

GUIDELINES FOR APPLICATION SUBMISSION TO THE RESEARCH REVIEW BOARD INC.

SUBMISSION OF PACKAGE

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The following information will assist you in preparing your informed consent document(s).

ICH Section 4.8 has been included for your reference. Please ensure you have included all the required information in your consent form document.

A. 4.8 Informed Consent of Trial Subjects

4.8.1 In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirement(s), and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB/IEC's written approval/favourable opinion of the written informed consent form and any other written information to be provided to subjects.

4.8.2 The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised written informed consent form, and written information should receive the IRB/IEC's approval/favourable opinion in advance of use. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.

4.8.3 Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.

4.8.4 None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.

4.8.5 The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally acceptable representative, of all pertinent aspects of the trial including the written information and the approval/favourable opinion by the IRB/IEC.

4.8.6 The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.

4.8.7 Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative.

4.8.8 Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion.

4.8.9 If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.

4.8.10 Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

- a. That the trial involves research.*
- b. The purpose of the trial.*
- c. The trial treatment(s) and the probability for random assignment to each treatment.*
- d. The trial procedures to be followed, including all invasive procedures.*
- e. The subject's responsibilities.*
- f. Those aspects of the trial that are experimental.*
- g. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.*
- h. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.*
- i. The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.*
- j. The compensation and/or treatment available to the subject in the event of trial-related injury.*
- k. The anticipated prorated payment, if any, to the subject for participating in the trial.*
- l. The anticipated expenses, if any, to the subject for participating in the trial.*
- m. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.*

- n. That the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.*
- o. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.*
- p. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.*
- q. The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.*
- r. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.*
- s. The expected duration of the subject's participation in the trial.*
- t. The approximate number of subjects involved in the trial.*

Research Review Board Inc. Guidelines and some suggested wording for the Informed Consent Form

A. STUDY IDENTIFICATION REQUIREMENTS:

An Informed Consent Document may not contain any data, information, or explanation that may be deemed coercive or encouraging the participant to the subject to participate in the study because they believe there is a certain benefit to them.

1. Study Centre/Principal Investigator's name must be identified and included in the header;
2. Version date must be included in the header or footer of each page;
3. Each page must be numbered (i.e. page 1 of ___).

B. INFORMED CONSENT / PATIENT INFORMATION AND INFORMED CONSENT FORM

The Informed Consent should be written in the second person, using the word "you" instead of the word "I". (Cf the Food and Drug Administration INFORMATION SHEETS for Institutional Review Boards and Clinical Investigators p. 42 Reprint 3/96).

"In informed consent documents, the use of the wording, "I understand..." may be inappropriate as many prospective subjects will not "understand" the scientific and medical significance of all the statements. Consent documents are more understandable if they are written just as the Clinical Investigator would give an oral explanation to the subject, that is, the subject is addressed as "you" and the Clinical Investigator as "I/we." This second person writing style also helps to communicate that there is a choice to be made by the prospective subject. Use of first person may be interpreted as presumption of subject consent, i.e., the subject has no choice.

C. INTRODUCTION SECTION (Insert the following sentences in this section)

"You have been invited to participate in a drug research study."

"For your information, this study is sponsored by (Name of Sponsor) and the study doctor is paid by the sponsor to conduct this study.

D. PROCEDURES SECTION

1. Identify any aspects of the trial that are "experimental".
2. Include a statement indicating the time commitment for the study participant at each study visit.
3. It is required that the information in this section be submitted as an itemized list or in a table format (See Option #1 and Option #2).

Option #1 (itemized/bulleted list of procedures at each study visit)

Example:

Screening

After you have signed the Informed Consent Form, you will be screened for up to __days to see if you are eligible for entry into this study. The screening assessments will take approximately (insert amount of time) and will include the following:

- Review of your medical history and any medications you have been taking.
- Physical examination, including measurement and recording of your vital signs (blood pressure, pulse, and temperature).
- Collection of blood samples (for routine lab tests),

Weeks 1 and 2 These study visits will take approximately (insert amount of time) and the following assessments will be performed:

- Review of any changes in your health or medications you have been taking.
- Physical examination, including measurement and recording of your vital signs.
- Assessment of your medical condition, etc.

