Guidance Document HREB Clinical Trial Application Part B

General Information

Part B must be completed by the Site Investigator as these tabs are specific to the LOCAL site.

If there are multiple local sites participating in a clinical trial, only one site is required to submit Part A. Once HREB approval is in place, other local applicants will be required to complete Part B only.

Please do not copy/paste symbols such as > into the application form. Doing so will result in misrepresented symbols upon submission. You must type out such as 'greater than or equal to' (e.g. questions 7.2 and 7.3)

Writing must be suitable for a lay audience. Avoid jargon terms and acronyms.

Ensure that the application is complete, all documents are submitted, consent form is clearly written, and consent form reading level is at or below the acceptable grade level to avoid delays with processing.

All questions marked with an asterisk (*) are required. Failure to answer a required question will cause delays in submitting an application for review.

All questions in the Project Info Tab are required to be completed (including questions not marked with an asterisk (*).

Tab 1: Site Submission Application Form for Ethics Review of a Clinical Trial. The site investigator must complete all tabs in this application

1.1: Number of participants anticipated for this site:

Please insert the anticipated number of participants at the local site only. To note, if the local site plans to recruit beyond the approved number, an administrative amendment must be submitted to the HREB for approval.

1.2: What treatment do you now use for patients who would meet the inclusion criteria for this study, i.e., how would you manage these patients if they did not go into this study?

In your clinical setting, what is the standard effective therapy you would use to treat eligible patients who do not participate in this study?

1.3: Does this site plan to deviate from/not participate in any aspect of the approved protocol (i.e. not recruit a particular participant type, or not participate in an exploratory substudy)?

For example, will your site not be participating in any of the optional research that was approved in the application submitted by the first site?

- o Yes (please complete question 1.4)
- o No

1.4: Please specify:

1.5: Has a clinical trial agreement (CTA) been negotiated for this study?

- o Yes (please complete question 1.6)
- o No

1.6: Please indicate who negotiated the CTA:

Please insert the parties who are involved in the clinical trial agreement (eg. xyz clinic & Sponsor; Eastern Health, Sponsor & PI; MUN, xyz University & PI).

1.7: Does this study involve a material transfer agreement (MTA) or a data transfer agreement (DTA)?

If data, blood and/or other biological samples collected as part of the study are being sent outside of the province of Newfoundland and Labrador, a data and/or material transfer agreement must be in place. The material transfer agreement is sometimes contained within the clinical trial agreement. If this is the case, you must still select the "YES" option below.

- o Yes (please complete question 1.8)
- o No

1.8: Please indicate the two parties of the MTA/DTA:

If a data/material transfer agreement is in place, please indicate the parties involved. If the DTA/MTA is contained in the CTA, please state here.

Please complete ALL fields below ACCURATELY. The information provided will be used for invoicing by the Health Research Ethics Authority for industry sponsored research. By completing below, you understand and agree that payment is due upon review by the HREB for services rendered and is not contingent upon securing approval by the HREB or executing a contract with the PI and/or Institution. Payment is expected within 60 days of the invoice date. To Note: If a Sponsor has outstanding review fees, any subsequent applications WILL NOT be reviewed by the HREB until full payment is received.

Tab 2: Invoicing Information

2.1: Is this project industry sponsored and subject to a review fee?

All industry sponsored research projects submitted to the HREB are subject to a review fee. For further information on review fees, please refer to the HREA website. A link to this can be found under 'Useful Links' on the Researcher Portal Homepage.

- o Yes (Please complete and attach the 'HREA Invoice for Industry Sponsored Research'.)
- o No (please skip questions 2.2 - 2.9)

2.2: Name of Sponsor:

2.3: Forward Invoice to:

- Site
- Sponsor/CRO

2.4: Company to be Invoiced:

Please provide the name of the Sponsor/CRO responsible for paying the invoice.

2.5: Complete Mailing Address:

Please provide the complete mailing address for the person responsible for paying the invoice.

2.6: Email Address:

Please provide the e-mail address for the person responsible for paying the invoice.

