Tips for Completing Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board Application Form for Ethics Clearance

(*in collaboration with the Kingston General Hospital Research Institute*)

This guide is to be used when submitting to the TRAQ ROMEO Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (HSREB) application system. 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/urs/ethics/guidelines). The Kingston General Hospital Research Institute (KGHRI) is able to assist you with completion of the form, if required. Please contact Lisa McAvoy at 613-549-6666, ext. 3344 or kghri@kgh.kari.net for further assistance.

While your submission to the HSREB will be supplemented by copies of your study protocol, information and consent form(s), recruitment materials, data capture forms, etc. it is important to remember that most members of the HSREB will not see this additional material. They will only see the HSREB submission 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 study participants and their personal information. HSREB membership contains those without clinical or scientific backgrounds so providing descriptions in lay language is essential.

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 submitting an industry contract to the Queen's University Research Services or KGHRI (if your funding is being managed at any of the affiliated hospitals (KGHRI, Hotel Dieu Hospital Kingston Research Institute (HDHKRI), Providence Care (PC)), in order to prevent any further delays in obtaining your HSREB approval once your funding has been secured. As a reminder a TRAQ DSS FORM application is also required to be completed at the same time for obtaining all necessary departmental and hospital approvals:

Project Team Info Tab:

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).

HSREB Submission Form Tab:

1. Information on Protocol:

Questions 1.1 and 1.2: All clinical trials and any study requiring subject participation (or use of participant data) 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. A copy of the review should be uploaded under the Attachments Tab. To expedite the HSREB approval of your research project, reviews should be submitted at the same time you are submitting your HSREB application.

Question 1.3: All students with research projects involving the use of human participants or their personal health information must have completed the "*Course on Research Ethics*" (CORE) (http://www.pre.ethics.gc.ca/eng/education/tutorial-didacticiel/). Copies of the completed course (passed certificate) must be uploaded under the Attachments Tab to the HSREB application.

Questions 1.4 to 1.6: If you are conducting a clinical trial please answer questions with a "yes/no" response and include the phase of your clinical trial.

2. Summary of Proposed Research:

Question 2.1: Abstract: a brief, lay, summary of the project to include the study rationale, its objectives, the study design (experimental, observational, cohort/case-control, or case series) and the outcome being assessed.

Question 2.2: 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.

Question 2.3: Study Design and Methodology: describe study design/methodology. Study designs are broken down into experimental and observational studies. Most experimental studies are randomized controlled trials (RCTs) but in this type, the investigator chooses the intervention to be studied. In double-blinded trials both the participant and investigator do not know what intervention the participant is receiving. In single-blinded trials, only the participant does not know the intervention received. In the observational study designs the intervention is not under the control of the investigator. 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 participants 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 participant. This often is the lengthiest section on the HSREB submission form.

Question 2.4: Outcome Measures: list the primary and secondary outcome measurements for the study. These will generally be those used for your sample size calculations.

Question 2.5: Criteria for premature withdrawal: list these for experimental studies. This is generally not applicable for observational designs.

Questions 2.6 and 2.7: 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. Include any provisions in place to reduce risks to participants assigned to placebo. 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 2 (2014)).

Questions 2.8 and 2.9: 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.

Questions 2.10 and 2.11: 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. Participants:

Questions 3.1 to 3.8: 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 participants expected for the entire study if this is a single centre study. Provide the date of anticipated completion of participation of participants. 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 participants that have formally requested not to participate in research studies or be contacted for research purposes/inquiries. A flag for this is within their electronic medical record (Patient Care System (PCS)) in the hospital and needs to be looked for. If a participant has withdrawn their consent to participate in research studies or be contacted for research purposes/inquiries, any data from that participant's medical record can not to be used for a research study.

Questions 3.9: Hospital Approval: "Yes/No" question. Reminder: all hospital approvals are obtained through the TRAQ DSS FORM application; a separate process from the TRAQ ROMEO HSREB application. Researchers are to complete the "TRAQ DSS" tab within the TRAQ DSS FORM application along with identifying all hospital operational directors impacted on the "Approval" tab if (1) their research project is being carried out or occurring in a hospital setting; (2) their research lab, unit, centre, space, and/or equipment is located in a hospital setting; (3) their research staff and/or their research offices are located in a hospital setting; and/or (4) they will be utilizing hospital resources (staff, equipment, supplies, space, medications, testing/procedures, etc.) for their research project.

