HREBA | Health Research Ethics Board of Alberta
Clinical Trials Committee

HREBA – Clinical Trials Committee
1500, 10104 - 103 Avenue NW
Edmonton, Alberta, T5J 4A7

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 (CTC).

Note: *The office of the 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.*

Procedures

Prior to the review of a research study, you must submit all of the information/documents detailed below and the applicable fee to the HREBA – CTC at the address below:

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Incomplete Submissions

- CTC administrative staff will inform you of the missing information/documents through IRISS.
- If you submit all missing information/documents by the following month's submission deadline, the protocol will then go to CTC for review.
- Note: Once the CTC administrative staff has sent the complete research application to the CTC reviewers, changes to the protocol or the informed consent form are not permitted until the CTC approves the research study originally submitted.
- Please refer to the *Check List for Submission of Research Study for Review* to ensure you include the appropriate number of all the required items in a submission.

Additional Information and Examples

- Information on HIA section 50 (how subject information is kept safe), declaration of conflict of interest, and justification of placebo are now found in the application form questions in the IRISS application and do not require a separate document.

Advertising

- If the Investigator/sponsor will be recruiting subjects by advertising, a copy of the advertising (e.g. posters, brochures, radio script, etc.) must be submitted 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.

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Check List for Submission of Research

To ensure all required items are included with your submission, please refer to the document *Check List for Submission of Research Study for Review*.

Clinical Trial/Financial Agreement

Document(s) Required for Review

- Please provide a copy of the Clinical Trial Agreement between the Investigator and the sponsor (signed by both parties).

Ongoing Information to Subjects

- Please describe how you will provide ongoing 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 ongoing information to subjects regarding safety and their participation in the study.

Publication Rights of Investigators

- Article 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.

Curriculum Vitaes

- The Investigator must submit a current typed Curriculum Vitae (for the present calendar year) for the Investigator and Co-Investigator(s).
- 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: listed investigators and co-investigators must be medical practitioners, registered with College of Physicians and Surgeons of Alberta, 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.

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 you are recruiting incompetent subjects, 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

Fee for Review

- The submission must include a photocopy of the applicable *review fee* and the cheque be mailed to the CTC.

Health Information Act (HIA) Requirements

Please provide a description of how you will meet the requirements of Alberta's Health Information Act.

- **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 *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 *Informed Consent Form Template – Standard Research Studies* for the requirements.)

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 *Informed Consent Form Template – Genetic Research Studies* for the requirements).

You may use the following 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, the parent or legal guardian must sign a consent form in order for the child to participate in the study.

Consent

- Used by children (approx. aged 12-17 years) who are "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 submit the most current version(s) of this/these document(s) for all drugs involved in the study.

Placebo-Controlled Trials

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.

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

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- 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.

Investigators should take great care 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.

Per-Item/Per Visit Budget

Please provide a budget for your study.

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."

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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 Compensation	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**

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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, 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 you reflect the cost amounts in your budget document.
- If you do research related testing at the research site, please list the individuals doing the testing in question #2.0 of the 'Research Methods and Procedures (continued)' section of the IRISS application form.