Being Able to Receive Study Treatment Following Termination of the Study

Due to the possibility of not being able to continue on treatment after a study is completed, the following wording should be included in the consent form. See the UBC Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB, page 21:

You may not be able to receive the study treatment after your participation in the study is completed. There are several possible reasons for this, some of which include: The treatment may not turn out to be effective or safe. The treatment may not be approved for use in Canada. Your caregiver may not feel it is the best option for you. You may decide it is too expensive and insurance coverage may not be available. The treatment, even if approved in Canada, may not be available free of charge.

Article 12.6: Quantification of Risks to Research Participants

UBC's REBs require numeric (usually percentage) quantification of risks wherever possible. Quantify the foreseeable risks of harms (side effects) or inconveniences (discomfort to incapacity) to the participant associated with each procedure (including radiation risks from X-rays, therapy, test, interview or other aspect of the study. For specific guidance on X-Rays, please see GN #17.Quantification should include information about the seriousness and consequences of the different types of adverse events that have been observed, as well as the probability of these events occurring. Quantification of these harms should emphasize the **incremental** risk with the experimental intervention as compared to placebo or no treatment, wherever possible.

Percentage Quantification: Qualitative terms such as "rare", "common", "infrequent" are not acceptable unless quantitative ranges are explicitly attached to them. The use of symbols (e.g. ≥ or ≤) is not acceptable. Quantifiers such as "more than 5%" are similarly not acceptable because they do not adequately define the magnitude of the risk.

It is generally acceptable to provide a qualitative description of the risks associated with standard blood drawing (venipuncture). For example, the consent form should state that the side effects of blood draw include pain and/or discomfort, bruising, fainting and/or light-headedness, and the rare possibility of infection.

UBCs REBs prefer researchers to list risks in descending order of frequency and/or to group them according to category of risk (e.g. by magnitude, severity, organ system, etc.). For example:

- Very Common (50% or greater)
- Common (20% - 50%)
- Less Common (5% to 20%)
- Uncommon (2% to 5%)
- Rare (Less than 2%)

Where no percentages are available: Where no percentages are available, specific discussion about risks encountered in case series/case reports, preclinical studies or studies involving similar drugs or procedures are required. If absolutely no relevant data about harms of the experimental procedures is available (e.g. a Phase 1 trial), Investigators are required to make their **best effort** to honestly inform participants about possible risks of participating in the research, even if they cannot be quantified. This quantification can be in the form of "for thirty participants, five experienced a particular side effect". This information must always be included in the consent form.

Unanticipated side effects: The consent form must include an explanation that unanticipated side effects, including severe or irreversible ones, could occur if a novel combination of drugs is being tested, even if the individual drugs are not expected to have these side effects.

Article 12.7: Benefits

Research benefits can be direct, e.g. a health condition improves, or indirect, e.g. the research benefits a group in which the participant belongs. As stated in the TCPS2, "researchers should be sensitive to the expectations and opinions of participants regarding potential benefits of the research. " [16]The consent form and the application should specify the benefits to the prospective participants. If there are no direct benefits to the participants from participating in the research, this must be stated explicitly. If any specific therapeutic benefits cannot be assured, but may be hoped for by the participant, state explicitly that the participant may or may not benefit from participation in the study. For sample wordings around the benefits of participating in a research project, see the Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB, section 11**.**

[16] TCPS 2, Chapter 4, Equitable Distribution of Research Benefits, p. 53.

Guidance Note #13

Informed Consent: General Principles and Application

Free and informed consent lies at the heart of ethical research involving human participants. The Tri-Council Policy Statement 2 (TCPS 2) defines consent to mean "free, informed and ongoing."[17] Individuals are generally presumed to have the capacity to make free and informed decisions about participating in research when properly informed of the purpose of the research and its risks and benefits. As a general rule, informed consent should be sought from all research participants (see GN #13 and GN #14 for exceptions to this standard).

The REB must be provided with a clear description of who will approach a potential participant, who will obtain consent, and what is the relationship between the person obtaining consent and the participant. All consent documents and methods must be approved by the REB before a potential participant is consented to take part in the research project.

Article 13.1: General Principles of Informed Consent

13.1.1 Consent Shall be Given Voluntary [18]

Consent should be given voluntarily, free of undue influence or coercion. **Undue influence** may arise when a person in a position of authority or a person in a dependency relationship is involved in the consent process, e.g. employers and employees, physician and patient, or professor and student. **Coercion** is a more extreme form of undue influence and can result in harm or perceived harm, if a potential participant fails to participate (see GN 10 on recruitment to ensure these situations are avoided). In order to maintain voluntariness, participants are free to withdraw from a research project at any time and without providing a reason. They do not need to express their desire to withdraw in writing. If there are any circumstances where a participant's data cannot be withdrawn, these circumstances must be clearly disclosed in the consent form.

13.1.2 Consent Shall be Informed[19]

[17] TCPS 2 Chapter 2 p. 27

[18] TCPS 2, Article 3.1

Researchers are responsible to ensure that a potential participant or authorized third party is provided with full disclosure of the necessary information needed to make an informed decision. A list of required elements for informed consent can be found in Article 2.2 of the TCPS2.

13.1.3 Consent Shall be an Ongoing Process[20]

Consent is an ongoing process. It is the duty of the researcher to ensure that participants are provided with all information relevant to their ongoing consent to participate in the research. Researchers must respect any display of dissent on part of a research participant. Any changes to the consent form or other documents given to participants must be approved by the Research Ethics Board prior to circulation to participants. See Article 13.5.1 below for further information about ongoing consent and new research risks.

13.1.4 Material Incidental Findings in Individual Research Participants[21]

Incidental Findings can be defined as unanticipated discoveries made in the course of research but that are outside the scope of the research. **Material Incidental Findings** are those incidental findings that may impact the welfare of participants, e.g. health related, psychological or social. This includes perceived abnormalities found on clinical research scans and tests as well as unexpected psychological or social findings. In research where incidental findings are more likely, researchers should submit a plan to the REB explaining how they will deal with such findings. Researchers must disclose any material incidental findings discovered in the course of research

13.1.5 Consent Shall Precede Collection of, or Access to, Research Data[22]

Research shall begin only after the participants, or their authorized their parties, have provided their consent. Exceptions to this are discussed in GN #13 and GN #14.

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[19] TCPS 2, Article 3.2

[20] TCPS 2, Article 3.3, ICH-GCP 4.8.2

[21] TCPS 2, Article 3.4

[22] TCPS 2, Article 3.5

Article 13.2: Consent Documentation

As stated in the TCPS 2, Article 3.12, evidence of consent shall be contained either in a signed consent form or in documentation by the researcher of another appropriate means of consent. In most circumstances, the UBC clinical REBs require that informed consent be documented by the use of a written consent form approved by the REB and signed and personally dated by the participant or the participant's legally authorized representative. The investigator should allow the participant or the legally authorized representative adequate opportunity to read the consent document before it is signed and dated. A signed and dated copy of the document must be given to the person signing the form. See UBC REB SOP 703 for further discussion of the documentation of informed consent.

The written informed consent document should be in plain language understandable to the participants of the study, e.g. at a grade 7 level. See the Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB for reference.

Where consent is not documented in a signed consent form, researchers may use a range of consent procedures, including oral consent, study notes and other strategies, for documenting the consent process. Consent may also be demonstrated solely by the actions of the participant (e.g., through the return of a completed questionnaire). Where there are valid reasons for not recording consent in writing, the procedures used to seek consent must be documented and approved by the REB.[23]

Exception: For research that is funded or supported by the US federal government, a REB may only waive the requirement for a signed consent form for some or all participants in accordance with applicable US Federal regulations, see UBC REB SOP 703, Article 3.3.

13.2.1. Translated Consent Documents

Translated consent forms must be submitted to the REB accompanied by an English version of the same. The researcher should ask for the translated version to be independently reviewed for accuracy. A copy of the translated consent document must be submitted to the REB for approval along with a statement signed by the interpreter confirming that the translation is accurate, stating the name and version date of the

[23] TCPS 2, Article 3.12

document they translated and their qualifications. This may be submitted as an amendment after the REB has approved the English version. The participant will sign the translated consent.

Note that a translated consent document does not replace the requirement for a translator/interpreter to be present during the consent process and throughout study. When using a translator for communication between the research team and participants, the research team should use someone who has appropriate command of the language to ensure accurate communication.[24] See Article 5.2 of the TCPS2 for ways to mitigate potential loss of confidentiality when using a translator.

If a translator assisting in the consent process is using the English consent form, the consent form must include a signature, printed name of the translator, and the name of the language it was translated into, on the signature page of the consent form.

13.2.2 Use of Facsimile, Mail or E-mail to Document Informed Consent

The REB may approve a process that allows the informed consent document to be delivered by mail, facsimile or e-mail to the potential participant or the potential participant's legally authorized representative and to conduct the consent interview by telephone when the participant or the legally authorized representative can read the consent document as it is discussed. All other applicable conditions for documentation of informed consent must also be met when using this procedure.

13.2.3 Oral Presentation of Informed Consent Information

Oral presentation of informed consent information may be used in limited circumstances such as when the proposed participant is illiterate or blind. In such cases, special care needs to be taken that the participant and/or the legally authorized representative are provided with all the elements of consent orally. The REB also must review and approve a written summary of the information that will be presented orally. This summary must be signed by a witness and the person consenting. The signature of the witness is intended to attest to the fact, and to state, that what is included in the summary was actually said to the participant or legally authorized representative. It does not attest to the comprehension of the participant.

[24] TCPS 3.2

Article 13.3: Directions for Obtaining Consent

The person obtaining consent must be sufficiently familiar with the study, the disease being treated (if applicable), and the process of informed consent. This will usually be the investigator or a designated research assistant. Consent in most cases should be obtained in a face to face discussion with the potential participant and legal representative, if applicable.

Article 13.4: Documentation of study participation in Medical Record

When medically relevant to the safety of participants, the investigator should independently document the obtaining of informed consent in the medical record, noting the date, the participant's full understanding of the risks and benefits of enrollment, the voluntary nature of participation, and if required, a copy the consent form. If participation in a clinical research study or if it is the intention or a likely consequence of the research that test results, which might affect treatment decisions or have important implications (e.g. HIV tests, genetic tests), will become part of the participants' health record, this must be disclosed in the consent form.

Article 13.5: Standard Consent Methods and Additional Information

The following is standard UBC guidance around specific research situations regarding informed consent. Standard informed consent disclosures can be found in the Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB. If you are unable to find appropriate guidance for your research, contact the applicable Research Ethics Board administration.

13.5.1 New Information about Risk:

When previously unknown/undisclosed risks of research become available, researchers are required to inform all relevant participants and their legal representatives (if appropriate) of this information within an appropriate timeframe. The timeframe depends on the nature of the study and the consequences of the risk. This may involve the following:

a) Informing the participants(s) verbally of additional risks or changes in procedures and ensuring that the communication of this information is documented in the study notes;

b) Informing the participants in writing of the additional risks via an addendum or amendment to the consent form. Note that in situations where the new information may affect the participants' willingness to remain in a study, the

participant should be informed of these changes in writing, e.g. revised informed consent form or addendum;[25] and

c) Informing the participants who have completed their study treatment if the newly identified risks could still affect them (e.g. irreversible or delayed adverse effects).

Any new or revised information given orally or in writing, including changes to the consent form (or consent addenda), information letters, or telephone scripts must be submitted to the REB for approval before use.

13.5.2 Timing of Consent:

The UBC REBs consider a consent given by a participant to be effective upon the signing the consent form or the giving of oral consent. The REBs do not recognize consent given after the fact, unless this was pre-approved by the REB for specific types of research, e.g. research in emergency situations, see Article 14.2 and UBC REB SOP 502, Article 3.1. As per Article 10.1.4, for studies involving more than minimal risk, twenty four hours is often considered an appropriate amount of time to give participants to think about participating in a study. However, the time to consent should be based on the nature of the study and should be justified in the application.

13.5.3 Consent for Participation in a Sub study:

The consent form should outline any plans for a sub study and either indicate that a new consent form will be provided or provide check boxes so that potential participant can decide whether they also want to participate in the sub study. If participation in the sub study is not optional, this should be clearly disclosed in the consent form and a justification provided to the REB.

13.5.4 Consent for Participation in an Extension Study:

If a study protocol includes a provision/plan for an extension study, the initial study consent form should mention that the participant might be offered an opportunity to participate in another longer-term study after this initial study is finished.

An entirely separate informed consent process must be administered at the time of enrollment into the extension study, using a specific consent form dedicated to the

[25] ICH-GCP 4.8.2.

extension study. In most cases, extension study must be submitted as a new application referencing the initial study so that the REB can review the results of the main study, e.g. safety data, before approval.

13.5.5 Consent in Tissue Banking and Data Registries:

There are specific consent requirements for studies that involve the creation of or an addition to a tissue bank or data registry. See GN #16 for information about the consent process in these situations. Please also see the CREB Guidance for Tissue Collection and Banking. Note that for studies that involve tissue banking and/or requests to enter participants' information in a data registry, this should be optional unless it is being collected for purposes directly related and integral to the study at hand. A specific tissue banking or data registry consent form should be prepared and participants consented separately from the main study. If the study poses no direct benefit to participants, researchers may require consent to both the study and the tissue bank or registry as a condition of participating. This is ethically acceptable because the study is not using the incentive of direct benefit to induce participants to participate in an unrelated procedure or activity. Thus, there is no prospect of undue influence in recruiting participants.

13.5.6 Consent and Studies that use Photography, Video recording, and Audiotaping:

If there are any plans to use photography (including digital photographs), video or audio recordings in the research, who will have access to the recordings and the methods used to protect the participant's identity must be described in the consent form. The eventual fate of the records must also be disclosed (i.e. where and for how long they will be stored, if there are any plans for secondary uses of the recordings, and whether they will be destroyed). If there are plans to use these materials for any other purpose than the research outlined in the consent form (e.g. for teaching purposes) and participants could be identified, a separate consent form is required.

13.5.7 Human Genetic Research:

Studies involving genetics that have the potential to identify disease predisposition must disclose this in the consent form and give participants the opportunity to choose what type of information they wish to know about themselves. Genetic counseling should also be made available and discussed in the consent form.[26]

Article 13.6: Standard and Mandatory Consent Disclosures

[26] TCPS2, Article 13.3.

UBC's REBs mandate standard required disclosures with respect to the following topics. Refer to the Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB for detailed information and standard wordings.

13.6.1 Confidentiality:

See section 16 of the Consent Form Guide and Template and Article 16.2 on Privacy and Confidentiality for information on confidentiality and specific consent form disclosures. Any alterations to the required wordings must be justified to the REB.

13.6.2 Disclosure of Personal Identifiers on Data sent Off-site:

If there is planned disclosure of personal identifiers (e.g. names, date of birth, or initials) outside the local study site, or if such personal identifiers are used on study documents or any research-related information or are part of the unique identifier, this must be justified to the REB. See Section 16, page 19, of the Consent form Guide and Template for further information.

13.6.3 Data Transferred out of Canada:

Research data that is being sent outside of Canada must be approved by the REB and clearly disclosed in the consent form. See Section 16, page 19, of the Consent Form Guide and Template for further information on specific disclosure requirements.

13.6.4 Child Abuse and other Reportable Offences:

Some research may involve an increased possibility of reports of child abuse or other reportable offences. The Child, Family and Community Service Act of B.C. requires that anyone who has reason to believe that a child may be abused, neglected, or is for any other reason in need of protection, must report it to the Director or a designated social worker (Ministry of Children and Family Development). See Child, Family and Community Service Act, Article 14. The REB may require that a sentence be included in the consent form disclosing to participants that reports or allegations of abuse must be reported to the proper authorities.