Option #2 (table)

Example:

	Study Visit 1 (15 min)	Study Visit 2 (30 min)	Study Visit 3 (30 min)	Study Visit 4 (30 min)	Study Visit 5 (30 min)	Study Visit 6 (30 min)	Study Visit 7 (30 min)	Study Visit 8 (30 min)	Study Visit 9 (30 min)	Study Visit 10 (30 min)	Study Visit 11 (30 min)	Study Visit 12 (30 min)	Study Visit 13 (30 min)	Study Visit 14 (30 min)
1. Procedure 1	✓			✓										
2. Procedure 2	✓			✓										
3. Procedure 3	✓	✓	✓	✓										
Etc	✓	✓	✓	✓										

For information about blood tests to screen for the Human Immunodeficiency Virus (HIV) and Hepatitis B or C HIC include the following statement:

A positive HIV test and/or a positive hepatitis test result will be reported to health authorities, as legally required, and you may be referred to public health for counseling.

For information about screening test for TB (Tuberculosis), include the following statement:

You will be tested for Tuberculosis. If it looks like you may have ‘latent’ (not active) tuberculosis, you will need additional tests, including a chest x-ray to determine if you can still participate in the study. If the chest x-ray confirms the presence of latent or active tuberculosis, public health authorities in your region will be contacted, as legally required.

Pregnancy Risk Statement:

If you are a woman:

It is not known how the study drug (s) may affect an unborn baby. Therefore, you may not take part in this study if you are pregnant or are nursing. You should discuss with your study doctor effective contraception methods to avoid pregnancy.

If you become pregnant during the study, you must tell the study doctor immediately to determine your future treatment with the study drug. The study doctor will ask for your consent to obtain information on the pregnancy outcome for you and the baby.

If you are pregnant, planning to become pregnant, or you are nursing a baby, you cannot be in this study.

If you are a man:

It is not known if women can be exposed to the study drug through sexual activity with a partner taking the study drug, or if the study drug has any effect on sperm. If you are male and you have a partner who could get pregnant, you should tell her that you are in this clinical study and use highly effective methods of birth control during your treatment with the study drug. Highly effective methods of birth control include abstinence, vasectomy, a latex condom or any nonlatex condom NOT made out of natural (animal) membrane (for example, polyurethane condom) in combination with hormonal birth control or barrier methods used by the woman. You and your study doctor must discuss your method(s) and agree that they are effective.

What Are the Risks and Side Effects of the Study?

Reference to frequency of side effects should use the following category list and include this definition of categories in the ICF:

- Very common (affecting more than 10 in every 100 patients);
- Common (affecting less than 10 in every 100 patients);
- Uncommon (affecting less than 1 in every 100 patients);
- Rare (affecting less than 1 in every 1,000 patients).

X-ray Risk

X-ray imaging does not cause pain. You may experience some discomfort from the temperature of the room, the position you must assume, or the equipment that is used. Radiation is used for x-ray imaging, and efforts are normally made to use the lowest possible levels of radiation necessary to achieve adequate imaging. There is a chance of damage to cells or tissue from x-ray radiation, and although there is no certain knowledge about risk of damage, many experts believe that if the radiation level is low and x-rays are infrequent the chance of significant damage is small.

Consider using the following information:

E. COSTS AND COMPENSATION

"There will be no costs to you for participation in this study. You will not be charged for the study drug or any research procedures. If you are physically injured then it will be determined whether this injury is related to the administration of the study drug and whether all parties including you have followed the study requirements. If both are true, then the sponsor of the study, [insert Name of Sponsor] will pay the medical expenses for the treatment of that injury that are not covered by any third party payer such as your insurance or a government program. Financial compensation for such things as lost wages, disability or discomfort due to the injury is not routinely available."