2.7: Contact Name:

Please provide the contact name of the person responsible for paying the invoice.

2.8: Telephone Number:

Please provide a telephone number for the person responsible for paying the invoice.

2.9: Protocol Title:

2.10: Protocol Number:

Tab 3: Blood and Other Biological Samples

Please note: the term "data" referenced within this application includes blood and/or other biological samples.

3.1: Does your study involve blood and/or other biological samples?

Please select 'Yes' if:

- your study involves the collection of any blood and/or other biological samples for the purposes of this study

OR

- archived and/or discarded blood and/or other biological samples are being accessed and used for this study

Please select 'No' if your study does not involve the access to or collection of any blood and/or other biological samples.

- Yes
- No (please skip questions 3.2 to 3.13)

3.2: List the blood and/or other biological samples, to be used in the study, the frequency of sampling and the amount of sample:

1. Explain which blood and/or other biological samples are mandatory for the clinical trial and which blood and/or other biological samples are optional (if applicable).

2. Please describe what blood and/or other biological samples will be taken, how often, and in what amounts, e.g. "xx ml of blood (xx teaspoons) will be taken over 'x' visits during the 'x' month study".

3. Please do not list every test being performed. Summarize tests when possible. For example, 'Routine safety bloodwork including chemistry, CBC, liver function tests'.

4. Is testing performed in local lab or central lab?

5. If archived blood and/or other /biological samples are being accessed, please attach '"Variable List"' (signed by the data custodian) under the "Attachments" tab of the application.

3.3: Will any blood and/or other biological samples now archived and/or discarded by a health care institution be used in the study? If yes, please include a variable list requesting access.

If you intend to use archived and/or discarded blood and/or other biological samples you must select 'Yes' below and upload the variable list (signed by data custodian) to the Attachments tab and select the Doc/Agreement as 'Variable List'.

- o Yes
- o No

3.4: Will any blood and/or other biological samples be sent outside the province?

Please select 'Yes' If any of the blood and/or other biological samples are going to be sent/shipped outside the province of Newfoundland and Labrador. If you select 'yes', please proceed to question 3.5.

If no blood and/or other biological samples will be sent/shipped outside of the province of Newfoundland and Labrador then you can select 'No'.

- o Yes (please complete question 3.5)
- o No

3.5: Please explain:

If you selected 'Yes' in question 3.4, please explain:

a) Where the blood and/or other biological samples will be sent (address location);

b) Who has custody and control of the blood and/or other biological samples at the location noted in (a) (e.g. name of lab)?

c) Are the blood and/or other biological samples being anonymized or de-identified prior to being shipped from the Site?

d) Describe the purpose for which the blood and/or other biological samples are being sent (e.g. for analyses).

3.6: Will any blood and/or other biological samples be kept after completion of the study?

Please select '"No"' if none of the blood and/or other biological samples collected will be kept after study completion.

Please select 'Yes' if any of the blood and/or other biological samples will be kept after study completion. If any of the blood and/or other biological samples collected will be kept after study completion, please complete question 3.7-3.13. It is important to note those questions 3.7-3.13 are in relation to blood and/or other biological samples retained after study completion only.

- o Yes (please complete questions 3.7 – 3.12)
- o No

3.7: Please indicate why the blood and/or other biological samples are being retained:

Please explain why the blood and/or other biological samples are being retained after completion of the study (e.g. specific research question, specific area of research, bio banking, unknown future research or use).

3.8: What specific research question will be addressed?

Please outline what specific research question will be addressed using these retained blood and/or other biological samples, if known.

3.9: How long will the blood and/or other biological samples be kept?

Please specify the time-period for which retained blood and/or other biological samples will be kept after completion of the study until destruction.

3.10: Where the blood and/or other biological samples will be stored?

Please provide the storage location (exact address) for any blood and/or other biological samples that are retained after completion of the study.

3.11: Please name the person or organization who will have custody and control of the blood and/or other biological samples that are retained after completion of the study.

3.12: Please indicate if blood and/or other biological samples can be withdrawn.

