HREBA | Health Research Ethics Board of Alberta
Clinical Trials Committee

HREBA – Clinical Trials Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 0H8

Items Required for Review

The following information outlines procedures and provides additional information with some examples regarding items required for review of a study by the Clinical Trials Committee.

Note: The office of the Clinical Trials Committee (CTC) must receive all required documents before review of a study proposal commences. Required documents include the signed and dated Clinical Trial Agreement, Budget and any applicable signed Service Provider Agreements.

Please be very specific when completing the IRISS application question, All questions should be complete even if "not applicable". The CTC members review the information in the application form and use the attached documents as support. The application should be the document of record, therefore provide detailed answers to all the questions by copying/pasting the answers directly from the applicable document (e.g., consent forms, protocol, investigator brochure). This application is a 'living document'; any changes to the study documents (e.g. protocol, IB, study staff) should be reflected in the IRISS application form.

IRISS Registration

Before you can start an application in IRISS, you need to register for IRISS. Please include the following documents:

1. Curriculum Vitae: the CV must contain the following applicable elements:
    - Research qualifications (listing both past and present research experience if any)
      Note: If you, the investigator, do not have any research experience, please confirm any training you have with respect to your obligation as a research under the ICH Good Clinical Practice Guidelines and/or the Tri-Council Policy Statement. If you have not received any training from the sponsor, you will be required to receive this training before approval can be granted.
    - Academic qualifications
    - Undergraduate/post-graduate training
    - Certifications
    - Affiliations
    - Publications
    - Note: Investigators and co-investigators must be medical/health profession practitioners, regardless of whether other personnel are considered co-investigators by the sponsors. For example, a PhD or RN could not replace the investigator for the purposes of supervising a study if an investigator is absent. The co-investigator replaces the investigator for the purposes of supervising the study if the investigator is absent. The co-investigator is also involved in study procedures and visits for subjects in the same role as the investigator when seeing subjects. Either the investigator or co-investigator can see the subjects for their study visits at the research site. It is the primary investigator though who is directly accountable for all documentation submitted to the Clinical Trials Committee.
2. Valid practice permit from your professional regulatory body.
3. Research ethics training completion certificate.
    - Tri-Council Policy Statement tutorial
    - CITI Program, (organization affiliation is under Alberta Innovates)

HREBA – Clinical Trials Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 0H8

Attaching Documentation to IRISS Application:

- For security purposes, please ensure all uploaded documents are in a PDF format (except the ICFs, which should be in Word format).
- Please do not upload any documents that are password protected. The IRISS platform is secure and only the reviewers and admin can access the files.
- When uploading documents, please ensure the document name, version and date are complete as this is what will appear on the approval correspondence. Please use the three separate fields provided when uploading a document.
- When adding a new version of a document, click the **Update** button beside the appropriate document.

Post Meeting Request resulting from CTC Review:

Please note once a study is submitted to the CTC in IRISS, any post meeting change requests from the Committee will be communicated in a Pending Approval Letter sent via the changes required activity. When responding to a Pending Approval Letter, please upload your response letter in the Other Documents section on the Documentation page in IRISS and make the applicable changes in the IRISS application. When updating documents on the documentation page, please add a clean and tracked changes version so the committee can see what change were made.

Additional Investigator Applications (Multi-site Studies):

1. Only fill out the IRISS Application questions in the following sections:
    a. Study Staff, Funding, Location
    b. Participant Information, Recruitment, and Informed Consent
    c. Data Privacy and Confidentiality
    d. Documentation – upload all documents requiring CTC approval.
2. For all other sections, because the information has already been reviewed and approved by the CTC for the lead site, please type “Reviewed and Approved for (insert approved file number here)”

Incomplete Submissions

- All new submissions for full committee review must be received by the submission deadline.
- CTC staff inform the research site, outlining the missing documents.
- If you submit all missing documents by the next day, the file will go for review for that month’s meeting. If the requested changes are not submitted by the next day, the file will miss the deadline and proceed to the following month’s CTC meeting for review.
- Note: After the CTC receives a complete research application, changes to the protocol or the informed consent form are not permitted until the Committee approves the research study originally submitted. Any new information outside of what is requested will delay the review and approval.
- Please refer to the “Checklists for Submission of a Research Study” to ensure all required items and the appropriate number of copies are included in a submission.

