

3.9 Contraception Requirements

Last Revised: 5/5/2025

1.0 Purpose

The purpose of this policy is to describe the contraception requirements for subjects participating in research involving drugs, devices or biologics.

2.0 Policy

It is the policy of the Organization that subjects must utilize appropriate contraception methods while participating in research with potential for reproductive toxicity.

- 2.1. Contraception requirements should be based on the investigator's data driven and good faith assessment of the risks to a fetus that are or might be associated with use of the drug or device during pregnancy.
 - 2.1.1. For studies utilizing devices, risks to fetuses include those risks associated with placement of the device, including but not limited to risks of drugs used for anesthesia or of radiographic procedures needed for placement of the device.
 - 2.2. Persons who are not of reproductive potential (premenarchal, postmenopausal, or surgically or otherwise unable to become pregnant) are eligible to participate in research without requiring the use of contraception.
 - 2.3. Person capable of producing seminal fluid, including those who have undergone successful vasectomy with resulting azoospermia or have azoospermia for any other reason, should use barrier contraception, or their partners should use appropriate contraception, unless the agent has been shown not to be present in seminal fluid, or the agent has been shown to have no genotoxic, reproductive, or developmental effects in nonclinical or clinical studies.
 - 2.4. It is the responsibility of the investigator (with the Research Subject Advocate and/or other qualified persons, as appropriate) to assist the potential study participant (as needed) to understand the risks and benefits of contraception choices so that they can make an informed choice.
 - 2.5. The discussion with the subject (or with an LAR or parent/guardian) regarding contraception requirements should be documented in the source/study record.
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3.0 Fetal Risk Categories

- 3.1. For FDA approved drugs which comply with FDA Pregnancy and Lactation Labeling Rule (PLLR), categories are determined by the investigator and are based on data in FDA approved “Prescribing Information” (especially sections 8.1 {Pregnancy} and 8.3 {Females and Males of Reproductive Potential}).
 - 3.2. For drugs not approved by the FDA, or approved drugs that do not comply with the PLLR, categories are determined by the investigator and are based on information in the Investigator’s Brochure related to teratogenicity and genotoxicity, and/or on the published medical literature, and/or on the FDA Use in Pregnancy Category.
 - 3.3. Categories
 - 3.3.1. Group 1: No systemic absorption of drug or biologic.
 - 3.3.2. Group 2: Review of clinical trials conducted in pregnant persons, pregnancy exposure registries, and other large scale epidemiologic studies show no evidence of adverse developmental outcomes.
 - 3.3.2.1. This would include drugs with FDA Use in Pregnancy category A.
 - 3.3.3. Group 3: In the absence of human data, animal studies show no evidence of adverse developmental outcomes.
 - 3.3.3.1. This would include drugs with FDA Use in Pregnancy category B.
 - 3.3.4. Group 4: Animal studies show evidence of adverse developmental outcomes, at dose levels higher than those to be used in this study.
 - 3.3.4.1. This might include some drugs in FDA Use in Pregnancy category C, depending on dose levels.
 - 3.3.5. Group 5: (1) Review of clinical trials conducted in pregnant persons, pregnancy exposure registries, other large scale epidemiologic studies, or well described case-series show evidence of adverse developmental outcomes; OR (2) animal studies show evidence of adverse developmental outcomes, at dose levels similar to those to be used in this study; OR (3) the mechanism of action of the drug suggests the possibility of adverse developmental outcomes
 - 3.3.5.1. This might include some drugs in FDA Use in Pregnancy categories C (depending on dose levels), D and X
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4.0 Allowable Contraception Requirements

- 4.1. Investigators may or must require contraception in accordance with data driven and good faith estimates of the likelihood of fetal injury due to in utero exposure to the drug as follows:
 - 4.1.1. Studies Involving Group 1 and Group 2 Drugs {no evidence of systemic absorption of drug (group 1), or no evidence of adverse developmental outcomes (group 2)} - The protocol may not require use of contraception.
 - 4.1.2. Studies involving Group 3 Drugs {No human data but animal studies show no evidence of adverse developmental outcomes} - The protocol may require the use of ONE form of effective contraception; this may include (but may not require) the use of a form of highly effective contraception.
 - 4.1.3. Studies involving Group 4 Drugs {Animal studies show evidence of adverse developmental outcomes, at dose levels higher than those to be used in this study} - The protocol must require the use of ONE highly effective form of contraception, or TWO concurrent forms of effective contraception.
 - 4.1.4. Studies involving Group 5 Drugs {evidence of adverse developmental outcomes; OR mechanism of action of the drug suggests the possibility of adverse

developmental outcomes} - The protocol must require the use of TWO forms of concurrent contraception, at least one of which must be highly effective.