In situations where there may be a breach of confidentiality, the researcher may state that a participant's "information may be disclosed if required by law."

13.6.5 Reportable Diseases:

Under the BC Health Act Communicable Disease Regulation, physicians/researchers are required to report some communicable diseases to provincial health authorities (e.g. Hepatitis B or C, Human Immune Virus (HIV), West Nile Virus, etc). If there is a possibility that a participant will be tested for one of the reportable diseases, this must be disclosed to the participants in the consent form. See Section 16, page 19, of the Consent Form Guide and Template for further information on specific disclosure requirements.

13.6.6 Primary Care Physician(s) and Specialist(s) Notification of Study Participation:

If notification of a participant's primary care physician or specialist is mandatory for the participation in a study, this must be disclosed in the consent form. If notification is optional, then a checkbox should be provided in the consent form. See Section 16, page 20, of the Consent Form Guide and Template.

13.6.7 Disclosure of Race and Ethnicity:

If applicable, collection of data on demographic features such as race/ethnicity, birthplace, gender, and sexual orientation must be justified in the ethics application and the reason for the collection explained to participants in the consent form. They must also be told that providing this information is voluntary. See Section 16, page 21, of the Consent Form Guide and Template.

13.6.8 Disclosure of Legal Rights:

The consent form should not contain language that causes or appears to cause the participant to waive their legal rights.[27] The participant should also not bear the cost of illness or injury arising from their participation in a research study. The Consent form should outline how potential injury or illness obtained as a result of participation in research will be covered. See Section 18, page 22, of the Consent Form Guide and Template for further information and required disclosures.

13.6.9 Receiving the Study Drug after Study Completion:

[27] ICH-GCP 4.8.4

For all studies that involve a study treatment that may not be accessible to participants after the study is finished for a variety of reasons, e.g. too expensive, not approved, not effective, this must be disclosed in the consent form. See Section 17, page 21, of the Consent Form Guide and Template.

Article 13.7: Informed Consent Form Administrative Requirements: UBC's REBs have administrative requirements for research consent forms in relation to the following topics. Refer to the Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB for detailed information and standard wordings.

13.7.1 Participants' Rights:

If research participants have concerns or complaints about their rights or experiences as research participants, they should contact the Research Subject Information Line in the UBC Office of Research Ethics by email at RSIL@ors.ubc.ca or phone at 604-822-8598 (Toll Free: 1-877-822-8598). This contact information should be outlined in the consent form making it clear that this line is not intended to answer questions about a participants' study treatment or to provide emergency medical care for a research related injury.

13.7.2 Required Signatures on the Consent Form:

The REB requires that the participant and the person obtaining consent sign and date the consent form. Except in special circumstances, e.g. where oral consent is necessary, the REBs do not require a witness signature on consent forms. Note that the Principal Investigator is responsible for ensuring the consent process is followed whether they conduct the process or not. For further information about required signatures, see section 23, page 26, of the Consent form Guide and Template.

13.7.3 Referencing the REB in the Consent Form:

The UBC REBs accept (but do not require) references in consent forms to the project having been reviewed and/or approved by the Research Ethics Board (REB). Appropriate references would be similar to the following: *This Board aims to help protect the rights of research participants.* Avoid using language that indicates that it is the role of REBs to ensure the well-being or safety of participants.

13.7.4 Use of Check Boxes in Consent Forms:

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

Exception to the above: Where a single consent form contains multiple optional sub-components, (e.g. tissue banking for genetic research) where participants 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 REB may require that *separate* consent forms fully describing a sub-component(s) of a project be developed in some cases.

13.7.5 Listing the Co-Investigators on the Consent Form:

The REBs prefers that all co-investigators, their institutional affiliation (i.e. use the local site in a multi-site trial) and appropriate titles be listed after the PI on the consent form. Where it is not practical to do so, the REBs accepts that only the PI (including their telephone number) be listed on the consent form. BCCA has separate requirements regarding listing co-investigators on the consent form. See the Consent Form Guide and Template, page 2, for further information.

Guidance Note #14

Departures from General Principles of Consent

This guidance note describes circumstances when some of the general principles discussed in GN #12 can be waived, altered, or temporarily suspended.

Article 14.1: Waiving Consent in Minimal Risk Research

The TCPS2, Article 3.7, states the REB may approve research without requiring that the researcher obtain the participant's consent where the REB is satisfied, and documents, that all of the following apply:

(a) the research involves no more than minimal risk to the participants;

(b) the lack of the participant's consent is unlikely to adversely affect the welfare of the participant;

(c) it is impossible or impracticable to carry out the research and to answer the research question properly, given the research design, if the prior consent of the participant is required;

(d) whenever possible and appropriate, after participation, or at a later time during the study, participants will be debriefed and provided with additional pertinent information in accordance with the TCPS 2, Articles 3.2 and 3.4, at which point they will have the opportunity to refuse consent in accordance with the TCPS 2, Article 3.1; and

(e) the research does not involve a therapeutic intervention, or other clinical or diagnostic interventions.[28]

It is the responsibility of the researcher to demonstrate that a particular research project fits into the above criteria. This should be done by listing each of the above criteria and an explanation as to why the research fits into it underneath. This may entered into the RISe application Box 6.6A..

Article 14.2: Waiver of Consent in Individual Medical Emergency Situations

[28] TCPS2, Article 3.7.

There are situations where an individual who requires urgent medical care is unable to provide consent for research due to loss of consciousness or capacity and the delay to seek authorized third party consent could seriously compromise that individual's health. In these cases and subject to all applicable legal and regulatory requirements, research involving medical emergencies may be conducted only if it addresses the emergency needs of the individuals involved, and then only in accordance with criteria established in advance of such research by the REB. **NOTE:** This section does not apply to publically declared emergencies, e.g. SARS. See TCPS2, Article 3.8 to read more about research conducted during publically declared emergencies.[29]

> As stated in the TCPS2, Article 3.8, the REB may allow research that involves medical emergencies to be carried out without the consent of participants, or of their authorized third party, if all of the following apply:
>
> (a) a serious threat to the prospective participant requires immediate intervention;
>
> (b) either no standard efficacious care exists or the research offers a realistic possibility of direct benefit to the participant in comparison with standard care;
>
> (c) either the risk is not greater than that involved in standard efficacious care, or it is clearly justified by the prospect for direct benefits to the participant;
>
> (d) the prospective participant is unconscious or lacks capacity to understand the risks, methods and purposes of the research project;
>
> (e) third party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so; and
>
> (f) no relevant prior directive by the participant is known to exist.
>
> When a previously incapacitated participant regains capacity, or when an authorized third party is found, consent shall be sought promptly for continuation in the project, and for subsequent examinations or tests related to the research project.[30]
>
> Research in emergency medicine must be reviewed by the REB, be restricted to the emergency needs of the participants, and be conducted under criteria designated by

[29] TCPS2, Article 3.8 (paragraph just above)

[30] Ibid, 3.8.

the REB. The above outlines the minimal conditions necessary for the REB to authorize a research without free and informed consent.

Article 14.3: Waiver of Consent and Secondary Use of Identifiable Information for Research Purposes

As stated in Chapter 5, Section D of the TCPS2, secondary use refers to the use in research of information originally collected for a purpose other than the current research purpose. Common examples are social science or health survey datasets that are collected for specific research or statistical purposes, but then re-used to answer other research questions. Information initially collected for program evaluation may be useful for subsequent research. Other examples include health care records, school records, biological specimens, vital statistics registries or unemployment records, all of which are originally created or collected for therapeutic, educational or administrative purposes, but which may be sought later for use in research. [31]

Researchers who have not obtained consent from participants for secondary use of **identifiable information** shall only use such information for these purposes if the REB is satisfied that the following TCPS2 (Article 5.5) requirements are met:

(a) identifiable information is essential to the research;

(b) the use of identifiable information 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;

(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; and

(f) the researchers have obtained any other necessary permission for secondary use of information for research purposes.

[31] TCPS, Chapter 5, Section D

The researcher must satisfy all of the above conditions for the REB to approve the research without requiring consent from the individuals to whom the information relates.[32] Researchers must ensure that they specifically address each of these requirements in the context of their application for waiver of consent by responding to each article individually.

For the purpose of these Guidance Notes, **identifiable information** is information that may reasonably be expected to identify an individual, alone or in combination with other available information. All research that involves the secondary use of identifiable information either must seek informed consent or request a waiver of informed consent using the above criteria. All research where the investigators only have access to de-identified information, but a link either does exist or did exist, must still submit for REB review; however, a request for waiver of consent is not required. Only secondary use of anonymous information, where information was collected anonymously, e.g. a link never existed, may qualify to be exempt from REB review as per Article 4.3.

Article 14.4: Secondary use of human biological Materials

Secondary use of biological material refers to the use in research of any material that was originally collected for a purpose outside of the current research purpose. Secondary use of biological material may include the use of materials left over from diagnostic examination or surgical procedures, or materials that were collected for an earlier project. Informed consent is required for the secondary use of identifiable human biological material unless the researcher can satisfy the REB that the criteria outlined in Article 14.3 of this Guidance Note are met. Note that secondary use of biological materials left over after diagnostic tests or surgery is only authorized for use when there is no further current or future clinical need for those materials. See the TCPS2 Chapter 12, Section C, for further discussion of consent and the secondary use of biological information.[33]

Article 14.5 Consent for contact for additional information after use of waived consent

In situations where a waiver of consent was granted by the REB or when a researcher wants to re-contact a former participant for further information without their explicit consent for re-contact, the researcher must provide the REB with a plan for making contact with the

[32] TCPS2 5.5

[33] TCPS2, Chapter 12, Section C.

participant. This plan must be approved by the REB before contact is made. The plan should include the following:

a) Demonstrate that the potential benefit of the follow-up contact clearly outweighs the risks to individuals;
b) Explain who will contact and invite the individuals to participate;
c) Describe the nature of the relationship of the above persons to the individuals.

The researchers must ensure that their method of contact complies with applicable privacy laws. The REBs prefer that the contact be made by the custodian of the original data set rather than the researcher.[34] The consent form should also explicitly state the process by which the waiver was authorized and indicate a contact who the potential participant can call or email, if they have further questions or concerns.

Article 14.6: Types of Research where a Consent Waiver or Alteration may be Appropriate

The following section provides examples where a waiver or alteration to the consent process may be appropriate.

14.6.1 Initial Contact by Telephone in Medical Emergencies

Research involving individual medical emergencies should follow TCPS2 Article 3.8, see Article 14.2 of this Guidance Note. However, if time allows, third party consent should be attempted before proceeding with a waiver of consent in an emergency situation. In these situations, the REBs allow a researcher to contact a legal representative or next of kin by telephone to give consent on behalf of the participant. This process should only be used when face-to-face consent with a legal representative or next of kin is not possible. The researcher should clearly describe for the REB the consent process that will be used ensuring to include the following: who will make initial contact and discuss the study over the phone, what consent form will be read over the phone, clarification that the participant will be given some time to decide, e.g. 30 minutes. A witness and the person reading the consent form should sign the original consent form. The time and date it was read, and the name of the participant must also be entered into the original consent form. The research team should obtain written consent when possible from the legal representative (e.g., by fax or e-mailing a scanned and signed form) and full informed consent from the participant when they are able.

[34] TCPS 5.6.

14.6.2 Research Involving Deception

Although clinical research involving deception is rare, clinical research that does involve deception requires justification of the deception by meeting all the requirements of TCPS2 Article 3.7 (See Article 14.1 of this Guidance Note). A simple test for possible deception is to ask yourself: "Is there any information in the procedures section of the ethics application that I would not be willing to tell the participant in the study prior to their participation?" If the answer to this is yes, then deception is involved. This deception information, and the rationale behind its exclusion from the initial consent form, must be provided to the participants in a debriefing after participation. Participants must also be able to indicate their consent or their refusal to include their information in the study at the end of the project, following the debriefing process.

14.6.3 Studies involving Questionnaires Only

Where a study involves the completion of a de-identified or anonymous questionnaire the return of a completed questionnaire may be taken as evidence of consent. The researcher should prepare an introductory letter/consent form and it must state the following or the like: *If you wish to participate in this research study and are comfortable with the procedures described in this letter/form, please complete the attached questionnaire and email/return it back to us.*

14.6.4 Chart Reviews

Clinical chart data or medical records used in research is considered secondary use of data. Informed consent or a clear argument for waiver of consent is required for collecting prospective and retrospective clinical data. See Article 5.5 of the TCPS2 and 14.3 of this Guidance Note for further information.

Chart reviews that involve the use of retrospective data only, generally fulfill the TCPS2, Article 5.5, criteria for waiver of consent for the use of secondary use of data in research. However, the request for waiver should still be outlined on page 6 of the REB application. Note that for the purposes of UBC REB review, retrospective data collection can only include data that is dated before the date of ethics approval. Any data that is

collected on an ongoing basis is considered prospective data collection and consent is generally required.

Guidance Note #15

Capacity to Consent and Research Involving Participants with Diminished, Diminishing, or Developing Capacity

The following sections deal with research involving participants with diminished, diminishing, or developing capacity to consent. It discusses determining capacity, situations where research is appropriate in populations with developing, diminished or diminishing capacity, including research with children, and lastly provides a framework for how to obtain consent and assent in these situations.

Article 15.1: Determining Capacity to Consent

Capacity is the ability of prospective or actual participants to understand relevant information presented (e.g. purpose of the research, foreseeable risks, and potential benefits), and to appreciate the potential consequences of any decision they make based upon this information.[35] The TCPS2 states that a participant may have developing or diminished capacity, i.e. a minor or person with a cognitive impairment, but still be able to decide whether to participate in certain types of research.[36] If a potential research participant has the capacity to consent, consent must be sought from them before research with them commences. If a person does not have the capacity to consent, they should still be involved in the consent process where possible and appropriate and given the opportunity to assent. If a person who lacks the capacity to consent declines to participate in research, his or her dissent must be respected and the person may not be included in the research, see Article 15.5 for further discussion on assent and dissent.

Capacity to consent to research is not a static determination; it may vary over time, and upon the complexity and circumstances of the decision being made. It is the responsibility of the Principal Investigator (PI) to determine and monitor participants' capacity to consent and to describe this to the REB in the context of the proposed study.

[35] TCPS 2, Chapter 3, C.

[36] Ibid.

Article 15.1.1 Capacity in those with cognitive impairments and diminishing or fluctuating capacity

Researchers should describe the population with whom they are doing research, and how they will assess capacity. This may include cognitive tests designed for determining a persons' capacity, e.g. the mini mental. The application should outline how the PI and study team will continue to monitor a participant's consent to participate when their capacity is diminishing or fluctuating. This should include details of obtaining consent from a third party, in the event that the participant can no longer consent to participate in the research. See Article 15.5.1 below for further information. If a participant regains capacity, the researcher must obtain their consent to continue to participate in the research. The REB may require that Investigators re-consent participants after taking into account the study's anticipated length and the condition of the individuals to be included (e.g., participants with progressive neurological disorders). Researchers are encouraged to contact a UBC REB for advice on specific situations involving people with fluctuating or diminishing capacity to consent.

Article 15.1.2 Capacity in those under the age of majority

The legal age of majority in BC is 19. However, depending on the nature of the research, a participant may have the capacity to consent well before the age of majority. BC law does not specifically prevent a person under the age of majority from consenting to participate in research. The common law has two well accepted doctrines that are applicable to the consent of minors. The first is the "emancipated minor" doctrine, and the second is the "mature minor" doctrine.

