INTRODUCTION
The UNMC IRB considers it important to balance two often conflicting duties: (1) to assure that patients may participate in potentially beneficial research without unnecessary restrictions and burdens, and (2) to minimize the risk of adverse effects on potentially pregnant subjects and/or fetuses. Toward this end, the UNMC IRB has developed the following policy regarding contraception.

GENERAL REQUIREMENTS

1. Eligibility criteria concerning contraception requirements should be based on the FDA Use-In-Pregnancy Categories\(^1\). If the FDA category is not available, the most appropriate template should be chosen by comparing the definitions of the categories with the reproductive toxicity data available for the protocol-specified medication of greatest concern. Phase III studies must provide animal data to support choice of template.

2. Female study volunteers who are not of reproductive potential (have reached menopause or undergone hysterectomy, oophorectomy, or tubal ligation) or whose male partner has undergone successful vasectomy with resulting azoospermia or has azoospermia for any other reason, are eligible without requiring the use of contraception. Male study volunteers, who have undergone successful vasectomy with resulting azoospermia or have azoospermia for any other reason, are eligible without requiring the use of contraception.

3. It is the responsibility of the investigator to discuss the risks and benefits of each form of contraception with potential study participants to ensure that subjects are making an informed choice. If applicable, the investigator must discuss with a patient why she is not of child-bearing potential and document that information appropriately.

FDA USE-IN-PREGNANCY CATEGORIES\(^1\)

1. **Category A: Controlled studies show no risk.** Adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester of pregnancy.

2. **Category B: No evidence of risk in humans.** Adequate, well-controlled studies in pregnant women have not shown increased risk of fetal abnormalities despite adverse findings in animals, or, in the absence of adequate human studies, animal studies show no fetal risk. The chance of fetal harm is remote, but remains a possibility.

\(^1\) 21 CFR 201.57(f)(6)(i)(a-e)
3. **Category C: Risk cannot be ruled out.** Adequate, well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking as well. There is a chance of fetal harm if the drug is administered during pregnancy; but the potential benefits may outweigh the potential risk.

4. **Category D: Positive evidence of risk.** Studies in humans, or investigational or post-marketing data, have demonstrated fetal risk. Nevertheless, potential benefits from the use of the drug may outweigh the potential risk. For example, the drug may be acceptable if needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective.

5. **Category X: Contraindicated in pregnancy.** Studies in animals or humans, or investigational or post-marketing reports, have demonstrated positive evidence of fetal abnormalities or risk that clearly outweighs any possible benefit to the patient.

**NOTE:** Deviations from this policy or the above language must be justified by the investigator and approved by the IRB.

**REQUIRED ELEMENTS FOR THE CONSENT DOCUMENT**

**Studies Involving Category A Drugs**

The investigator is not required to mandate use of contraception, and the IRB strongly discourages the investigator from doing so (since adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester of pregnancy). Should the investigator choose to mandate contraception, the mandate must be justified to the IRB.

The investigator may, at their discretion, include some or all of the following standard language in the Risks section of the consent form:

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It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone you want to have present.
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If contraception is required, the IRB concurs with the requirement for contraception, subjects should be informed that they should not participate in a contraception process. If participating in sexual activity that could lead to pregnancy, the subject and his/her partner should use one reliable form of contraception while on study and for a specified number of months afterwards. The following IRB approved language must be used in the Risks section of the consent form:
It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

If contraception is required, and the IRB concurs with the requirement for contraception, subjects should be informed that they should not participate in a conception process. If participating in sexual activity that could lead to pregnancy, the subject and his/her partner should use ONE reliable form of contraception while on study and for a specified number of months afterwards.

The following IRB approved language must be used in the Risks section of the consent form:

It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study, and you are strongly advised not to do so.

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use one of the following forms of birth control:

- Condoms (male or female) with our without a spermicidal agent.
- Diaphragm or cervical cap with spermicide
- IUD
- Hormonal-based contraception

The Investigator will discuss the risks and benefits to each of the different forms of contraception available to you in an effort to provide you with the information necessary for you to make a fully informed decision as to which form of contraception you will use. There is specific information available about the risks of each form of contraception and there is also information available about the “failure rates” of each form.

By signing this and being in the study, you are agreeing to use the birth control methods listed above while you are on the study [“and for x months afterwards” for drugs with
potential for residual effects.] Should you become pregnant while on this study, you must immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

Studies Involving Category B Drugs

The investigator is not required to mandate use of contraception. Should the investigator choose to mandate use of contraception, subjects should be informed that they should not participate in a conception process. If participating in sexual activity that could lead to pregnancy, the subject and his/her partner should use ONE reliable form of contraception while on study and for a specified number of months afterwards.