- 4.2. Highly effective forms of contraception (<1 pregnancy per 100 person-years) include long-acting reversible contraception (LARCs), copper or hormonal IUD, or tubal ligation.
 - 4.3. Effective forms of contraception (6-12 pregnancies per 100 person-years) include injectable, oral, transdermal or local (vaginal) hormonal therapy, double barrier methods, diaphragm plus spermicide, or other single barrier methods plus spermicide.
 - 4.4. Persons who practice total abstinence, when this is in line with the preferred and usual lifestyle of the subject may participate in research without requiring the use of contraception. Total abstinence does not include methods of “periodic abstinence” (such as calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal.
 - 4.4.1. Persons not participating in sexual activities that could lead to pregnancy (including but not limited to total abstinence in line with their preferred and usual lifestyle) may be required to utilize barrier or double barrier contraception as above should they deviate from this preferred and usual lifestyle.
 - 4.5. Persons who are not of reproductive potential (premenarchal, postmenopausal, or surgically or otherwise sterile) are eligible to participate in research without requiring the use of contraception.
 - 4.6. Exceptions to this policy must be approved by the full IRB after adequate justification by the PI.
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5.0 Additional Requirements

- 5.1. The duration of contraception must be stated in the IRB Application and in the ICF. If contraception is required for longer than the time the drug is being administered, justification must be provided.
 - 5.2. For all groups described above, the ICF must include the corresponding standard Contraception language in Addendum 1, except:
 - 5.2.1. For Group 5 drugs, if the sponsor mandates specific contraception language be included in the ICF this language may be used in lieu of the standard language in Addendum 1, provided the IRB determines that the specified language is as protective of the potential fetus, and does not create undue burden on the subject.
 - 5.2.2. If PI wishes to list specific forms of birth control in any of the above categories (rather than the generic “effective method(s) of birth control” found in the IRB-approved template), and use of an effective form of contraception is allowed per section 4.0, then the list must include at least barrier or double barrier methods with a spermicidal agent.
 - 5.3. The IRB Executive Chair is authorized to negotiate with sponsors and/or PIs to address requests for specific language modifications in the ICF provided the requested modifications are at least as protective as the requirements found in the IRB-approved template.
 - 5.4. In the case of minors and those with impaired decision-making capacity, risks to those who can become pregnant or contribute to a pregnancy, as well as contraception requirements, will be discussed in a developmentally and cognitively appropriate manner.
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6.0 Additional Consideration for research involving devices

- 6.1. Investigators may or must require contraception in accordance with data driven and good faith estimates of the likelihood of fetal injury associated with:
 - 6.1.1. placement of the device, including
 - 6.1.1.1. drugs used for anesthesia, if required to place the device or assure its safe operation; or
 - 6.1.1.2. radiographic procedures, if required to place the device or assure its safe operation; and
 - 6.1.2. use of the device (including, but not limited to, risks related to electrical or electromagnetic safety of the device)
 - 6.2. For risks associated with use of drugs for placement of the device or to assure its safe operation, contraception may be or must be used as described above for research involving drug products.
 - 6.3. For risks associated with radiographic procedures required to place the device or assure its safe operation, contraception requirement should reflect best clinical practice related to exposure of persons of childbearing potential to standard diagnostic procedures involving radiation.
 - 6.4. For risks associated with use of the device (including, but not limited to, risks related to electrical or electromagnetic safety of the device), contraception requirements should reflect best clinical practice and/or manufacturer recommendations regarding use in persons of childbearing potential, or in pregnant persons.
 - 6.5. For research involving devices that pose risks to a fetus, the ICF must include the corresponding standard Contraception language in Addendum 1, modified as described in Addendum 2.
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ADDENDUM #1