The emancipated minor doctrine, which is commonly applied by UBC's REBs, provides that persons under the age of majority who are "emancipated" in the sense of living on their own, earning their own income, etc. are generally capable of consent, because they are "emancipated from parental control and guidance."

The mature minor doctrine is a common law rule that takes the varying abilities of young people into account, and recognizes that some minors are able to make decisions for themselves. Generally, at common law, if a minor has reached a level of intellectual and emotional maturity such that he or she is capable of understanding and appreciating the nature and consequences of a particular treatment / decision, together

with its alternatives they can be considered capable of consenting. Put another way, if it can be determined that a minor in fact understands the proposed interventions, can properly weigh the risks and benefits of various procedures, understands other courses of action and their implications, and it is not prohibited from consenting by legislation, a minor may give a legally valid consent.

There is some debate concerning whether the mature minor doctrine applies in instances where treatment is not beneficial or therapeutic, but increasingly the "rights of minors" to decide are being recognized, except in the most extreme cases, e.g. life and death situations.

The ability to consent to research is not based upon on a participants age or whether they have reached the age of majority. In accordance with the TCPS2 and in keeping with Article 15.1 above, capacity to consent to research is premised upon an individual's ability to understand the nature of the research and the consequences of participation in the research project. The Panel on Research Ethics (PRE) stresses that no two research studies or research participants are the same. Therefore, the researcher plays an important role in determining whether a particular research participant is capable of consenting on their own behalf or whether an authorized third party should be used. [37] Within the same research project, there may be some minors who are capable of consenting and others who are not. As per Article 15.1 above, the researcher should describe to the REB how the study team will determine capacity to consent to the research for those proposed participants who are under the age of majority. The PRE advises that factors to consider in making the decision to seek consent from children should include the following: the level of risk the research may pose to participants, provincial legislation and other applicable legal and regulatory requirements related to legal age of consent, and the characteristics of the intended research participants.[38]

[37] Panel on Research Ethics: http://www.pre.ethics.gc.ca/eng/policy-politique/interpretations/consent-consentement/

[38] Ibid

Article 15.2: Conditions for Research with People lacking in Capacity to Consent

Research involving individuals who lack the capacity, either permanently or temporarily, to decide for themselves whether to participate, must meet at a minimum the following conditions in order to be considered for REB approval:

a) the researcher involves participants who lack the capacity to consent on their own behalf to the greatest extent possible in the decision-making process;
b) the researcher seeks and maintains consent from authorized third parties in accordance with the best interests of the persons concerned;
c) the authorized third party is not the researcher or any other member of the research team;
d) the researcher demonstrates that the research is being carried out for the participant's direct benefit, or for the benefit of other persons in the same category. If the research does not have the potential for direct benefit to the participant but only for the benefit of the other persons in the same category, the researcher shall demonstrate that the research will expose the participant to only a minimal risk and minimal burden, and demonstrate how the participant's welfare will be protected throughout the participation in research; and
e) when authorization for participation was granted by an authorized third party, and a participant acquires or regains capacity during the course of the research, the researcher shall promptly seek the participant's consent as a condition of continuing participation. [39]

Article 15.3: Who can be an Authorized Third Party and Obtaining Third Party Consent

An **authorized third party** is any person with the necessary legal authority to make decisions on behalf of a prospective participant who lacks the capacity to consent to participate, or to continue to participate, in a particular research project. This person should not be part of the research team and should adequately know the person whom they are representing to take into account any previously expressed opinions regarding participating in research. Family members and friends may also provide information to the authorized third party about the interests and previous wishes of prospective participants.

When an authorized third party is being used to consent on behalf of a person with diminished or developing capacity, the Consent Form Guide for UBC Clinical REBs and Fraser Health

[39] TCPS2 3.9

Authority REB should be used to develop the consent form and it should be amended to be clear that the third party is consenting on behalf of the research participant. The following paragraph or the like is required to appear in the consent form in cases where the participant assents to participate in the research:

The parent(s)/guardian(s)/authorized third party and the investigator are satisfied that the information contained in this consent form was explained to the child/potential participant to the extent that he/she is able to understand it, that all questions have been answered, and that the child/potential participant assents to participating in the research.

Inclusion of this statement in the consent form places the obligation on the authorized third party, who is providing consent, and on the investigator to ensure that the participant/child assents and understands the information in the consent form to the extent that he/she is able.

A separate assent document with wording aimed at the level of the potential participant may also be appropriate and is not precluded by the addition of this statement to the consent form. See Article 15.6 below**.**

Article 15.4: Research Directives

Where individuals have signed a research directive indicating their preferences about future participation in research in the event that they lose capacity or upon death, researchers and authorized third parties should be guided by these directives during the consent process.[40] If a person who has signed a research directive retains sufficient capacity to assent or dissent to the research, and they decline to participate, their dissent must be respected.

Article 15.5: Assent

Where an authorized third party has consented on behalf of an individual who lacks legal capacity, but that individual has some ability to understand the significance of the research, the researcher should determine the wishes of that individual with respect to participation. If this person "assents" to the research, they are agreeing with or concurring with the consent of their authorized third party. While the individuals assent would not be sufficient to permit them to

[40] TCPS2 3.11

participate in the absence of consent by an authorized third party, their expression of dissent or signs suggesting they do not wish to participate must be respected and precludes their participation. Those who may be capable of assent or dissent include:

a) those whose capacity is in the process of development, such as children whose capacity for judgment and self-direction is maturing;
b) those who once were capable of making an autonomous decision regarding consent but whose capacity is diminishing or fluctuating; and
c) those whose capacity remains only partially developed, such as those living with permanent cognitive impairment.[41]

UBC's REBs do not consider lack of assent or dissent to be equivalent to refusal to participate. Caution and special care should, however, be taken in these circumstances. The research must fit all of the criteria outlined in Article 15.2 and the third party decision maker must take into account any previous preferences regarding participation in research expressed by the potential research participant. The researcher should document the lack of assent or dissent in the research record. The researcher must respect any expressions or displays of dissent during participation in the research.

Article 15.5.1 Obtaining Assent from a Research Participant with Third Party Consent

When a third party is used for consent of a person who lacks capacity, the researcher still must determine the willingness of the prospective participant to take part in the research. This is generally done through a face-to-face interview with the prospective participant and the principal investigator. This interview must convey the main information contained in the consent form using concepts and terms that are developmentally and cognitively appropriate. If the prospective participant is able to read, an assent form should be prepared in a language that is appropriate to the participant. **Note**: For studies starting after Sept. 2012, the CREB no longer accepts an assent statement attached at the end of a consent form, but rather all participants who are capable of assenting should sign a separate form labeled as such. This may be similar to the main consent form, if the person is capable of reading the language in the main consent, but should be labeled as an assent form. The following elements should be included in the assent form:

[41] TCPS2 3.10

a) a description of the purpose, procedures and the potential risks, discomforts, and hoped for benefits of participation, including possible benefits to others. The CREB recognizes that it will often be appropriate to give this information summarily and with less precision than is normally found in a consent form. Nevertheless, the information should not be so scant that a participant is surprised by aspects or consequences of their participation;
b) a statement of the amount of time that participation in the study will take;
c) a statement that the participant's confidentiality will be respected, e.g. that the participant's involvement will be kept private;
d) a statement that participation is voluntary, that the participant may refuse to participate at any time without giving reasons, e.g. no one connected with the study will be angry if a decision to leave the study is made after giving assent, and that all other health care will remain available.
e) statements that prospective participant has had the opportunity to ask questions, is encouraged to discuss his or her participation with relatives or friends, and that all questions have been answered.
f) a statement that questions are encourages and may be asked at any time.

The assent form should be as brief as reasonably possible, e.g. for children under 12 it should not exceed 2 pages. Merely technical information, such as the name of the sponsor, disclosure of an investigator's financial interest, advice that legal rights are not limited by participating etc. can typically be omitted. The participant must receive a copy of the assent form and have had adequate time to review it and to discuss it with relatives or friends and the principal investigator (or delegate) prior to assenting.

15.5.2 Preparing Assent Forms for Younger Children (7-13)

In addition to the above, when preparing assent forms for children it is especially important to convey information that is sensitive to their perspectives on the procedures, risks, discomforts, and inconveniences that they will encounter. For example, it may be appropriate to explain to children what they will experience simply by being in a hospital (for example, that they will be in a room with other children, that they will have to spend most of their time in a hospital bed and will not be able to get up and walk around without immediate supervision or that they will be able to walk around unsupervised, that their parents will not be able to be with them all the time, that they will spend a certain number of nights away from home, that they will be

looked after by nurses and doctors, etc). Also, it will typically be appropriate to describe how the research procedures will change how they feel or look (for example, that a medication will make them dizzy or itchy, or that they will be connected by tubes to a machine, or that they will have a scar and what it will look like). For an example of a template suitable for children click here.

15.5.3 Assent in Children Younger than 7

Children who are under 7 years old and who are capable of assent will not normally be capable of reviewing an assent form. Investigators should follow the procedures as per Article 15.6. Any dissent from the child must be respected.

Article 15.6: Informing and Obtaining agreement of Parents of Consenting Children

When a child under the age of majority is deemed to have the capacity to consent, they can consent for themselves, unless there is a legislative prohibition, which restricts their ability to consent in particular circumstances. In BC, there is no legislation that has been interpreted as restricting children with capacity to consent, from consenting to research.

However, in some situations parental agreement may be appropriate or necessary. For example, the research may be taking place in institutions that have specific requirements about research involving children or it may be sponsored by a company that also has requirements in this regard. In these cases, a parental consent form as well as a child's consent form may be necessary. For example, the Vancouver School Board requires parental consent for all research that is taking place in its schools. In these situations, researchers should seek consent from the capable child and consent from the parents, using separate forms. Both parties must consent before the research can take place. If the child consents and the parent does not, the child cannot participate in the research despite being fully able to consent. This is not UBC's REBs policy, rather it is due to the school board's requirements. In order to be able to conduct research within the Vancouver School Board, their requirements must be complied with. The same is true for sponsored studies where adult / parental consent is a requirement of the Sponsor.

In the same way that there are clearly examples of cases where it would be inappropriate or possibly even harmful to inform the parents of children capable of consenting to certain

research about their child's participation, (e.g. some kinds of research concerning abortion or other sensitive subjects) there may be other instances where it would be appropriate or courteous to obtain the agreement of a capable child's parents, or at least to ensure that they are informed that the research is taking place. Researchers should consider the specific nature and context of their research, and determine what they deem to be appropriate. UBC's REBs will make the final determination as to what they deem to be necessary in the context of the research that they are reviewing.

Guidance Note #16

Creation of Research Databases and Registries

Research Databases and Registries

This guidance note applies to research databases and registries, including databases for general research purposes and databases for multiple research uses over an extended period of time. It regulates the creation, maintenance, and use of repositories that collect and store information about humans specifically for use in subsequent research. The information may include personally identifying information, clinical files, clinical test results, x-rays, MRIs, information about race, age, or place of origin, etc., that is collected retrospectively or prospectively. This guidance note does not apply to databases and registries that are created specifically for clinical/health purposes.

Article 16.1: Informing Potential Participants and the REB

The information described below must be conveyed in the consent form and in the Application for Ethical Review in ways that will be meaningful to prospective participants and the REB:

i) The type(s) of data to be collected and the period over which they will be collected (which in this guideline includes identifying data, such as names, initials, telephone numbers, addresses, personal health numbers, etc.);

ii) The purpose(s) for which the data will be used;

iii) The limits on the use, disclosure, and retention of data, including descriptions of access by other researchers, any planned linkages to other databases, and types of studies to be conducted;

iv) The entity or person(s) who have custodianship of the data and the address of the database or registry;

v) The measures in place for protecting the security of the data and participant confidentiality, including a description of the de-identification or coding of the data and of what steps will be taken to ensure the security of the database (e.g., password protections, data encryption, secure rooms, etc.);

vi) A description of who will have access to identifying data, the nature of that information, and who will have a key linking coded data to identifiable participants;

vii) A description of any identifying data, or linked or coded data, or data that is fully de-linked and anonymised, that will be sent outside Canada, and to whom it will be sent (e.g. individuals, organizations, regulatory agencies), and where it will be stored (provide local address and country);

viii) The risks associated with possible disclosure of identifying data, including non-physical risks associated with accidental disclosure of genetic or other information that could result in discrimination by employers, insurance providers, or others;

ix) A description of any commercial uses for which the data may be used, including any disclaimers about participant remuneration;

x) Any foreseeable circumstances where disclosure of identifying data is required by law (e.g., for reportable diseases or child abuse [LINK]);

xi) Any anticipated secondary uses of identifying data from the research, and whether participant consent will subsequently be sought for such uses;

xii) Any anticipated linkage of the data gathered in research with other data about participants (whether those data are contained in public or personal records);

xiii) Any modes of observation (e.g., photographs or videos) or access to information (e.g., sound recordings) in the research that allow identification of particular participants (see Article 13.5.6);

xiv) Any access participants have to the data and rights to amend or withdraw data or to withdraw permission to obtain data, including a description of who to contact for these purposes (requests to withdraw permission to obtain data must not be required in writing);

xv) A description of how long the data will be retained and whether identifying data will be destroyed or returned to the participant.

Article 16.2 Further Requirements for Information Disclosure to the REB

In addition to the information described above, researchers must satisfy the REB of the following in the Application for Ethical Review:

i) A full description is provided of the data stewardship processes for overseeing the management and use of the data, including the main rules governing use of the database, the process by which access requests will be reviewed, and the organization to whom the researcher is accountable for the proper management of the data;

ii) Data is being obtained from research participants only insofar as it is necessary for the research.

iii) Specific and appropriate justification has been provided for collection and use of identifying data, including any use of identifying data on case report forms or other database or registry documents (e.g., names, initials, telephone numbers, addresses, personal health numbers, etc.).

iv) De-identification of data will occur as quickly as possible.

v) Access to identifying data and to the key linking identifying data to de-identified data has been limited to the minimum number of properly trained personnel that is reasonable in the circumstances.

vi) Database personnel have appropriate training in, and comply with, security and privacy safeguards.

vii) Identifying data will not be retained for longer than is necessary to fulfill research purposes (at which time they should be destroyed or returned to the participant– see A. xvi above). [See AGN 8.6 and Food and Drug Act Regulations: Division 5 Section C.05.012 (4) regarding retention of records.]

Changes to 16.1 or 16.2 above require REB approval through the normal study amendment process.

The CREB may require additional information in the consent form or in the Application for Ethical Review.

Article 16.3: Definitions

Identifying/Identifiable Data: information that can directly or indirectly identify an individual. This includes information: a) that contains an individual's personally identifying information (e.g., name, initials, address, telephone number, date of birth, personal health numbers, full face photographic images, etc.), or b) for which there is a reasonable basis to believe the information could be used to identify an individual.

De-identified Data: information where an individual's identifying information has been removed, and where there is no reasonable basis to believe that the information could be used to identify an individual. De-identified data may nevertheless be coded (e.g. via a confidential master list created by the researcher) so that the information can be linked to the individual and his/her clinical or other records. See AGN 8.4 for further directions on coding that is consistent with de-identification of data.

Anonymous/anonymised data: this refers to information that cannot be linked back to an individual either directly or indirectly (i.e., the information contains no identifying information, no master list or coding remains anywhere linking a participant to the information, and there is no reasonable basis to believe that the information could be used to identify a participant).