If contraception is NOT required, the following language must be used in the consent form:

It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study, and you are strongly advised not to do so.

If contraception is required, the following IRB approved language must be used in the Risks section of the CF:

It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study, and you are strongly advised not to do so.

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use one of the following forms of birth control:

- Condoms (male or female) with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
IUD
Hormonal-based contraception

The Investigator will discuss the risks and benefits of each of the different forms of contraception available to you in an effort to provide you with the information necessary for you to make a fully informed decision as to which form of contraception you will use. There is specific information available about the risks of each form of contraception and there is also information available about the “failure rates” of each form.

By signing this and being in the study, you are agreeing to use the birth control methods listed above while you are on the study ["and for x months afterwards" for drugs with potential for residual effects.] Should you become pregnant while on this study, you must immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

Studies Involving Category C Drugs

The investigator should mandate use of contraception, since there are no definitive studies which demonstrate the safety of these drugs for the fetus. However, due to the unknown magnitude of the risk to the fetus, the investigator may, at his discretion, require the use of either one or two forms of contraception.

Subjects should be informed that they should not participate in a conception process. If participating in sexual activity that could lead to pregnancy, the subject and his/her partner should use **ONE or TWO** reliable form(s) of contraception while on study and for a specified number of months afterwards.

The following IRB approved language must be used in the Risks section of the consent form:

It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study, and you are strongly advised not to do so.
[Investigator: use one of these two clauses]

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use ONE of the following forms of birth control every time you have sex:

- Condoms (male or female) with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
- IUD
- Hormonal-based contraception

[OR]

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use TWO of the following forms of birth control every time you have sex:

- Condoms (male or female) with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
- IUD
- Hormonal-based contraception

[Include for all]

The Investigator will discuss the risks and benefits of each of the different forms of contraception available to you in an effort to provide you with the information necessary for you to make a fully informed decision as to which form of contraception you will use. There is specific information available about the risks of each form of contraception and there is also information available about the “failure rates” of each form.

By signing this and being in the study, you are agreeing to use the birth control methods listed above while you are on the study [“and for x months afterwards” for drugs with potential for residual effects] Should you become pregnant while on this study, you must immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

**Studies Involving Category D Drugs**

The investigator should mandate use of contraception, since studies of the drug in humans, or investigational or post-marketing data, have demonstrated fetal risk.

Subjects should be informed that they should not participate in a conception process. If participating in sexual activity that could lead to pregnancy, the subject and his/her partner should use **TWO** reliable forms of contraception while on study and for a specified number of months afterwards.
The following IRB approved language must be used in the Risks section of the consent form:

It is possible that the medicines used in this study could injury a fetus if you or your partner becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study, and you are strongly advised not to do so.

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use two of the following forms of birth control every time you have sex:

- Condoms (male or female) with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
- IUD
- Hormonal-based contraception

The Investigator will discuss the risks and benefits of each of the different forms of contraception available to you in an effort to provide you with the information necessary for you to make a fully informed decision as to which form of contraception you will use. There is specific information available about the risks of each form of contraception and there is also information available about the “failure rates” of each form.

By signing this and being in the study, you are agreeing to use the birth control methods listed above while you are on the study (“and for x months afterwards” for drugs with residual effects.) Should you become pregnant while on this study, you must immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

**Studies Involving Category X Drugs**

The investigator/sponsor should mandate use of contraception, since studies of the drug in humans, or investigational or post-marketing data, have demonstrated fetal risk.

Subjects should be informed that they should not participate in a conception process. If participating in sexual activity that could lead to pregnancy, the subject and his/her partner should use the contraception requirements as directed by drug package insert, medical
alert, or investigator’s brochure while on study and for a specified number of months afterwards.

The following IRB approved language must be used in the Risks section of the consent form:

**It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.**

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks involved, you and your partner should not become pregnant while you are participating in this study, and you are strongly advised not to do so.

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use:

*Specify contraception requirements as directed by drug package insert, medical alert, or investigator’s brochure.*

The investigator will discuss the risks and benefits of each of the different forms of contraception available to you in an effort to provide you with the information necessary for you to make a fully informed decision as to which form of contraception you will use. There is specific information available about the risks of each form of contraception and there is also information available about the “failure rates” of each form.

By signing this and being in the study, you are agreeing to use the birth control methods listed above while you are on the study (“and for x months afterwards” for drugs with residual effects.) Should you become pregnant while on this study, you must immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask you to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

**Administrative Approval:**

**Signed:** [s] Ernest D. Prentice, Ph.D.

**Title:** IRB Executive Chair and Associate Vice Chancellor for Academic Affairs