ICF Pregnancy Risk Statements Group 2 drugs {no evidence of adverse developmental outcomes}:

PREGNANCY RISKS

- There is no evidence that the drug(s) used in this research could injure a fetus {OR an unborn child}, if you, or your partner, become pregnant while taking them; however it is possible. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

Group 3 drugs {No human data but animal studies show no evidence of adverse developmental outcomes}:

PREGNANCY RISKS

- It is possible that the medicines used in this study could injure a fetus {OR an unborn child} if you, or your partner, become 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, you, or your partner, must not become pregnant while you are participating in this study. Persons who can become pregnant must have a negative pregnancy test before entering the study {and before each treatment – as appropriate}.
- If you are sexually active and can get pregnant, or can get your partner pregnant, you must use ONE effective form of birth control every time you have sex, or you must not have sex.
- You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate's Office at (402) 559-6941.
- You will need to continue to use birth control to avoid pregnancy for X months after finishing the research.
- By signing this and being in the study, you are agreeing to not get pregnant while you are on the study and for X months after. Should you become pregnant while on this study, you should 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.

Group 4 drugs {Animal studies show evidence of adverse developmental outcomes, at dose levels higher than those to be used in this study}:

PREGNANCY RISKS

- It is possible that the medicines used in this study could injure a fetus {OR an unborn child} if you, or your partner, become 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, you, or your partner, must not become pregnant while you are participating in this study. Persons who can become pregnant must have a negative pregnancy test before entering the study {and before each treatment – as appropriate}.
- If you are sexually active and can get pregnant, or can get your partner pregnant, you must use ONE {or TWO} effective method(s) of birth control every time you have sex, or you must not have sex.
- Because of the possible risk to the fetus {OR an unborn child}, methods of natural family planning are not, by themselves, reliable enough to avoid pregnancy.
- You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate's Office at (402) 559-6941.
- You will need to continue to use birth control to avoid pregnancy for X months after finishing the research.
- By signing this and being in the study, you are agreeing to not get pregnant while you are on the study and for X months after. Should you become pregnant while on this study, you should 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.

Group 5 Drugs {evidence of adverse developmental outcomes; OR mechanism of action of the drug suggests the possibility of adverse developmental outcomes}:

PREGNANCY RISKS

- It is possible that the medicines used in this study could injure a fetus {OR an unborn child} if you, or your partner, become 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, you, or your partner, must not become pregnant while you are participating in this study. Persons who can become pregnant must have a negative pregnancy test before entering the study {and before each treatment – as appropriate}.
- If you are sexually active and can get pregnant, or can get your partner pregnant, you must use TWO effective methods of birth control every time you have sex, or you must not have sex.
- Because of the possible risks to a fetus {OR an unborn child}, methods of natural family planning are not, by themselves, sufficiently reliable to avoid pregnancy.
- You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate's Office at (402) 559-6941.
- You will need to continue to use birth control to avoid pregnancy for X months after finishing the research.
- By signing this and being in the study, you are agreeing to not get pregnant while you are on the study and for X months after. Should you become pregnant while on this study, you should 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.

ADDENDUM #2 (For Studies Involving Devices)

ICF Pregnancy Risk Statements are as described in Addendum #1, except the first paragraph of the Pregnancy Risks statement should be replaced with:

- It is possible that the device {or substitute the actual name} or the procedure to put in the device if appropriate} used in this study could injure a fetus {OR an unborn child} if you are pregnant or become pregnant. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

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? Revised: 11/21/2017 - revision not documented

? Revised 11/27/2024 - Revised to base contraception requirements on PLLR rather than previous FDA Use-In-Pregnancy category; revised to use gender neutral language; added comment that risks to those who can become pregnant or contribute to a pregnancy, as well as contraception requirements, will be discussed in a developmentally and cognitively appropriate manner (section 5.4); stylistic changes.

? Revised 5/5/2025 - Revised purpose to specify policy addresses contraception requirements for subjects participating in research involving drugs, devices or biologics; added additional considerations for research involving devices (sections 2.1.1 and 6.1 thru 6.5); added ADDENDUM #2 (ICF Pregnancy Risk Statements for studies involving devices); minor stylistic changes and correction of typographic errors.

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