

GUIDELINES FOR RESEARCH ETHICS REVIEW INVOLVING HUMAN PARTICIPANTS

All research projects involving physicians, staff (including staff acting as investigators outside the Institution), students (i.e., research within the institution or using institutional resources), or patients, must obtain ethical approval from the Research Ethics Board (REB) before research can begin. The REB is responsible, on behalf of the institution, for ensuring that all research involving human participants under the auspices of its institution meets current ethical standards. Heads of departments /divisions /programs are responsible for ensuring that all such research is submitted for ethics review.

Proposals are reviewed by the full board at a scheduled meeting, or in a delegated manner, depending on level of risk associated with the study, and on prior review. Regardless of the type of review, a full application form must be completed. A complete research proposal/and or protocol must also be submitted.

TYPES OF REVIEW

- I. **FULL BOARD REVIEW:** This is the level of REB review assigned to studies which involve greater than minimal risk. This is the default that will apply unless there is sufficient justification for delegated review.

Please submit signed the scanned application form and supporting documents to the REB office (reb@hrh.ca) prior to the submission deadline, including:

- HRH Initial Prospective Application Form, including HRH Research Impact Form
- Consent Form(s)
- Protocol
- Budget Information
- Questionnaires, Recruitment Tools, etc.
- Investigator's Brochure/Product Monograph/Device Manual (as applicable)
- Health Canada No Objection Letter (as applicable)

- II. **DELEGATED REVIEW:** Submissions for delegated review are accepted on a rolling basis (i.e., not subject to a submission deadline). For delegated review, please submit the scanned and signed version of the appropriate Application Form and accompanying study documents to the REB Office.

Studies that may qualify for Delegated review are considered either minimal-risk and non-invasive (e.g. retrospective chart reviews, non-intrusive questionnaires or surveys, non-invasive assessments, use of existing samples), or studies involving only current standards of care.

The investigator must include the justification for requesting delegated review. The decision of whether a study qualifies for delegated review rests with the REB Chair. Where delegated review is not granted, the investigator will be informed that a full board review will be required.

THE APPLICATION FORM - INSTRUCTIONS

Electronic application Forms are available from the Research Ethics Board website. If this is a multi-centre study, a complete application must be submitted to each local REB. Ensure that the appropriate signatures are obtained for each site. The entire form must be completed. If a section does not apply, indicate N/A. Do not refer to or attach other documents in response to questions except where indicated. The following are

further explanatory notes regarding some items on the application form. The numbering corresponds to the items on the application form.

SECTION I: GENERAL INFORMATION

1. PRINCIPAL INVESTIGATOR

The Principal Investigator is the responsible leader of the research team and must be clearly designated for each site. **There should be one PI per site per protocol. Students/trainees cannot be listed as the PI. Where the investigator is a student, the supervisor should usually be designated as the PI and sign this section.** Some institutions require the PI to be a staff member at the institution where the research will take place. Check with your institution.

For “clinical studies” as defined by Health Canada (i.e. involving an investigational drug or medical device), the Principal Investigator must be a Qualified Investigator (a physician or, where applicable a dentist, and a member in good standing of a professional medical or dental association).

2. FULL STUDY TITLE

Include the full title as it appears on the protocol.

4. INVESTIGATORS

4C. Contact Person

For studies originating from outside of the institution, a staff member must be involved as the institutional liaison who will accept responsibility for the research activities at the institution, as well as serve as the administrative contact with the REB. The role of institutional liaison applies only at those institutions that do not require the PI to be a staff member and only for studies where the PI is not a staff member.

Signatures

All applicable signatures must be obtained before the REB reviews the application. All sections of the form must be completed before signatures are obtained.

5. DEPARTMENT/DIVISION/PROGRAM APPROVAL

The application forms for all projects submitted for review will require the signature of the Division/Department Head/Program Director where the research is to be conducted. The signature indicates agreement that the Division/Department/Program supports the project and that the PI is qualified by education, training, and experience to perform his/her role in the study. When the Division/Department Head/Program Director is the investigator, the signature of an individual one level above the investigator is required.