- o Yes
- o No

3.13: Please describe the process for withdrawal or provide rationale for why blood and/or other biological samples cannot be withdrawn:

If you selected "Yes" to question 3.12, please describe how participants may request to have their blood and/or other biological samples withdrawn and the process in which the request to withdraw takes

place (e.g. participant informs the local site verbally and local site contacts the data custodian of the retained blood and/or other biological samples). Also explain what will happen to the data collected from the blood and/or other biological samples once the blood and/or other biological samples are withdrawn.

If you selected "No" to question 3.12, please provide a rationale (e.g. blood and/or other biological samples have been de-identified and link has been destroyed).

Tab 4: Recruitment and First Contact

4.1: Please describe in detail the means you will use to identify and contact eligible participants:

It is important to describe the means of identifying and contacting eligible participants. For example, the first contact may be verbal or in writing and simply informs the potential participant that a study is underway. If they are interested, they may leave their contact information with the person approaching, the community agency, someone in the physician's office or be given a telephone number to contact the research team directly.

In the case of patients, the HREB expects that the person making first contact will be in the participant's circle of care. Examples include, but not limited to: The patient is contacted by the PI who is also providing clinical care; the clinician providing care asks participant if interested in meeting PI/RC/RA as applicable; Letters mailed from primary clinician. For participants in the community, it may include contact by random digit dialing, community agency, support group, workplace manager, newspaper ads, posters, etc.).

4.2: Will contact be made with potential participants?

- o Yes (please complete question 4.3)
- o No

4.3: Who will make the first contact to provide information about the study?

For participants in the community, it may include a community agency, support group, workplace manager, newspaper ads, posters, contact by random digit dialing, etc.

In the case of patients, the HREB expects this person to be in the patient's circle of care. Examples include, but are not limited to: The patient is contacted by the PI who is also providing clinical care; the clinician providing care asks the patient if they are interested in meeting with the PI/RC/RA as applicable; or a letter is mailed from the primary clinician to the patient informing them of the study.

4.4: Please specify the means of contact. Check all that apply. Copies of letters, telephone scripts, ads and posters must be included with the application:

Please upload copies of letters, telephone scripts, ads, posters, etc. to the Attachment tab and select the Doc/Agreement as "Recruitment Document" and include in the Description the type of document that it is, i.e. invitation to participate letter, telephone script, ad, poster, etc. An ad template is available on the 'Attachments' tab.

- o In person

- o Letter
- o Telephone
- o Advertisement
- o Poster
- o Other (e.g. email, social media) (Please complete question 4.5)

4.5: Please specify:

<u>Tab 5: Consent Process</u>

The Principal Investigator is the person ultimately responsible for the consent process.

5.1: Who will obtain the consent?

Examples include: Principal Investigator, Research Assistant, Research Coordinator

5.2: Explain, in detail – setting, timing, person approaching and persons to be approached - the procedure you will use to obtain consent. Special consideration is required if the study involves individuals with an altered or diminished capacity to consent (e.g. children, incompetent persons, etc.). If applicable, describe in detail how proxy, community and/or parental consent and child assent will be obtained:

For further information on obtaining consent, please refer to the 'HREB Guidelines for Consent' available under the Attachments tab.

This section should explicitly outline the details of the consent process.

- Where and when will consent take place?
- Who will be approaching the participant and conducting the consent process?
- What is the timeline for consenting to participate? Will participants be permitted to take consent form home?
- How will consent for individuals with an altered or diminished capacity to consent be achieved?

5.3: Does this study involve deception?

Please refer to the TCPS2 for further information re: deception in research.

- o Yes (please complete question 5.4)
- o No

5.4: Please describe and justify the use of deception and outline the process you will use to debrief participants:

Please complete this section if you answered 'Yes' in 5.3.

5.5: Does this study involve a waiver of consent?

Please refer to the TCPS2 for further information re: waiving requirements of consent.

- o Yes (please complete question 5.6)

- o No

5.6: Please describe and justify the requirement of a waiver of consent:

Please refer to TCPS2, Chapter 3.7A and confirm that the five requirements for waiver of consent are met.

