

Tips for Completing an Ethics Submission for the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board

From the Kingston General Hospital (KGH) Clinical Research Centre

This guide is to be used when completing the Health Sciences Research Ethics Board (HSREB) submission form. It has been developed particularly to assist new or junior researchers who do not often complete these forms. This form is available on the HSREB webpage (<http://www.queensu.ca/ors/researchethics/REB.html>). The form is updated periodically so be sure to use a current version of the form. The KGH Clinical Research Centre has staff that is able to assist you with completion of the form, and can be contacted through Mary Pope, in the Office of Health Sciences Research, which is located within KGH (Empire 2).

While your submission to the HSREB will be supplemented by copies of your study protocol, information and consent forms, and data forms, it is important to remember that most members of the HSREB will not see this additional material. They will only see the HSREB form and the consent form. Hence this submission form must stand alone in providing a brief overview of the purpose of your study and its design as well as more details of the procedures that will be in place to protect subjects and their personal information. HSREB membership contains those without clinical or scientific backgrounds so providing descriptions in lay language is essential.

Staff and investigators associated with the KGH Clinical Research Centre are willing to share copies of completed HSREB applications, consent forms and subject information sheets from approved applications. These may be helpful templates for your application.

The following are some tips on completing the required elements of this application. It is highly recommended that you submit your HSREB application at the same time that you are submitting an internal/external grant application to a funding agency or an industry contract to the Queen's Office of Research Services Contracts Office, in order to prevent any further delays in obtaining your HSREB approval once your funding has been secured:

Signature Page (page 2):

Under the "Principal Investigator", if you are a site investigator for a multicentre trial where the PI is not from Queen's, just replace "Principal" with "**Site**" and bold this so it is noticed. List all PI's if more than one with the contact PI listed first. "Status" refers to your University Rank (e.g. Associate Professor).

1. Information on Protocol:

- a. These questions are straightforward. The question on Clinical Trial is asking whether it is an RCT or other experimental trial and the "phase" question only refers to these.

- b. All clinical trials and any study requiring subject participation in providing information must be reviewed scientifically by an appropriate person independent to the research team. In some cases, the person may need to be someone from outside the hospital/university in order to avoid conflict of interest. This review is provided by peer-review funding agencies. For non-funded projects, such a review should be arranged by the investigator and/or department. An independent review will also be required for industry sponsored studies. The HSREB will not approve an application until the peer review has been received. Copies of the review are to be sent to the HSREB. To expedite the HSREB approval of your research project, reviews should be submitted at the same time you are submitting your HSREB application.

2. Summary of Proposed Research:

- a. Abstract: a brief, lay, summary of the project to include the study rationale, its objectives, the study design (RCT/experimental, observational, cohort/case-control, or case series) and the outcome being assessed.
- b. Rationale and Hypothesis: present a more detailed description of why the study is important, what new knowledge will come from it and/or how it will have the potential to inform future work. List the specific study questions/objectives being addressed. Avoid cutting-and-pasting extensive sections from the protocol.
- c. Study Design:
 - i) Describe study design/methodology: study designs are broken down into experimental and observational studies. Most experimental studies are RCTs but in all of these, the investigator has control over who does or doesn't get the intervention under study. In the observational study designs the intervention is not under the control of the study management. These designs include cohort, case-control and case series designs. This section should identify one of the study designs, the target population, how and where the target population will be identified initially and in follow-up and briefly how study information will be collected. It is important to explain how subjects will be identified, how informed consent will be obtained and by whom. This section needs to explain step by step how the study will be conducted from the perspective of the subject. This often is the lengthiest section on the HSREB submission form.
 - ii) Primary outcome measures: list the main outcome measurements for the study. These will generally be those used for your sample size calculations.

