

Guidance Notes

For RQHR Research Ethics Board Application Form



GUIDANCE NOTES

The following Guidance Notes (GNs) are intended to ensure that applicants have the necessary information to be able to fill out the Application for Research Ethics Review correctly and to construct consent forms that meet RQHR REB standards. The RQHR REB procedures comply with, the pertinent Tri-Council Policy Statement (TCPS) on 'Ethical Conduct for Research Involving Humans' (1998) as well as with the ICH Good Clinical Practice Guidelines (ICH GCPs) (1997).

The purpose of the RQHR REB is to determine whether the research question or hypothesis is scientifically and therefore ethically valid; and, if so, whether the research is in compliance with the relevant ethical requirements for carrying out research involving human subjects. In accordance with TCPS Article 1.1 and ICH GCP Article 3.3.6, the research study cannot begin until the REB issues its written approval of the research proposal. All investigators are responsible for understanding and adhering to the TCPS and other relevant guidelines. These Guidance Notes are not intended to be a substitute for this responsibility. Refer to the original documents for complete information.

These notes are offered as guidance to investigators. They are not intended to apply to every situation. The Board may, under certain circumstances, require different procedures than those described here. Similarly, investigators may request that a process other than that described here be followed for a particular project.

Acknowledgement

The RQHR Research Ethics Application Form, Guidance Notes, and Consent Form template were adapted with permission from the forms used by the University of British Columbia Clinical Research Ethics Board.

How to Use the Guidance Notes With The Application Form

The GN's are numbered and correspond to the same numbered box in the Application Form. There are no direct links from the application form to this document so both documents must be opened and viewed. It is the responsibility of the researcher(s) to ensure that the information contained in each GN is applied in a manner appropriate to each individual study for both the Application Form and any accompanying documentation. The REB requires a complete response to each question in the Application Form.

If, after reading the question and the corresponding guidance note, a box does not apply to your study, enter "N/A" in the box instead of leaving it blank.

Submitting the Application

Application for ethical approval of research proposals is made by submitting 1 original and 19 copies of the application form and other attached forms to the Research Ethics Board, Research and Performance Support, 2180-23rd Ave., Regina, SK, S4S 0A5, along with 3 copies of the complete research protocol. If your research qualifies for expedited review, you will only need 1 original and 2 copies of the application form, along with 3 copies of the complete research protocol. All applications must be typewritten. No hand-written applications will be accepted.

All signatures requested must be obtained prior to submission to the Board. Applications with missing signatures will be returned to the investigator without review.

Please note that beginning March 2011, principal investigators of chart audit studies must complete the *McMaster Chart Audit Tutorial*, available at <http://ethics.mcmaster.ca/chart/>, prior to submission to the Board. Principal investigators of chart audit studies prior to March 2011 are exempt from this requirement.

Similarly, principal investigators of studies involving contact with patients (e.g. patient interviews, patient surveys, focus groups, etc.) must complete the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS)* tutorial, available at <http://www.pre.ethics.gc.ca/eng/education/tutorial-didacticiel/>, prior to submission to the Board. Principal investigators of studies involving contact with patients prior to March 2011 are exempt from this requirement.

Applications received at least ten working days prior to a scheduled meeting will be reviewed at that meeting. The application is recorded and forwarded to the Chair of the Board. Following review by the Committee, the Chair will communicate the decision regarding suitability to the applicant in writing. For the REB meeting dates, please see the link on the website: http://www.rqhr-rps.ca/page/reb_meeting_dates/

The outcome of the first review of the application through either a Full Board or an Expedited Review will be one of the following four decisions:

Approval: The Certificate of Approval will be issued for a term of one year.

Conditional Approval: The REB endorses the study with some changes and authorizes the Chair to grant approval when the concerns addressed to the researchers in the Notice of Ethical Review (i.e., the provisos) have been satisfactorily addressed.

Deferral: Based on the documentation provided, the REB is unable to make a final decision. The decision is deferred for full board review at such time as the researchers submit the supplementary information or documentation as specified by the REB in the Notice of Ethical Review.

Not Approved: The REB does not authorize the conduct of the research in the RQHR.

This decision will be forwarded to Administration for information and to the applicant with an outline of the requested changes, if any. **Research projects must not be initiated until "Approval without changes" is granted.**

Whom to Contact for Assistance

Questions regarding preparation of an application should be directed to the office of Research and Performance Support at 306-766-5451.

The RQHR Research Ethics Application form consists of 10 sections. The type of project determines which sections need to be completed. The following table summarizes this information.

	Prospective Research Involving Human Subjects	Retrospective Research Using Identifiable Health Information (e.g., Chart Audit)	Database Research (i.e., using de-identified health information)
Part 1: Identification	✓	✓	✓
Part 2: Department Approvals	✓	✓	✓
Part 3: Research Summary	✓	✓	✓
Part 4: Use of Health Information	NO	✓	NO
Part 5: Human Subjects	✓	NO	NO
Part 6: Project Details	✓	NO	NO
Part 7: Informed Consent	✓	NO	NO
Part 8: Privacy Protection	✓	✓	✓
Part 9: Investigator Profile	✓	✓	✓
Part 10: Attachments	✓	✓	✓

Table of Contents:

Part 1: Identification

Part 2: Department Approvals

Part 3: Summary of Research Proposal

Part 5: Studies Involving Human Subjects

Part 6: Project Details

Part 7: Informed Consent

Part 8: Privacy Protection

Part 9: Investigator Profile

Part 10: Attachments

PART 1: IDENTIFICATION

GUIDANCE NOTE 1.1: PRINCIPAL INVESTIGATOR

The "principal researcher" is the individual who is ultimately responsible for the actions of those acting with delegated authority. He/she is the person responsible for the conduct of the clinical trial at a trial site or the responsible leader of the team.