Question 3.10: The participant information sheet and consent form are critical components of the HSREB application. You need to explain who will approach the potential participant(s) to explain the study 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 to the participant 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.).

Questions 3.11 and 3.12: 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. Check off all identified target populations from the list that will be included in your study.

Questions 3.13 to 3.15: 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. Participants 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 (Legally Authorized Representative, LAR).

Questions 3.16 to 3.18: All investigators and research staff/students/trainees must have hospital credentials/appointments specifically to allow involvement in clinical research activity in a hospital setting. Clinicians (MD) with hospital patient care credentials need nothing further. Researchers (Ph.D., non MD), Queen's research staff (and hospital staff when research is not part of their job description), students, and trainees require research hospital appointment to carry out research within the

hospital(s). For more information or assistance about research hospital appointments at KGH and HDH, please contact Gina Morey at 613-549-6666, ext. 4260 or moreyg@kgh.kari.net. For research hospital appointments at PC, please contact Sally Lake at 613-548-5567 ext. 5645 or lakes@providencecare.ca for further assistance.

Questions 3.19 to 3.21: These questions are straightforward.

Question 3.22: 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 participant information sheet and consent form addressing whether or not the participant consents to having his/her primary care physician notified of his/her participation in the study.

Question 3.23: This question is asking how physicians will identify potential research participants and get this information to the principal investigator of a study or their study personnel who are assisting with participant recruitment.

Questions 3.24 and 3.25: Enrollment of a single participant in multiple studies may compromise scientific validity of the studies or affect participant care. It may also be overly burdensome for some participants. This question asks whether this is likely.

Question 3.26: Describe how participation in a research study could potentially benefit a participant's future care as a patient. Participation in a research study should not negatively affect a participant's future care as a patient. If it might, this information needs to be documented. There is a wide range of considerations here from infection control to violence. Research staff members also need to be protected and the potential for harm should be considered a priority and addressed both for participants and research staff.

4. Study Interventions or Procedures Involving Humans:

Questions 4.1 and 4.2: 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 participant/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 (e.g., PK, RNA sampling) would be considered not part of their usual standard of care and required solely for research purposes. Some vitals are collected routinely in some clinics but others are beyond standard of care (pre and post treatment vitals). Be clear on what is different from the standard of care.

5. Risk/Benefit Estimates:

Questions 5.1 and 5.2: Benefits: this refers to potential personal and clinical benefit as a result of participation either during or after the study. This may include contribution to the advancement of knowledge. List all anticipated benefits.

Question 5.3: Potential Harm: describe potential harms (injury, discomfort, inconveniences, psychological distress, etc.) to the participants. 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". If there are no risks, this should be documented.

Question 5.4: Placebo: 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 2 (2014).

Question 5.5: Unexpected Risks: 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 serious 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 serious 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

Questions 5.6 to 5.13: Third party and Reproductive Risks: these are considerations only for experimental studies and generally include 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. If it is not, please forward these questions to the Sponsor/CRO for clarification and a response.

6. Confidentiality and Privacy:

Question 6.1: Personal Identifiers: this is part of best practices, as reflected in Ontario's privacy legislation and related parts of the TCPS 2 (2014), which indicates that participants 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 participants with participant identifiers on a password protected computer within their research setting or in a paper log filed under lock and key. 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. In your response to this question, also identify who will have access to the participants' records.

Question 6.2: Personal Health Information: describe all types and sources of collecting personal health information. Personal health information (defined as "identifying" or "potentially identifying" information about a participant) may be required to be collected on data forms as part of the primary and secondary outcome measures. The sources of identifying information may be from the participant, from hospital or clinic medical records or from proxies.

Question 6.3: Access to Medical Records: permission to access existing medical records is obtained from the individual who controls data access (e.g. hospital medical records department) through the TRAQ DSS FORM application. For research studies where there is no direct contact of participants and patient data is being used, researchers need to review all medical charts to ensure that participants 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 participant 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 participants to collect any additional research data, there will be an expectation to gain approval to access their medical record and contact the participant from the HSREB. When participants 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, participant's primary physician, etc.) through the participant information and consent form.