- iii) Criteria for premature withdrawal: list these for experimental studies. This is generally not applicable for observational designs.
- iv) Use of placebo: again for experimental studies only. The HSREB will expect the choice of placebo and how it will be presented to be fully discussed including why a placebo arm is required and what the associated risks are for being in the placebo arm. The rationale for use of a placebo should clearly conform to the requirements dictated in the Tri-Council Policy Statement: *Ethical Conduct for Research Involving Humans* (TCPS).
- v) Use of deception or nondisclosure: this again is primarily for experimental studies but may also be a consideration for some observational/cohort studies. In general there is an expectation for full disclosure of the study design, the interventions under study and the outcomes being measured. Nondisclosure or incomplete disclosure may be appropriate for some studies where disclosure is likely to affect the measurement of outcomes and/or scientific validity. In that case you will need to present a clear statement on why deception/non-disclosure is needed.
- vi) Withholding standard therapy: again generally for experimental studies. This question is fairly straightforward. Also include here if there will be a delay in access to standard therapy through participation. The risks of withholding standard therapy must also be covered.

3. Subjects/Participants:

- a. Provide total number of participants expected for entire study including all study sites. List the number to be recruited in Kingston; these numbers would be the same as the total number of subjects expected for the entire study if this is a single centre study. There will be an expectation to justify the sample size in any analytic design (RCT, Cohort, Case-Control) with an appropriate sample size calculation. You should also demonstrate that the sample size is feasible to attain, generally through use of a medical record search. A qualitative justification of the sample size may be sufficient for pilot studies of any design or for case series (e.g. convenience sample). Identify the sources of potential subjects: hospital, clinic, medical record search, telephone survey etc. Finally, there is a small group of hospital-based subjects that has formally requested not to participate in research studies or be contacted for research purposes/inquiries. A flag for this is on their PCS electronic medical record and needs to be looked for. These subjects' data are not to be used for a research study.
- b. The subject information sheet and consent form are critical components of the HSREB application. You need to explain who will approach the subject to explain

the study to the subject and who will obtain informed consent. There are templates for the information sheet and consent form on the HSREB webpage. It would be prudent to use an acceptable template to fulfill HSREB expectations. In addition, investigators in the KGH Clinical Research Centre have made available copies of these forms for different study designs. These can be used as templates by other investigators. Just contact the KGH Clinical Research Centre. In addition to the subject information sheet and consent form you need to also include a copy of all recruiting methods (i.e. telephone scripts, newspaper/radio advertisements, posters, brochures, etc.).

- c. The easiest way to complete this section on study population is simply to provide the inclusion and exclusion criteria from your study protocol and defend these.
- d. Check off all identified target populations from the list that will be included in your study. If mental competency is one of your inclusion or exclusion criteria then it will be important to make clear the criteria used to make this decision.
- e. Subjects who may not be competent to consent include young children, individuals with mental illness and critically ill hospital patients. The proxy for signing consent is generally a family member, a legal guardian or the person who has power of attorney for personal care.
- f. All staff must have hospital credentials specifically to allow involvement in clinical research activity. Clinicians with hospital patient care credentials need nothing further. But other hospital or university staff, such as nurses or research assistants do need to apply for hospital credentials for their research activities.
- g. There is an expectation to inform clinical colleagues of the details of a proposed study that may involve their patients as participants. It is a good idea to include a statement in the subject information sheet and consent form addressing whether or not the subject consents to having his/her primary care physician notified of his/her participation in the study.
- h. This question is asking how physicians will identify potential research subjects and get this information to the principal investigator of a study or their study personnel who are assisting with subject recruitment.
- i. Enrollment of a single subject in multiple studies may compromise scientific validity of the studies or affect subject care. It may also be overly burdensome for some subjects. This question asks whether this is likely.
- j. Straightforward.
- k. There is a wide range of considerations here from infection control to violence. Research staff needs to be protected and the potential for harm should be considered a priority.

4. Study Interventions or Procedures:

In parts a and b identify the interventions/testing procedures/questionnaires/etc. under study and determine whether they are or are not part of the usual standard of care/usual practice for this particular subject/target population. For example, certain laboratory blood work may be routinely collected for a particular target population as part of their usual care however any additional laboratory testing above this would be considered not part of their usual standard of care and required solely for research purposes. Be clear on what is different from the standard of care.

