HREBA | Health Research Ethics Board of Alberta Clinical Trials Committee

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

Reviewer Form

The Clinical Trials Committee (CTC) members use a Reviewer Form to assist them in assessing protocol submissions. The CTC believes that awareness of the context that reviewers use to assess protocols may assist Investigators in developing their submissions. Investigators might find the Reviewer Form a useful reference. Considering the Reviewer Form in conjunction with the existing CTC template for submissions may be helpful, particularly when an Investigator is developing the informed consent document.

We have divided the document into the following three sections:

1) Standard Consent Form—Administrative/Committee Review (The CTC Coordinator/Committee members use this section as a guideline when reviewing the consent form)
2) Genetic Consent Form—Administrative/Committee Review (The CTC Coordinator/Committee members use this section as a guideline when reviewing a genetic consent form)
3) Required Documentation—The Chair of the Committee is required to review all the documents found in this section

Please note that we have provided this document only as a resource for Investigators to assist in organizing an informed consent form/protocol submission.

Standard Consent Form

1. **Initial Mandatory Requirement:**
   a. Is this statement included and verbatim?
2. **Background/Rationale:**

   This section should include a description of the following four points if applicable:

   a. Information for subjects – why should this disease/condition be studied?
   b. Information – what impact does this disease/condition have on subjects?
   c. Why the study drug/procedure has potential for subjects
   d. Why the study drug dose or type of procedure is proposed
3. **Purpose/Objectives:**
   a. Is the primary study objective stated (in lay terms) according to the protocol?
4. **Study Design:**
   a. Have randomization and blinding been explained?
   b. If single blind, is that addressed?
   c. In double blinded, have the details of when and how a code may be broken been explained?
   d. If deception is necessary for the research, debriefing is required. Is a description of the final consent process after debriefing included?
5. **Use of Placebo Section:**

   Placebo controlled trials must adhere to the principles outlined in the Tri-Council Policy Statement 2nd edition (TCPS2) Article 11.2 and demonstrate adherence to the principles described by this statement.

   a. Is this a placebo-controlled study?
   b. Does information provided include treatments currently used for this treatment of the disorder and discussion of effectiveness of the treatment?
   c. Does this section explain why placebo is necessary?

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

d. Is there an explanation of risks to the subject during any period that standard treatment is withheld?

e. Does information include measures taken to reduce the risk to subjects?

6. Study Procedures:

a. Is there a detailed description of what participation will entail for the subject (regular routines, nature of tests and procedures, amount of time spent at clinic visits)? Does this include time spent at home (i.e. filling in diaries, travel to and from site and labs, any other forms that need to be completed at home?)

b. Is there identification of procedures which are not part of usual clinical care – if applicable?

7. Risks and Discomforts:

a. Is a description of any discomforts and inconveniences associated with participation included?

b. Are known or suspected short- and long-term risks included?

c. Are risks categorized in percentages? If risks are not in percentages please advise why.

d. Are risks presented in tables for easy reference?

8. Reproductive Risks:

a. Are the risks regarding reproduction, lactation and fetal development explained?

b. Are the acceptable methods of contraception listed?

c. If required, is there a statement indicating that permission will be requested to follow a pregnancy according to the protocol?

d. If the pregnancy is to be followed, is the reason(s) for following it stated (e.g. explicit safety reasons)?

9. Benefits:

a. Is this section free from inducements for the subject to participate (e.g. close physician monitoring, free provision of services and/or medications)?

b. Does the consent form present a fair and honest view of the potential benefits?

c. This section **should not**

- Over-emphasize the benefits of participation.
- Present unproven benefits as potential benefit?
- Emphasize compensation or other benefits in a way that could induce participation

d. This section **should**:

- Indicate that randomization to the control group could mean the subject will not receive the active study treatment?
- Indicate that non-participation will not have any negative consequences for the subject including access to standard care?

10. Alternatives to Participation:

a. Are the alternatives to participating in the study listed?

b. Are trade names of commonly used medications listed?

c. Is there discussion of the risks and benefits of the alternatives or a statement indicating that the physician will discuss the risks and benefits of the alternative treatments with the subject?

d. If the drug is available without participating in this study, is this clearly stated?

