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Effective date: September 2009	RESEARCH PROTOCOLS THAT MAY POSE A RISK TO A FOETUS AND/OR SUBSEQUENT CHILD AND PROTOCOLS WHERE THERE IS A REQUIREMENT FOR CONSENT TO COLLECT INFORMATION ON PREGNANCY AND ITS OUTCOME FROM FEMALE PARTNERS OF MALE RESEARCH PARTICIPANTS		

1. In cases where there is

- **a) a request to exclude pregnant women or women of childbearing potential or**
- **b) impose mandatory birth control, the REB gives consideration to the following questions and issues:**

- a) Is there enough of a prospect of genuine benefit to the subject that justice issues are raised in arbitrary exclusions?
- b) What is the risk posed to a foetus or subsequent child?
- c) Is the information to be gained of such importance for the greater common good that justice issues are raised in arbitrary exclusions?
- d) What is the evidence with respect to reproductive risk?

The researchers must address the issues as follows:

- a) If there are justice concerns raised in arbitrary exclusions the investigator must defend the exclusion of pregnant women or women of childbearing potential.
- b) If the exclusion seems to be warranted the investigator must defend the position that it is important enough to usurp the woman's ordinary position as the arbiter of foetal risk. (i.e. the REB's position is that one that prefers an exclusion by warning the subject of the risk, rather than by issuing a dictum.)
- c) If it is warranted to exclude rather than just warn, the REB expects that the exclusion would be effected in a respectful manner. If the decision to exclude pregnant women or women of childbearing potential is appropriate and urgent enough that the woman shouldn't be the decision maker (generally a case of serious potential for foetal harm with only modest benefit for the woman):
- d) The Letter of Information should explain the issue rather than just demand compliance
- e) The contraceptive requirement should only be extended to women who may become pregnant during the course of the study
- f) There should be an explanation for specific contraceptive choices
- g) Contraceptive use must be considered a research risk and factored into the risk/benefit calculation

Case Scenario:

A sponsor insisted on oral contraceptives even for sexually abstinent women or lesbians. Asked if they would still make that requirement if a nun were the subject, they said "Yes". The REB felt there was also the issue that oral contraceptives might be a religious concern for nuns. But more seriously it was easy to calculate that the contraceptive use would create a risk of death (from thrombosis) that was far greater than would have been the risk of pregnancy without oral contraceptives.

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2. Monitoring and Follow up of pregnancies occurring during a clinical trial

In many instances if a woman becomes pregnant or a man fathers a child while in a study the pregnancy should be monitored to ascertain the health of the mother and child. In some cases it may be necessary/prudent to monitor the child once it has been born. In all cases, the request to monitor the pregnancy and/or the child should be made in a respectful manner.

When applicable, the Information / Consent documentation should:

- include a statement that the treatment or procedure may involve risks, which are currently unforeseeable, to the participant or to the foetus or child, if the participant is or may become pregnant or is breastfeeding.
- it may also be necessary to warn male participants or partners about the danger of fathering a child while involved with the study

3.0 Examples of wording for the Information / Consent Documentation

(These should be adapted to meet the needs of the particular study)

- We know that the treatment involved in this study poses significant risks to a foetus and/or a child that is being breast fed by a woman taking the drug. Therefore it is extremely important that you not become pregnant nor breastfeed while taking part in this trial. To ensure that you are not pregnant at the start of the study you will be asked to have a pregnancy test before undergoing any treatment. If it is possible that you may become pregnant during the course of the study you will also be asked to use an approved method of birth control for the course of the study and have periodic pregnancy tests.
- If you are or become pregnant during the course of this study, the treatment or procedure may involve risks, which are currently unforeseeable, to you or to the foetus.
- Because we do not yet know very much about the safety of this drug in pregnancy, we want to know what happens if any of the participants become pregnant (father a child) while taking the drug. If you get pregnant (father a child) during this study you must inform your study doctor right away. We would then appreciate it if you'd allow us to record information about the outcome of the pregnancy (the child's health etc.) This will also involve asking you to permit us to contact you annually for the next five years to ask about the health of your child.

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4. The HSREB requires written consent documentation be provided to female partners of male study participants if it is evident in the REB submission and participant informed consent documentation that there may be a risk to the woman and/or her foetus; and, there may be a need to collect information on the pregnancy and its outcome. This documentation must be presented to the HSREB at the same time as the initial study submission and the process discussed in the REB submission.

BACKGROUND

If a sponsor or investigator has concerns that the drug or treatment under study may cause harm to a woman and/or her foetus if the child is fathered by a patient on a clinical trial, the sponsor and investigator are obligated to make reasonable efforts to ensure the woman is informed of this possibility. The ethical considerations and responsibilities of the sponsor and the investigator would, in these instances, extend beyond the actual study participant (patient).