Guidance Note #17

Special Categories of Research: Research Involving Radiation Exposure

(Note: this Guidance Note is in Draft Form, May, 2012)

Article 17.1: Research Involving Radiation Exposure

UBC's REBs make case-by-case judgments about the merits of research in light of the risks posed. As radiation exposure escalates, expectations of risk minimization and prospect of direct benefit will proportionally escalate. This guidance focuses on improving communication with research participants about radiation risk.

When using radiation or radioactive materials in human participants, the study should be designed to use minimum radiation doses following prevailing medical radiation exposure guidance, and those that are as low as reasonably achievable (the "ALARA" principle).

Radiation exposure includes the dose from all radionuclide procedures and all diagnostic radiology procedures related to the research study, together with doses from other research studies in which the participant may be participating or has participated in previously. Repeated use of the same volunteers for different projects involving radiation exposure is discouraged. Similarly, it may be inappropriate to involve participants with substantial prior radiation exposure. UBC's REBs understand that the risk of exposure to radiation is cumulative over a lifetime.

While radiation is categorized by the FDA as a known carcinogen, considerations pertaining to informing participants of radiation risks need to be tailored to the particular circumstances of the study population. For example, communication of risk to cancer patients who may be participating in studies that involve exposure to radiation would be quite different than communication of risk to adults without cancer. Similarly, risks to adults over 50 are somewhat lower, and risks to children are higher, due to their heightened sensitivity.

Article 17.2: Assessment/ Categorization of Radiation Risk

UBC's REBs base their understanding of the risks of radiation on the European Commission document noted below.

"Radiation protection 99, Guidance on Medical Exposures in Medical and Biomedical Research, 1998"
http://ec.europa.eu/energy/nuclear/radioprotection/publication/doc/099_en.pdf

The European Guidance describes the following primary categories of radiation risk:

> **Category 1:** Effective doses less than 0.1 mSv (adults)
> This category involves a risk (total detriment from the radiation exposure for normal participants of less than one in a million.
>
> **Category 2a:** Effective dose range 0.1 – 1 mSv (adults)
> This category involves risks of the order of one in a hundred thousand.
>
> **Category 2b:** Effective dose range 1 – 10 mSv (adults)
> This category involves risks to the irradiated individual of the order of one in ten thousand.
>
> **Category 3:** Effective doses greater than >10 mSv (adults)
> Here the risks to the irradiated individual are estimated at greater than one in a thousand.

The risks referenced in the categories, are "lifetime risk of death [from cancer] due to hematologic or solid organ malignancy".

The categories noted apply to healthy adults (those without cancer) under 50 years of age. The dose figures may be increased by a factor of 5 – 10 for individuals over 50. In the event that approval is being sought for research on children, the corresponding dose figures should be reduced by a factor of 2 or 3.

Article 17.3: Informing / Disclosing risks of radiation to research participants

UBC's REBs (with the exception of the BC Cancer REB) recommend that the following principles be adhered to in all study-related communications about the risk of radiation exposure:

1. State the effective dose (or dose range) in mSv.

   The conversion factor between the mSv and Radiation Equivalent Man (REM) units is 10mSv=1 rem.

2. Describe the exposure in terms of common life events, such as:

Chest radiograph	0.02 mSv[42]
Natural Background radiation	2.4 mSv / year[43]

A guide to the exposure associated with various other procedures is available at http://www.radiologyinfo.org/en/safety/index.cfm?pg=sfty_xray#3

3. Describe the risk in absolute based on the categories and age adjustments in section 20.1.2. and disclose that the risk being referred to is "your lifetime risk of dying from cancer".
   For example, the additional risk of fatal cancer from a single 20 mSv exposure in a person <50 years old is 1 in 1000 or 0.1%.

4. Mention the time horizon over which the risk occurs. For example, "If it were to occur, it could take many years or decades for you to develop cancer related to this study."

   The latent period for cancer induction is estimated to be 6 to 10 years for blood borne cancers (leukemia, lymphoma) and 10 to 25 years for solid organ cancers.

5. Disclose to research participants that the risk from all sources of radiation is cumulative over a lifetime.

Investigators requiring assistance in estimating the levels of risk or the practical equivalents should speak with the Radiation Protection Officer of their institution. Researchers conducting studies with participants who have cancer should consult with the BC Cancer REB concerning the need to include any specific information pertaining to radiation risks in their proposed studies.

Article 17.4: Positron-Emitting Radiopharmaceuticals (PERs)

Researchers conducting studies utilizing positron-emitting radiopharmaceuticals should consult with the 2006 interim compliance policy and guidance documents found at:

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[42] The Royal College of Radiologists. Making the best use of clinical radiology services: referral guidelines. London: The Royal College of Radiologists, 2007, page 17, Table 2.

[43] Mettler FA, Bhargavan M, Faulkner K, Gilley DB, Gray JE, Ibbott GS, Lipoti JA, Mahesh M, McCrohan JL, Stabin MG, Thomadsen BR, Yoshizumi TT. Radiologic and nuclear medicine studies in the United States and worldwide: Frequency, radiation dose and comparison with other radiation sources – 1950 – 2007.

http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/radiopharm/research_per_recherche_prep-eng.php

http://www.hc-sc.gc.ca/dhp-mps/compli-conform/info-prod/drugs-drogues/pol_0053_tc-tm-eng.php

References

Health Canada:

http://www.hc-sc.gc.ca/dhp-mps/compli-conform/clini-pract-prat/docs/gui_68_tc-tm-eng.php

Health Canada:
"Factors considered in the assessment of risks involved in the use of positron emitting radiopharmaceuticals in basic research involving humans"

FDA:
http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Oncology/ucm196484.htm#dose

International Commission on Radiological Protection)[§ 361.1(b)(3)(iv)].
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=361.1

Medical Internal Radiation Dose Committee of the Society of Nuclear Medicine
http://www.snm.org/index.cfm?PageID=1372

The European Commission document *"Radiation protection 99, Guidance on Medical Exposures in Medical and Biomedical Research, 1998*"
http://ec.europa.eu/energy/nuclear/radioprotection/publication/doc/099_en.pdf

Radiology Info: A guide to the exposure associated with various other procedures is available at
http://www.radiologyinfo.org/en/safety/index.cfm?pg=sfty_xray#3

RISe Application Guidance Notes (AGNs)

The Application Guidance Notes (AGNS) provide question by question guidance for filling out the UBC Clinical research ethics application. It is recommended that researchers have the AGNs close at hand while filling out the application for quick reference. Along with the AGNs, the right hand side of the application is also a useful resource, so it is recommended that researchers read the application thoroughly as they are filling it out.

The AGNs are connected with the main UBC Clinical Guidance notes (GNs). The main GNs are UBC's overarching clinical guidance notes and are a less administrative discussion of UBC's ethical framework. There are links between the two sets of guidance notes, where applicable, to avoid redundancies.

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Application Page 1: Study Team, TCPS2, and Study Title

The Application Guidance Notes following this Introduction correspond to the questions in the UBC online Application for Ethical Review. The online application form is divided into pages or views with required fields in each view which will prevent you from proceeding to the next page unless you have completed all of the required fields. Required fields are marked by a red asterisk. While only some fields are "required", it is recommended that all fields are completed in the application form, marking "N/A" for questions which do not apply to your study.

STUDY TEAM:

1.1 PRINCIPAL INVESTIGATOR (Required field)

The Principal Investigator (PI) bears the overall responsibility for the conduct of the study, including the activities of co-investigators, who are assumed to be acting under the delegated authority of the PI, and is required to adhere with the requirements of TCPS2 and other relevant guidelines. The PI accepts this responsibility by submitting the completed CREB application by clicking "OK" in the Submit Activity view on the application homepage. Based on security in the RISe system, only the PI listed in Question 1.1 on the application has access to this Submit Activity button for initial submission on the application homepage. The PI's signature attests to the following:

> *By signing below, I certify that I have read this application together with its attachments and that all information provided herein is accurate and complete. If circumstances should arise that materially affect the accuracy and completeness of the information provided, I will immediately report the new information in writing. I will abide by all applicable laws, regulations and international guidelines, and the policies of the UBC CREB regarding the conduct of research in humans [UBC Policy, #87 and #89], including UBC's conflict of interest policy [Policy # 97] and the Tri-Council Policy Statement for Ethical Conduct for Research Involving Human Subjects.*

Department Head Signature

The PI's Department Head must also approve the application by clicking "OK" in the Approval Activity view on the application homepage to indicate that the PI has the qualifications, experience, and facilities to carry out their research. If the PI is a Department Head, the Dean of the Faculty or the Head of Division must sign the form.

Division Heads for the Department of Medicine, Faculty of Medicine are permitted to sign the application forms on behalf of the Head of the Department of Medicine. A Division Head who is also the PI must have the Head of the Department of Medicine sign the application form.

Once a PI hits Submit on an application form, it does not appear in the Research Ethics Board's (REBs) in-box until the Department Head has signed off on it. If an application is submitted close to a deadline, it is a good idea to follow-up with the Department Head so that the application does not miss a CREB deadline. The CREB is very strict about its deadlines. See the following link for CREB deadlines: http://research.ubc.ca/ore/creb-meeting-dates-deadlines . Note only full board applications have deadlines.

Who can be a Principal Investigator?

a) UBC Faculty
The Principal Investigator must have a Faculty Appointment (for example, Assistant Professor, Associate Professor, Professor, or Emeritus Professor). This includes Clinical Faculty appointments in the Faculty of Medicine.

b) Hospital Employees
The UBC Research Ethics Boards also review research carried out at affiliated teaching hospitals by employees who do not have Faculty appointments and who are not UBC students. In this case, the employee should be listed as the Principal Investigator and the employee's Hospital Department Head should sign the application.

Non-UBC Researchers
Faculty and students from other educational institutions wanting to conduct clinical research on UBC premises, including the UBC-affiliated hospitals, must have a UBC-affiliated Principal Investigator who is willing to take on the above mentioned responsibility. It is the responsibility of the non-UBC researcher to find an appropriate UBC PI.

1.2 PRIMARY CONTACT
The primary contact is the only other person listed on page 1 of the RISe application who will receive all correspondence from the RISe system about the application. The primary contact may also be listed as a co-investigator. For graduate research, it is recommended that the student who is completing the thesis list themselves as both the primary contact and a co-investigator.

Note that the PI may change the primary contact on an application without submitting an amendment. This can be done from the study homepage by clicking on the "**Change Primary Contact**" button under Activities on the left hand side of the screen.

1.3, 1.4, and 1.5 CO-INVESTIGATORS AND ADDITIONAL TEAM MEMBERS (with and without online access)
All co-investigators, including students, medical residents, and other study team members should also be listed in box 1.3, 1.4, or 1.5 of the application form. Note that anyone who interacts with study participants or their data should be listed on page 1 of your RISe application. Researchers may interact with individuals who are not directly involved in their research but who also have

access to participant data, e.g. people managing charts, databanks or research registries. These people do not need to be listed on page 1 as access and proper management of this data is part of their terms of employment.

OTHER INFORMATION ABOUT STUDY TEAM

Designating Signing Authority

Once an ethics application has been approved, the Principal Investigator can designate one or two co-investigators to act as "co-investigators with full signing authority" to submit post-approval activities to the Research Ethics Board.

It is important to emphasize that the PI will continue to be entirely responsible for the research study. The PI must ensure that designated "co-investigators with full signing authority" are completely conversant with all aspects of the study. This option may be particularly helpful in situation where the PI is absent for a short time; however, if the PI will be away for longer periods the REB expects to be formally notified of a change of PI (see below).

In order to designate signing authority, the PI should go to the study homepage. Under the Activities menu on the right, click on "**Designate Signing Authority**" then select **"Add"** to display the list of co-investigators on the study. You may then designate up to two co-investigators with full signing authority. Click "Ok" to complete the activity. Click here for visual directions.

Examples of additional study team members who you may wish to have online access to the application include Clinical Trial Coordinators and Research Assistants who play an intricate part in managing the research in question.

Change in Principal Investigator

When the PI terminates his or her employment/association with UBC or his or her role on a study, the PI must inform the CREB by submitting an amendment that a new PI (meeting the above criteria in 1.1) will assume this role for the study for the CREB approval to be considered valid. If you need to change the PI permanently or temporarily, submit an Amendment to the REB using the RISe system. This involves completing the **Change of PI form** located in the Amendment PAA Coversheet in RISe. The form requires the signature of the following and then to be reattached in the PAA Coversheet as a .pdf file;

-the current PI
-the new PI
-the new PI's Department Head.

-What if the PI is not available to sign the form?

Provide a thorough explanation on the form as to why they are not available to sign it.

-What if the PI is not available to submit the amendment?

A co-investigator with signing authority listed in RISe can submit the amendment. The PI can access RISe from any location where they can access the internet.

1.6. TRI-COUNCIL POLICY STATEMENT TUTORIAL (Required field)

All non-Faculty personnel who are associated with a research project and who will have contact with the research participants are expected to have completed the TCPS online tutorial 'CORE' (Course in Research Ethics) before the application is submitted to the CREB. This includes (but is not limited to) undergraduate and graduate students, medical residents, research assistants, research coordinators, etc. The CREB requires that all Principal Investigators be familiar with the TCPS2 and recommends that Principal Investigators also complete the TCPS tutorial, especially when the Principal Investigator supervises or teaches classes for graduate students or medical residents. TCPS Certificates do not need to be attached to applications; however, you may enter details in the comment box in this section, e.g. date of completion. Copies should be retained by the Principal Investigator and be available on request.

The tutorial is free. It takes around two hours to complete and can be found at the following:
http://www.pre.ethics.gc.ca/eng/education/tutorial-didacticiel/ (English) TCPS 2: CORE
http://www.ger.ethique.gc.ca/fra/education/tutorial-didacticiel/ (French) EPTC2: FER
The following tutorials are acceptable substitutes for CORE: past completion of the previously offered TCPS tutorial or the CHRPP (Course in Human Research Participant Protection) tutorial.

1.7 PROJECT TITLE (Required field)

The title given in the application form must correspond to the title on the consent form and other study documents. If the study is supported by research grant or contract funding that is being administered by the University or one of the teaching hospitals, the title should also correspond to the title on the grant or contract. If the research project is supported by multiple grants with different titles, ensure that all of the grants are clearly listed on page 2 of the application and the title is thematically similar to the grants listed.

1.8 PROJECT NICKNAME (Required field)

The project nickname or short title will appear in your inbox for applications and post approval activities (amendments, renewals, etc.). The nickname will not be printed on the Certificate of Approval. It will be used to serve as a quick reference to identify the project.

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Application Page 2: Study dates, Funding Sources and Conflicts of Interest

2.1 PROJECT PERIOD (Required field)
The start date should correspond to the beginning of the period during which you anticipate collecting data and should not pre-date this application. In multi-phase projects include the period that involves research with human participants (i.e. the beginning of the project for the purposes of this application should not pre-date the application).

The end date can be an estimate of when you expect to have completed data collection and can be extended by an application for renewal or amendment.

For chart reviews, the dates entered here should be the dates the study will be conducted. The date range of charts to be reviewed should be indicated on page 5 of the RISe application form.

2.2 SOURCE OF FUNDING
2.2 A. Type of Funds (Required field)
Select the type of funding the research has received to conduct the study. If "Other" is selected, please provide details. For-profit studies will be charged a fee of $3000. If the sponsor is only collaborating on a project and not fully funding it, e.g. they are providing the study drug or laboratory space only, select "Other" and provide details on the sponsor's role in the study. Researchers must inform the CREB office of any changes or additions to the funding source(s) using the Post Approval Activity "Amendments to Study". See the Post Approval Activity Guidance Notes for Amendments . The UBC Office of Research Services can only release the funds for awards/grants when the CREB Certificate of Approval has been updated to reflect the addition or change of a funding agency, should this occur.

