



Title:	Pregnancy Testing Requirements		
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1 PURPOSE

The UNC IRB has developed this SOP to describe a series of consistent, deliberate steps to mitigate fetal exposure to risk in clinical research studies among women of child-bearing potential (CBP). These procedures are intended for: 1) research studies in which fetal harm from a study intervention is known or can be plausibly inferred, or is unknown; 2) research studies in which the prospect of direct benefit to the woman, the fetus, or both cannot be justified because of fetal risk, and 3) research studies in which the exclusion of pregnant women is scientifically justified. This SOP describes pregnancy-testing requirements for enrollment and continued study participation of women of CBP, as defined below. This SOP does not address requirements for male participants, noting that exposure to interventions in that population may also contribute to adverse outcomes in offspring.

2 PROCEDURE

2.1 Defining “Child-bearing Potential” in Adults

2.1.1 Women are considered *of* CBP if they (a) are anatomically and physiologically capable of becoming pregnant. Menarche (first menstrual cycle) is the most feasible clinical indicator of the biological potential for pregnancy, thus menstruating females, regardless of age, are considered CBP. Women who have had a hysterectomy or a bilateral oophorectomy are not considered of “CBP”.

2.1.2 A woman is considered past CBP if:

- She is 60 years old or greater, or
- She is age 50 to 59 years and has not menstruated for 12 months or has a follicle stimulating hormone level > 40 mIU/L

2.2 Procedures For Inclusion of Women of CBP in Research

The IRB application and informed consent form should include procedures for inclusion of women of CBP in research. Minimum procedures are outlined below.

- 2.2.1 For protocols that involve study interventions with known or suspected fetal teratogenicity (i.e., thalidomide, vitamin A, ACEi or ARB class of drugs, testosterone and other endocrine disruptors, pheytin, valproic acid, warfarin, diazepam, chemotherapeutic agents or other anti-cancer agents, radiation, and others), enrolled women of CBP must have a negative pregnancy test (urine or serum) confirmed prior to each study drug administration. Participants should be advised and agree to contraceptive use. Appropriate female contraception is described in section 2.3.1. Participants should also be advised that a negative pregnancy test does not preclude the presence of a very early gestation.
- 2.2.2 For protocols involving study interventions with unknown fetal effects, eligible women of CBP must
1. Have a negative pregnancy test (urine or serum) prior to enrollment
 2. Be advised and agree to contraceptive use, which is reaffirmed prior to each study intervention. Appropriate female contraception is described in section 2.3.1
 3. Be assessed for likelihood of pregnancy prior to each study drug administration, or monthly at a minimum (i.e., asking and documenting answer to 'Is there a possibility that you could be pregnant?') and also
 4. Have a negative pregnancy test (urine or serum) prior to study intervention if investigator deems there is possibility of pregnancy (i.e. participant reports 'yes' to question #3, or reports not using contraception despite sexual activity, or reports missed menstrual period).
- 2.2.3 For protocols for which there is no anticipated risk for fetal harm but exclude pregnant women solely for scientific reasons (i.e. pregnancy biology may alter or skew results), eligible women of CBP should have pregnancy testing at the discretion of the investigator. Contraception recommendations are also at the discretion of the investigator. Pregnancy testing and contraception recommendations should reflect the protocol's design regarding discontinuing or withdrawing women if discovered to be pregnant while participating in the study.

2.3 Acceptable methods of birth control for studies that include known teratogens or other interventions that pose a high fetal risk

- 2.3.1 For protocols that entail the use of known or suspected teratogens or other interventions that pose a high risk to the fetus, women and male participants with female partners, must use reliable and highly effective methods of birth control during the study. Reliable and highly effective methods of female birth control include: two forms of barrier contraception (e.g. condoms and foam; e.g. condoms and diaphragm); long-acting reversible contraception (e.g. subdermal contraceptive implant, intrauterine device, contraceptive injections), and oral contraceptive pills.
- 2.3.2 Contraceptive measures such as Plan B™, sold for emergency use after unprotected sex, are not acceptable methods for routine use.

- 2.3.3 Contraceptive requirements may be waived for women who engage in same-sex intercourse or report monogamous heterosexual intercourse with a partner who has had a vasectomy.