Tab 6: Safeguards of participant's confidentiality and information

The protection of the privacy and confidentiality of all research participants and their information is the responsibility of all members of the research team. This pertains to any personal information and personal health information collected from identified participants or their records. The following privacy protections are recommended by HREB. Please check those currently in place for this study. If you plan exceptions for these requirements please provide, in detail, the rationale for this decision.

6.1: The following privacy protections are recommended. Please check those currently in place for this study. Organizational safeguards are the responsibility of the Principal Investigator:

A template "Oath of Confidentiality" can be found under "Useful Links" on the Researcher Portal Home page.

All members of the research team have been briefed on their responsibility for privacy protection.

All members of the research team have signed an oath of confidentiality.

Any data-sharing agreements between the researcher and other institutions have been signed prior to providing access to data.

Consequences for breach of confidentiality are clearly stipulated to the research team.

All computer files pertaining to the study will be password protected.

All paper abstract forms and printouts of electronic files will be kept in secure storage – limited number of storage areas, limited access rooms, locked filing cabinets.

6.2: If you did not check all of the boxes in Question 6.1, please provide, in detail, the rationale for the exception to the recommended privacy protections:

6.3: List below the names of ALL members of the research team who will have access to identifiable data. Please describe why their access is necessary, their role in relation to the project, and how and where they will be accessing the data throughout the project:

All members listed here must also be listed under the Project Team Info tab. TCPS2 certificates must be provided for all people on this list. In order to protect participant privacy, please limit the number of people requiring access, as much as possible.

Tab 7: Retention of Data

Health Canada (HC) regulations, Division 5 requires that clinical trial data (collected for HC regulated trials) must be available for monitoring, auditing and inspection for 25 years.

Please note: the term “data” referenced within this application includes blood and/or other biological samples.

7.1: How will data be collected?

7.2: Will any data be shared outside of your institution? If so, how (e.g. secure file transfer, encrypted USB, etc.)?

7.3: Will you be linking the data to other data sources? How will the linkage occur?

7.4: Where will the data be stored? Provide the exact street address including room/office number.

1. Please provide the exact location where local data will be stored while the study is active.

2. If applicable, please describe how data will be transferred from the local site to the Sponsor and what safeguards are in place to protect the data in transit.

3. Please provide the exact location where local data will be stored when the study is closed.

4. Please provide the exact location where all study data will be stored when the study is closed.

7.5: Who will have custody and control of the study data? Provide their name and contact information:

Please provide the full name or role and contact information (including telephone and/or e-mail contact) of the person who will have custody and control of the study data, including who is responsible for the data while the study is active and who is responsible for the stored data after the study closes.

Please note, data custodians (e.g. Eastern Health) require that supervisors be responsible for the data generated by student’s projects.

7.6: Describe how the data will be disposed of after the retention period.

e.g. Paper records will be shredded by local NAID certified shredding facility. Electronic data will be disposed of by ensuring the drives on the device are appropriately sanitized (securely deleted or destroyed) prior to the disposal or repurposing of the system or any storage components.

7.7: List any participant identifiers – name, postal code, study code, to be retained and give the rationale for retention:

If you will be retaining any participant identifiers please list them individually and provide an explicit rationale for the retention (e.g. name and MCP numbers will be kept to identify participants and link to health record in the event of a regulatory inspection.)

Tab 8: End of study responsibilities and reimbursements

There is an expectation that research results will be disseminated to the academic community and, where appropriate, to participating individuals or communities in a timely manner. For research involving an Indigenous community, community leaders or partners should vet final reports, manuscripts and other dissemination materials for cultural and factual accuracy. However, there should

be no restrictions placed on publishing: instead, researchers should allow for dissenting views to be expressed in publications.

8.1: Explain the plan and timeline for debriefing participants at the end of the trial. Explain how study results will be disseminated (including how you will provide feedback to participants):

Be explicit on method of dissemination, such as disseminated to participants on an individual basis, in a group setting, community, workplace or any other process.