The Principal Investigator for a study must notify the REB office in writing when this responsibility is going to be assumed by a different researcher. Principal Investigators must also ensure that a process is put into place to ensure the ongoing safety of research subjects in the event that the Principal Investigator leaves or retires from their RQHR affiliated position and the study remains ongoing. Principal Investigator must be affiliated with the Regina Qu'Appelle Health Region.

Multiple Investigators

Investigators can request that multiple "sites" conducting the same study operate at the same institution (e.g., a stroke researcher and a cardiologist researcher wish to each act as the principal investigator for separate "sites" of a multi center trial being conducted at one hospital). In such cases, a legitimate reason for operating in this way must be provided to the REB. Furthermore, the REB will request that the two "sites" coordinate all interactions with the REB (e.g., amendments, renewals, SAE's) as a method of streamlining the approval processes and preventing divergence in consent form disclosures.

Address

The REB office will send all Notices of Ethical Review, Acknowledgements, and Certificates of Approval to the address provided for the Principal Investigator.

GUIDANCE NOTE 1.2: AFFILIATION

All Principal Investigators must have a staff appointment at a RQHR affiliated institution. The Principal Investigator 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 Principal Investigator.

GUIDANCE NOTE 1.6: PROJECT TITLE

The title given in Part 1 of the Application Form and the title of the protocol submitted should be the same and correspond to the title of any consent form(s) also submitted.

GUIDANCE NOTE 1.9: EXPEDITED REVIEW

All new applications for clinical research must be submitted using the "Application for Research Ethics Review" form, including those that qualify for expedited review.

Minimal Risk Studies:

The process used to review new applications varies according to the level of risk (i.e. is proportionate to the level of risk) that the subject could experience as a result of the particular type of research procedure used, and is described below. Minimal risk studies are eligible for an expedited review.

Submission Criteria

Minimal Risk is defined in the TCPS as: "...if potential subjects 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 subject in those aspects of his or her everyday life that relate to the research then the research can be regarded as within the range of minimal risk" [TCPS C1]. Risks of daily life mean those risks encountered in the daily lives of the subjects of the research, considering their actual life situations, as opposed to the daily life of "normal persons" or "healthy volunteers" as the case may be.

Types of Minimal Risk Research Studies Qualifying for Expedited Review

Studies that may meet the criterion for minimal risk include research that is *limited* to the following sources of data and may undergo expedited review by the REB Chair:

Primary Sources of Data Obtained for Prospective Research

- Collections of hair, nail clippings, deciduous teeth, excreta, salivary secretions, additional swabs, or other external secretions that have been collected in a non-invasive manner and that may also be collected as part of routine clinical care;
- Placenta or amniotic fluid collected as a consequence of normal labour and delivery;
- Data recorded using non-invasive procedures routinely employed in clinical practice (e.g. EEG or EKG);
- Blood samples collected by venipuncture and that may also be collected as part of routine clinical care;
- Output data obtained as a result of moderate exercise undertaken by healthy volunteers;
- Other clinical non-invasive data that may be collected as part of routine clinical care and used for observational research;
- Interview or filling in a questionnaire for a fully competent adult subject
- Use of previously collected research data, without record linkage
- Existing data, documents, or records
- Existing pathological or diagnostic specimens
- Response to provisos issued by REB
- Amendments
- Annual review
- Open label extensions

Secondary Sources of Data Used for Retrospective Research

- Studies of a clinical nature using existing databases/registries or linking information between databases.
- Previously collected pathological or diagnostic specimens whereby the tissue is frozen and the cells are dead.

All studies that do not meet the criteria described above must be submitted for full board review. The REB Chair also reserves the right to refer any study for full board review for any reason and will notify the applicant of a change.

Expedited Review Not Allowed

- Studies with greater than minimal risk to the subject
- Research on a sensitive topic that could cause distress to the subjects
- Action research
- Deception
- Collection of tissue/blood for the purpose of creating or adding to a tissue bank or for the purpose of genetic research.
- Group interview or focus group
- Studies whose purpose is the derivation of stem cell lines from human somatic tissue, umbilical cord or placenta OR research involving the grafting of stem cell lines into humans must be submitted for full board review.
- Data linkage
- Recruitment via telephone or on the internet
- Any subjects who are less than 18 years of age
- Any subjects who are unable to be fully informed, such as those with mental disability or dementia
- Video/audio recording
- Payments/gifts-in-kind of value more than \$20 per research subject

GUIDANCE NOTE 1.12: PROJECT PERSONNEL

All members of the research team must be listed in this section. In addition to their RQHR and/or University affiliation, their role in the research project must also be reported (i.e., co-investigator, study coordinator, research assistant, or student).

GUIDANCE NOTE 1.14: SOURCE OF FUNDING

Researchers must send a letter to the REB office informing them of any changes or additions to the funding source(s).

GUIDANCE NOTE 1.17: ETHICS REVIEW FEE

The fee for ethical review of industry sponsored studies is \$1,000.00 and applies only to research that receives its funding from an industry sponsor (i.e. pharmaceutical/medical devices company or an agent thereof). The fee covers the submission of the initial request for ethical review, subsequent amendment and renewal applications, as well as the submission of serious and unexpected adverse event reports in the case of clinical trials.

