

HSREB Guidance Document	Female Partner Preliminary & Pregnancy Information
Effective Review	Delegated & Full Board
Version Date	September 2009

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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 female partners of male research participants

When does this guidance apply?

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:

- i. Is there enough potential of a genuine benefit to the subject 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 pregnant women or women 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 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.)
- 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 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):
- iv. The Letter of Information should explain the issue rather than just demand compliance
- v. The contraceptive requirement should only be extended to women 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 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.

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:

- 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 male 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 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.
- 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.

Female Partners of Male Participants

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.

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 their consent has been created to assist researchers in ensuring that female participants 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 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.