2.2.B. For Industry sponsored studies please provide a sponsor contact (i.e. study monitor or CRO contact).

2.3 RESEARCH FUNDING APPLICATION/AWARD ASSOCIATED WITH THE STUDY THAT WAS SUBMITTED TO THE UBC OFFICE OF RESEARCH SERVICES
Research grants or contracts administered by the University or affiliated institutions will not be released until the project has been reviewed and approved by the appropriate Research Ethics Board. The information entered into these boxes will be used to cross-reference the Application for Ethical Review with a research grant or contract that may be flagged as pending ethical review in the Research Services database. Your Certificate of Approval will list the title that was entered in box 1.7 of the RISe application, as well as titles of all grants or other funds listed in boxes 2.3 and 2.4

2.4 RESEARCH FUNDING APPLICATION/AWARD ASSOCIATED WITH THE STUDY NOT LISTED IN QUESTION 2.3

2.5. U.S. FUNDING (Required field)

US Department of Health and Human Services (DHHS) Funded Research
If the study is funded by the DHHS, attach the actual grant application to box 9.8 of the ethics application. The DHHS requires that the UBC REB review the actual grant application to compare it to the protocol being approved to ensure that they are the same.

2.6 CONFLICT OF INTEREST (Required field)

As defined in UBC Policy #97: Conflict of Interest and Conflict of Commitment, Article 12.4, "*in the research context, Conflict of Interest includes a situation where financial or other personal considerations may compromise, or have the appearance of compromising, an investigator's professional judgment in conducting or reporting research. Conflicts of interest may be potential, actual or apparent*".

Even though Investigators may supply the information requested in the application to their departments or hospitals, the REB must consider whether this information has any bearing on the ethics of the research study. Furthermore, as stated in Procedure 2 of UBC Policy #97, assessors of annual conflict of interest disclosures by UBC members (with members being defined as faculty, clinical faculty and staff) will disclose the existence of the conflict of interest to the relevant REB where the conflict of interest relates to a particular research project. Note that "immediate family members" includes partners and children (whether living in the household or not). The REB does not require that the researcher declare holdings in managed mutual funds in the conflict of interest statements.

Participants must be informed of significant individual financial conflicts of interest in the consent form. At a minimum, potential conflicts must be disclosed to the Board and to potential participants. The Board may require further action of the researcher to minimize or abandon a conflict, require formal oversight procedures for the research (including audits, independent data safety monitoring processes, regular reports to the CREB), or may disallow the research altogether. The Board may also inform the investigators' Department Head or Dean of Faculty about the conflict of interest.

Investigators are also advised of the following relevant national policies and guidelines:

- TCPS2 Chapter 7 D. Researchers and Conflicts of Interest http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter7-chapitre7/#toc07-1d
- NSERC Schedule 14: Conflicts of interest in Research http://www.nserc-crsng.gc.ca/NSERC-CRSNG/Policies-Politiques/MOURoles-ProtocolRoles/14-Conflict-Conflits_eng.asp

If “yes” is answered to question 2.6., an extra page (page 3) will open and further detail will be requested.

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Application Page 3: Conflict of Interest

3.1

This box should describe all potential benefits
Answer questions A through E, giving as much detail as possible.

Recruitment Fees

The Canadian Medical Association Policy Guidelines for Physicians in Interactions with Industry 2007 states:

12. Because of the potential to influence judgment, remuneration to physicians for participating in research studies should not constitute enticement. It may cover reasonable time and expenses and should be approved by the relevant research ethics board. Research subjects must be informed if their physician will receive a fee for their participation and by whom the fee will be paid.

13. Finder's fees, whereby the sole activity performed by the physician is to submit the names of potential research subjects, should not be paid. Submission of patient information without their consent would be a breach of confidentiality. Physicians who meet with patients, discuss the study, and obtain informed consent for submission of patient information may be remunerated for this activity.

3.2

Clarify how much money the investigator has received from the funder, as well as why the money has been received.

Preceptor Agreements

Disclosure to potential subjects is required where Preceptor agreements exist between a PI and a sponsor whereby the PI is consulted by the PIs at community sites for the same study; and where Preceptor agreements exist between a PI and a sponsor whereby the PI is consulted by the PIs at community sites for the same study.

3.3

Disclose whether any of the investigators and/or their partners/family members are directly involved with the sponsor financially.

3.4

Disclose whether any of the investigators and/or their partners/family members hold patent or intellectual property rights

3.5

Clarify whether all UBC COI declarations for the Principal Investigator and Co-Investigators (if UBC Faculty) are up to date

Faculty members must disclose the extent, nature, and timing of their Extra-University Activities, their use of University resources for any Extra-University Activities, and any Financial Interests they or their Related Parties have in entities related to the Members employment at the University. This disclosure must be current and renewed at least annually.

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Application Page 4: Research Ethics Board, Location, Risk Level, and Pandemic Research

4.1 UBC RESEARCH ETHICS BOARDS (Required field)

UBC's REBs have signed a one board of record agreement. Studies taking place at multiple UBC sites require review and approval by only one UBC-affiliated REB. The choice of Board should be determined by the PI's primary appointment and/or the main location of the research. See the following link to the UBC Clinical Guidance Note #2 on the jurisdiction of the UBC-affiliated REBs

Ensure to appropriately select whether the application is clinical or behavioural for each of the applicable boards as the application changes according to your selection. See the right side of the application for further discussion of the differences between clinical and behavioural research. BC Cancer Agency, Providence Health, and Children's and Women's REBs all review both behavioural and clinical research.

4.2 INSTITUTIONS AND SITES FOR STUDY (Required field)

You may add more than one site under this question. The letterhead of all recruitment and consenting documents are required to correspond to the selected institution(s).

VCHA – Vancouver Coastal Health Authority: All research conducted at any of the institutions within the authority of Vancouver Coastal Health (VGH, etc.) must be approved for resource utilization by the Vancouver Coastal Health Research Institute (VCHRI) in addition to the UBC Behavioural or Clinical REB.

C&W – Children's and Women's Health Centre of BC: Any research conducted at Children's Hospital, Sunny Hill Hospital, and Women's Hospital, collectively known as C&W, must be reviewed by the C&W REB. Please check the CFRI web page for the Children's & Women's REB deadlines.

PHC – Providence Health Care: Any research involving human participants conducted at a Providence Health Care (PHC) site must be reviewed and approved by the UBC-PHC Research Ethics Board. The UBC-PHC REB also needs to review any research protocols in which patients who are receiving care at a PHC site are enrolled.

BCCA – BC Cancer Agency: Researchers at the BC Cancer Agency should submit their new applications for ethical review to the UBC-BCCA REB for all clinical projects and in the case of behavioural projects to either the UBC-BCCA REB or the UBC Behavioural REB. However, anyone conducting research, behavioural or otherwise, at the BC Cancer Agency, must make sure they obtain approval from any BCCA Department whose resources are affected by the conduct of the study. The Principal Investigator is responsible for identifying and meeting those requirements.

4.2 B. All other locations*:* Please describe other locations where research participants will be recruited and / or where data collection will occur.

4.3 RELATIONSHIP WITH OTHER PROPOSALS

If this proposal is closely linked to any other proposal previously or simultaneously submitted to the CREB, please indicate this here and describe the relationship of this proposal to the others**.** Ensure to clearly indicate the related RISe file number, e.g. H11-00000.

Extension or Sub-studies

Indicate whether the study is an extension or a sub-study of a primary study. For example, in an extension study, the study period could be extended in order to give participants the opportunity to undergo an extra regimen of treatment with the experimental drug. A sub-study is a concurrent study on a sub-sample/population of the original study sample/population. The CREB reserve the right to require that a sub study or extension study be submitted as a new application.

4.4 LEVEL OF RISK (Required field)

UBC's REBs use a proportionate approach to review research involving human participants. They review applications in accordance with the level of risk that the proposed study poses to the research participants: the lower the level of risk, the lower the level of scrutiny; the higher the level of risk, the higher the level of scrutiny. In accordance with the TCPS2, full review by a fully convened REB is the default requirement unless the REB has determined that the research is of minimal risk and that delegated review by one or more experienced reviewers appointed by the REB is appropriate.

Minimal Risk is defined in the TCPS2 as follows: "*research in which the probability and magnitude of possible harms implied by participation in the research is no greater than those encountered by participants in those aspects of their everyday life that relate to the research*". See Guidance Note #5, Article 2 for a more thorough discussion of minimal risk research and specific examples.

Differences in Review Processes for Minimal Risk versus Full Board

-Full Board: The CREB reviews all greater than minimal risk applications at the full board. Full board meetings take place on the 2nd and 4th Tuesday of each month, with the exception of December, when only one meeting takes place. The CREB full board meeting deadlines are strictly followed and are at noon on the Friday which is 11 days before the meeting. See the following link for a list of upcoming deadlines and meetings: http://research.ubc.ca/ore/creb-meeting-dates-deadlines . Studies that are reviewed at a full board meeting on a Tuesday can expect to hear back about the review before Friday of the same week.

-Minimal Risk: There are no deadlines for applications that meet the minimal risk criteria. The application will be assigned for review to designated members of the CREB. The turnaround time depends on the volume of applications received and the availability of reviewers; generally, it is approximately two weeks.

4.5 PEER REVIEW (Required field)
All studies submitted to the CREB which are more than minimal risk require a peer review or scholarly review, or an accepted argument about why one has not been obtained. The application will be sent back before it is reviewed if appropriate peer review information is not included. See Guidance Note #8, Article 2 on Required Information for a thorough discussion of peer review requirements.

4.6 HARMONIZED REVIEW OF MULTI-JURISDICTIONAL STUDIES (Required field)
A multi-jurisdictional study is a research study that requires review and approval by more than one Canadian research ethics board (i.e. by more than one Canadian REB as well as a UBC affiliated REB) as a result of the requirements of the TCPS2 and/or UBC's and/or another institution's human ethics policies.

UBC has entered into partial reciprocity and collaborative review arrangements with certain other institutions and entities in situations where a study requires review and approval by more than one Canadian Research Ethics Board. For detailed guidance on harmonization processes and requirements click here.

List of institutions with which UBC has a reciprocity or collaborative review agreement:
Simon Fraser University
University of Alberta
University of Northern British Columbia
University of Saskatchewan University of Victoria

If Box 4.6 is marked "Yes", the application will skip to View E

4.7 CREATION OF A RESEARCH DATABASE, REGISTRY OR TISSUE BANK
Research databases or registries are repositories that collect and store information about humans specifically for use in subsequent research. The information may or may not include personally identifying information, clinical files, clinical test results, x-rays, MRIs, information about race, age, or place of origin, etc., that is collected retrospectively or prospectively.
Biorepositories (also known as biobanks) are types of repositories that collect and store human biospecimens specifically for use in subsequent research. Biospecimens are defined as human biological materials obtained from a participant and may include solid tissues, blood samples and fluids.

The information associated with the biospecimen may or may not include personally identifying information. Research databases, registries, and biorepositories can be of any size.

If Box 4.7.A is marked "Yes", the application will skip to View C

4.8 CLINICAL CHART REVIEW

Important Note: Studies that are exclusively retrospective chart reviews where no consent is being sought and no contact with participants is being proposed will be re-directed to a shortened application form for retrospective chart reviews only.

A retrospective chart review for the purpose of this application includes charts that were collected before the date of ethics approval (dates in the past), e.g. Sept. 2005-Sept. 2011.

If Box 4.8.D is marked "Yes", the application will skip to View A

If Box 4.8.D is marked "No", but Box 4.8.E is marked "Yes", the application will skip to View A

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Application Page 5: Summary of Study and Recruitment

NOTE ON TERMINOLOGY

Although the TCPS2 guidelines specify a preference for the term 'participant', applicants may use the term of their choice (e.g. 'participant' or 'subject') as long as they are *consistent* throughout their application rather than switching back and forth. It is also important to be clear in your terminology. For example, if your study involves collaborators and participants, and these are distinct groups, do not use the term 'participants' interchangeably to refer to both.

5.1 A. SHORT SUMMARY (Required field)

Provide a short summary in lay language in 100 words or less.

5.1 B. SUMMARY OF RESEARCH (Required field)

The research proposal should be separated into 6 different headings: **Purpose, Hypothesis, Justification, Objectives, Research Method, and Statistical Analysis**. Read the right hand side of the application carefully for the required elements, when relevant, under each of the different headings. See the below for a discussion of each heading:

1. **Purpose**: This is the main reason that the study is being conducted (e.g. to determine efficacy, equivalence, safety, dosage levels, effectiveness) and should include the direct implications/applications of the research. Specify whether or not optional studies that may be part of a protocol are being conducted at the local site.

2. **Hypothesis or Aim:** This specifies the precise research questions being evaluated in the study.

3. **Justification for the study**: This includes background evidence that explains the need for the study. In particular, this section should explain what is unique about the study and what new research questions can be answered in order to support the ethical tenet that the proposed research has value.

   For clinical trials, this information should provide evidence of *clinical equipoise*, which is defined as "...a genuine uncertainty on the part of the expert medical community about the comparative therapeutic merits of each arm of a clinical trial." The justification must include the differences between what is considered the current standard of care and the experimental intervention.

Some studies are conducted in order to satisfy requirements for Health Canada or FDA approval. This is not a sufficient ethical justification for the study. Ensure that a more precise justification is provided which explains why additional studies are needed and warranted.

4. **Objectives**: This includes the specific outcomes/endpoints of the research.

5. **Research Method:** This should include a description of the target population and/or sample, sample size, sampling method (e.g. randomization), type of research design (e.g. experimental parallel group or cross-over design) and the statistical analysis plan. It should also include a justification for the use of deception or placebo or for the need to carry out research in emergency health situations, if applicable.

5.2 INCLUSION CRITERIA

The selection of participants must take TCPS2 Article 4.1 into consideration, which states that: "*Taking into account the scope and objectives of their research, researchers should be inclusive in selecting participants*". The TCPS2 cautions against recruiting participants into research studies solely because they are easy to access or manipulate and highlights researchers' special obligations toward individuals or groups whose circumstances may lead to or increase their vulnerability in the context of a specific research project or study. For a thorough discussion of inclusion criteria, see Guidance Note #9, Article 1

When filling out the application form, ensure that all inclusion criteria as listed in the protocol are stated. Otherwise, indicate how these criteria differ from that in the protocol.

5.3 EXCLUSION CRITERIA

Provide all exclusion criteria as described in the protocol. Otherwise, indicate how these criteria differ from those in the protocol. The exclusion criteria should not just mirror the inclusion criteria. It should clearly list characteristics that would exclude individuals who could otherwise participate based on the inclusion criteria. For a more thorough discussion of exclusion criteria, see Guidance Note #9, Article 3

5.4 RECRUITMENT

The described recruitment method should be free from undue influence, as per Guidance Note #10, Article 1.2**,** and include the following elements:

h. The source (i.e. its original purpose, if relevant) of the contact information, and how the researcher gained access to it;
i. Who will collect the contact information;
j. Who will make the initial contact with the prospective participant(s);
k. How the prospective participant will be initially contacted;
l. When the prospective participant will be initially contacted;

m. The relationship, if any, of the study team members to the participants (e.g. treating physician, teacher); and
n. All recruitment materials such as letters, advertisements, flyers, television or radio scripts, internet/e-mail messages

Ensure this section contains sufficient detail. If appropriate information is not included, the board will request clarification. For a more thorough discussion on recruitment, including examples of appropriate recruitment methods, see Guidance Note #10 .If contact information is being obtained from **Medical Records, Databases, or Registries,** see Guidance Note #11for guidance on using this information appropriately and ensure that this is disclosed in the application form. In box 5.6 (further described below) indicate why the Principal Investigator and/or other study team members have access to this information.