Payment of the required fee, or a letter stating that the fee will follow and by when, must accompany the Application for Research Ethics Review for all industry-sponsored research. It is the responsibility of the Principal Investigator to ensure that their sponsor is aware of this requirement and to submit the cheque or letter at the time of the submission to the REB. The REB will review the research only if the fee or a letter accompanies the application.

Waiver Criteria

The fee is waived for:

1. Studies receiving a grant-in-aid (normally an investigator-initiated study with partial funding-e.g. supply of drugs or devices or a very limited amount of funding from an industry sponsor);
2. Studies that are funded by not-for-profit agencies;
3. Studies that receive internal grants either from RQHR-affiliated institutions (including self-funded);
4. Studies funded by CIHR, NSERC, CHSRF, and NIH (including NIH Institutes), and;
5. Studies without funding.

Mechanism for Submitting the Fee

For cheques sent to the REB office AFTER the submission of the initial application: Accompany the cheque with a memo that identifies the study by citing the Principal Investigator's name and the exact study title. Requests for invoices sent to the REB office after an application is submitted, must include the exact title of the research study and the Principal Investigator's name.

Requirements for Fee Refund

The fee will be totally refunded if the associated research study is withdrawn prior to review. \$500.00 of the fee amount will be non-refundable if the associated research study is withdrawn after the review.

GUIDANCE NOTE 1.18: SCIENTIFIC PEER REVIEW

For research with more than minimal risk, the REB must be satisfied about both the value and the scientific validity of the study. Under some circumstances and depending on the level of risk, the REB may request that a peer review be conducted as a condition of approval. Research that poses minimal risk will not usually require peer review.

Independent Peer Review Information

Peer review is considered independent when experts in the field, who are not affiliated with the institutional department carrying out the study or who are not affiliated with the company sponsoring a clinical drug/device trial, have evaluated the study for its scientific appropriateness.

An independent peer review may be either 'internal' or 'external'. The appropriate type of review is dependent on the nature of the study.

Peer reviews conducted by granting agencies or by Health Canada, for investigational drugs or devices, are considered to be acceptable types of 'external' peer review.

Provide a description of any independent peer review conducted and attach a copy of the peer review report.

If a peer review has not been conducted, explain why this is the case. Do not use 'not applicable' to complete this Box since there are no categories of research which are automatically exempted from peer review.

GUIDANCE NOTE 1.20: OBTAINING REGULATORY APPROVAL

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 Licence must submit the appropriate application for regulatory approval to Health Canada before research can begin.

It is the duty of the principal investigator to be certain that Health Canada has issued a NO OBJECTION LETTER before the study begins enrollment. 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).

All clinical trials, including Phase IV trials, must be conducted in accordance with good clinical practices as specified by ICH Good Clinical Practice Consolidated Guidelines. However Phase IV clinical trials are not subject to the Clinical Trial Application filing requirements with Health Canada.

Industry Sponsored Clinical Trials

Specify the date of the application to Health Canada and the Health Canada control number for all clinical trials. The control number must be submitted once obtained if not available at the time of submission to the REB.

Investigator-Initiated Clinical Trials

Specify the date of the application to Health Canada. A copy of the Health Canada NO OBJECTION LETTER (NOL) must be submitted to the REB once obtained.

PART 2: DEPARTMENT APPROVALS

GUIDANCE NOTE 2: DEPARTMENT APPROVALS

This page must be completed for all studies accessing or using RQHR resources. This includes internally funded projects that do not involve a direct exchange of money, but rather, are funded through 'donations-in-kind' from various departments. Signatures are necessary to ensure that prior to commencement of the investigation, department heads and unit managers have had an opportunity to assess the impact of the proposal on their area.

PART 3: SUMMARY OF RESEARCH PROPOSAL

GUIDANCE NOTE 3: SUMMARY OF RESEARCH PROPOSAL

The RQHR REB requires that a research protocol/research plan be submitted for ALL types of studies, including pilot studies and retrospective chart reviews. The research proposal submitted to granting agencies may be used to meet this requirement; in this case, ensure that the appropriate section of the grant application is referenced. For all other studies, including those that are submitted for expedited review, investigators must submit a protocol that uses the following suggested headings. Append no more than 2 additional sheets.

Introduction

Include background information that leads up to the specific study being proposed.

Purpose & Objectives

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. Also include the specific outcomes/endpoints of the research.

Hypotheses or Aim

This specifies the precise research questions being evaluated in the study.

Research Methods

This should include a description of the target population and/or sample, sample size, sampling method (e.g. randomization), and type of research design (e.g. experimental parallel group or cross-over design). 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.

Analyses

A brief description of the intended analyses, and if appropriate, who will be responsible for conducting them, should be provided. That is, if the statistical expertise is not present on the research time and an external consultant will support the analyses, this should be stated.

Potential Significance/Justification

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.

PART 5: STUDIES INVOLVING HUMAN SUBJECTS

GUIDANCE NOTE 5.5: INCLUSION CRITERIA

Provide all inclusion criteria as described in the protocol. Otherwise, indicate how these criteria differ from that in the protocol.

The selection of subjects must be considered equitable and should strive to achieve a demographically representative sampling, subsequent to the constraints of the research.

Note that the inclusion of legally incompetent subjects must meet the requirement of TCPS Article 2.5c, which states "individuals who are not legally competent shall only be asked to become research subjects when the research does not expose them to more than minimal risks without the potential for direct benefits for them."

Special consideration must be given to the potential for inclusion of vulnerable subjects who are not competent to give a legally or ethically valid consent or who have relatively little social or economic power. The research 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.