8. POTENTIAL CONFLICTS OF INTEREST

The term “conflict of interest” refers to situations in which financial or other personal considerations may compromise, or have the appearance of compromising, a researcher’s professional judgments. The bias such conflicts could conceivably impart may inappropriately affect the goals of research.

“Apparent” or “perceived” conflicts of interest refer to situations which appear to present a conflict to an outside observer, although they may not give rise to an actual conflict. The mere appearance of a conflict may be as serious and potentially damaging as an actual conflict. Immediate family includes an investigator’s spouse and dependent children (including stepchildren). For more information, you may refer to the University of Toronto policy on Conflict of Interest at the following internet location:

<http://www.utoronto.ca/govcncl/pap/policies/conacad.html>

9. OTHER ETHICS/SCIENTIFIC/ SCHOLARLY REVIEW

Indicate in the table where this application is being submitted, including sites where an application has been or will be submitted, and REB review status. The relevant documentation (REB review letter, reply to any concerns, approval letter) must be provided.

11. CLINICAL TRIAL REGULATIONS

This section need only be completed if the research study is a clinical trial. Health Canada, under Division 5 defines a clinical trial (requiring Health Canada approval) as “an investigation in respect of a drug for use in humans that involves human participants and that is intended to discover or verify the clinical, pharmacological or pharmacodynamic effects of the drug, identify any adverse events in respect of the drug, study the absorption, distribution, metabolism and excretion of the drug, or ascertain the safety or efficacy of the drug.

Investigational drugs or devices include all drugs (including biologics and natural health products) or medical devices requiring Health Canada approval, as well as all approved drugs being tested for a new indication (e.g., age group, disease entity), dosage or method of administration.

Studies involving investigational drugs or medical devices must apply for authorization for research use from Health Canada. For investigational drug trials a “Clinical Trial Application” form must be submitted to Health Canada. Provide a copy of the authorization or “No objection” letter from Health Canada as soon as it becomes available. Final REB approval of the study will not be granted until the no objection letter has been received. For certain medical device studies (class III and IV devices), however, Health Canada requires REB approval first.

If results are to be submitted for US Food and Drug Administration (FDA) approval, provide the IND number (drug studies) or PMA number (device studies).

SECTION II: STUDY SUMMARY

A size limit has been set for some of the items in this section, as indicated on the form.

12. ABSTRACT

Ensure that the abstract is described using lay language.

11. RATIONALE AND HYPOTHESIS/RESEARCH QUESTION

Ensure that the rationale and hypothesis are described using lay language For studies involving investigational new drugs or devices or use of an approved product for a new indication, provide justification to support the investigational use in this project.

14. STUDY DESIGN

14A. Design/methodology

Describe the basic study design and method. If this is a randomized trial, explain how participants will be assigned to each group. If this is a pilot study, indicate briefly how the data will be used to develop a full follow up study.

14B. Primary outcome measures

List the primary endpoints, or key data items that are required to answer the study question.

14C. Criteria for Early Withdrawal

Indicate what endpoints or stopping rules will serve as triggers/thresholds for early withdrawal for subject safety (e.g. regarding treatment failure/adverse events), such as blood pressure levels, laboratory values, disease status assessments, etc.

14D. Placebo

The Tri-Council Policy Statement (TCPS) indicates that, with some exceptions, placebo should not be used for conditions where an effective treatment is available. If the research involves placebo, explain the justification for its use and what provisions are in place to reduce any increased risk associated with the use of placebo.

14E. Deception or Lack of Disclosure

The TCPS permits the REB to approve a consent procedure which does not include, or which alters some information about the study only when the deception or lack of disclosure poses no more than minimal risk, the research could not practicably be carried out in another way, the participants are provided with full disclosure at a later date (where possible) and the deception or lack of disclosure does not involve a therapeutic intervention. Deception or lack of disclosure is used most often in social science or psychology research, where full disclosure would likely affect the responses of the participants and thus invalidate the research.

14F. Study Restrictions

List in this section any restrictions on medications/treatments or lifestyle, such as diet, exercise, smoking, exposure to sun, driving, etc. Specify the duration of restrictions and the reasons the restrictions are necessary.