5.5 RECRUITMENT OF NORMAL/CONTROL PARTICIPANTS

If the study is recruiting control participants and the recruitment method differs from that described in box 5.4., clearly describe the recruitment strategy based on the criteria outlined in box 5.4. If the study is using controls and the recruitment method is the same, state this. If the study is not using controls, then *N/A* may be used in this box.

5.6 USE OF RECORDS

If the study is using existing records, e.g. health records, clinical lists, or other records/databases, for recruitment purposes, clearly disclose why the Principal Investigator or another study team member has access to this information. An example of this may be that the Principal Investigator is a doctor in a specialized clinic and, therefore, has access to patient records within the clinic. In these cases, special care needs to be taken to ensure that the patients' rights are not violated. See Guidance Note #11, Article 5 for further information for appropriate use of these lists The method of contacting people on these lists should be clearly disclosed in box 5.4.

5.7 SUMMARY OF PROCEDURES (Required field)

Describe in a step-by-step manner the research procedures and how they differ from normal, non-research activities (ensure to clearly describe what is normally done, i.e. standard of care, and what is being done for research purposes). Describe the period during which the procedures will be carried out, how long each procedure will last, and the frequency of the procedures.
The description should include the sampling method (e.g., random sampling), group assignment (e.g., randomization), and type of research design (e.g., double blind).
The application and the consent form should include a description of the method of being assigned to one group or another in a study comparing two or more different experimental conditions. The researcher should provide a separate consent form for each group describing the experimental procedures that will affect the participant directly.

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Application Page 6: Participant Time, Risks and Benefits, and the Consent Process

6.1 TIME TO PARTICIPATE

Indicate the amount of time a participant will be asked to dedicate to the project. The time should be above that which the participant would do regardless of participating in the research as part of standard of care. Include both the minutes/hours of the actual experimental procedure and the length of time the participant will be asked to do this, e.g. "*the participants will attend the clinic once a week for a 1 hour appointment for 7 weeks. The total amount of time participants are being asked to dedicate to the project is 7 hours over 7 weeks.*"
Your times may be estimates where the exact time is unknown, e.g. 15-30 min; however, there must be consistency throughout the application and on all study documents.

6.2 TIME TO PARTICIPATE – NORMAL/CONTROL PARTICIPANTS

Using the criteria outlined in 6.1 indicate the amount of time that controls will be asked to dedicate to the project. If the research does not involve a control group, this box may be marked *N/A*.

6.3 RISKS/HARMS

Describe the potential risks or inconveniences to the participant associated with each procedure, test, or other aspect of the study. Please also address, where applicable, the broader impacts of the study on individual participants and the groups to which they belong. Such impacts may include: social stigmatization, threats to reputation, the creation of unfair stereotypes, and/or psychological harms such as anxiety, regret, or guilty feelings. Describe strategies to be used to minimize or manage the study impacts for participants and other affected individuals.

Clinical risks should be listed as bullet points and quantified using percentages, where possible. Ensure that there is consistency between this box and study documents, especially the consent form. See Guidance Note #12 for a detailed discussion of required information around risks.

6.4 BENEFITS

Specify the potential benefits to the participants. If there are no direct benefits, state this explicitly, and ensure this is disclosed in the consent form. If any specific benefits cannot be assured, but may be hoped for by the participant, state explicitly that the participant may or may not benefit from participation in the study. If benefits at a community or broader societal level are expected, these should be mentioned. See Guidance Note #12, Article 7 for Benefits.

6.5 REIMBURSEMENT

Voluntary consent must be free of undue influence in the form of inappropriate inducements. The amount or kind of payment should not be such that the participant will base his/her decision to participate on the potential material rewards.

TCPS2 page 29 states, "*In considering the possibility of undue influence in research involving financial or other incentives, researchers and REBs should be sensitive to issues such as the economic circumstances of those in the pool of prospective participants, the age and capacity of participants, the customs and practices of the community and the magnitude and probability of harms*".

The CREB will weigh the amount of remuneration offered against the amount of time and inconvenience to the participant on a case-by-case basis. It is considered unacceptable to have payment depend on completion of the project. However, reimbursement may be pro-rated based on the time a participant was enrolled in the study.

Ensure that a clear discussion of reimbursement and payments is in the consent form, including a schedule for pro-rating the reimbursement, if applicable. However, do **NOT** include reimbursements or payments on recruitment materials, see Guidance Note #10, Article 1.3, Exclusion of Remuneration from Recruitment Materials.

No Remuneration or reimbursement:
If the participant will not be remunerated for participation or reimbursed for expenses, this should be clearly stated in the consent form.

Lotteries and Draws:
As an incentive to participate in studies, researchers frequently offer participants a chance at a prize in a draw. If such a draw does not include those who decline to participate, technically it becomes a lottery and is illegal in British Columbia (without a license). You must have a license from the province of British Columbia to run any kind of lottery scheme. This includes draws where the subject pays or "barters" for a chance at a prize by completing some aspect of the research project. Consequently, researchers must ensure that participation in the draw is not contingent on participation in the research, and any subjects who withdraw must also have the opportunity to have their names included in such draws.
The CREB considers the use of draws as an acceptable incentive if the names of those who withdraw from the study are also included in the draw.

Reimbursement of Expenses:
Include specific details of the reimbursement of expenses related to transportation and parking and when these will be paid. The timing of the reimbursement should be appropriate to the length of time the study is to continue i.e. if a study is 2 years long, consider reimbursement of expenses every 6 months and not at the end of the study.

6.6 OBTAINING CONSENT

This box should clearly indicate who will explain the consent form to potential participants and obtain consent. The person obtaining consent must be sufficiently familiar with the study, the disease being treated (if applicable), and the process of informed consent. Ensure to disclose the relationship between the person obtaining the consent to the potential participant, e.g. doctor – patient. For a detailed discussion on the general principles of informed consent and on obtaining consent, see Guidance Note #13. If the study involves a departure of the normal principles of consent or involves assent, see as well Guidance Note #14 and #15
Refer to the UBC Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB for guidance on developing an appropriate consent form.

6.7.A WAIVER / ALTERATION OF CONSENT

In the TCPS2, Article 3.7 and Article 5.5 outline specific criteria for requesting a waiver or alteration of the consent in certain circumstances. The REB will consider an alteration or waiver of consent when outlined criteria are met. See the right hand side of the application for a list of the criteria. Ensure that your response to each of the criteria is labelled with the article indicating that criteria, i.e. i. *The proposed research is not more than minimal risk, ii. Participants' rights will unlikely be adversely affected as [insert description of confidentiality method and research sensitivity], iii…, iv….etc.* See Guidance Note #14 for further information on alteration or waiver of consent.

Note that retrospective chart review (access to past chart information only), generally fulfills the criteria for waiver of consent. However, prospective chart review (ongoing review of charts) does not meet the requirements for waiver of consent.

6.7.B WAIVER OF CONSENT IN INDIVIDUAL MEDICAL EMERGENCIES

Refer to TCPS2 Article 3.8 for further information on the following criteria.
a. A serious threat to the prospective participant requires immediate intervention
b. Either no standard efficacious care exists or the research offers a realistic possibility of direct benefit to the participant in comparison with standard of care
c. Either the risk is not greater than that involved in standard efficacious care, or it is clearly justified by the prospect for direct benefits to the participant
d. The prospective participant is unconscious or lacks capacity to understand the risks, methods and purposes of the research project
e. Third party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so, and
f. No relevant prior directive by the participant is known to exist

6.8 TIME TO CONSENT

Prospective participants should have adequate time to make a fully informed decision about participating in a study. For studies involving more than minimal risk, twenty-four hours is often considered an appropriate amount of time to give participants to think about participating in a study. However, the time given to consent should be based on the nature of the study in question.

The TCPS 2 states that the time required for initial consent should "*depend on such factors as the magnitude and probability of harms, the complexity of the information conveyed, and the setting where the information is given*". See Guidance Note #10, Article 1.4 for further information.

6.9 CAPACITY TO CONSENT

Indicate whether or not the research will include participants who lack the capacity to consent on their own behalf.

The Principal Investigator must judge the potential participant's capacity to consent on his or her own behalf, in all participants, in all research projects, regardless of age. The TCPS2 cautions around treating a group as inherently vulnerable. For example, within a group of 15 year olds, some may have the capacity to consent while others will not. It is the responsibility of the PI to determine this. Ensure that the research proposal indicates a method for determining capacity. For research involving individuals who lack the capacity to consent, either permanently or temporarily, these individuals should be given information and involved in decision making to the extent possible. See the related discussions in TCPS2 (Article 3.9, Articles 4.4, 4.5, 4.6). Also, see Guidance Note #15 for further discussion of capacity and obtaining consent in those who lack the capacity to consent.

6.10 RENEWAL OF CONSENT

TCPS2 Article 3.3 states that "*consent will be maintained throughout the research project. Researchers have an ongoing duty to provide participants with all information relevant to their ongoing consent to participate in the research*". Renewal of consent might be particularly appropriate in the context of clinical trials research where risks become known as the trial progresses. In these cases, a clear description of how the participants will be told of new risks should be outlined in your application. Note that depending on the nature and urgency of the risks, the participant may be told verbally of new risks or presented with an updated consent form. If the participant is told verbally, this should be clearly disclosed in the investigator's study notes. When the nature of the risks has the potential to affect a participants' decision to continue to participate, written re-consent is generally required.

Once the risks are known, an amendment must be submitted to the CREB in order to update the application form and submit any new materials that may be given to participants. For most cases (non-emergency), the amendment should be granted REB approval before the participants are contacted. In emergency situations, please contact the CREB as soon as possible to discuss the situation.

6.11 PROVISIONS FOR CONSENT

Describe any provisions planned for participants (or those consenting on a participant's behalf) to have special assistance, if needed, during the consent process (e.g., consent forms in Braille, or in languages other than English). Attach copies of contact letters or consent forms that have been

translated into other languages to page 9 of the application.

6.12 RESTRICTIONS ON DISCLOSURE

Describe any restrictions regarding the disclosure of information to research participants (during or at the end of the study) that the sponsor has placed on investigators, including those related to the publication of results.

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Application Page 7: Regulatory Approvals

7.1 MULTI-CENTRE STUDIES

Mark "yes" when the study is occurring in one or more site that is outside of UBC's one board of record agreement e.g. sites not including PHC, C&W, VCHRI, and UBC.

TCPS2 Article 8.3(b) states, "*Research conducted under the auspices of a Canadian research institution and conducted outside its jurisdiction, whether elsewhere in Canada, or outside Canada, shall undergo prior ethics review by both: (i) the REB at the Canadian institution under the auspices of which the research is being conducted; and (ii) the REB or other responsible review body or bodies, if any, at the host research site*". Please indicate the agency having jurisdiction over the site of the research and whether approval has been applied for or received. If approval has been received, append this to box 9.8 of the RISe application.

7.2 NUMBER OF PARTICIPANTS

This section must be completed. It is acceptable to provide an estimate for the number of participants if the exact number is not known in advance. However, the number provided should be consistent throughout the application.

7.3 DRUG APPROVALS

Enter the generic name for all experimental drugs or marketed drugs used in the study outside of their approved indication. See 7.8 below for further information on regulatory approvals for the use of these drugs in research.

7.4 MARKETED DRUGS

Enter the generic name of all marketed drugs used within their approved indication.

7.5 NATURAL HEALTH PRODUCTS

Enter the name of any Natural Health Product used in the study. Natural Health Products include vitamins and minerals, herbal remedies, homeopathic medicines, traditional medicines such as traditional Chinese medicines, probiotic, and other products like amino acids and essential fatty acids. All Natural Health Products must be safe as over-the counter products. If they need a prescription to be sold, they are regulated under the food and drug regulations. See the following Health Canada link for further information: http://www.hc-sc.gc.ca/dhp-mps/prodnatur/index-eng.php .

7.6 EXPERIMENTAL DRUGS AND DEVICES

Enter the name of all investigational devices or marketed devices used outside of their approved indication. See 7.8 below for further information on regulatory approvals for the use of these devices in research.

7.7 STUDIES INVOLVING POSITRON-EMITTING RADIOPHARMACEUTICALS (PERS)

Enter the name of any positron-emitting radiopharmaceuticals used in the study. For further information, please consult with the Health Canada 2006 interim compliance policy and guidance documents found at:

http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/radiopharm/research_per_recherche_prep-eng.php

http://www.hc-sc.gc.ca/dhp-mps/compli-conform/info-prod/drugs-drogues/pol_0053_tc-tm-eng.php

7.8 HEALTH CANADA REGULATORY APPROVALS

Investigators conducting clinical trials involving either investigational drug(s), device(s), or natural health products formulated for therapeutic purposes OR involving a drug/device/natural health product used for an indication outside those specified in the Health Canada Drug Identification Number, Notice of Compliance or Medical Device License, must submit the appropriate application for regulatory approval to Health Canada before research can begin. Note that the CREB will not release a Certificate of Approval until the Health Canada No Objection Letter (NOL) has been received. In these situations, once a study has been approved in principle, the CREB administration will issue an additional proviso requesting that the study team attach the NOL once received. When the study team receives the NOL, attach it to Box 9.1.B. of the application and re-submit for REB approval.

The Clinical Trial Application (CTA) for drugs/natural health products or the Investigational Testing Authorization (ITA) for devices must be filed with the appropriate directorate within the Health Protection and Food Branch of Health Canada:

1. Clinical trials for drug and devices: http://www.hc-sc.gc.ca/ahc-asc/branch-dirgen/hpfb-dgpsa/tpd-dpt/index-eng.php
2. Clinical trials involving natural health products formulated for therapeutic purposes: http://www.hc-sc.gc.ca/ahc-asc/branch-dirgen/hpfb-dgpsa/nhpd-dpsn/index-eng.php

Compliance with the Food and Drug Act

All investigators conducting clinical trials must be familiar with the details of the Food and Drugs Act and Regulations: http://www.hc-sc.gc.ca/fn-an/legislation/acts-lois/act-loi_reg-eng.php

C.05.001 of the Regulations empowers the Research Ethics Boards to review, approve and conduct periodic reviews of biomedical research involving human participants to ensure the protection of their rights, safety and well-being.

Several of the important new regulations are summarized below:

- These regulations apply to clinical trials for both new investigational drugs and some marketed drugs. The use of a marketed drug outside of its approved indication now requires Health Canada approval for use in a clinical trial (whether investigator or industry initiated).
- A 'Sponsor' is defined in the Regulations as an individual, corporate body, institution or organization that conducts a clinical trial.
- All clinical trials, including Phase IV trials, must be conducted in accordance with good clinical practices as specified by ICH GCP. However, Phase IV clinical trials are not subject to the Clinical Trial Application filing requirements with Health Canada.
- Each clinical trial must have a 'Qualified Investigator' who is responsible to the sponsor for the conduct of the trial and who has appropriate medical qualifications (see the definition under C.05.001).
- All information collected in a clinical trial must be stored in accordance with C.05.012, which includes the requirement for the sponsor to store records for 25 years.

7.9 DETAILS OF HEALTH CANADA REGULATORY APPROVALS

If as per the above questions, if the study needs a Health Canada NOL, ITA, NOA, it must be listed here. Note that is also must be attached to the application in Box 9.1.B or C (if US).