GUIDANCE NOTE 5.6: EXCLUSION CRITERIA:

Provide all exclusion criteria as described in the protocol. Otherwise, indicate how these criteria differ from that in the protocol.

Ensure that a justification is provided if subjects are excluded on the basis of such attributes as culture, language, religion, race, mental or physical disability, sexual orientation, ethnicity, gender or age.

GUIDANCE NOTE 5.7 & 5.8: IDENTIFICATION, INITIAL CONTACT, AND RECRUITMENT OF POTENTIAL SUBJECTS

In some studies, the Investigator requires information from a third party's records in order to invite prospective subjects to participate in a research study. Details of how initial contact via a vis third party records will be accomplished and copies of any letters sent to either the third party or to the subject via the third party must be provided for review by the REB. In addition, any recruitment materials, such as letters, advertisements, flyers, radio or television scripts, or Internet messages must be included with your application in Part 11 as attachments.

Specifically, the REB requires information on how subjects are identified and initially contacted to participate in a research study. In particular, this information should include a description of:

- i. the source (i.e. its original purpose, if relevant) of the contact information;
- ii. who will make the initial contact with the prospective subject;
- iii. how the prospective subject will be initially contacted;
- iv. when the prospective subject will be initially contacted, and;
- v. the Investigator's relationship, if any, to the subjects (e.g., treating physician).

The following procedures for identifying and making initial contact with prospective subjects are acceptable to the REB:

Identifying and Contacting Prospective Subjects From Primary Health Care Provider Records

In some situations, the prospective subject's primary care (i.e. family doctor) physician (or other primary health care provider) holds the subject's personal contact information. In this case, permission to use the contact information must be obtained from the subject by the primary care physician before the Investigator can use the information for recruitment purposes. The primary care physician must either verbally ask the prospective subjects' permission to release their names to the Investigator or distribute an introductory letter describing the study to the prospective subjects, with details on how to contact the Investigator if they are interested in participating.

Note that private practice physician's fall under the provisions of the Saskatchewan Health Information Protection Act (HIPA). Section 29 of the Act regulates the disclosure by physicians of personal information for research or statistical purposes. Section 29 sets out the rules under which trustees can use or disclose personal health information. It requires all research proposals to be approved by a recognized research ethics committee, and whenever practicable, the consent of the individual received.

Information Held by Disease Specific Registries

Subjects who have previously consented to be included in a registry for research purposes and this consent included contact for future research studies must first be contacted by mail via the contact information included in the Registry. The letter must explain how their contact information was obtained in addition to the purpose of the contact.

Identification And Initial Contact Of Prospective Subjects Attending Specialized Medical Clinics

In some situations, Investigators who are not acting as health care providers are attached to a hospital department/clinic/medical unit that offers clinical care, and conduct research on the patient populations that attend that particular medical unit. It is acceptable for these Investigators to obtain prospective subject names from the patient lists of their hospital's medical units for initial contact purposes. In this situation, the subjects may be contacted in writing to explain how their personal contact information was obtained, and the Investigator's relationship to the medical unit or hospital.

Initial Contact with Prospective Subjects Under the Investigator's Care or Authority

Ensuring Non-coercive Contact

Special care needs to be taken during the initial contact when the Investigator is in a fiduciary relationship with prospective research subjects. For example, whenever the relationship between the Investigator and research subject is such that coercion could be perceived to be a factor (e.g., when the Investigator is also providing medical care to a prospective subject, non-coercive means for inviting participation should be used. A typical example of the latter would be posting notices to invite volunteers from the entire group concerned, for example, in the waiting room of the medical clinic.

This leads to the recommendation that a treating physician/care provider not be the person making initial contact with subjects unless this is absolutely necessary.

Direct Initial Contact by Study Nurses

The REB permits study nurses/co-ordinators who co-ordinate studies out of a specialized medical clinic to make direct initial contact with a prospective subject who is attending that clinic for patient care or for research purposes. The study nurse must identify his/herself and the relationship to the clinic/medical department at the time of contact with the prospective subject.

Initial Contact by Mail

Prospective subjects under the Principal Investigator's care may also be contacted by mail via an initial contact letter, which can be followed up by a telephone call within a reasonable length of time. The letter should stipulate who will make the follow-up phone call and when this will occur. The RQHR REB prefers that the follow up telephone contact be made by a study nurse/co-ordinator in order to minimize the possibility of coercion, perceived or otherwise. The Principal Investigator must sign the initial contact letter unless a compelling reason why someone else should sign is provided.

The Principal Investigator is invited to become involved in the consent process whenever explanations are required which the person making initial contact cannot provide.

Initial Contact with Prospective Subjects Who Provide Personal Data to Sponsors' Call Centres

Subjects may choose to contact a Call Centre directly to indicate that they would like to participate in a clinical trial and to provide their contact information. The local study centre, upon receiving this information from the Call Centre, may contact the prospective subject directly by phone, explaining how their name and phone number was obtained. A description of this procedure must be included in Box #4.9 of the Application Form along with the script used by the Call Centre to receive calls and all screening scripts.

The REB is concerned about how personal information (including contact information) given to central screening agencies is handled by these agencies. Investigators are required to describe the planned disposition of the information by the Call Centre. For example, the REB would not permit this information to be provided to the sponsor for possible use in marketing or for contacting patients for reasons unrelated to the research project.