It is the view of the HSREB that it is an ethical imperative to ensure that reasonable efforts are made to ensure that all parties who may be (inadvertently) affected by the study are notified of any potential risks or requests in a proactive manner. Once the woman becomes pregnant she in fact becomes a research participant in the trial in that the sponsor is required to request information from her even though the data are not kept as part of the regular study dataset. These “secondary” participants must be afforded the same respect and concern for their well being and confidentiality as the actual clinical trial participants.

PROCESS

The HSREB recommends a two stage informed consent process.

Stage 1

Once a person agrees to participate in a clinical trial the study participant should tell his female partner(s) (of child bearing potential) of potential risks to her and any child she may bear with her partner, while her partner is taking part in the clinical trial. She should be told that if she becomes pregnant she should inform study doctor and that she may be asked to provide information about that pregnancy and its outcome to the sponsors of that study to add to the body of information on the safety of the drug or treatment.

The HSREB is well aware that some relationships are fluid, unstable and not monogamous. We recognize that the patient may not be entirely truthful with the site staff or may opt not to pass along the information to his partner(s). The HSREB also accepts that neither the site nor the sponsor can force a patient to be truthful or compliant. It is the stand of the HSREB that “reasonable” efforts be made to inform anyone that may be potentially harmed or approached as a result of the patient’s participation in the study. The primary method being to tell the study participant that they should inform any partners of childbearing potential of the potential risk by giving them a copy of a Female Partner Preliminary Letter of Information.

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Depending upon the situation it might also be prudent to occasionally remind the man over the course of the study that if he has a new partner(s) he should pass along the Female Partner Preliminary Information Letter.

In most studies it will be acceptable for the Female Partner Preliminary Letter of Information to be given to the female partner(s) by the study participant without requiring that the female partner attend the study site for a discussion of its contents or return a signed acknowledgement.

A signed acknowledgement of the Female Partner Preliminary Letter of Information by the female partner is not required unless the HSREB feels the risks and consequences of a pregnancy are sufficiently severe to warrant obtaining formal consent from the female partner at the start of the study or when she becomes a partner. This would be determined by the HSREB on a study by study basis. However, in all cases it should be documented by the study site that the research participant was informed that, for the duration of his participation in the study, he should give his female partner(s) (current and/or future) a copy of the Female Partner Preliminary Letter of Information as soon as possible.

Stage 2

The second stage occurs if the female partner becomes pregnant and the study site is notified. A formal consenting process should be undertaken to ensure the woman is fully informed as to what is being asked of her and is made aware of her rights. The female partner should be invited to attend the study site and be given a Female Partner Pregnancy Letter of Information (note that this letter differs from the Preliminary Letter in that it is specific to the fact that the woman is now pregnant). The woman will be asked to voluntarily provide information about her pregnancy and its outcome or authorize her health care provider to do so. If travel to the site is not possible or desirable then it would be acceptable to send the Pregnancy Letter of Information to the woman and ask her to sign it and return it by mail. The site coordinator or study investigator could make themselves available by telephone to discuss the Letter and answer any questions the woman may have.

Sample Letters and Consent forms

The sample documentation for informing the woman and obtaining her consent has been created to assist researchers in ensuring the woman is fully informed. The wording of the samples provided by the HSREB should be modified to fit the situation. The HSREB will also consider alternative documentation provided by the sponsor that accurately reflects the risks, requirements and time periods etc of the trial in question.

Other issues

It is not expected that the process as described above will interfere with the process and conduct of the trial nor compromise the data from the local site. Neither will it impinge upon the confidentiality of the female partner, as the study site will not have access to the female partner's name until such time as she opts to disclose that she is pregnant.

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SAMPLES

Female Partner

Letters of Information & Consent forms **Version Feb. 2009**

1a Preliminary Letter of Information

1b Preliminary Acknowledgement

2a Pregnancy Letter of Information

2b Pregnancy Consent Form

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FEMALE PARTNER - PRELIMINARY LETTER OF INFORMATION

Study title

LOCAL STUDY DOCTOR: *Name and affiliation*

INTRODUCTION

Your partner is participating in a research study involving the use of drugs or treatments which may harm a foetus (unborn child). He has been advised not to father a child during the time he is taking the drugs or treatments **and for a period of XXXX after**. This letter is to inform you that there may be risks to the foetus should you become pregnant with your partner. You and your partner should use an effective birth control method such as barrier method (condoms, diaphragm); oral, injectable, or implant birth control; or abstinence to avoid becoming pregnant. If you do become pregnant it is important to inform your partner's study doctor as soon as possible.

If you become pregnant while your partner is taking part in this study; we will ask you to voluntarily provide us with information concerning your pregnancy and its outcome. You will receive another letter explaining the request and a consent form to sign. Only information, relating to your pregnancy and the outcome of the pregnancy, will be collected and/or analyzed. You may provide this information yourself or give permission to your health care provider to release it directly to your partner's study doctor. The purpose of collecting this information is to determine how the drug or treatment may have affected the foetus.