Question 6.4: Use of Personal Health Information: There are two questions here. First, personal health information may be used as variables integral to the analysis. Second, research data collected directly from participants 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 Queen's and/or the hospitals (KGH, HDH, PC), a very clear description of this process is required.

Questions 6.5 and 6.6: Consent to the Disclosure of Personal Health Information: 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 participants and there is no potential for their being identified during the research or in presentations of results.

Questions 6.7 and 6.8: Harms and Benefits from Use of Personal Health Information: 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 participant 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 participant or their caregiver? There is generally little potential for harm from accessing personal health information providing care is taken to protect the participant's privacy.

Question 6.9: Personnel Access to Personal Health Information: 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 to personal health information. Provide the names of persons from other centres if it is a multicentre project. Note members of your Data Safety Monitoring Board if applicable. Note members of the HSREB, the sponsor/CRO, and regulatory bodies (FDA, Health Canada if audited) for industry-sponsored studies who will have full access on request for other auditing purposes. This information should also be noted in the participant information sheet and consent form.

Question 6.10: Conflict of Interest: is there a 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 participants?

Questions 6.11 to 6.13: Database Sharing: will the individual participant data be shared with others outside of your local research group who are not listed in Question 6.9 above? If you respond "yes" here then you are 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:

Questions 7.1 and 7.2: 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, a response to this question might look like this:

> *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.*

Questions 7.3 to 7.6: Straightforward. In an industry-sponsored clinical trial, the participating site collects the data and the Sponsor analyzes it, unless the site plans on publishing site specific data. Consider whether data will be transferred electronically or by another method such as a disk sent by courier. KGHRI staff may be able to help with data encryption. For this question, you must provide the type of encryption used to ensure secure transmission of data. You can obtain this information from the IT department of a Vendor being used in an industry-sponsored clinical trial.

Here are some examples from industry-sponsored submissions:

> *Study data may be transferred electronically via secured servers between Site and Sponsor, Sponsors and Vendors. They use 256bit SSL encryption.*
>
> *Participant data is transferred electronically via secured servers between Sponsor and the vendors.. The cryptographic protocols used to secure transmission of data in transit between a Rave end user's web browser and the Sponsor's servers are Transport Layer Security/TLS and Secure Socket Layer/SSL.*

Question 7.7: 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).

Question 7.8: Researchers will want to keep full original data with identifiers, including copies of data forms (hardcopy or electronic media /storage devices) for a specified period of time depending on the study type and terms of the funding agency/oversight authority. CIHR 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://cihr-irsc.gc.ca/e/34848.html). 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 hospital medical records departments 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 related to drug trials be kept for a minimum of 25 years.

Question 7.9: 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 Question 7.8 above, you may want to keep anonymized data in perpetuity.

Question 7.10: Long-term storage should meet same criteria as in 7.1 above.

8. Payment to Participants:

Questions 8.1 to 8.3: 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. Provide details of participant compensation. This should match what is listed in your attached approved final budget and participant information and consent form.

9. Monitoring:

Question 9.1: 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 Question 9.4 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 to obtain a visitor's pass from the KGHRI. Please contact Lisa McAvoy at 613-549-6666, ext. 3344.

Questions 9.2 and 9.3: 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.

Question 9.4-9.6: A Data Safety Monitoring Board (DSMB) 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. If the makeup of the DSMB is known at the time of submission, this information should be provided to the HSREB.

Question 9.7: The research plan should include a definition of a serious adverse event (SAE), how they will be identified and how research staff will be trained to identify potential SAEs and report them to the PI/local site investigator and HSREB. There is an SAE form on the TRAQ/ROMEO site that defines the reportable data elements.

10. Conflict of Interest/Investigator Financial Disclosure:

Questions 10.1 to 10.15: The checklist here is fairly straightforward. If you hold stock in a company it generally needs to be declared. All conflicts of interest whether real, potential or perceived ought to be stated here. The TCPS 2 (2014) requires disclosure on all financial issues related to research studies. This has become especially critical for industry-sponsored projects. Financial conflicts (receiving benefits) can be an ethical concern and for this reason we must have budget

information for the study. Conflicts can exist for the researcher or his/her family with the sponsor, the institution or research participants. Note: if any of the following conflicts apply, append a letter detailing these activities to the Chair of HSREB. Please disclose all contracts and any conflicts of interest (actual, perceived, or potential) relating to this project.