Identification and Contact of Subjects by Third Parties

The RQHR REB does not permit investigators to ask their subjects to invite other people (e.g. family members) to participate in a proposed research study. While recruitment of subjects by subjects may be methodologically desirable and convenient, it may put the index subject and the people they contact in a variety of potentially uncomfortable and coercive situations and is therefore not permitted. At no time should there be any obligation placed on the subject to recruit subjects for the investigator. In some situations (with REB approval) it is permissible for subjects to be asked to provide the investigators with names of other potential subjects (e.g. a sibling who might consider participating as a subject), but no further obligation may be placed on the subject.

RECRUITMENT METHODS AND MATERIALS

Letters

Letters used for initial contact purposes may be followed by a telephone call. In this situation, the letter must explain when the telephone call will occur, such that there is a reasonable length of time between receiving the letter of invitation by mail and the follow up telephone call. It is preferred that the initial contact letter be accompanied by the full consent form so potential subjects can be more informed and prepared for the subsequent telephone contact.

Initial Contact by Telephone for Obtaining Consent in Emergency Situations

Any proposal to make initial contact with a potential subject by telephone should include a detailed description of the procedure and provide adequate justification. Contacting potential participants by telephone is generally unacceptable and should be avoided, except under unusual circumstances, such as research being conducted in a hospital emergency department.

1. This consenting procedure may be used only when the next-of-kin or legal representatives have not arrived with the potential study subject and are not expected at the hospital within the time limit of the study initiation.
2. The principal investigator or designate will present the information in the consent form over the phone and provide any clarification required.
3. Once the next-of-kin or legal representative of the patient has been fully informed of the patient's medical condition by the attending physician, the study will be discussed by one of the Investigators. The Principal Investigator or Co-investigator will read the entire consent form over the telephone and provide any clarification requested by the next-of-kin or legal representative.
4. When all questions have been answered to the satisfaction of the next-of-kin or legal representative, the call will be terminated to provide an opportunity for the next-of-kin or legal representative to consider the study. In approximately (but not before) 30 minutes have passed, the Investigator (and witness) will again contact the individual for their decision (This is done so the family does not have to bear the costs of long distance charges).
5. A witness to the telephone consent, in addition to the Investigator reading the consent form, will be on the telephone line to hear the reading of the consent form and the verbal granting or refusal of consent by the next-of-kin or legal representative.
6. The identity of the witness will be disclosed to the next-of-kin or legal representative prior to the reading of the consent form.
7. The date and time that the telephone consent is obtained, the names of the next-of-kin or legal representative, the Investigator (reader), and the witness will be entered into the original consent form.
8. Whenever possible the consent form will be faxed to the next-of-kin or legal representative prior to the reading of the form, enabling them to follow along as it is read to them. If the next-of-kin or legal representative agrees to participate they will be instructed to sign the form and fax it back to the principal investigator.
9. Written evidence of consent will subsequently be obtained in a timely manner after obtaining verbal consent.

GUIDANCE NOTE 5.10 & 5.11: TIME REQUIREMENT

Report the exact time requirements for participation by the subject, including:

- duration of each procedure;
- duration of overall study, and;
- total number of visits.

GUIDANCE NOTE 5.12: REMUNERATION

Where researchers plan to provide remuneration to subjects, the REB will assess the value of the remuneration on a study-by-study basis. In general, remuneration should not be so substantial as to induce subjects to trade accepting potential risks for financial gain.

For most studies, remuneration that is considered reasonable is within the \$25.00 to \$100.00 range for participation. Randomly provided monetary remuneration (e.g., via entry into a draw) is considered an acceptable form of remuneration. This does not include reimbursement of any expenses incurred by the subject during participation in the research.

Include any specific details about the reimbursement of expenses related to transportation and parking and when these will be paid.

If the subject will not be paid for participation or reimbursed for expenses, this should be stated in the consent form.

Subjects must be eligible for remuneration according to their actual amount/duration of participation with no rewards for completing the study or withholding of owed remuneration from those who withdraw.

The monetary value of the remuneration for participation must not be disclosed at the time of recruitment. This mitigates the possibility of inducing subjects to trade accepting potential risks for financial gain. In addition, a prospective subject 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 subjects into thinking that they will automatically be enrolled into the study.

GUIDANCE NOTE 5.13: SUBJECT FEEDBACK

Regardless of the type of study, all participating subjects should be offered access to the study's findings. Depending on the type of study, the way in which this requirement is accomplished will vary. Some acceptable methods for providing subject feedback include:

- Attaching a separate 'sign up' sheet to the consent form for subjects to indicate their interest in receiving a copy of the findings. Note, providing subjects with a copy of the scientific summary is not considered suitable feedback. As such, any summaries intended for the subject should be written in lay terms. The list of interested subjects should be stored separate from the consent form, and when the study is completed, a summary should be mailed.
- An invitation to review the study findings with the subject upon completion of the study (e.g., during their next office visit).
- Placing posters in the waiting room to indicate that the study results are in, and inviting participating subjects to request a copy from the receptionist.
- Host a public presentation of the findings and invite all participants.

Note that whatever method providing subject feedback is chosen, it is to be disclosed in the Subject Study Information/Consent Form.

PART 6: PROJECT DETAILS

GUIDANCE NOTE 6.2: RESEARCH PROCEDURES

Specify precisely which procedures are research-related and how they differ from standard care. This information must be transferred to the consent form in such a way that the subject understands how participating in the research may be different from the treatment normally received with standard care.

GUIDANCE NOTE 6.3: RISKS AND BENEFITS

Specify the benefits to the subjects. If there are no benefits, state this explicitly. If any specific therapeutic benefits cannot be assured, but may be hoped for by the subject, state explicitly that the subject may or may not benefit from participation in the study.