8.2: Do you intend to reimburse participants for expenses incurred?

- o Yes (please complete question 8.3)
- o No

8.3: Please specify what expenses will be reimbursed:

Please list eligible expenses and describe how reimbursement will be made. Please include whether receipts are required from participants prior to reimbursement being issued.

8.4: Will there be any payment for referral of patient participants?

- o Yes (please complete question 8.5)
- o No

8.5: Please specify the amount that will be paid per patient.

If you selected 'Yes' to section 8.4, please complete this section.

8.6: Do you intend to provide a gift, honorarium, or lottery opportunity to participants?

- o Yes (please complete question 8.7)
- o No

8.7: Please describe. At what point in the study would this be offered?

The HREB requests details on any gift, honorarium or lottery opportunity and the point at which the offer is made.

Best practices dictate that participant compensation is provided at the time of consent as opposed to later in the process as the TCPS 2 requires that participants not be penalized for withdrawing from a study.

If you selected 'No' to question 8.6 please do not complete this section.

Tab 9: Potential Conflict of Interest

The HREB requires disclosure of any real, potential or perceived individual conflicts of interests, as well as any institutional conflicts of interests of which you are aware that may have an impact on your research and explain how you intend to manage this conflict, particularly situations where any of the investigators will be paid to be involved in the study, own shares in the sponsor company, receive honoraria for lectures, workshops, or stand to gain personally.

9.1: Does any investigator have direct or indirect financial interests in any device, drug, intervention being using in this study?

- o Yes (please complete question 9.4)
- o No

9.2: Does any investigator function as an advisor, employee, officer, director or consultant for any funder(s)?

- o Yes (please complete question 9.4)
- o No

9.3: Will any investigator receive an honorarium or other benefits from any funder(s) (apart from fees for service)?

- o Yes (please complete question 9.4)
- o No

9.4: Please describe and explain how the conflict is being managed to ensure participant rights and welfare are not affected:

Please disclose to the HREB any real, potential or perceived individual conflicts of interests, as well as any institutional conflicts of interests of which you are aware that may have an impact on your research and explain how you intend to manage this conflict.

Tab 10: Checklist

Please review the items below to ensure your application is complete and that necessary supporting documents have been attached.

10.1: Please provide the HREB file number for the Part A Clinical Trial this study is associated with.

Please contact the Sponsor or Sponsor Designate for their HREB file number.

10.2: All questions have been answered in the space provided ('see attached' is not acceptable).

- o Yes
- o No

10.3: The site budget is included:

Please upload the site budget to the Attachments tab and select the Doc/Agreement as "Budget". In the description, please enter "Site Budget".

- o Yes
- o No

10.4: The site Principal Investigator has no conflicts of interest to declare or has explained in Question 8.4 how any conflict will be managed.

- o Yes

- o No
- o Not Applicable

10.5: The site Principal Investigator is in good standing with the NL College of Physicians and Surgeons.

- o Yes
- o No

10.6: Will this contract be administered through the University Finance Office? (If you are not affiliated with MUN choose "Not Applicable") If yes, copies of the HREB approval will be forwarded to the Office of Research Services.

- o Yes
- o No
- o Not Applicable

10.7: A copy of the TCPS2 Tutorial Certificate of Completion is included if a first time applicant.

Please upload your TCPS2 Tutorial Certificate to the Attachments tab and select the Doc/Agreement as "TCPS2 Certificate". In the description, please enter "TCPS2 Certificate - [your name]".

- o Yes
- o No
- o I have already submitted my TCPS2 Tutorial Certificate of Completion.

10.8: A copy of a current curriculum vitae for the site Principal Investigator is included if a first time applicant:

Please upload your current curriculum vitae to the Attachments tab and select the Doc/Agreement as "Curriculum Vitae". In the description, please enter "Curriculum Vitae - [your name]".

- o Yes
- o No
- o I have already submitted my curriculum vitae.

10.9: A copy of the Informed consent document is included.

Consent form templates are available for download and modification from the Attachments tab. When completed, please upload the informed consent document to the Attachments tab and select the Doc/Agreement as "Informed Consent Form."