5. Risk/Benefit Estimates:

- a. Financial benefits will be asked for later. This refers to potential clinical benefit as a result of participation either during or after the study.
- b. Potential harm should be considered. There is generally at least an inconvenience of time. In addition for clinical trials all potential risks and discomforts should be listed including those related to use of the study drug, therapy, or device, withholding medications, pregnancy, and any tests or procedures carried out in the study. For industry studies this information can usually be found in the study Investigator's Brochure or Product Monograph provided by the sponsor. The standard for disclosure of risks is "full and frank disclosure."
- c. List all risks associated with using a placebo, washout or withholding of treatment. Placebo related risks are generally related to not providing or deferring a standard of care intervention. Again, refer to the requirements regarding use of placebo in the TCPS.
- d. There is an expectation for having a plan to identify and manage risks/adverse events and for the reporting of these adverse events. This generally refers to experimental trials. For observational studies such troubles are generally related to mishandling of confidential subject information. Adverse events are certainly reported to PIs or site investigators. For RCTs adverse events are also reported to the Data Safety Monitoring Board. All adverse events for any study are to be reported to the HSREB. There is a form available on the HSREB website to be used for adverse event reports in industry/multicentre studies. For local studies, a summary of the event signed by the PI is to be sent to the HSREB Chair.
- e. Third party or reproductive risks are considerations only for experimental trials; generally this includes toxic or teratogenic effects of pharmaceutical agents and may also include infectious risks. For industry studies, this information can usually be found in the study Investigator's Brochure or Product Monograph provided by the sponsor.

6. Confidentiality and Privacy:

- a. It is part of best practice, as reflected in Ontario's privacy legislation and related parts of the TCPS, that subjects are identified on data collection forms by study number only. Therefore research staff may need to create and maintain a table linking the study number to subjects with subject identifiers on a password protected computer within their research setting. However if research staff do need some form of personal identifier on data collection forms in order to be time-efficient and not make data collection errors (as is often the case) this needs to be justified on the HSREB form.
- b. Generally personal health information (defined as "identifying" or potentially identifying information about a subject) is required. The sources of information may be from the subject, from hospital or clinic medical records or from proxies.
- c. Permission to access existing medical records where there is never any subject contact is generally obtained from the manager/director of the data source who controls access (e.g. KGH/HDH Medical Records Department). The researcher will need to assess all the medical charts to ensure that subjects included in the data analysis have not had their consent to participate in research activities withheld/withdrawn. If consent has been withheld, then the chart will not be further assessed and any collected data on that subject will be destroyed permanently. Permission for such access is conditional on approval from the HSREB for your research project. Where there is a requirement for direct contact with subjects to collect any additional research data, there will be an expectation to gain consent to additionally access their medical record from the HSREB. Note that it is the hospital and not the researcher who must obtain prior consent for subjects to be contacted directly, if the research requires direct contact. When subjects are actively participating in the research study, it is important to obtain consent to extract personal health information through various sources (e.g. medical charts, subject's primary physician, etc.) through the subject information and consent form.
- d. There are two questions here. First, personal health information may be used as variables integral to the analysis. Second, research data collected directly from subjects are often linked to databases such as hospital medical records. Describe how this will be done. If there is a linkage to be done to databases external to our Health Sciences Centre, a very clear description of this process is required.
- e. Consent is "not applicable" only if there is never use of personal health information. If verbal or written consent is being sought then check "yes". No consent may be justified where medical records alone are being used for research with no contact being made with subjects and there is no potential for their being identified during the research or in presentations of results.