11. Confidentiality:

a. Is there an explanation of who will have access to the information collected?

b. If disclosure of health/registration information is required from another custodian, does the consent meet requirements of Alberta Health Information Act section 34(2)?

c. Is the CTC included as having access to the information?

d. Is HREBA - CTC spelled out in full and is it correct?

e. If notifying the primary care physician of the subject's participation is optional, is the mandatory wording present and correct?

The confidentiality clause should inform subjects of the following:

a. That personal health information will be collected as part of the study

b. What is included in "personal health information"

c. That information will be kept confidential

d. How confidentiality will be protected (i.e. use of code numbers, etc.)

e. That study records will be kept separate from medical records

f. That in some circumstances, sponsor and/or investigator may be required by law to release personal health information about subjects

g. The purpose for which the information collected will be used (should be limited to the purposes of the study)

h. The sponsor's representatives will check the health information collected from time to time against medical records by. This means that representatives of the drug company paying for this research will be able to view your medical records.

i. Other persons may also need to view subject's records, including representatives from the Health Research Ethics Board of Alberta-Clinical Trials Committee, the Health Products and Food Branch of Health Canada (if applicable), the United States Food and Drug Administration (if applicable), and/or other foreign regulatory agencies

j. That where the groups/persons who need to see subjects' medical records are outside Canada, the privacy laws in these other places may be less strict than those in place in Canada.

k. That study records must be kept for 25 years.

l. That subjects have a right to check health records and ask for corrections to be made.

m. That by signing the consent form they give investigator and sponsor permission to collect, use and disclose medical records as outlined in this section.

n. If providing notification of participation to the subject's primary care physician is <u>optional</u>, the following must be included[1]:

If you have a personal physician, it is important that s/he know that you are entered into a research study and may be taking a drug that could affect your health. With your permission, we will notify your personal physician that you are enrolled in this study.

"I consent to my primary care physician being notified of my participation in this study.

❑ YES ❑ NO

Subject's Initials_____"

[1] If the investigator is the subject's primary care physician, this statement is not required.

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

o. If there is an optional genetic component to the protocol, please provide a separate genetic consent form. If the genetic component is mandatory, include the following paragraph in the main informed consent form:

"There may be risks to your eligibility for employment, life insurance, mortgage insurance or private health insurance if the results of genetic testing were to be inadvertently disclosed to certain parties. Safeguards have been established to ensure that such disclosure will not occur. For example, we have taken steps to ensure that a coded number, rather than your name, will be used to identify your sample and that your name will not be disclosed in association with the sample at any time. In addition, the results of genetic testing will not be placed upon your medical record. Despite these efforts, we cannot guarantee you with 100% certainty that your genetic information could never be linked to you."

Rationale: the risk of individual harm arising from participating in genetic research is unclear. Inclusion of the preceding paragraph may offer some clarity but should only be inserted IF it reflects what you and the sponsor are actually doing. Otherwise, the paragraph could be modified, as needed, to reflect the reality.

12. Cost to Patients:

a. Is there a statement indicating that AHCIP (spell out in document) will not be billed for visits, treatments or procedures related to the study?

b. Is there a description of any financial costs that the subject may incur and whether these costs may be reimbursed?

c. Is there a statement advising who will be responsible for the cost of remedies to treat side effects?

d. If this drug is not approved for marketing in Canada, is the mandatory statement included?

e. If subjects are to receive fees for participating in this research protocol, then a statement must be included in this section that states the nature of this reimbursement. If the amount is specifically stated in the budget then this amount must be included in the consent form document.

The Statement should include:

i. How the subject may apply to receive reimbursement

ii. Maximum amount of reimbursement

iii. What sort of costs will be covered by reimbursement (i.e. travel, daycare, over the counter medicines)

13. Compensation:

Is the mandatory statements included, if yes, is it verbatim?

All Informed Consent Forms must include a statement regarding the sponsor's policy on compensation for subjects who are injured as a result of their participation in the research.