7.10 STEM CELL RESEARCH

As of 30 June, 2010, the updated CIHR Guidelines for Human Pluripotent Stem Cell Research apply to all new or ongoing human stem cell research that is:

1. funded by the CIHR agencies;
2. conducted under the auspices of an institution that receives any agency funding, whether on site or off site or;
3. conducted elsewhere with any source of funding by faculty, staff or students from an institution that receives Agency funding.

See the above guidelines and the GN on Stem Cell Research for a more thorough discussion of the types of research the SCOC must approve and the types of research that does not need to conform to these guidelines**.**

CIHR requires that stem cell investigators seek REB approval for their **non-clinical research**, in addition to approval from the UBC Animal Care Committee (when appropriate) and the UBC Biosafety Committee.

7.11 REGISTRATION FOR PUBLICATION OF CLINICAL TRIALS

The TCPS 2, Article 11.3, states that all clinical trials should be "*registered before recruitment of the first trial participant in a recognized and easily web-accessible public registry*." Note that the CREB requires that all clinical trials must be registered with a registry that meets the requirements of the International Committee of Medical Journal Editors (ICMJE), e.g. ClinicalTrials.gov and Controlled-trials.com.

The PI of a clinical trial being done at UBC/affiliated sites is responsible for ensuring that the trial is registered with an acceptable international registry. Ordinarily, multi-centre studies will have been registered by the sponsor so the PI at UBC/affiliated sites need only verify that the trial has been registered by the sponsor and note the registry on the application form.

The CREB expects that the PI will ensure that the trial is registered and appropriately updated when the trial is complete or results are published. Note you may register your trial in ClinicalTrials.gov prior to getting approval from the CREB, provided the trial is not yet recruiting. Before the first participant is recruited, REB approval must be obtained and the protocol record updated on the site according to that approved by the REB. Please refer to http://prsinfo.clinicaltrials.gov/faq.html for more information.

7.12 US REGULATORY REQUIREMENTS

If the study is conducted or funded by the US Department of Health and Human Services (DHHS) or is required to comply with either the US FDA or any other US regulations, this must be indicated on the application See the right hand side of the application and the list below for further information.

Office of Human Research Protections (US Department of Health & Human Services)
Food and Drug Administration (FDA)
US National Cancer Institute (NCI)
National Institutes of Health (NIH)

UBC Clinical Research Ethics AGNs

Application Page 8: Data Monitoring, Data Security, Confidentiality, and Data Retention

8.1 UNBLINDING IN AN EMERGENCY

For applicable research, the CREB requires that sufficient information to reveal treatment assignment in the event of a medical emergency be held locally. An emergency contact number (available 24 hours a day, 7 days a week) of a person who can break the code must be identified on the consent form(s). If the code cannot be held locally, the CREB requires a detailed explanation of how the code can be broken in an emergency and how quickly this can occur. For applicable research, the emergency contact's name and telephone number must be clearly identified in the consent form.

There are a number of circumstances where research participants or caregivers may need to be able to access information about a clinical trial on an "emergency" basis. At present, CREB requires that an emergency number be available for studies involving clinical interventions 24 hours a day, 7 days a week.

While a true 24-hour, 7-day a week access telephone number is optimal, it may not be possible, practical or even realistic for every study. For this reason, access to information/research personnel should be, to some degree, individualized based on the risk associated with the study.

In clinical trials where patients are treated with a drug or device (or other form of treatment), there are a few types of "emergency" information that could be required at some time:

1) unblinding to reveal treatment assignment
2) information about the nature and risks of the particular treatment the participant is or has received
3) access to the Principal Investigator for advice about the nature and risks associated with a particular treatment

The CREB recommends that all participants enrolled in a clinical trial involving drug administration in which they are not continually in a controlled environment (hospital, research clinic, etc.) should be provided with a wallet card describing the basic information about the trial.

An example of such a card could be as follows:

1. Name of Participant
2. Name of Study
3. Participant Study Number (if applicable)

4. Name of Principal Investigator
5. Treatment they are receiving (or which they could be receiving if they are in a blinded study)
6. Contact information of investigator/research staff (not necessarily 24/7)

OPTIONAL INFORMATION AS DICTATED BY THE NEED OF THE PARTICIPANT

1. Phone number for immediate unblinding
2. Website for more detailed information about the study
3. Contact information of investigator/research staff (24/7)
4. "Key information for clinicians". There may be some particularly important issues that need to be highlighted. For example, there could be important information that would be required for life-threatening situations - information that treating physicians might not have time to obtain by contacting the investigators.

8.2 DATA MONITORING PROCEDURES

The TCPS2 Article 11.7 states: "*Researchers shall provide the REB with an acceptable plan for monitoring the safety of participants, including a plan for the tabulation, analysis and reporting of safety data, and the sharing of other new information in a form that permits REBs to interpret and respond appropriately*." Provide this information in detail, if applicable to your study.

8.3 STUDY STOPPAGE

The TCPS2 Article 11.8 states that "*When new information is relevant to participants' welfare, researchers shall promptly inform all participants to whom the information applies (including former participants). Researchers shall work with their REB to determine which participants must be informed, and how the information should be conveyed*." Outline any set stopping rules for the study and the way in which participants will be informed in the event that the clinical trial is stopped, if applicable to your study.

8.4 PERSONAL IDENTIFIERS

The TCPS2 Article 5.3 states: "*Researchers shall provide details to the REB regarding their proposed measures for safeguarding information, for the full life cycle of the information: Its collection, use, dissemination, retention and/or disposal*."

The CREB expects that research-related documents (except the master randomization schedule, consent forms, or screening logs) do not include information that would allow the participant to be identified. To this end, spaces/fields for participant's name, the first or last three letters of a participant's name, actual initials, reversed initials, birth date, hospital medical record number, provincial personal health number, social insurance number, address or phone number are not permitted on study-related documents.

Information is considered de-identified if the following conditions are met:

1. the unique study code is not derived from or related to the information about the individual;
2. the unique study code could not be translated to identify the individual, and;
3. the investigator or their institution could not use OR disclose the unique study code for other purposes OR disclose the mechanism for re-identification.

It is not necessary to use a personal identifier (for example, birthdate) as a secondary identifier in order to confirm the identity of the participant. This can be accomplished by using any two unique identifiers.

Participant Enrolment Logs, documents or databases, which correlate participant names with study code numbers, must be kept on the locked premises of the PI or in an appropriately secured electronic form.

As per the above discussion, Box 8.4 of the application should specifically state that a *unique study code,* not derived from or related to the information about the individual, i.e. name, SIN, PHN, hospital number, DOB, address, or unique characteristic, will be used. A proviso will be sent back if this is not directly specified.

8.4A USE OF PERSONAL HEALTH INFORMATION OR IDENTIFIERS

If you will be collecting personal identifiers, this must be indicated and justified. If the full date of birth will be collected, justify why this is necessary as opposed to only collecting the month and year of birth.

8.5 DATA ACCESS AND STORAGE

Give the names (if known) of those who will have access to the raw data, which may include information that would identify the participants. The research participants must also be told in the consent form who will have access to his/her data and what use will be made of it, either now or in the future. Temporary student assistants and clerks may be referred to by their role instead of name.

8.6 DISPOSITION OF STUDY 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 *after publication* within a UBC facility, but may be retained for a longer period provided that they are 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 Principal Investigator.

Please note that if it is not stated specifically in the response to this box that a study's data will be maintained for *at least five years after publication*, a specific statement explaining why not must be provided. If not, a proviso will be issued to ensure that data will be maintained the appropriate amount of time.

If your study is regulated by Health Canada, the data retention period is 25 years.

Describe any future use of the data beyond the conclusion of this research project (e.g., justification for future studies, publication, etc.) and indicate whether subject consent will be obtained now in the current consent procedure or the subject will be contacted later to obtain consent. Either possibility must be described in the consent form. If consent is to be obtained now, the future use of the data must be described in full in the consent form included with the current application. If consent for future use of the data is to be obtained later, full details, including the consent form, must be submitted to the CREB for review and approval before the research begins.

8.7 DATA TRANSFER TO OTHER INSTITUTIONS

If information will be sent outside of the local site, please indicate the type of information to be transferred and in what form it will be in when transferred.

The TCPS2 identifies 5 different categories of data collected from research participants, each with different implications for the privacy of participants (see TCPS2, Chapter 5, P. 56 – also below). When sending data off site, the data should be coded. Justification for sending directly identifying information or indirectly identifying information off site must be provided and approved by the CREB before data is transferred:

- 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 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.

8.8 DATA TRANSFER TO INSTITUTION

Give details about any data being received from other sites, if applicable.

8.9 DATA LINKAGE

If data is to be linked to any other data source (including a biorepository) the data set, how the linkage will occur and how confidentiality regarding shared information will be reserved needs to be identified and elaborated upon.

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Application Page 9: Documentation

Assign a version date to all attached documents created by the researcher. This version date must be included as a footnote on each page of the study documents. Pagination of attached documents should be in the form 'page X of XX'. Please ensure the date listed on the RISe application form matches what is on the actual document. The Certificate of Approval generates the date listed on the RISe application form; if this does not match what is in the document, your Certificate of Approval will be incorrect.

Identifiers on Research Documents
As per box 8.4., all study documents including participant information should be marked with a unique study number only. See discussion in Box 8.4**.**

9.1 PROTOCOL OR PROPOSALS
All applications for CREB review require a research protocol to be attached to this box. See Guidance Note #8, Article 1 for further discussion of what should be included in a research protocol. Note that research proposals submitted to granting agencies may be used to meet this requirement.

9.1B and 9.1C REGULATORY APPROVALS
Enter regulatory information when applicable. See Application, page 7, for further information about regulatory approvals.

9.2 CONSENT FORMS
Participant Consent Form – Informed consent is often documented by means of a written, signed, and dated informed consent form, following a process by which a participant voluntarily confirms his or her willingness to participate in a particular study, after having been informed of all aspects of the study that are relevant to the participant's decision to participate. The UBC Clinical Boards and Fraser Health Authority have developed a common consent form guide and template. See the following link to the UBC Consent Form Guide and Template for UBC Clinical REBs and Fraser Health Authority REB . The document can be downloaded in Word, saved to your desktop, and edited to meet the needs of a particular study. Note sections that are not relevant to your study do not need to be included.
If you are obtaining oral rather than written consent, you must describe the procedures you will use to obtain consent, including a script of how consent will be broached and obtained. Please note that even if you obtain oral consent, it may be advisable to leave a written statement of the information conveyed in the consent process with the participant. However, researchers should

not leave any documentation with a participant if it may compromise their safety or confidentiality or if it is culturally inappropriate to do so. See TCPS2 Article 3.12 and Article 10.2 for further discussion.
See Guidance Notes #13, #14 and #15 for thorough discussions of consent and consent processes.

9.3 ASSENT FORMS

Assent Form – TCPS2 Article 3.10 stipulates that the assent of a participant is required in situations where free and informed consent has been obtained from an authorized third party, and where the individual substantially understands the nature and consequences of the research. Also, see Guidance Note #15 for UBC specific assent procedures. Finally, refer to the CREB Assent Form Template.

9.4 INVESTIGATOR BROCHURES/PRODUCT MONOGRAPHS

The most recent Investigator Brochure (IB) for all investigational drugs must be attached to the CREB application. The IB should be updated via amendment as updates become available. For products that have Health Canada approval, the most recent product monograph should be attached to the application.

9.5 ADVERTISEMENTS

Advertisement to Recruit Participants – This includes any type of communication (e.g., flyer, radio/television script, poster, newspaper ad, Internet message) that is directed to potential participants for the purpose of recruitment.

All recruitment material used must be approved by the REB in the form it will be used in before recruitment begins, e.g. a newspaper ad and a poster should be submitted separately even if the text is only slightly different. Recruitment materials should give potential participants a basic understanding of the research, what would be expected of them (including time commitment), and their potential eligibility for the study. Include directions for the potential participant to contact the research team, if they are interested in the study. All recruitment material should be labelled with a version date. Do not include any payment or remuneration value for participation on the recruitment material; however, you may mention an honorarium, gift, or small token of appreciation will be given. Refer to Guidance Note #10, Article 1.3

9.6 QUESTIONNAIRES

Ensure that all questionnaires, surveys, tests, interview scripts etc. are attached as separate documents to this box. They should be in their final form. If they are included as an appendix in the protocol or study proposal, they still must be attached to this box as separate documents.

9.7 LETTER OF INTIAL CONTACT

Attach any letters of initial contact that are being used for the study. Ensure that they include the required elements listed in Guidance Note #10, Article 1.1

9.8 OTHER DOCUMENTS

Attach all other documents relevant to the study and REB approval in this box. This could include but is not limited to the following: peer review reports, clinical trial agreement, other REB approvals, transcript of audio visual item, data transfer agreement, website content, DHHS Grants. See the right hand side of the application for further information.

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Application Page 10: Fees

A fee for ethical review applies *only* to sponsored research studies (i.e., those funded by industry or for-profit sponsors). Please note that if the study team is collaborating with a sponsor, e.g. a sponsor is supplying the study drug or laboratory space but no other funding, the study does not need to pay for REB review.

Sponsored Research Fees

An initial application fee of $3,000 CAD per application covers the cost of the submission and initial review of the application. As of April 1, 2012, an annual renewal fee of $500 CAD will be levied (at the time of the annual renewal) to cover the cost of the annual renewal and other on-going oversight, including amendments and unanticipated events (Refer to the Annual Renewal Update posted below). The Principal Investigator must ensure the sponsor is aware of these fees.
Payment of the fee, or a letter stating the date payment is expected to be made, must accompany the Application for Clinical Ethical Review on RISe (See Page 10 of the Application Form). Review the Wire Payment Instructions document for advice on paying the review fee via wire transfer.
The Certificate of Approval will not be released until the review fee has been received. **If you have outstanding fees, no new CREB reviews will be undertaken until your account is brought into good standing**. For a current statement of your fee account or other specific queries relating to CREB fee payment, please contact (604-875-4111 x68917).

Fee for Renewal of Sponsored Research

Effective April 1st, 2012, all applications for annual renewal of ethics approval for **current** (active and approved prior to April 1, 2011) privately sponsored (industry funded) research studies will be subject to an annual renewal fee of $250 upon submission of the renewal. All new studies submitted for initial ethics approval subsequent to April 1st, 2011 will be subject to an annual renewal fee of $500 upon submission of the renewal.

For further information about the renewal fee and CREB procedures in this regard, see the notice of Fee for Annual Renewal on the CREB website at http://research.ubc.ca/ore/creb-forms-guidance-notes

UBC Clinical Research Ethics AGNs

VIEW A – RETROSPECTIVE CHART REVIEW

A.1 (Required field)
Summarize the research proposal using the following headings:
1) Purpose
2) Hypothesis
3) Justification
4) Objectives
5) Analysis of Data

A.2 (Required field)
Describe how permission to access the medical records and to collect and use these records will be obtained.

A.3
Briefly describe the type of data that you intend to collect (e.g., disease, diagnosis, outcome, demographic, aggregate, personal-level).
Important Note: If you intend to collect personally identifiable information, a data collection / data extraction form must be appended to Box 9.8.A. of the application form.

A.4
Specify the minimum number of charts / records required to conduct the study.

A.5 Personal Information (Required field)
A.5 Personally identifying information is any information that may reasonably be expected to identify an individual, alone or in combination with other available information, e.g. name, SIN, PHN, date of birth, address, or unique personal characteristic etc.

A.5.1 Types of personally identifiable information include but are not limited to the examples above. For example gender, e-mail address, telephone number, healthcare provider, discharge dates, photographs, postal codes etc. can all constitute personally identifiable information.

