

<b>HSREB Guidance Document</b>	Female Partner Preliminary & Pregnancy Information
<b>Effective Review</b>	Delegated & Full Board
<b>Version Date</b>	November 16, 2022

## Contents

When does this guidance apply?.....	1
Monitoring and Follow up of pregnancies occurring during a clinical trial .....	2
Examples of wording for Letters of Information & Consent Documents .....	2
Female Partners of Male Participants .....	3
Sample Letters and Consent Forms .....	4
Other Issues .....	5

**Note from the REB:** Participation in studies involving drugs or devices which may affect a foetus or newborn baby ask that any pregnancy during the study, or a specified time after participation in a study, is followed. This is always voluntary. The details and wording outlined below refer to the biological parents, i.e. the individuals whose reproductive systems produced the foetus/baby.

### This Guidance is intended for:

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 pregnant partners of biologically male research participants.

### When does this guidance apply?

In cases where there is

- a) a request to exclude pregnant individuals or people of childbearing potential
- OR**
- b) impose mandatory birth control

### The REB gives consideration to the following questions and issues:

- i. Is there enough potential of a genuine benefit to the participant or partner that justice issues are raised in arbitrary exclusions?
- ii. What is the risk posed to a foetus or subsequent child?
- iii. Is the information to be gained of such importance for the greater common good that justice issues are raised in arbitrary exclusions?
- iv. What is the evidence with respect to reproductive risk?

### The researchers must address the issues as follows:

- i. If there are justice concerns raised in arbitrary exclusions the investigator must defend the exclusion of a pregnant person or people of childbearing potential.
- ii. If the exclusion seems to be warranted the investigator must defend the position that it is important enough to usurp the pregnant partner’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 participant or partner of the risk, rather than by issuing a dictum.)
- iii. 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 a pregnant person or person of childbearing potential is appropriate and urgent enough that the person shouldn't be the decision maker (generally a case of serious potential for foetal harm with only modest benefit for the individual):
  - iv. The Letter of Information should explain the issue rather than just demand compliance
  - v. The contraceptive requirement should only be extended to people who may become pregnant during the course of the study
  - vi. There should be an explanation for specific contraceptive choices
  - vii. 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 individuals. Asked if they would still make that requirement if a nun were the participant, 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.

### **Monitoring and Follow up of pregnancies occurring during a clinical trial**

In many instances if a person becomes pregnant or a participant impregnates their sexual partner 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:**

- a) 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.
- b) It may also be necessary to warn participants or partners about the danger of fathering a child while involved with the study

### **Examples of wording for Letters of Information & Consent Documents**

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

- a) 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 participant who is taking the drug. Therefore, it is extremely important that you do 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.
- b) 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.

- c) 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.

## Partners of (Biologically) Male Participants

The HSREB requires written consent documentation be provided to partners (who can become pregnant) of study participants if it is evident in the REB submission and participant informed consent documentation that there may be a risk to the partner and/or potential 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 person who can become pregnant and/or foetus if the child is fathered by a participant in a clinical trial, the sponsor and investigator are obligated to make reasonable efforts to ensure the person who can become pregnant 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 person who can become pregnant becomes pregnant, that person in fact becomes a research participant in the trial in that the sponsor is required to request information from that person 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 their partner(s) (of child bearing potential) of potential risks and risks to any child that may be created with their partner, while they are a participant in the clinical trial. The participant's partner should be told that if they become pregnant the study doctor should be informed and that the pregnant partner 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 participant may not be entirely truthful with the site staff or may opt not to pass along the information to their partner(s). The HSREB also accepts that neither the site nor the sponsor can force a participant 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 participant'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 Partner Preliminary Letter of Information.

Depending upon the situation it might also be prudent to occasionally remind the participant over the course of the study that if there is a new partner(s) the Partner Preliminary Information Letter should be given to them.

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

A signed acknowledgement of the Partner Preliminary Letter of Information by the 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 partner at the start of the study or when they become 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 the participation in the study, he should give his partner(s) (current and/or future) a copy of the Partner Preliminary Letter of Information as soon as possible

## Stage 2

The second stage occurs if the partner becomes pregnant and the study site is notified. A formal consenting process should be undertaken to ensure the pregnant partner is fully informed as to what is being asked and is made aware of any rights. The partner should be invited to attend the study site and be given a Partner Pregnancy Letter of Information (note that this letter differs from the Preliminary Letter in that it is specific to the fact that the partner is now pregnant). The pregnant partner will be asked to voluntarily provide information about the current pregnancy and its outcome or authorize a 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 pregnant partner, ask for a signature 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 pregnant partner may have.

As a reminder Western's HSREB will only allow for collection of data related to the current pregnancy as it pertains to the participant's inclusion in the study. Do not state, that past medical records including abortions, miscarriages, etc. will be collected from the pregnant partner

## **Sample Letters and Consent Forms**

The sample documentation for informing the pregnant partner and obtaining their consent has been created to assist researchers in ensuring that participants who can become pregnant are 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 a partner who can become pregnant, as the study site will not have access to the partner's name until such time as they opt to disclose that they are pregnant.