15. PARTICIPANTS/CONTROLS

Selection of participants must be equitable. Include the rationale for the choice of control group if applicable. If a vulnerable population is used (e.g., children, incompetent adults), include justification for this choice (e.g., has the research question been previously addressed in a less vulnerable populations). Justification is not required at institutions where these vulnerable populations are the primary patient population (e.g., paediatric or geriatric centres). If a group (e.g., women of childbearing potential, the elderly) is excluded from a study involving a general patient population, justify. Where women of childbearing potential are excluded will consideration be taken for inclusion of women who are not at risk of becoming pregnant?

15E. Sample Size Justification

For quantitative studies, include sample size calculations and source for standard deviation. For qualitative studies indicate approximate sample size and rationale. You may refer to the protocol for this information.

16. STUDY INTERVENTIONS OR PROCEDURES INVOLVING HUMAN PARTICIPANTS

16A. Usual Standard of Care

This section must specify what is standard care specifically as it relates to the population under study and any study interventions, and how participation in the study will alter standard care if applicable (i.e. what would happen if the study were not being done).

16B. Changes/additions to Standard of Care

Describe any procedures that are being done in the study that are not part of standard of care, including any procedures performed purely for research purposes (e.g. extra blood samples, evaluations, telephone surveys, questionnaires). If participants are required to meet certain eligibility criteria that necessitate changes to or termination of treatments, describe them too. Include all patient contact and be as specific as

you can. Attach a copy of all instruments (i.e. questionnaires (non-standardized), interview scripts and rating scales) that will be administered during the study.

SECTION III: ETHICAL ISSUES

18. RECRUITMENT AND CONSENT

18B. Identification of potential participants.

Specify how potential participants will be identified and by whom. Respect for patient privacy requires that patient records be reviewed by persons within the patient's circle of care, who have access to patient information as part of their normal professional duties, or their delegates (e.g. study coordinator working on behalf of investigator who has access).

Health Records include but are not limited to: slides (e.g. pathology), radiology films/reports, surgical lists and databases.

The REB must review all study-related materials that will be given to participants, including advertisements or letters regarding recruitment. Note that no specific dollar amount of payments to participants should be listed in the advertisement.

Finder's Fees include money or other reward given to a physician (or group of physicians, or other health care providers) in payment for identifying or recruiting a patient into a study or a trial. Finder's fees are prohibited. For more information the University of Toronto Policy on finder's fees can be found at: http://www.facmed.utoronto.ca/scripts/index.asp?action=31&U_ID=0&N_ID=13&P_ID=9976

18C and D. Initial contact with participants and consent process.

Issues to consider include whether the contact person is known to the subject/authorized third party, has access to patient information as part of their normal professional duties, or is able to assess capacity to consent.

18F. Checklist of Study Participants

The purpose of this checklist is to flag for the REB any research scenarios that may raise special concerns. "Participants unable to communicate" refers to patients who are mentally competent, but who, because of certain conditions (e.g. stroke), are unable to communicate or have difficulty communicating their intentions. "Marginally incompetent" refers to patients who fall in the grey area between competent and incompetent, and whose capacity may fluctuate over time.

18G. Enrollment in Multiple Studies

There may be occasions where a number of different research projects focus on a particular patient population, and individual patients may be eligible for more than one study. Enrollment in multiple studies raises concerns whether the studies are ongoing simultaneously or in succession. In this situation, investigators must explain what procedures are in place to avoid enrollment of patients in multiple studies. If enrollment in multiple studies is anticipated, justify and explain what extra precautions are in place to ensure patient safety and welfare.

SECTION IV: RISKS, BENEFITS AND SAFETY

19. RISK/BENEFIT ESTIMATES

It is the expectation of the Tri-Council Policy Statement that proposed research will be designed to benefit participants where possible. Studies that involve significant risk without a balance of significant benefit may be inappropriate.

19A. Potential Harms

Describe all risks associated with the study procedures and the likelihood of these events occurring. Please list all the risks documented in the protocol and study consent form(s).