The statement must:

1. Be in plain language
2. Accurately describe the sponsor's compensation policy. For example, if the policy is that health care costs are covered, but that loss of wages or future earning capacity are not covered, then subjects need to be aware of this.
3. Explain to subjects that if they are injured due to participation in a research study, their private health insurer (i.e. prescription drug, dental coverage) may not cover their medical care costs. They will need to familiarize themselves with their policy in order to determine what is included in coverage.
4. Explain who will determine whether an injury is study-related. Where the policy is to have the study doctor and the sponsor (or sponsor's representative) make this determination, it must be clear how conflicts among the decision-makers are to be resolved. The CTC suggests that where there is a

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

disagreement between the sponsor and study doctor as to whether an injury is study-related, an independent third party should make the final decision.

5. Explain to subjects that if they do not receive compensation voluntarily from the sponsor, they are entitled to sue to receive compensation. The legal costs of a claim will be the subject's responsibility, and these costs can be very significant

14. Withdrawal from Study:

a. Does this section contain information regarding what will happen to patients who are screen failures, withdrawals or when subjects complete the study?

b. If a subject withdraws and final procedures are to be performed for safety reasons, are the reasons clearly stated?

c. If not for safety reasons, is there a statement that the procedures are not mandatory and subject can refuse to do?

d. That they may withdraw from the study, and that in order to do so, they will need to notify the investigator in writing.

e. That even if they withdraw from the study, the information collected will not be destroyed.

f. That even if they withdraw from the study, there may be some continued use of the personal information collected about them. For example, the information will be used or disclosed if necessary to preserve the scientific integrity of the study; that study data already integrated into the database will not be withdrawn; that anonymized information will continue to be used.

15. Ethical Review:

a. If this mandatory statement is included, is it verbatim?

16. Signature Page:

a. Does this section conform to the mandatory wording?

17. Document Footer:

a. Does this section contain version date, page #s and space for subject initials?

Genetic Consent Form

1. Initial Mandatory Requirement:

a. Is this statement included and verbatim?

2. Risks Section:

a. Does this section conform to the mandatory wording?

When there is a genetic component to the study, subjects must be informed about the nature of genetic information, and risks of inadvertent disclosure of genetic information. Please note that the risk of individual harm arising from participating in genetic/pharmacogenetic/biomarker research is unclear. Inclusion of the following paragraph may offer some clarity but should only be inserted IF it reflects what you and sponsor are actually doing. Otherwise, the paragraph could be modified, as needed, to reflect the reality.

"There may be risks to your eligibility for employment, life insurance, mortgage insurance or private health insurance if the results of genetic testing were to be inadvertently disclosed to certain parties. Safeguards have been established to ensure that such disclosure will not occur. For example, we have taken steps to ensure that a coded number, rather than your name, will be used to identify your sample and that your name will not be disclosed in association with the sample at any time. In addition, the results of genetic testing will not be placed upon your medical record. Despite these efforts, we cannot guarantee you with 100% certainty that your genetic information could never be linked to you."

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

3. **Signature Page:**

   a. Does this section conform to the mandatory wording?

4. **Document Footer:**

   a. Does this section contain version date, page #s and space for pt initials?

Required Documentation

1. **Clinical Trial Agreement:**

   a. Has it been signed by the investigator and sponsor?

   b. Does the investigator have the ability to publish research findings?

      Complete prohibitions on publication are unethical, as they give the Sponsor ultimate control over whether information from the study reaches the public. It is acceptable for Sponsors to require advance notice from the investigator and to delay publication to ensure that the Sponsor's intellectual property rights are protected. The investigator must have final authority over the content of the publication (Tri-Council Policy Statement 2, Article 11.12)

   c. Does the investigator have the ability to disclose information needed to safeguard subjects' health and safety?

      Investigators must be able to disclose what is reasonable in order to publish their research, and they must be able to disclose what, in their clinical judgment, is needed to safeguard subjects' health and safety.

   d. Does the Investigator have discretion to determine when disclosure should be made to subjects and what that disclosure should include?

      Regardless what the CTA says, investigators owe legal obligations to research subjects. Obligations agreed to between investigator and sponsor in the CTA do not relieve investigators of their duty to research subjects.