HREBA – Clinical Trials Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 0H8

Items Required for Review

Advertising

- If the Investigator/sponsor will be recruiting subjects by advertising, a copy of the advertising (e.g. posters, brochures, radio/TV script, etc.) must be uploaded to the Documentation page for review.
- If you use a telephone screen to determine a subject's eligibility for participation in the research study, statements regarding the following must be included in the script at a point prior to the section that collects personal identifiable information:
    - What will happen to collected information if the subject is ineligible to participate? Will you discard gathered information? How long will it be retained? What is the purpose for retaining it?
    - What degree of confidentiality can you guarantee to the potential subjects? How will you accomplish this?
- Note: All participating sites must submit a copy of any telephone screening scripts for review.
- Please use the following as guidance when creating advertising.

Acceptable wording:

- extra care, free care,
- cost of medication included,
- compensation/reimbursement for time/travel,
- physician access (US wording) as Canada always has free access

Unacceptable wording:

- promise of compensation for participation
- compensation without a qualifier (e.g. for time and travel)
- access to a new "treatment" (research is not a treatment)
- promise of a procedure and/or treatment that is not ordinarily free (e.g. ophthalmology studies)
- accelerated access to care

Check List for Submission of Research

- To ensure all required items are included with your IRISS submission, please refer to the document Checklists for Submission of a Research Study.

Clinical Trial Agreement

Document(s) Required for Review

- Please upload a copy of the contract(s) between the Investigator and the sponsor (signed by both parties) to the Documentation Page (section 11.0) in the IRISS application.

On-going Information to Subjects

- Please describe how you will provide on-going information to subjects regarding safety and their participation in the study.
- The Clinical Trial/Financial Agreement and/or Protocol must conform to Sections 4.8.2 and 4.8.10(p) of the ICH Harmonized Tripartite Guideline for Good Clinical Practice

which states that investigators must be able to provide on-going information to subjects regarding safety and their participation in the study.

Publication Rights of Investigators

- Section 11.12 of the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans 2nd Edition states: *"Institutions and REBs should take reasonable measures to ensure that sponsors, researchers and institutions publish or otherwise disseminate the analysis of data and interpretation of clinical trial results in a timely manner without undue restriction."*
- All investigators entering into agreements with sponsors need to ensure that a paragraph on publication rights is included.
- In order that the publication accurately reflects the results of the study, the investigator's access to the data generated from the study should not be restricted. Any unreasonable restrictions, implied or specific, preventing the publication by the investigator(s) of the results, including significant or serious adverse events, is unacceptable.

Entire Research Protocol

Standard Research Protocol

- The protocol must include the following items:
  - Type of study (pilot, clinical trial, drug (phase), placebo, sequel to previous study, multi-centre)
  - The number of sites engaged in the project
  - The number of subjects in the total study
  - Rationale (background to justify this particular research)
  - Hypotheses
  - Purpose
  - Objectives
  - Study Design
  - Recruitment/ Population description (sample size, inclusion and exclusion criteria)
  - Methods and Procedures (identify which are standard care and which are additional)
  - Outcome Measures
  - Statistical Analysis
  - Indication of whether all potential subjects would be able to give consent to participation (e.g. minors, mentally incompetent subjects, etc.)
- Note: If incompetent subjects are to be recruited, the protocol must identify the process for obtaining consent from a legitimate proxy.

Genetic Studies

- The following information must be provided:
  - Rationale for the use of the data and the sample
  - Description of personal/demographic data that will accompany the sample
  - Distribution of any personal data and samples
  - Information and justification for access by subjects/relatives
  - Duration of storage and statement regarding destruction of samples/data • process whereby the personal data and samples will be anonymized.

HREBA – Clinical Trials Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 0H8

Fee for Review

Research studies which receive funding from industry (e.g. pharmaceutical/medical device companies) or other for-profit organizations are charged an administration fee for the initial ethics review. There are no fees for ongoing review activities, nor for the initial review of studies which are unfunded or funded by cooperative groups, internal funds, or grants.

Once the ethics certificate is released (i.e. the study is approved) an invoice will be sent from Alberta Innovates for the amount indicated below (GST will be added if applicable). **Please do not send in the administration fee until you receive an invoice.**

Type of Review	Fee
Full Review	$5,000.00
Delegated Review Includes minimal risk, additional investigator (multisite) and reciprocal reviews.	$2,000.00

Health Information Act (HIA) Requirements

On the Data Privacy and Confidentiality section of the IRISS application, please provide a description of how you will meet the requirements of Alberta's Health Information Act.