11. Funding:

Questions 11.1 to 11.7: Funding is usually required for a research project even if the source is a departmental research fund. Please site all sources and status of funding.

12. Contract:

Questions 12.1 to 12.4: This generally doesn't apply to peer-reviewed grants but is rather for industry and government contracts. However we increasingly see subcontracts/sub-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/KGHRI site. For assistance in contract related issues, please contact the Queen's University Research Services' Contracts Office (Heather Webster at 613-533-6000 ext. 75844) for all contracts where the funds will be held in research restricted accounts at Queens and KGHRI (Veronica Harris-McAllister at 613-549-6666 ext. 3653) for all contracts where the funds will be held in research restricted accounts at KGHRI.

13. Publications/Dissemination of Results:

Question 13.1: This is relevant to externally managed multicentre studies where Queen's is a study site. It includes both industry and peer-reviewed funded research.

Questions 13.2 and 13.3: Straightforward.

Question 13.4: Again straightforward but should remember that even for multicentre peer-reviewed grant funded research you want access to your own data without restriction.

Questions 13.5 and 13.6: Generally only a consideration for industry-sponsored studies

14. Liability:

Question 14.1: Liability insurance is not needed for peer-reviewed grants: Queen's has insurance for this. This is for industry sponsored studies. HIROC covers hospital staff for research purposes. The HIROC liability policy states that all employees (nurses included) are additional insureds and as such are covered for their work done for and on behalf of the hospital. The coverage includes but is not limited to healthcare professional liability. Please note, as protection is limited to actions that

are within the employee's obligations at the hospital there is no coverage for work outside of his/her duties at the hospital. All research staff at Queen's would be covered by Queen's liability policy. HIROC does not cover physicians. CMPA covers the physicians for their research activities. HIROC Certificates of Proof of Insurance can be issued on a request only basis through KGHRI by contacting 613-549-6666 ext. 3344.

Questions 14.2 and 14.3: Again, compensation for out-of-pocket medical expenses related to injury is relevant mainly for industry-sponsored studies and responsibility for this should be clear in the contract and defined in the participant information and consent form.

15. Investigational Drugs or Devices:

Questions 15.1 to 15.8: This section is fairly straightforward. Note that all clinical trials need to be registered. A clinical trial is any research study that assigns participants 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 participant 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 KGHRI (Lisa McAvoy; 613-549-6666 ext. 3344).

16. Handling and Disposition of Study Drugs:

Questions 16.1 to 16.8: This section needs only be completed if you are participating in a clinical drug research study. Please describe the steps related to drug ordering and receipt, drug storage requirements, drug labelling, drug dispensing procedures, drug use by participants, drug returns and disposal, and drug record keeping. These guidelines are intended as a resource for investigators to ensure study protocols contain all necessary information about the handling and disposition of study drugs:

Ordering and Receipt: Describe the steps for ordering and receipt of study drugs including shipping, packaging, receipt and record keeping. Where a cold chain must be maintained details for temperature monitoring are required at each step.

Storage: Describe the storage requirements for the study drugs, including:

- Where the study drugs will be stored;
- How the study drugs will be stored (refrigerator, freezer, locked cupboard).

Inventory Monitoring and Record Keeping: Identify who will be responsible for monitoring and replenishing the inventory of study drug supply. Describe the process for inventory monitoring (e.g., inventory counts, expiry date checks).

Labeling: Describe the study drug label when it is received and dispensed; include a sample label of each.

Dispensing: Describe how the study drugs are prepared for patients on active and placebo treatment arms. Describe how patients are assigned to a treatment arm in a randomized trial. Identify who is responsible for study drug preparation and dispensing. Describe the process for providing information to study subjects on how to take study medications including precautions and other instructions.

Drug Returns and Disposal: Describe the process for return of study drugs from the patients and disposal of returned or unused study drug at the study site.

Record Keeping: Describe the records that will be maintained for all study drugs and who is responsible. Include a sample of the study drug accountability form.