- f. There is an expectation of benefit of new knowledge for all studies and this does not need to be noted here. The specific benefit to a subject may be a change in their medical management that may be enlightened by a detailed review of their records during the research process. How will this information be transmitted to the subject or their caregiver? There is generally little potential for harm from accessing personal health information providing care is taken to protect the subject's privacy.
- g. Provide a table here listing the position title, name of the person taking on the role if known, their primary tasks, qualifications required and why access is needed. Provide the names of persons from other centres if it is a multicentre project. Note members of your Data Safety Monitoring Board if applicable. N.B. members of our HSREB and the sponsor if an industry sponsored study, will have full access on request for other purposes: this should be noted in the subject information sheet and consent form.
- h. Is there potential for conflict of interest based on funding (especially for industry sponsored work)? Will access to this information conflict with or affect your clinical responsibilities to the subjects?
- i. Will the individual subject data be shared with others outside of your local research group that is listed in g. above? If you respond "yes" here then you're also going to be linking your data to other databases even if you are just merging your data with others within a multicentre trial. It would be an expectation for you to remove all personal identifiers and to replace these with the study number before providing such data to those outside your local research group. This would include removing the full birth date (provide age; or month and year of birth only).

7. Protection of Data:

- a. Protection of stored data is of key interest to the HSREB. Check all forms of data storage that will be used. For computerized files, there is an expectation to maintain data on a network drive accessible only to study personnel with secure backup procedures and password protection. Non-computerized information should be stored in a locked cabinet/compartment behind a locked door. Data that can or might be used to identify individuals should not be removed from the research setting/hospital on portable electronic devices/laptops. For Example:

All data forms will have an assigned study number with/without personal identifiers. These data forms will be kept locked in a filing cabinet in the Clinical Research Centre. All data entered in the database will be stored on a password-protected computer in the Clinical Research Centre and will be backed up nightly on the hospital computer system. The data will not be removed from the Clinical Research Centre on any portable electronic devices/laptops.

- b. Straightforward.

- c. Consider whether data will be transferred electronically or by another method such as a disk sent by courier. CRC staff may be able to help with data encryption.
- d. Generally information being transferred outside your research group should not contain any personal identifiers (full date of birth, CR number, initials, and names must be removed).
- e. Researchers will want to keep full original data with identifiers, including copies of data forms (hardcopy or stand) for a specified period of time depending on the study type and terms of the funding agency/oversight authority. “CIHR now requires grant recipients to retain original data sets arising from CIHR-funded research for a minimum of five years after the end of the grant. This applies to all data, whether published or not.” (ref.: CIHR Policy on Access to Research Outputs, September, 2007; <http://www.cihr-irsc.gc.ca/e/34846.html#5.1>). Industry studies generally require these data to be maintained for a minimum of 25 years. Some data sources/providers will have their own restrictions that need to be complied with. The KGH/HDH Medical Records have their own policies on how long medical records are retained. For clinical trials, researchers need to inform this department about their study in order to ensure that these paper and electronic records that are part of their source documents are retained past the Hospital policy. Most Hospital policies only call for a record retention of 10 years, while Health Canada requires that all source/study documents be kept for a minimum of 25 years.
- f. A separate anonymized file stripped of identifiers can be created that you can use for analysis. The original data can be stored safely. While you may destroy data files with personal identifiers as in e. above, you may want to keep anonymized data in perpetuity.
- g. Long-term storage should meet same criteria as in a. above

8. Payment to Subjects:

It is okay to compensate subjects for travel, parking, and other direct costs of participation at reasonable rates. It is generally not acceptable to compensate subjects for their time by money or gifts. If this is deemed necessary it will need to be justified.

9. Monitoring:

- a. This question is asking about monitoring primarily for industry sponsored studies. It does not include monitoring by a Data Safety Monitoring Board: this is addressed in c. below. Describe the monitoring committee and whether they are independent from the study/industry sponsor. Note also that if a study monitor

comes to a hospital-based site they will need credentials to do so from the hospital credentials committee and medical records. There is a bit of red tape in organizing this and KGH CRC staff can provide some advice on this.