Information on harms must be included and must be consistent with the information on harms provided in the protocol and Investigator's Brochure (IB)/Product Monograph. If information is not available from the protocol or IB, indicate the source of the risk data provided.

Quantify the foreseeable risks of harms (side effects) or inconveniences (discomfort or incapacity) to the subject associated with each procedure (including radiation risks from x-rays), therapy, test, interview, or other aspect of the study.

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.

The Board requires numerical (usually percentage) quantification of risks wherever possible. Qualitative terms such as "rare", "common", "infrequent" are not acceptable unless quantitative ranges are explicitly attached to them. Quantifiers such as ">5%" are similarly not acceptable since they do little to define the magnitude of risk.

It is helpful to list risks in descending order of frequency and/or group them according to category of risk (e.g., by magnitude, severity, organ system). See the example of categories provided below.

- i. Very Common (50% or greater)
- ii. Common (20% to 50%)
- iii. Less Common (5% to 20%)
- iv. Uncommon (2% to 5%)
- v. Rare (Less than 2%)

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

Box 6.3, as well as the consent form should 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.

GUIDANCE NOTE 6.4: MINIMIZING HARMS

The information in Box 6.4 should include an explanation of any strategies put in place to minimize and/or manage the harms for subjects and other affected individuals (e.g., reporting side effects to the investigator, rescue medication, early withdrawal from the study).

In studies where the interaction with other drugs is unknown, disclose whether the research necessitates that certain medication or treatments not be administered during the study so subjects can evaluate this in the context of their current health.

Studies With Wash-Out Periods or Requirements for Stopping Medication

The consent form must explain the symptoms/signs that subjects could experience from being taken off of any medication. Advice on procedures that must be followed in special cases is included in the following sections.

Social and Psychological Harms

Note that harms to the subject may also include social harms such as breach of confidentiality, social stigmatization, threats to reputation, and psychological harm.

Harms Requiring Special Counselling

Some studies (e.g. genetic tests) may provide results to subjects, which identify them as belonging to a high-risk group on the basis of the result (e.g. genetic status, biochemical test result). In the case of research involving families and groups in genetic research, the researchers must "reveal potential harms to the REB and outline how such harms will be dealt with as part of the research project." In this regard, Article 8.4 requires that "genetic researchers and the REB shall ensure that the research protocol makes provision for access to genetic counselling for the subjects, where appropriate."

In addition, the RQHR REB believes that it is the Principal Investigator's responsibility to ensure that research subjects experience no avoidable harm, such as psychological distress, arising from any knowledge that they could obtain as a result of their participation in any type of research study.

The REB expects to see evidence of measures taken to ensure that counselling services are made available to research subjects if the study tests could lead to information which would have serious consequences for that individual and/or their family.

Harms Related to Testing for Reportable Diseases

Pre-test counselling for subjects tested for reportable diseases includes the implications, some of which may be life-altering, of having a positive test. These may include the legal obligation for mandatory reporting by the investigator, medication implications for sexual partners as well as the impact of a positive test on a subject's insurance policies.

PART 7: INFORMED CONSENT

GUIDANCE NOTE 7.1: CONSENT REQUIREMENTS

Consent should in most cases be obtained after a face to face discussion with the subject/legal representative has taken place.

Written evidence of the subject's/legal representative's informed consent/assent must be obtained and documented before participation in the study begins.

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

- i. chart or medical record reviews
- ii. provincially regulated databases/registries
- iii. disease specific registries with data collected from subjects who have already consented to its use for the sort of research being done.

The requirements for seeking consent are subject to federal and provincial privacy legislation and investigators are responsible for compliance with these laws that relate to their research. The RQHR REB does not have the authority to authorize any procedure which contravenes these laws.

The information included in Box 7.1 should include details of the following:

- Who would approach the subject to obtain consent [note that this contact should occur a minimum of 24 hours after initial contact, except in the case of emergency situations];
- Who would inform and take the consent from the subject;
- What is the relationship of the person obtaining consent to the subject?

Use of Mailed/Faxed Consent Forms

Consent forms with an introductory letter may be mailed or faxed to potential subjects who live in areas outside of the geographical catchment area for a study. In these circumstances, the Principal Investigator or designate can sign the consent form after receiving the signed consent form back from the subject, or after having obtained telephone consent (see telephone consent procedures).

Questionnaires/Interviews Conducted by Telephone

Consent forms with an introductory letter (indicating that a follow up phone call will be made) may be mailed or faxed to prospective subjects when the study involves questionnaires/interviews that must be conducted by telephone. A follow up telephone call can then be made after a reasonable period of time to the subject to obtain their verbal consent in order to proceed with the interview or questionnaire. The complete written consent form should be read to subjects over the phone and their verbal consent documented prior to proceeding with the interview/questionnaire. The subject's signed written consent form must be returned to the investigator as evidence that written consent has been obtained. The investigators must maintain a verifiable record detailing when and who obtained verbal consent by phone.

Studies Using Questionnaires Only

The returned questionnaire may be taken as evidence of implied consent. Note that subject ID number should only identify the questionnaire.

GUIDANCE NOTE 7.2: AVOIDANCE OF COERCION

Whenever the relationship between the Investigator and research subject is such that coercion could be perceived to be a factor (e.g., when the Investigator is also providing medical care to a prospective subject), special care must be taken to avoid actual or perceived coercion. This leads to the recommendation that a treating physician/care provider not be the person making initial contact with subjects or obtaining subject consent unless this is absolutely necessary.