A.7. (Required field)
Describe the risks associated with the possible disclosure of the data. Include any foreseeable circumstances where disclosure of identifying data may be required by law.
A.8 (Required field)

Describe how the identity of the participants will be protected both during and after the research study, including how the participants will be identified on data collection forms.

Unique Study Code
UBC REBs require the use of a unique study code not derived from or related to the information about the individual i.e. name, SIN, PHN, hospital number, DOB, or unique characteristic.

A.9 (Required field)
Explain who will have access to the data at each stage of collection, processing and analysis, and indicate whether a current list of the names of study personnel (including co-investigators) and their delegated tasks will be maintained in the study file. If a list will not be maintained, please explain.

A.10 (Required field)
Describe how the data will be stored (e.g. computerized files, hard copy, video-recording, audio-recording, personal digital device, other).
For example, study documents must be kept in a secure locked location / filing cabinet, computer files should be password protected and encrypted and data should not be stored or downloaded onto an unsecured computer or a portable laptop.

A.11 (Required field)
Describe the safeguards in place to protect the confidentiality and security of the data. Reference procedural measures, technical measures, and physical measures planned for the protection of data. If a coding procedure is being used, describe the procedure in detail.

A.12 (Required field)
Describe what will happen to the data at the end of the study, including how the data will be destroyed, and what plans there are for future use of the data, including who will have access to the data in the future and for what purpose.
Please clarify that data will be stored according to UBC's Policy #85
http://www.universitycounsel.ubc.ca/policies/policy85.pdf
Original data for any given study must 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).

A.13 Data Transfer (Required field)
Will data be transferred outside of UBC or its affiliated hospitals?
If yes, please describe the type of data to be transferred, who the data will be transferred to, where the data will transferred, and how the data will be sent.

Note that if this changes in the future an amendment must be submitted before data is transferred.

A.14.A Data Linking (Required field)
Do you plan to link the data to any other data? Note that if this changes in the future an amendment must be submitted before data is linked.

A.14.B
Identify the data set, how the linkage will occur, and provide a list of data items in the other database. Also, identify what personal information will be used to link the databases and how confidentiality regarding this shared information will be preserved.

UBC Clinical Research Ethics AGNs

VIEW C – Creation of a Research Database, Registry or Biorepository

C.1 (Required field)
What is the scope and purpose of the database, registry or biorepository?
Some institutions may request that a Privacy Impact Assessment (PIA) be completed when creating a research database or registry. Consult your hospital or institutional privacy office for more information.
In addition to other attributes, biorepositories may be considered as: a) mono-user biobanks (i.e., a collection aimed at supporting a specific, single research project; b) an oligo-user biobank (i.e., a collection aimed at supporting several research projects, a research group or a research consortium); or c) a poly-user biobank (i.e., a collection aimed at supporting undetermined, multiple users with REB-approved research projects, through a defined access/application mechanism).

C.2 (Required field)
What are the anticipated public and scientific benefits of the database, registry or biorepository?

C.3
Over what period of time will data be collected? Include a clear date range of the information that will be included in the registry or biorepository. If data will be collected indefinitely, clearly indicate that data will be collected indefinitely or until the participant withdraws, if applicable.

C.4.A What information source(s) are you accessing?
Elaborate on the recruitment method. Answer C.4.A. and B if your project involves creation of a database or registry. Answer C.4.C. if your project involves creation of a biorepository. Tissue biospecimens are any human biospecimens or biological material comprised of whole solid tissues, cells isolated from solid tissues and fluids other than blood.
C.4.B. Provide specific details about the source(s), i.e. including name of the database or type of health records, location etc.
C.4.C. What are the sources of your biospecimens, check all that apply.
Direct from live subject (procedure conducted for research purposes)
Indirect from live subject (procedure conducted for clinical purposes and excess tissue leftover after clinical diagnosis obtained for research)
Post mortem tissue collection

C.5. A. Confidentiality (Required field)

Are you collecting personally identifying information/will the biospecimens be linked to personally identifiable information? [If not, skip to C.9] (if no, form should truncate to C.9) **Personally identifying information** is any information that may reasonably be expected to identify an individual, alone or in combination with other available information, e.g. name, SIN, PHN, date of birth, address, or unique personal characteristic etc.

C.5.B
Indicate the type of personally identifying information you will be collecting/that will be linked to the specimens. Include a justification for its inclusion in the registry or database and/or retention of the link. Important Note: For databases or registries, a data collection form should be attached to question 9.8. of the application.

C.5.C
How long will data remain identifiable/ specimens be linked (i.e. when, if ever, will it be irreversibly anonymized). Justify why data/specimens need to remain identifiable, if this is the case.

Irreversibly Anonymized data are 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 to very low. Refer to the appendix of definitions at the end of this document.

C.5.D.
List the individuals (who are not already listed on page 1 of the application) who will have access to personally identifying information at any stage in the data collection or review/abstraction of the data,/analysis of the specimens including those who will have access to master lists of keys linking identifiable participants to research data/specimens.

C.6.A. Consent (Required field)
Will participants consent to be included in the database or registry?/Have their specimens included in the biorepository? [If no, skip to C.7.]
Important Note: Attach a copy of the consent form to Box 9.2 of the application.
Click here for the required elements of the Consent related to banking:
UBC Guidance Note #16
CREB Guidance Notes Related to Tissue Collection and Banking
Pre-procedure consent is consent obtained prior to the individual undergoing a medical procedure (e.g. surgery or biopsy to remove a tumour). Post-procedure consent is consent obtained after the individual has undergone a medical procedure. For additional information click here.

C.6.B.
Specify who will explain the consent form and invite participants to contribute. Include details of where consent will be obtained and under what circumstances. For biorepositories, please explain whether the consent process is pre-procedure or post-procedure.

C.7

If you do not plan to obtain individual participant informed consent please provide justification for not doing so following the criteria outlined on the right. Please address each criterion individually. Refer to TCPS2 Articles 3.7 and 5.5 for further information on the following criteria.

A. Explain why inclusion in the registry or database/biorepository involves no more than minimal risk to the participants;

B. Confirm that the lack of participants' consent is unlikely to adversely affect the welfare of the participants;

C. Demonstrate that the purpose or aim of the registry/database/biorepository would be impossible or impracticable to carry out, if the prior consent of the participant is required;

D. Explain why the public interest in conducting this research using this registry or database exceeds the public interest in protecting the privacy of individuals;

E. Demonstrate that whenever possible and appropriate participants will be provided with information regarding their participation in the database, registry, or biorepository;

F. Demonstrate compliance with any known preferences previously expressed by individuals about any use of the information/ their specimens; and

G. Confirm that any other necessary permission for secondary use of information for research purposes are in place.

C.8.A. Participant access to data and withdrawal (Required field)

Will individual participants have the right to access their data, or right to amend or withdraw their information?

C.8.B.

Provide details of the process for accessing and/or withdrawing data, including what data can be withdrawn.

C.9. (Required field)

What is the entity or who is the person that will have custodianship of the database or registry/bio-repository?

A **data/biorepository custodian** is an entity or person who is responsible for overseeing the management and use of the data/biorepository, including the main rules governing use of the database/ biorepository, the process by which access requests will be reviewed, and the organization to whom the researcher is accountable for the proper management of the data/biospecimens.

C.10. (Required field)

What will be the address of the database, registry or the location of the biorepository? This should be a mailing address; however, if there is a URL, please also provide it.

C.11. (Required field)

What steps will be taken to ensure the security of the data/biospecimens? Reference procedural measures, technical measures, and physical measures planned for the protection of data. If a coding procedure is being used, describe the procedure in detail in this box.

C.12 (Required field)
For databases and registries, describe the risks associated with the possible disclosure of the data/. Include any foreseeable circumstances where disclosure of identifying data may be required by law.

C.13.A. (Required field) Data/Biospecimen Transfer
Will data/biospecimens be sent outside of the institution? [If no, skip to C.14]

C.13.B.
Explain why it is necessary to send the data/biospecimens outside of the institution, and indicate what data/biospecimens will be sent, where it/they will be sent, who it/they will be sent to, how it/they will be transferred (faxed, emailed, couriered, encrypted electronic transfer etc.) and where it/they will be stored.

C.13.C.
Will there be a data transfer/material transfer agreement? If so attach a copy of the data transfer agreement to box 9.8. of the application.

C.14.A. (Required field) Data Linking
Do you plan to link all or some of the data or the biospecimens to another data source (e.g. database, biorepository)? Note that if this changes in the future an amendment must be submitted before data is linked.

C.14.B.
Identify the data set, how the linkage will occur, and provide a list of data items in the other database. Also, identify what personal information will be used to link the databases and how confidentiality regarding this shared information will be preserved.

C.15.A. (Required field) Data Retention
How long are you planning to keep the data/biospecimens?

C.15.B.
If the data/biospecimens will be destroyed, indicate the planned method for erasure/destruction of the data/biospecimens.
Please clarify that data will be stored according to UBC's Policy #85
http://www.universitycounsel.ubc.ca/policies/policy85.pdf

Original data for any given study must 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).

C.16.A. Future Use (Required field)
Will the information in the database/biorepository be retained as an ongoing database/biorepository (or as part of an ongoing database/biorepository) for future research? [If no, skip to C.17]

C.16.B.
Provide a full description of the data/biospecimen stewardship process, including whether the dababase / biorepository will have formalized SOPs. Reference who will have access to the database in the future and under what circumstances, what will happen if an individual data custodian leaves the institution, where the ongoing database will be stored or maintained, and what security measures will be in place

UBC's REBs encourage researchers who are creating biorepositories to consider certification of their biorepository with the Canadian Tumour Repository Network (CTRNet) Biobank Certification Program or accreditation with the College of American Pathologists (CAP) Biorepository Accreditation Program.

C.17.A. (Required field)
Describe any commercial uses for which the data/biospecimens may be used, including any disclaimers concerning participant remuneration for such use.

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VIEW E – Harmonized Review of Multi-Jurisdictional Studies

THIS VIEW IS ONLY AVAILABLE TO APPLICANTS SUBMITTING TO THE HOSPITAL RESEARCH ETHICS BOARDS)

E.1 (Required field)
Is this the first/initial application for review of the multi-jurisdictional study at any of the sites where the research is going to be conducted? The **first/initial application for review** is the first application for ethical review of the research submitted to any of the Institutions with which UBC has a signed reciprocity agreement.
UBC has entered into partial reciprocity and collaborative review arrangements with certain other institutions and entities in situations where a study requires review and approval by more than one Canadian Research Ethics Board. For more information on streamlining processes being implemented at UBC click **here.** For a list of institutions with which UBC has a reciprocity or collaborative review agreement click **here.**

E.2. (Required field)
Are you the Lead Investigator for this multi-jurisdictional study? The Lead Investigator is the **only** Investigator conducting the multi-jurisdictional study at various sites external to UBC or the Investigator chosen from amongst numerous Investigators from various sites external to UBC to lead the multi-jurisdictional study. The Lead Investigator is the Investigator who submits the first/initial application for ethical review of the multi-jurisdictional study at any of the sites where the research is going to be conducted. The Lead Investigator is required to submit the initial application for review of the research to his or her home institution's REB regardless of where the research is taking place.
If this is an initial application for review of the study and you are NOT the lead investigator, you cannot continue with this submission.
If you are a UBC faculty member, you cannot answer 'no' to question E.1 and 'yes' to question E.2 because UBC must perform the review of initial/first application since UBC is your home institution.

E.3. Please indicate which external institution with UBC has a signed reciprocity agreement is your home institution.
University of Saskatchewan
University of Alberta
University of Victoria
Simon Fraser University
University of Northern British Columbia
If your institution appears on this list the application will truncate to section 9, where you will need to append all UBC site specific documents as applicable. Please append to section 9 all available

documentation and information from the Lead PI and his/her REB, including the Lead PI's REB Application, Certificate of Approval, Informed Consent and recruitment documents and all available correspondence between the Lead PI's REB and the Lead PI, including, if available, the minutes from the Lead PI REB's review of the study.

If your institution does not appear on this list, you will be directed to 4.8 and will need to fill out the full CREB application.

Appendix: Acronyms and Glossary

Acronyms:

AGN: Application Guidance Note

BCCA: British Columbia Cancer Agency

C&W: Children & Women's

CREB: Clinical Research Ethics Board

GN: Guidance Note

PHC: Providence Health Care

PI: Principal Investigator

QA/QI: Quality Assurance/Quality Improvement

REB: Research Ethics Board

TCPS2: Tri-Council Policy Statement (2nd version)

U.S. DHHS: United States Department ofHealth and Human Services

VCHRI: Vancouver Coastal Health Research Institute

Glossary:

For a complete guide to ethics definitions please refer to the Glossary of the TCPS2. The most common definitions have been added below.

Authorized third party: Any person with the necessary legal authority to make decisions on behalf of a prospective participant who lacks the capacity to consent to participate, or to continue to participate, in a particular research project. In other policies/guidance they are also known as "authorized third party decision makers."

Autonomy: The capacity to understand information and to be able to act on it voluntarily; the ability of individuals to use their own judgment to make decisions about their own actions, such as the decision to consent to participate in research.

Clinical Equipoise: The existence of a genuine uncertainty on the part of the relevant expert community about what therapy or therapies are most effective for a given condition.

Duty of Care: The obligation of clinicians to act in the best interest of patients. In the context of clinical trials, researchers are concerned with the welfare of individual participants, but are also focused on the generation of new knowledge that may or may not confer direct benefits on participants. Nevertheless, researchers do have a duty of care to ensure that the participant is an integral part of the research design and conduct. Refer to Chapter 11 of the TCPS2 for more information.

De-identified Data: information where an individual's identifying information has been removed, and where there is no reasonable basis to believe that the information could be used to identify an individual. De-identified data may nevertheless be coded (e.g. via a confidential master list created by the researcher) so that the information can be linked to the individual and his/her clinical or other records. See AGN 8.4 for further directions on coding that is consistent with de-identification of data.

Human Participants: An individual whose data, or responses to interventions, stimuli, or questions by a researcher are relevant to answering a research question; also referred to as "participant," and in other policies/guidance as "subject" or "research subject."

Human biological materials: Tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva, and other body fluids. The term also includes materials related to human reproduction, including embryos, fetuses, fetal tissues and human reproductive materials.

Identifiable information – Information that may reasonably be expected to identify an individual, alone or in combination with other available information. Also referred to as "personal information."

> **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 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.

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.

Multi-jurisdictional Study: A multi-jurisdictional study is a research study that requires review and approval by more than one Canadian research ethics board (i.e. by more than one Canadian REB that is not a UBC affiliated REB) as a result of the requirements of the TCPS2 and/or UBC's and/or another institution's human ethics policies.

Retrospective Data: Data collected from charts dated on or before the date of ethics approval

Prospective Data: Data collected on an ongoing basis (i.e. chart information is taken from patients who are seen after the date of ethics approval)

Secondary use of data: The use in research of information or human biological materials originally collected for a purpose other than the current research purpose.

Therapeutic Misconception: A misunderstanding, on the part of participants, of the purpose, benefits, and/or risks of clinical trials. Often participants do not understand that research is aimed primarily at producing knowledge and may not provide any therapeutic benefit to them.

Vulnerability: A diminished ability to fully safeguard one's own interests in the context of a specific research project. This may be caused by limited capacity or limited access to social goods, such as rights, opportunities and power. Individuals or groups may experience vulnerability to different degrees and at different times, depending on their circumstances. See also "Autonomy." Refer to Chapter 4 of the TCPS 2 for more information.