- b. There is an expectation for an interim analysis for clinical trials and occasionally for cohort studies. An interim analysis may not be required if the study is a small sample size or if the study is run over such a short time interval of recruitment that the results would not be helpful in directing the study. There may not be a need for such an analysis if the intervention is of very low risk. If an interim analysis is conducted, describe how this information will be used: for example describe stopping rules for study.
- c. A data safety monitoring board is an expectation for RCTs. Members should be independent from the research team. For instance, CIHR requires DSMB members not to have collaborated on projects/publications with research team members in the previous five years.
- d. Seems to have been skipped on the form.
- e. The research plan should include a definition of an adverse event, how they will be identified and how research staff will be trained to identify potential adverse events and report them to the PI/local site investigator. There are AE reporting forms on the Queen's HSREB website that defines the reportable data elements.

10. Financial Disclosure:

The checklist here is fairly straightforward. If you hold stock in a company it generally needs to be declared.

11. Funding:

Funding is near always required even if the source is a departmental research fund.

12. Contract:

This generally doesn't apply to peer-reviewed grants but is rather for industry and government contracts. However we increasingly see subcontracts/agreements as being part of grant funded multicentre studies where the PI is not based at Queen's. The PIs host institution may develop a contract/agreement with the Queen's site. For assistance in contract related issues, please contact the Queen's Office of Research Services Contracts Office (Laurie Vaughan-Evans; 613-533-3290). Within the KGH Clinical Research Center we also have expertise in managing these various forms of contracts that can also assist you with some of your questions (Veronica Harris-McAllister; 613-549-6666 ext 3653).

13. Publications/Dissemination of Results:

- a. This is relevant to externally managed multicentre studies where Queen's is a study site. It includes both industry and peer-reviewed funded research.
- b. Straightforward.
- c. Again straightforward but should remember that even for multicentre peer-reviewed grant funded research you want access to your own data without restriction.
- d. Generally only a consideration for industry sponsored studies

14. Liability:

- a. Liability insurance is not needed for peer-reviewed grants: Queen's has insurance for this. This is for industry sponsored studies.
- b. Again, compensation here is relevant mainly for industry sponsored studies and responsibility for this should be clear in the contract.

15. Investigational Drugs or Devices:

This section is fairly straightforward. Note that all clinical trials need to be registered. A clinical trial is any research study that assigns subjects to one or more health-related interventions (i.e. drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes) in order to evaluate an outcome (i.e. effectiveness of a drug/device/diagnostic tool, improvement in quality of life). Registration of a clinical trial must be done before any subject is recruited. There are different options for doing this and the choice may be dictated by the funding agency. If a funding agency has not specified a certain registry, the registry that Queen's supports is the NIH website (<http://clinicaltrials.gov/>). For industry-sponsored clinical trials, usually the sponsor registers the trial. For investigator-initiated clinical trials the investigator would register the trial. If help is needed for the registering of clinical trials, please contact the Clinical Research Centre (Veronica Harris-McAllister; 613-549-6666 ext 3653).

16. Handling and Disposition of Study Drugs:

This section needs only be completed if you are participating in a clinical drug research study. There are detailed guidelines that need to be followed here. The information provided in this section is useful for the KGH/HDH Pharmaceutical and Therapeutics Committee who reviews and additionally approves all HSREB applications for drug studies. A copy of this HSREB Submission Form, along with a copy of your protocol and Investigator Brochure/Product Monograph

automatically gets forwarded to the KGH/HDH Pharmaceutical and Therapeutics Committee. Note: The KGH/HDH Pharmaceutical and Therapeutics Committee must approve all clinical drug trials prior to the enrollment of subjects into the clinical drug trial, even if the researcher has already obtained approval from the HSREB or other committees (i.e. Radiation Safety Committee, Biohazards Committee, Animal Care Committee). You will receive a letter of approval from the KGH/HDH Pharmaceutical and Therapeutics Committee, if your study is approved. For more information regarding the KGH/HDH Pharmaceutical and Therapeutics Committee, please consult the HSREB's *Guidelines for Handling of Drugs in Clinical Studies* (<http://www.queensu.ca/ors/researchethics/REB.html>), KGH Policy 14-100 *Clinical Drug Trials* and/or contact directly the KGH/HDH Pharmaceutical and Therapeutics Committee at 613-549-6666, ext. 3654 or kghphids@kgh.kari.net.