      If an investigator enters into a CTA that purports to leave the determination of what must be disclosed to protect subject safety with the Sponsor or any other party (including an arbitrator, for example), then the investigator risks legal liability either to him/herself (as a result of breaching his legal obligations to inform the subject of risks of participating in research) or to the Sponsor, as a result of breaching his / her contractual obligations.

   e. Does the CTA say anything about what law governs disputes arising pursuant to the agreement?

      Investigators should be aware that different jurisdictions may have different legal rules. Clauses that say that the law of some other jurisdiction will govern disputes may create unexpected problems for investigators.

2. **Budget:**

   a. Does the budget accurately reflect the work being performed at the Investigator's site?

   b. Does the budget accurately reflect the Clinical Trial Agreement?

   c. Is the budget free from any inducement for either the investigator or subjects to participate?

   d. If no, is the inducement appropriate?

3. **Service Provider Agreements:**

   a. Is there a separate Service Provider Agreement(s) for third party services (e.g. laboratory, x-ray, pharmacy) outlined in the budget?

4. **Health Information Act Requirements:**

   Note: The investigator must provide the CTC acceptable written documentation of the investigator's methods for compliance with requirements of Alberta's Health Information Act.

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

a. [HIA Section 50(1)(b)(iii)] – detailed in the 'Data Confidentiality and Privacy' section of the IRISS application.

   Are methods documented for complying with the *Health Information Act* requirements to safeguard subjects' personal health information?

   Do the documented safeguards conform to this section of *HIA*? If 'no' please explain.

b. [HIA Section 34(2)] – A consent referred to in subsection 34 (1) must be provided in writing and must include:

   - Authorization for the custodian to disclose the health information specified in the consent,
   - The purpose for which the health information may be disclosed,
   - The identity of the person to whom the health information may be disclosed,
   - Acknowledgment that the individual providing the consent has been made aware of the reasons why the health information is needed and the risks and benefits to the individual of consenting or refusing to consent,
   - Date the consent is effective and date, if any, on which the consent expires. The purpose of an expiry date is to notify the custodian of the health information the duration that they are permitted disclose the requested information. The custodian will not know the date at which "at the end of my participation in this study" occurs without further documentation. This process is facilitated by the determination of an exact date.
   - Statement that the consent may be revoked at any time by the individual providing it
   - Do the documented safeguards conform to this section?

c. Do references to other privacy legislations conflict with the Health Information Act?

5. IB/Product Monograph:

a. Has the investigator provided the IB or Product Monograph for *all* drugs being used?

b. Is the IB or product monograph provided by the Investigator the most current one available (i.e. what is the date on each document?)

6. Advertising:

a. Is advertising being proposed? If yes, has a sample been included?

b. Does the advertising adhere to the following principles?

   - Clearly state that the project is research.
   - Err on the side of underestimating benefits and overestimating risks.
   - Do not make claims of safety, equivalence, or superiority.
   - Avoid phrases such as "new treatment," "new medicine", or "new drug".
   - Avoid using the term *free* in reference to treatment and procedures.
   - Do not emphasize compensation.
   - Obtain approval to post advertisements from all applicable groups.

c. Is the cost of advertising included in the budget?

7. CVs

Note: An investigator must provide to the CTC, an acceptable typewritten documentation outlining their qualifications to do the research and listing both past and present research experience. If the investigator does not have any research experience, please confirm any training with respect to ICH Good Clinical

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

Practice Guidelines and/or the Tri-Council Policy Statement CORE training tutorial. If the investigator has not received any training from the sponsor, training will be required before approval can be granted.

a. Has a CV for each physician been included with the submission?

b. Does each physician have the appropriate qualifications for carrying out the study?

8. Conflict of Interest Forms:

a. Has a completed and signed document for each physician been included?

The College of Physician's and Surgeons of Alberta Conflict of Interest policy, is as follows: "Conflict of interest is defined as a clash between an individual's duty to act in the public's best interest, and that individual's opportunity for personal gain. It must be distinguished from bias. Bias refers to "… a tendency to support or oppose a particular person or thing in an unfair way by allowing personal opinions to influence ones judgement". Every person has biases; awareness of them is crucial to endeavoring to exercise judgement as objectively as possible."