Insert a statement about Compensation/ Payment for being in the study, e.g. "You will be reimbursed \$(amount) for each scheduled study visit that you complete. If you withdraw from the study before completion, or if the study doctor withdraws you from the study, compensation will only be made for the scheduled study visits attended. If you do not receive payment, please contact Dr. (Name) at (area code and phone number).

Will you receive compensation if you have an injury/illness related to your participation in the study?

(Name of Sponsor) will pay you back for reasonable medical expenses for the treatment of any injury or illness resulting from the procedures required by the study protocol related to (Name of study drug) and/or placebo if the procedures were done correctly and the injury or illness occurred only because you are participating in the study.

F. CONFIDENTIALITY

[Name of sponsor] (the sponsor), its designee(s), members of the Research Review Board Inc., and various government health agencies such as the Food and Drug Administration (FDA) and the Health Products and Food Branch (HPFB) may inspect and/or copy the records of this study. If you decide to participate in this study, the results will be reported to (Name of Sponsor), the study sponsor and their affiliates and federal regulators.

With your permission your primary care physician/family physician/other physicians may be informed if you agree to be in this study. If you grant permission the study doctor may contact your other physicians to obtain medical records.

G. YOUR ROLE IN THE STUDY

Your responsibilities as a study subject include the following:

- At every study visit provide accurate and complete information about any side effects you are experiencing or problems you are having and any other prescription medications you are taking, as well as over the counter medications and herbal supplements.
- Provide accurate information about your medical history and current conditions.
- Come to your study visits as scheduled.
- Give yourself the study drug as instructed.
- Return the used and unused study drug containers to the study site at each visit or as instructed by the study staff.
- Tell the study staff of any health problems you are having even if you don't think they are important.
- Tell the study staff if you want to stop taking part in the study and come back for the final visits.
- Do not change any of your medicines without checking with your study doctor.
- Do not give the study drug to any other person. The study drug must be kept out of the reach of children and persons of limited capacity to read or understand.
- Store all study medications as instructed by the study staff.

H. VOLUNTARY PARTICIPATION / INVOLUNTARY WITHDRAWAL

Your participation is voluntary. You may refuse to be in this study or you may quit at any time.

If you decide not to be in the study, it will not affect your entitlement to future treatment. If you withdraw from the study you will not be penalized or lose any benefits you are entitled to.

Your participation in this study may be stopped by the study doctor, the study sponsor, [name of sponsor], the Research Review Board Inc., the United States Food and Drug Administration (FDA), the Health Products and Food Branch (HPFB) of Health Canada and possibly other government agencies at any time. Your study doctor will explain the reason for ending your participation and assist you with arrangements for your continued care if necessary.

If you decide to withdraw from the study, we encourage you to talk to the study doctor and your primary care physician first. There may be health consequences to suddenly leaving the study.

The study doctor can help you make that decision. If you stop taking the study drug, leave the study, or are removed from the study before it ends, blood tests and physical evaluations may still be required.

You *must* permanently stop the study drug if:

- a) You become pregnant. The study drug must be *immediately* discontinued.
- b) You have a medical emergency that makes it necessary to stop the study drug.

You may have the study drug permanently stopped for the following reasons:

- a) At the discretion of the study doctor or study sponsor for medical reasons or for not following the rules of the protocol.
- b) If the study is discontinued.

You will be withdrawn from the study for the following reason:

- a) You are unwilling or unable to follow the rules of the protocol.

I ADDITIONAL INFORMATION

A description of this clinical trial will be available on [http:// www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. It may be many years; however, before research results are posted.

Or

A description of this study will be available on <http://www.ClinicalTrials.gov>, as required by United States law. This website will not include information that can identify you. At most, the website will include a summary of the study results. You can search this website at any time.

J. QUESTIONS

If you have questions concerning your rights as a research subject, you may contact:

The Research Review Board Inc. at 905-508-2747 or info@researchreviewboard.com

The Research Review Board (RRB) Inc. is a group of people who review research studies to protect the rights and welfare of research subjects and is not affiliated with the trial doctor or the sponsor. The RRB Inc. has reviewed this study.