The REB permits study nurses/co-ordinators that co-ordinate studies out of a specialized medical clinic to obtain the subject consent. The study nurse must identify his/herself and the relationship to the clinic/medical department at the time of contact with the prospective subject.

GUIDANCE NOTE 7.3: ALLOWING SUFFICIENT TIME FOR PROSPECTIVE SUBJECTS TO CONSIDER PARTICIPATION

Recruitment must be done in such a way that prospective subjects 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, prospective subjects who are attending a clinic for elective or scheduled procedures should not 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.

GUIDANCE NOTE 7.4: COMPETENCE

This section is intended to provide guidance on the requirements for obtaining consent or assent for research involving subjects who would not be considered legally competent to give their own consent. The determination of legal competence is the responsibility of the principal investigator or designated representative. Competency must be assessed not only at the time of obtaining initial consent but also must be assessed on an ongoing basis throughout the duration of the study. Should a legal authorized representative of the subject consent on behalf of a subject, the principal investigator or delegated representative is also obligated to assess that representative's competence to consent.

Types of subjects who may fall into this category include:

- i. individuals with permanent or transient cognitive impairments (e.g. subjects with Alzheimer's Disease, subjects who are sedated/ventilated; subjects with a variable/permanent mental illness);
- ii. children who do not yet meet the tests for competency.

Substitute Decision Makers

TCPS Article 2.5 states, "Subject to applicable legal requirements, individuals who are not legally competent shall only be asked to become research subjects when:

- i. The research question can only be addressed using individuals within the identified group(s);
- ii. Free and informed consent will be sought from their authorized representative(s); or
- iii. The research does not expose them to more than minimal risks, without the potential for direct benefits to them."

TCPS Article 2.6 specifies the following minimum conditions that must be met for research involving incompetent subjects:

- i. "The researcher shall show how the free and informed consent will be sought from the authorized third party, and how the subject's best interests will be protected.
- ii. The authorized third party may not be the researcher or any other member of the research team.
- iii. The continued free and informed consent of an appropriately authorized third party will be required to continue the participation of a legally incompetent subject in research, so long as the subject remains incompetent.

- iv. When a subject who was entered into a research project through third-party authorization becomes competent during the project, his or her informed consent shall be sought as a condition of continuing participation.

TCPS states that competence (capacity to consent) consists in "the ability of prospective subjects to give informed consent in accord with their own fundamental values. It involves the ability to understand and to appreciate the potential consequences of a decision..." (TCPS, page 2.9, emphasis added).

There are thus two thresholds or tests that must be met to establish capacity to consent: capacity to understand, and capacity to appreciate one's decision. Understanding is the ability to discern in significant measure the nature of the research and the consequences of choosing/forgoing participation in it. Appreciation is the ability to give reasons for participation that reflect, or are consistent with, the prospective subject's own fundamental values. It assumes adequately developed adult capacities for forming and revising personal values.

The Principal Investigator must judge the potential subject's ability to consent to research on his or her own behalf, in all patients, in all research projects, regardless of the prospective subject's age.

Incompetent subjects should be informed and involved in decision making with respect to their participation to the extent possible. These subjects may not be able to participate in research if they dissent or do not assent, even though third party consent has been obtained.

Obtaining Assent from legally Incompetent Subjects, Including Children and the Mentally Impaired.

According to TCPS, legally incompetent subjects may be ineligible to participate in research unless they assent to participation. The procedures that the researcher plans to adopt for obtaining assent must be described in Box 7.5b of the Application Form.

GUIDANCE NOTE 7.5: OBTAINING ONGOING CONSENT

The consenting process is continual and requires vigilance on the part of the Principal Investigator to ensure that information that may in any way alter a subject's decision to remain in the study be conveyed in a timely manner to that subject. Information that may affect the subject's safety may be relayed to the subject verbally as quickly as possible.

Provisions should be made to ensure that any new information which has the potential to change a subject's decision to continue participation is conveyed in written form to the subject. The information may take the form of a letter or an addendum to the consent form unless it is more appropriate to administer the revised consent owing either to the special circumstances of the subject or to the importance of the new information.

Verbal confirmation of a subject's decision to continue participating may be obtained if informed by letter or verbally and should be documented accordingly. The subject should be given a copy of the consent as part of the process for deciding whether or not to continue participation in the study. Revised consents, addendums or letters must be submitted to the REB for approval prior to their use unless another prior arrangement is made with the REB.

The following sections provide information on provisions required in special cases:

Incompetent Subjects Who Become Competent

The informed consent of a subject who was incompetent at the time of enrolment but who becomes competent during the project should be sought as a condition of continuing participation. This means that although subjects who were incompetent cannot give consent to receive the experimental intervention(s) after they have been administered, that the subject must consent to continue participating in the study (i.e., consent to receive any remaining procedures).

Competent Subjects Who Become Incompetent

In situations where a subject becomes incompetent during a study, and where the investigator intends to continue to include the subject in the research, the Principal Investigator is obliged to find an appropriate third party who will agree to monitor consent accordingly on behalf of the subject, as long as the subject remains incompetent. If a third party does not exist, the best approach is to consult the REB for guidance.

New Information About Risks

When previously unknown/undisclosed risks of research become available, investigators are required to inform all subjects/legal representatives, to whom this information may be relevant using appropriate means within an appropriate time, depending on the nature and consequences of the risk. This may involve:

- i. informing the subject(s) verbally of additional risks or changes in procedures and ensuring that the communication of this information is documented in the study notes of the investigator and;
- ii. informing subjects who have completed their study treatment if the newly identified risks could still affect them (e.g. irreversible or delayed adverse effects).