19A.v) If participation in the study may affect a patient's options for future care (e.g., making them ineligible for other standard therapies or the possible development of antibodies which might prevent future treatment with the investigational agent), explain what options will and will not be available.

20. PAYMENTS

Participants should not be expected to incur expenses as a direct result of participation in a research study; reimbursement for out-of-pocket expenses (e.g. travel) is encouraged. Payment should not be used in such a way that it could be construed as an undue inducement to participate (e.g. unreasonable amount, payment tied to completion of study). Reimbursement should be for expenses, time or inconvenience, but should not be used to encourage participants to accept increased risk. If reimbursement for time is proposed, explain. It is expected that expenses will be fully covered and any payments for time (including honoraria) will be pro-rated for partial participation.

21. MONITORING

Monitoring refers to oversight activities performed by groups other than the REB, such as the study sponsor (e.g. site visits to check for GCP compliance, interim analysis of results by a data and safety monitoring board or steering committee).

22. PUBLICATION/DISSEMINATION OF RESULTS

Since the contribution to knowledge is one of the primary purposes of medical research, researchers are encouraged to publish the results of their research. Furthermore, where possible, researchers are strongly encouraged to share the study results of the research with the participants who made the research possible, and/or with the relevant patient communities.

Any document that will be viewed by a study participant **must be submitted to the REB for review and approval**. If any of the above material has not yet been developed and is intended for use at a later date, **it must be submitted as an Amendment prior to implementation**.

SECTION V: ETHICAL ISSUES

23. COLLECTION AND USE OF PERSONAL HEALTH INFORMATION

During collection and storage data and samples must be kept secure from theft, interception, unauthorized reading and copying. Investigators must state their means of protecting study data or samples from such violation, for instance by coding systems and/or security systems.

The Personal Health Information Protection Act (Bill 31) which came into force in Ontario on Nov. 1, 2004, requires that for research studies involving the collection, use and disclosure of personal health information the REB must receive a description of what information will be collected, and how it will be collected, used and stored. The act defines personal health information as follows (s. 4):

Personal Health Information means identifying information about an individual in oral or recorded form, if the information,

- a) Relates to the physical or mental health of the individual including information that consists of the health history of the individual's family,
- b) Relates to the providing of health care to the individual, including the identification of a person as a provider of health care to the individual,

- c) Is a plan of service within the meaning of the *Long-Term Care Act, 1994* for the individual,
- d) Relates to payments or eligibility for health care in respect of the individual,
- e) Relates to the donation by the individual of any body part or bodily substance of the individual or is derived from the testing or examination of any such body part or bodily substance,
- f) Is the individual's health number, or
- g) Identifies an individual's substitute decision-maker.

Identifying Information means information that identifies an individual or for which it is reasonably foreseeable in the circumstances that it could be utilized, either alone or with other information, to identify an individual.

SECTION VI: FUNDING, CONTRACTS AND AGREEMENTS

23. BUDGET

27. AGREEMENTS Refer to the HRH Impact Form for details regarding submission of contracts or research agreements.

MATERIAL TRANSFER AGREEMENT

This refers to agreement for transfer of biological materials (e.g., tissues, cell lines) from the institution to another institution or other entity.

The agreement usually originates from the institution sending out the materials. If biological material (e.g., tissues, cell lines) is to be transferred from this institution to another institution or entity, indicate what arrangements are in place to ensure that appropriate consent has been obtained for this use and that donor confidentiality will be protected.

INFORMATION SHARING AGREEMENT

An information sharing agreement is recommended when a health information custodian shares a patient's personal health information with a researcher from another hospital or institution. The agreement should specify who are the information custodians, and the outside researcher with whom the information is being shared. The agreement should also describe the use, storage and disposal of the information.

28. Liability

Please indicate who will cover the costs of treatment not covered by the provincial health plan in case of injury directly resulting from participation in a research study (i.e. sponsor, institution, other).

29. Publication Agreements

Agreements regarding publishing of medical research should not prevent the publication of results or the communication of information important to subject safety.

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