Guidance:
In any research study involving a procedure or test agent unapproved for use in the study population, the consequences of female subjects becoming pregnant during the study should be considered. This should include the need for information in the consent form on pregnancy and risk to the fetus, pregnancy testing requirements, and abstinence from unprotected sexual activity. Sexual activity and the possibility of pregnancy can be a complicated matter in pediatric and adolescent populations. For these reasons, the IRB has prepared this evidence-based guidance for the community.

Given the sensitivities of the pediatric and adolescent populations in regards to sexual activity and pregnancy, pregnancy testing should not, therefore, routinely be included in a protocol. If pregnancy is a contraindication for inclusion, pregnancy testing should be justified in the protocol and the frequency of pregnancy testing specified.

Children may be at various stages of puberty when enrolling into a research study. Since the beginning of menses is unpredictable, female subjects may begin menstruation at any time during a study. Menses now begins at younger ages, and most adolescents who have begun menses are not sexually active. Although very unlikely, a subject could become pregnant prior to onset of menses. Parents may not be aware of their child’s sexual activity. Based on national and local research on teenage pregnancies, if pregnancy testing is appropriate, it should generally be required for any female 11 years or age or older or who has begun menses. There is template language that should be included in informed consent documents.

Because protocols may not exclude females based on their potential to become pregnant, numerous issues involved with drug use/exposure/procedure in pregnancy arise when performing studies in this age group. These include the high rate of unplanned pregnancies in adolescents, contraceptive failure due to inconsistent use of contraception, inadvertent exposure during pregnancy (treatment initiated prior to pregnancy and discontinued when pregnancy is recognized, resulting in exposure during critical periods of development), and therapeutically essential treatment during pregnancy. These issues need to be carefully considered in studies in which adolescent girls are enrolled.

For male subjects, including language about the complications that could arise were they to father a child while enrolled in the study and for a period thereafter is important for studies that include males over the age of 11. Again, there is template language that can be used in these instances.
Instructions:

When writing a research protocol, investigators should make sure the following issues are addressed:

1. Any protocol involving a procedure/experimental agent should discuss the potential of the procedure/experimental agent to adversely affect a pregnancy or fetus; adverse effects should not be assumed in the absence of data. Information on the effects of the drug or procedure during pregnancy is typically derived from laboratory animal studies, and not from human studies. The standard is to use laboratory animal studies to assess any potential risk to human pregnancy, even though results in laboratory animals are not always predictive of human responses.

2. The age criteria of 11 or the onset of menses should generally be a requirement for pregnancy testing in protocols having the potential for adversely affecting a pregnancy. If laboratory animal or human studies of the agent do not show a potential for producing adverse effects on pregnancy, no pregnancy testing is necessary unless pregnancy is otherwise an exclusion criteria for participation in the study.

3. In protocols having the potential for adversely affecting a pregnancy or fetus, the plan for pregnancy testing must be fully disclosed in the informed consent document. This should include:
   - who will be tested (generally, any female 11 years of age or older or who has begun menses)
   - the type of pregnancy test (blood or urine)
   - the frequency of testing (prior to, during the study)
   - what will happen if results are positive
   - who will be informed of the results
   - how confidentiality will be maintained

4. In protocols having the potential for adversely affecting a pregnancy or fetus, subjects should be informed about the need to avoid pregnancy during the course of the research, and this should be explained in the informed consent. Suggested language is as follows:

   “The effects of drug X/procedure Y on pregnancy or a fetus are [choose either] “unknown” or “known to be potentially harmful from laboratory animal or from human studies”. For this reason, subjects taking drug X/undergoing procedure Y should not become pregnant or father children during the study and for a period of X weeks after taking the drug/undergoing the procedure. For entry into this study, we require that all participants agree to either abstain from sexual intercourse for the duration of the study and for X weeks thereafter, or agree to use reliable, effective contraception for this period. If you become pregnant or father a child during this period, you must contact the investigators immediately so that they may provide medical assistance and counseling.”
5. Subjects who have questions about how to avoid pregnancy should be offered information on contraception at the time of enrollment. Information specifically designed for teenagers can be found at the website [http://www.medem.com “Tool Kit for Teen Care: Contraception”].

6. The following language was developed to provide templates for informed consents documents:

**For females:**
If you are pregnant or nursing, you should not take part in this research study. The effects of _DRUGS/DEVICES/INTERVENTIONS_ on an unborn baby are [“unknown” or “known to be potentially harmful from laboratory animal or human studies”] (Choose one or both phrases, whichever is appropriate). Because of this, if you are eleven years old or have already started having periods, you will be given a pregnancy test before starting this study [and at _____ times during the study] (add if pregnancy test will be repeated). The results will be shared with you (the child) and not with your parent(s). We encourage you to tell your parents the results. If you are found to be pregnant, you will not be able to continue participation in the study. You need to take safety measures to prevent pregnancy (such as not having sexual intercourse, or using a medically accepted form of contraception while you are receiving _DRUG/DEVICE/INTERVENTION_. If you have questions about how to avoid pregnancy, talk to your doctor or the researcher and they will provide you with information on contraceptive choices. You should tell _INVESTIGATOR_____ at once if you become pregnant during this research study.

**For males:**
You should not father a baby while on this study. You need to take safety measures to prevent pregnancy (such as not having sexual intercourse or using contraception) while you are receiving _DRUG/DEVICE/INTERVENTION_. If you have questions about how to prevent pregnancy, talk to your doctor or the researcher and they will provide you with information on contraceptive choices. Include a statement about possible sterility when appropriate.

This guidance was prepared by: The IRB in conjunction with Donald Schwarz, M.D., Chief, Division of Adolescent Medicine, and Jeanne Manson, Ph.D., M.S.C.E., Division of Human Genetics and Molecular Biology.