VOLUNTARY PARTICIPATION

Your agreement to provide information on your pregnancy and its outcome is voluntary. You do not have to make a decision about whether or not you want to provide this information at this time. You may refuse to provide this information, refuse to answer any questions or withdraw your consent for data collection at any time with no effect on the care of your partner who is participating in the clinical trial. Should you decide to withdraw your consent for data collection regarding your pregnancy and its outcome, we would no longer request information from you or your health care provider, however information collected prior to your withdrawal of consent may continue to be used in future analyses of the safety of the drug or treatment.

CONFIDENTIALITY & PRIVACY ISSUES

The study in which your partner is enrolled is sponsored by *Sponsor [insert name]*. The information about your pregnancy and its outcome would be forwarded to the sponsor or companies working on behalf of the sponsor, where it would be analyzed and stored in their safety database. The sponsor may also be required to forward the information to health authorities worldwide, and the information may also be used in reports for scientific presentations or publications. The results may also be used for future safety assessments.

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All information collected with regard to your pregnancy and the outcome of your pregnancy would be kept confidential to the limit allowed by law. The information would not be given to your partner. The data would be coded to hide your identity and the identity of your baby. Specifically, your name and other identifying information would not be sent to the sponsor of the study. If the results of the trial are published, your identity and that of your baby would remain confidential.

Representatives of **Sponsor**, regulatory agencies such Health Canada **and the Food and Drug Administration (FDA – USA)**, and The University of Western Ontario Health Sciences Research Ethics Board may need to examine your original medical records to verify the information and monitor the conduct of the study. In these cases, they would see your name and the name of your baby, but no identifying information would be attached to any information collected from your records.

RISKS

There are no known risks to providing this information other than those mentioned above.

BENEFITS

It is unlikely that you would benefit directly by providing us with this information however it might provide important safety information to the company that makes this drug.

CONTACT INFORMATION

If you have any questions about the conduct of the study or your rights in this matter you may contact Dr. David Hill, Scientific Director, Lawson Health Research Institute at 519-667-6649.

If you have any questions about the study and data collection you may contact the study doctor **XXXXX at XXXXX**

Please keep this letter for your records.

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FEMALE PARTNER - PREGNANCY LETTER OF INFORMATION

Study title

LOCAL STUDY DOCTOR: *Name and affiliation*

INTRODUCTION

You are receiving this letter because you have become pregnant while your partner is taking part in this study.

Your partner is participating in a research study involving the use of drugs or treatments which may harm a foetus (unborn child). He had been advised not to father a child during the time he is taking the drugs or treatments **and for a period of XXXX after**. This letter is to inform you that there may be risks to a foetus fathered by your partner.

We are asking you to voluntarily provide us with information concerning your pregnancy and its outcome. Only information, relating to your pregnancy and the outcome of the pregnancy, will be collected and/or analyzed. You may provide this information yourself or give permission to your health care provider to release it directly to your partner's study doctor. The purpose of collecting this information is to determine how the drug or treatment may affect the foetus.

VOLUNTARY PARTICIPATION

Your agreement to provide information on your pregnancy and its outcome is voluntary. You may refuse to provide this information, refuse to answer any questions or withdraw your consent for data collection at any time with no effect on the care of your partner who is participating in this drug study. Should you decide to withdraw your consent for data collection on your pregnancy and its outcome, we will no longer request information from you or your health care provider, however information collected prior to your withdrawal of consent may continue to be used in future analyses of the safety of the drug or treatment.

CONFIDENTIALITY & PRIVACY ISSUES

The study in which your partner is enrolled is sponsored by *Sponsor [insert name]*. The information about your pregnancy and its outcome will be forwarded to the sponsor or companies working on behalf of the sponsor, where it will be analyzed and stored on their safety database. The sponsor may then be required to forward the information to health authorities worldwide, and the information may also be used in reports for scientific presentations or publications. The results may also be used for future safety assessments.

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All information collected with regard to your pregnancy and the outcome of your pregnancy will be kept confidential to the limit allowed by law. The information will not be given to your partner. The data will be coded to hide your identity and the identity of your baby. In particular, your name and other identifying information will not be sent to the sponsor of the study. If the results of the trial are published, your identity and that of your baby will remain confidential.

We will do our best to protect your confidentiality however, representatives of **Sponsor**, regulatory agencies such Health Canada and the Food and Drug Administration (FDA – USA), and The University of Western Ontario Health Sciences Research Ethics Board may need to examine your original medical records to verify the information and monitor the conduct of the study. In these cases, they will see your name and the name of your baby, but no identifying information would be attached to any information collected from your records.

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There are no known risks to providing this information other than those mentioned above.

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It is unlikely that you will benefit directly by providing us with this information however it may provide important safety information to the company that makes this drug.

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