- **Section 50(1)(b)(iii)**
  - This section states that *"The ethics committee must assess whether, in the opinion of the ethics committee, adequate safeguards will be in place at the time the research will be carried out to protect the privacy of the individuals who are the subjects of the health information to be used in the research and the confidentiality of that information".*
- The Investigator must take reasonable steps to maintain the safety of subject information. This document must outline the safeguards specific to the research site. Examples of adequate safeguards include, but are not limited to:
  - **Administrative**
    - Access restricted to authorized users
    - Security checks on key employee positions
    - Oath of confidentiality
    - Regular review of access privileges
    - Authentication of users (passwords)
    - Education of staff re: policies and consequences following a breach
    - Access, use, disclosure log – audit ability
  - **Technical**
    - Secured from unauthorized access
      - Eavesdropping, interception and diversion
    - Encryption (storage and transmission)
    - Secured from inappropriate access, accident, viruses and system failure
    - Disaster recovery safeguards
    - Procedures to restore, recreate or replace when damaged, lost or destroyed
  - **Physical**
    - Controls on facility, office, information retrieval equipment and systems
    - Card locks, physical security access such as keys, digital card keys, and cipher lock barriers
    - Bolting equipment to the floor, locked desks and rooms

- **Section 34(1) & (2)**
  - If the investigator needs access to individually identifying health and/or registration information from another custodian, consent must be obtained from the individual who is the subject of the information and the consent must meet the requirements outlined in section 34(2).
  - This consent may be included as a "Consent for Disclosure" section in the study's informed consent form or may be a separate consent form altogether. Please refer to our Consent to Disclose Health/Registration Information template.

Informed Consent Form(s)

Standard Research Studies

- Please modify the study's informed consent form to the Committee's requirements and place it on the Investigator's letterhead (refer to the Consent Form Template – Standard Research Studies for the requirements).
- Please upload the initial consent forms in Word format.

Genetic Research Studies

- Please modify the study's informed consent form to the Committee's requirements and place it on the Investigator's letterhead (refer to the Genetic Informed Consent Form Template for the requirements).
- Please upload the initial consent forms in Word format.

The following may be used as a guideline to determine when to use an assent form versus a consent form for minors:

Assent

- Used and signed by children (approx. aged 7 – 12 years) who are, in the judgement of the investigator, able to understand and sign a simple form but lack the maturity to give consent on their own. In addition to the assent, a consent form must be signed by the parent or legal guardian in order for the child to participate in the study.

Consent

- Used by children (approx. aged 12-17 years) who are deemed "mature minors" (i.e. children who have the capacity to consent because they have sufficient intelligence and maturity to understand the nature, consequences and responsibilities of the study.
- It is the responsibility of the investigator to make the evaluation and judge the capacity of the child to consent on his/her own.
- In Canada, according to common law, a "mature minor" can legally consent to participate in research without parental consent.

Investigator's Brochure/Product Monograph

Please upload the most current version for *all* drugs involved in the study to the Documentation Page of the IRISS application.

Justification for Placebo (for Placebo-Controlled Studies Only)

It is the responsibility of the researcher or sponsor to provide justification to the Clinical Trials Committee for the choice of a placebo control group, as opposed to the other possible choices of control group (e.g., active control, wait-list control, dose-response and combination therapies). The criteria below are to ensure that this type of clinical trial design is used only in situations that do not compromise the safety and welfare of participants.

The justification for the use of the placebo must follow the requirements outlined in Article 11.2 of the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans 2nd Edition (TCPS 2). The comments must address the specific item(s) in the TCPS 2 that applies [i.e. 11.2 (1) to (5)] and the discussion must support this. Please include this information on the Clinical Trials Page of the IRISS Application.

Article 11.2 of the Tri-Council Policy Statement, 2nd edition, states that:

- A new therapy or intervention should generally be tested against an established effective therapy.
- As with all alternative choices of a control, a placebo control is ethically acceptable in a randomized controlled clinical trial only if:
    - its use is scientifically and methodologically sound in establishing the efficacy or safety of the test therapy or intervention; and
    - it does not compromise the safety or health of participants; and
    - the researcher articulates to the REB a compelling scientific justification for the use of the placebo control.
- For clinical trials involving a placebo control, the researcher and the REB shall ensure the general principles of consent are respected and that participants or their authorized third parties are specifically informed (see Article 3.2):
    - about any therapy that will be withdrawn or withheld for purposes of the research; and
    - of the anticipated consequences of withdrawing or withholding the therapy.