Written re-consent is required in situations when the information concerning risks has the potential to affect the subject's decision to continue participation in the study. ICH GCP 4.8.2 states that "the written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent".

Any revised written information or consent form (e.g., consent addenda) must be submitted to the REB for approval before use.

GUIDANCE NOTE 7.6: PROVISIONS FOR OBTAINING CONSENT FROM SUBJECTS WHO REQUIRE SPECIAL ASSISTANCE

The Principal Investigator is responsible for ensuring that for "English as a second language" (ESL) subjects either a consent form in the most appropriate language or an appropriate translator is present during the initial informed consent process.

Translated Consent Forms

Translated copies of the consent form(s) will be required for acknowledgement after the REB has approved the English version of the consent form. A copy of the translator's signed and appropriate confirmation of the accuracy of the translation must accompany this; or, Consent forms originally written in other languages must be translated into English and the back translation submitted for ethical review. If a translator enrolling a subject is using an English consent form, the consent form must include the signature and printed name of the translator and the name of the language it was translated into.

GUIDANCE NOTE 7.7: SPECIFICATION OF STOPPING RULES

Specify any stopping rules for discontinuing the research-related procedures/treatment.

GUIDANCE NOTE 7.8: UNBLINDING IN THE EVENT OF AN EMERGENCY

For applicable research, the RQHR REB requires that sufficient information to reveal treatment assignment in the event of a medical emergency be held locally and that an emergency contact (24 hours, 7 days a week), who can break the code, be identified on the consent form(s). If the code cannot be held locally, the Board 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 phone number must be clearly identified in the consent form.

*****For specific guidance on creating the consent form, please see our [Consent Form Template and Guidelines](#).***

PART 8: PRIVACY PROTECTION

As with all research and other activities, assuring patient privacy and confidentiality is of utmost importance. As a result, it is the responsibility of the principal investigators and associated research personnel to maintain patient confidentiality of all information to which they are privy in the context of their research activities. Specifically, this requires that subjects not be identified in any way in all research reports and/or documents generated through the

research activity (e.g., no names, initials, or unique identifiers). In addition, it is the responsibility of all investigators and research personnel to be familiar with the Freedom of Information and Protection of Privacy Act (FOIPPA) and other relevant legislation and requirements concerning confidentiality.

GUIDANCE NOTE 8.3: ACCESS TO INFORMATION

It is the Principal Investigator who assumes ultimate responsibility to ensure the protection of the research subjects' privacy.

GUIDANCE NOTE 8.5: CONSENT TO USE EXISTING HEALTH INFORMATION

NOTE: REGARDING TISSUE AND/OR DATA OBTAINED FROM TISSUE AND DATA BANKS

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

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

GUIDANCE NOTE 8.6: DOCUMENT STORAGE AND RETENTION REQUIREMENTS

Storage Requirements:

All research documents must be securely stored in a specified area (e.g., in a locked filing cabinet located in the principal investigator's hospital office.) Documents or files that link de-identified data to their primary source must be stored separately from the study data.

Retention Requirements:

For clinical trials, the applicant is referred to the following sources for information on the document retention responsibilities of Investigators.

1. ICH GCP 4.9.5

Refer to: <http://www.ncehr-cnerh.org/english/gcp/>

2. Health Canada's Food and Drug Act Division 5 C.05.012 (4)

Refer to: http://www.hc-sc.gc.ca/food-aliment/friia-raaii/food_drugs-aliments_droques/act-loi/pdf/e_e-drugs.pdf.

For all other types of research studies, the REB requires that study records be maintained for no less than a 5-year period. Destruction of study records should be treated as confidential waste and disposed of in that manner. The exact length of time the records will be stored (e.g., 5 years, 25 years) must be disclosed and adhered to.

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.

Regulated databanks may also have specific requirements for record retention, which should be adhered to for studies using data from these sources.

GUIDANCE NOTE 8.7: PROTECTION OF SUBJECT IDENTITY

When it is not possible to anonymize research related records (i.e. anonymity is defined as the removal of all personal identifiers from a subject's records), the use of a unique study code or scrambled initials is considered acceptable by the REB.

The REB expects that research-related documents (except the master randomization schedule, consent forms, or screening logs) do not include information that would allow the subject to be identified.

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

- the unique study code is not derived from or related to the information about the individual;
- the unique study code could not be translated to identify the individual, and;
- 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 subjects. This can be accomplished by using any two unique identifiers.

GUIDANCE NOTE 8.8: ACCESS TO IDENTIFIABLE STUDY LOGS

Subject Enrolment Logs, documents or databases, which correlate subject names with study code numbers, must be kept on the locked premises of the Principal Investigator or in an appropriately secured electronic form. They should be stored separately from any of the other data.

GUIDANCE NOTE 8.9: DISCLOSURE OF INFORMATION

Include information on what measures are taken to prevent unauthorized access to the research data.

Include information on the provisions in place to protect the anonymity of data when it is transferred to other study sites outside of the local site (e.g. countries outside of Canada, sites in other parts of Canada).

PART 9: INVESTIGATOR PROFILE

GUIDANCE NOTE 9.2: PUBLICATIONS

Include information for each investigator and/or student. Attach no more than 2 additional pages per investigator.

PART 10: ATTACHMENTS

GUIDANCE NOTE 10: ATTACHMENTS

The REB office will NOT check the content of each copy or collate attachments. Applications that are submitted without complete protocols or consent forms will be deferred by the REB and will have to be resubmitted to another board meeting. Ensure that the documents submitted include all pages in the correct order.