2.4 Pregnancy and Minors

- 2.4.1 North Carolina State law requires healthcare professionals to report abuse and neglect of minors to state and local authorities. A positive pregnancy test in a minor does not, however, indicate abuse or criminal sex act. Hence, researchers do not need to file a report for each positive pregnancy test. The statute leaves it up to the healthcare professional to exercise his/her judgment to assess whether a criminal act has been committed.
- 2.4.2 Disclosure of a pregnancy to the child's parent should occur when:
- The adolescent agrees to the disclosure or;
 - The adolescent is under 12 years of age or younger or;
 - The adolescent appears to not understand what is happening or becomes emotionally dysregulated after hearing that they are pregnant (i.e., they do not seem in control of their emotional state or are stating that they are a danger to themselves or others) or;
 - The adolescent discloses that they may be in physical danger from their partner or someone else due to the pregnancy.

Disclosure of the minor's pregnancy to the child's parent in any of the above circumstances should not occur if the adolescent has disclosed unreported or unresolved maltreatment from the parent.

In the rare situation in which the adolescent is not safe to leave the research study for any reason (unreported or unresolved maltreatment in the home where they are currently afraid that they will be seriously injured, suicidal crises with plan, access, and intent, or the situation described here where revealing the pregnancy has precipitated a crisis) the researcher should contact the proper authorities to insure the adolescent's safety (e.g., Orange County mobile crisis unit 1-877-967-8844).

Per North Carolina State law, if a study participant is less than 18 years of age, and the PI or researcher has cause to suspect that the minor participant is dependent, abused or neglected by a parent, guardian, custodian, or caretaker, then the PI or researcher must report the case of the participant to the Director of the Department of Social Services in the county where the child resides or is found.

- 2.4.3 When pregnancy testing is required, females 10 years and older should be asked if they have started menstruating both in the presence of their parents and privately. Females age 12 or older, or who started menstruating regardless of age, require pregnancy testing if study interventions pose potential for fetal risk.

2.5 Pregnancy testing conducted outside of the UNC Health Care System

- 2.5.1 Researchers administering urine pregnancy tests at locations outside of the UNC Health Care System (e.g., BRIC, off-campus research facilities) must ensure that the tests are U.S. Food and Drug Administration (FDA) approved and used prior to the date of expiration. Pregnancy tests should only be read by an appropriately trained member of the research team.

2.6 Pregnancy testing and MRI research

- 2.6.1 The IRB does not require urine pregnancy testing (unless required by the study protocol) for females of CBP who participate in research using FDA-approved Magnetic Resonance Imaging (MRI) machines without contrast unless when asked, they respond that they are or suspect that they are pregnant. Females who verbally state that they are not pregnant do not require pregnancy testing.
- 2.6.2 Urine pregnancy testing is required within 36 hours prior to all studies using Non FDA-approved MRI machines with or without contrast.

2.7 Pregnancy testing and research using non-FDA-approved coils

- 2.7.1 A coil is a large inductor with a considerable dimension and a defined wave length, commonly used in configurations for MR imaging. The MRI image quality depends on the signal to noise ratio (SNR) of the acquired signal from the patient. MR imaging coils are necessary to handle the diversity of applications.
- 2.7.2 Receive-only coils do not introduce any additional energy into the participant and do not change the functioning of the MRI machine. Because no additional energy is introduced, pregnancy testing is not required.
- 2.7.3 Transmit-Receive coils may introduce additional energy. Because additional energy is introduced, pregnancy testing is required.

2.8 Recommended consent form language:

2.8.1 Parental permission

Pregnancy testing is required for participation in this study; all girls age 12 and older or those older than 10 years who are menstruating, will be tested for pregnancy. Only those testing negative will be allowed to participate. If your child is 12 years and younger, we will share pregnancy test results with you. If your child is 13-17 years of age, we will share pregnancy test results with you if your child 1) agrees that we can share this information with you, 2) is pregnant and does not appear to understand the situation, becomes highly emotional or expresses the potential of harming herself or 3) your child discloses that they may be in potential harm from a partner or someone else due to the pregnancy.

2.8.2 Assent (7-14) and (15-17)

If you are 12 years or older or are 10 years old and have started having your period, pregnancy testing is required for participation in this study. You can only be in the study if you are not pregnant. If you are 12 years or younger, we will tell your parents about your test results. If you are 13 or older, we will tell your parents about your test results if: 1) you agree that we can share this information with them or, 2) you are pregnant and do not appear

to understand the situation, or if you become very emotional or expresses the potential of harming yourself or you feel that are in potential harm from a partner or someone else due to the pregnancy.

2.8.3 Adults (18 years and older)

If you are capable of becoming pregnant, pregnancy testing is required for participation in this study. Only those testing negative will be allow to participate. If you've had a hysterectomy (surgical removal of your uterus) or a bilateral oophorectomy (surgical removal of both ovaries), or tubal sterilization (tubes tied or cut), pregnancy testing is not required