Great care should be taken to avoid abuse of placebo comparators. However, they are acceptable in any of the following situations:

1. There are no established effective therapies for the population or for the indication under study;
2. Existing evidence raises substantial doubt within the relevant expert community regarding the net therapeutic benefit of available therapies;
3. Patients are resistant to the available therapies by virtue of their past treatment history or known medical history;
4. The trial involves adding a new investigational therapy to established effective therapies: established effective therapy plus new therapy vs. established effective therapy plus placebo;
5. Patients have provided an informed refusal of established effective therapy, and withholding such therapy will not cause serious or irreversible harm.

The determination of response satisfaction and refusal of treatment must take place outside the context of recruitment for the clinical trial and prior to offering trial participation to the prospective participant, and both must be documented.

The use of a placebo comparator in situation (5) is permitted because prospective trial participants are not using established therapies and therefore are not benefiting from therapy. For that reason, such participants would not be further disadvantaged if enrolled in a placebo-controlled trial than participants in a trial for whom there are no established effective therapies for the indication under study. Research proposals submitted to CTC must include sufficient support and justification of the trial design and use of placebo comparator. The text above is available in: Justification for Placebo - Guidelines.

HREBA – Clinical Trials Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 0H8

Service Provider Agreements

- Please provide evidence that appropriate arrangements are in place between the Investigator and the relevant service providers (e.g. Laboratory, x-ray, pharmacy, MRI, etc.) for compensation of research related testing.
- Evidence may be provided in the form of a signed and dated contract or letter of agreement referencing the study title and protocol number (if applicable).
- Please ensure the cost amounts are reflected in your budget document.
- Please upload the applicable service provider agreements to section 11.0 on the Documentation Page in the IRISS application.

Per-Item Per-Visit Budget

Please upload a budget for your study to the Documentation Page in the IRISS application.
Article 7.4 of the Tri-Council Policy Statement 2 states:

> *"The REB should examine budgets to ensure that there are no inappropriate payments to be made or other unexplained expenses that may raise questions about conflict of interest. Further, payment provisions should be scrutinized to ensure they do not create ethically inappropriate incentives to recruit quickly, at the expense of a careful review of the suitability of prospective participants. Unreasonable payments or undue inducements may place the researcher, and sometimes the institution, in a conflict between maximizing financial remuneration on the one hand and protecting participants and meeting the scientific requirements of the project on the other. Disclosure of the kinds and amounts of payments and other budgetary details encourages the researcher to identify and appropriately manage potential conflicts of interest and helps the REB to assess them. Management by institutions and/or REBs may include prohibiting certain forms of payment."*

Sample Per-item/Per-visit Budget

Study ABC -Investigator: Dr. Jane Doe

Fixed Costs	**Amount**
Investigator – Review of Protocol and Confidential Investigator's Brochure	$2,550.00
Coordinator – Review of Protocol and Confidential Investigator's Brochure	$1,500.00
REB – submission, reporting (fees)	$3,750.00
Pre-Screening Log	$800.00
Pre-Study Visit	$500.00
Broadband Internet Access (1 Year)	$1,800.00
Advertising (if applicable)	$1,500.00
Pharmacy setup (if applicable)	$7,00.00
Total	**$13,100.00**

Direct Costs	**Frequency**	**Amount**
Investigator ($150/hour)		
Informed Consent	1	$150.00
Medical History	1	$150.00
Complete Physical Examination	1	$150.00
INCL/EXCL Assessment	2	$150.00
Laboratory Assessment	3	$112.50

AE Review/Assessment	4	$150.00
Case Report Forms Review/Revision	4	$300.00
Coordinator ($50/hour)	5	$125.00
General Patient Management		
Vital Signs	3	$37.50
Review of Prior/Concomitant Medication	3	$37.50
Dietary Compliance Monitoring	1	$12.50
Management of Study Medication	3	$75.00
AE Review	4	$200.00
Post-Study AE Follow-up (telephone)	1	$12.50
CRF Completion, Review/Revision and Audit	6	$750.00
Laboratory Tests/Services		
Laboratory Draw/Processing	3	$60.00
Hematology	3	$75.00
Serum Biochemistry	3	$105.00
Serum B-hCG (women only)	3	$45.00
ECG, 12-lead	1	$50.00
Miscellaneous	5	$250.00
Patient Expense Reimbursement	2	$50.00
Pharmacy Management		
Office Supplies	5	$125.00
Administrative Support	5	$125.00
Sub-Total		**$3,297.50**
20% Administrative Overhead		**$659.50**
Total per Patient		**$3,957.00**
Total Study Budget (Direct Costs and Fixed Costs– 12 Patients)		**$60,584.00**