- o Yes
- o No

10.10: Optional consent sections (or separate consent form) for DNA/tissue storage/use, or optional substudy consent forms, are included, if applicable:

Please refer to the HREB Policy Manual for information on clinical trial substudies. Consent form templates are available for download and modification from the Attachments tab. When completed, please upload the informed consent document to the Attachments tab and select the Doc/Agreement as "Informed Consent Form" or “Substudy Consent Form.”

- o Yes
- o No
- o Not Applicable

10.11: The consent form has been assessed at a reading level of... (must be grade 9 or less):

Tips for writing in plain language and more information on how to test the readability of a document can be found under 'Useful Links' on the Research Portal Home page.

10.12: Study specific questionnaires, recruitment advertisements, covering letters, etc. are included:

Please upload these documents to the Attachments tab. Any document that pertains to the collection of data for the purpose of the study should have a Doc/Agreement as "Research Instrument." Any document that pertains to the recruitment of participants for the study should have a Doc/Agreement as "Recruitment Document." Any document that pertains to the secondary use of data should have a Doc/Agreement as "Variable list".

- o Yes
- o No

Tab 11: Additional Requirements

Researchers should be aware that institutions, organizations, or other groups under study may have requirements for allowing access to their sites and to participants, and that some of these may have established mechanisms or guidelines e.g., school boards, Indigenous communities, correctional services, Regional Health Authorities, and community groups. Therefore, once your study has received ethics approval from the HREB, organizational approval may also be required. Organizational approval is not another ethics review; it is a separate and distinct process. It is possible that studies may be approved by the HREB but be unacceptable to an authority, agency or institution because of overuse of a particular group of patients, unavailability of space, personnel, equipment at the time of the proposed trial or incompatibility with the values of the community in which the trial will be conducted. It is your responsibility to seek the necessary organizational approval from the Regional Health Authority or other organization as appropriate prior to commencing your study.

11.1: I have read and acknowledge the above statement:

Further information on obtaining organizational approvals can be found on the HREA website: www.hrea.ca.

- o Yes, I have read and acknowledge the above statement.

11.2: Does your study involve a Regional Health Authority (RHA)?

- o Yes (please complete question 11.3)
- o No

11.3: Check all that apply:

- o Eastern Health Regional Health Authority
- o Central Health Regional Health Authority

- Western Health Regional Health Authority
- Labrador Grenfell Health Regional Health Authority

Tab 12: Declaration

Note: this tab must be completed by the site Principal Investigator. By submitting this application, I assume full responsibility for this research study and verify that the information provided in this application is accurate and complete. I request the Health Research Ethics Board (HREB) to act as the research ethics board of record for this study.

12.1: I verify that the information provided in this application is accurate and complete.

- Agree
- Disagree

12.2: I will conduct the study according to applicable laws, regulations and guidelines.

- Agree
- Disagree

12.3: I will conduct the study consistent with applicable ethical norms:

- Agree
- Disagree

12.4: I will conduct the study according to the approved protocol and consent form(s):

- Agree
- Disagree

12.5: I will accept the authority of, and abide by, the decisions of the HREB as the board of record:

- Agree
- Disagree

12.6: I will comply with the HREB requirements, including timely filing of documents as required by the HREB and provide access to study documents for any random or for cause monitoring by the HREA:

- Agree
- Disagree

12.7: I will ensure there will be no changes to the research without prior HREB review and approval, except where necessary to eliminate an immediate hazard to participants.

- o Agree
- o Disagree

12.8: I will report immediately to the HREB any unanticipated problems in the research, significant deviations from the study protocol, or changes increasing the risk to participants or affecting significantly the conduct of this study:

- o Agree
- o Disagree

12.9: I will report promptly to the HREB all adverse reactions that are both serious and unexpected and new information that may affect the participant's willingness to participate in the research:

- o Agree
- o Disagree

12.10: I will request an annual ethics renewal for each year this study is active and submit a final report once this study is complete:

- o Agree
- o Disagree