**Duke Health IRB**

**Required Elements on Reproductive Risks for Informed Consent Forms**

***Examples of Standard Language***

Note that the Duke Health IRB requires each of these elements in the ICF rather than specific language. If the sponsor’s suggested ICF language contains all these required elements, addition of Duke sample language is not required, although sponsor language may be revised/edited during the IRB review process.

**Required Elements**

• Description of rationale for preventing pregnancy during study, and which subgroups are excluded

• Description of pregnancy testing requirements (women/girls only)

• Description of duration and type of contraception required

• Description of actions taken in event of pregnancy

• Description of any potential risks to future fertility if noted in protocol

**I) Description of rationale for preventing pregnancy during study, and which subgroups are excluded**

* **Women: Sample Language**
  + *Known human teratogen:* [Study drug] is known to increase the risk of birth defects and miscarriage in humans when taken during pregnancy and may have risks for breastfed infants. Therefore, women who are pregnant, planning a pregnancy, or breastfeeding are not allowed to participate in studies using [study drug].
  + *Teratogen in animal studies, human effects unknown:* In animal studies, [study drug] increased the risk of some birth defects; whether these effects are also seen in humans is unknown. To reduce the risk of any harmful effects, women who are pregnant, planning a pregnancy, or breastfeeding are not allowed to participate in studies with [study drug].
  + *Unknown risks*: The effects of [study drug] on a developing pregnancy or breastfeeding infant are unknown. To reduce the risk of any harmful effects, women who are pregnant, planning a pregnancy, or breastfeeding are not allowed to participate in studies using [study drug].
  + *No risks:* Although [study drug] is generally considered safe to use during pregnancy, the changes your body goes through during pregnancy may affect some of the things we are measuring in this study. Therefore, women who are pregnant or planning a pregnancy are not allowed to participate in this study.
* **Men: Sample Language**
  + *Known risk with paternal exposure:*  An increased risk of certain birth defects has been observed in pregnancies where the father was taking [study drug] at the time the pregnancy began. Therefore, men who are trying to become fathers are not allowed to participate in studies using [study drug].
  + *Unknown risk, no concern about seminal transmission:*  It is unknown whether pregnancies that began while the father was taking [study drug] are at increased risk for birth defects, miscarriages, or other bad outcomes. To reduce the risk of any harmful effects, men who are trying to become fathers are not allowed to participate in studies of this drug.
  + *Unknown risk, concern about seminal transmission:* It is unknown whether pregnancies that began while the father was taking [study drug] are at increased risk for birth defects, miscarriages, or other bad outcomes. In addition, [study drug] may be present in semen and transmitted to a partner during sexual activity. To reduce the risk of any harmful effects, men who are trying to become fathers are not allowed to participate in this study.

**II)** (**Women/girls only) Description of Pregnancy Testing Requirements**

* **Description should include**
  + Who is Required to Be Tested?
  + If Blood Test Required, Risk of False Positive/Indeterminate Blood Test
  + If Additional Testing Required, Description of Type, Frequency, and Consequences of Positive Result
* **Sample Language**
  + If you are a woman who could possibly become pregnant (you have not completed menopause, had a hysterectomy and/or both tubes and/or both ovaries removed) and you have a partner who is able to father children, a [blood/urine] pregnancy test will be performed, and it must be negative in order to continue in the study.
  + If serum pregnancy test used: In women 40 years old and older, blood pregnancy tests may sometimes give a false positive or “indeterminate” result and additional testing may be required to confirm your eligibility for the study.
  + If additional tests required: You will also have additional [blood/urine] tests at some study visits, as described above, and they also must be negative for you to continue in the study.

**III) Description of Duration and Type of Required Contraceptive Methods**

* **Description should include**
  + Statement that complete abstinence from vaginal intercourse for the study-specified duration of contraception is acceptable.
  + Duration of need for abstinence or contraception, including starting time and ending time
  + Specific methods which (a) meet the protocol-specified level of effectiveness and (b) are compatible with the study population (for example, combination oral contraceptives are contraindicated in many populations because of increased risk of venous thrombotic events).
  + Statement that the study team will assist with any required changes to contraceptive methods.
  + Statement of possibility of pregnancy even with highly effective methods and need to notify study team
  + For males,
    - If specified by protocol and appropriate for clinical population, statement that donation of sperm is prohibited for same duration as contraception requirement
    - If concern is seminal transmission, a statement that condoms are required for all types of intercourse if partner is currently pregnant or breastfeeding
  + “Highly effective methods” (<1% failure rate)
    - “Typical use”
      * Partner vasectomy
      * Bilateral tubal ligation
      * IUDs
      * Progestin implants (Implanon)
    - “Perfect use” (acceptable with some sponsors, FDA, ICH/EU guidance)
      * Other hormonal methods (OCPs, injections, patches, rings)
  + “Effective Methods”
    - Any of the above, or
    - Barrier (condom, diaphragm, cervical cap) plus spermicide
  + If protocol specifies dual methods, specific combinations (e.g., barrier method plus other method) must be specified. A list of all methods and statement that two must be used is not acceptable.
* **Women: Sample Language**
  + You and your partner must agree to either abstain completely from vaginal intercourse for the duration of the study and for [X time] after your last dose of study drug, or use a highly effective method of contraception for the same length of time These methods include (a) partner vasectomy, (b) bilateral tubal ligation, (c) intrauterine devices (IUDs), (d) hormonal implants (such as Implanon), or (e) other hormonal methods (birth control pills, injections, patches, vaginal rings). If you and your partner are not currently using one of these methods your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness required for this study. Because no birth control method is 100% effective, you should notify your study doctor immediately if you think there is any chance you could be pregnant.
    - If protocol requires ongoing pregnancy testing: you should notify your study doctor immediately if you think there is any chance you could be pregnant, *even if you have had a recent negative pregnancy test.*
* **Men, No Concern about Seminal Transmission: Sample Language**
  + If you have a partner who could possibly become pregnant (she has not completed menopause, or has not had a hysterectomy and/or both tubes and/or both ovaries removed), you and your partner must agree to either abstain completely from vaginal intercourse for the duration of the study and for [X time] after your last dose of study drug, or use a highly effective method of contraception for the same length of time. Highly effective methods include (a) vasectomy, (b) bilateral tubal ligation, (c) intrauterine devices (IUDs), (d) hormonal implants (such as Implanon), or (e) other hormonal methods (birth control pills, injections, patches, vaginal rings). If you and your partner are not currently using one of these methods your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness required for this study.
  + You should not donate sperm for the duration of the study and for [X time**]** after your last dose of study drug.
* **Men, Concern about Seminal Transmission, Pregnancy Risk Only: Sample Language**
  + If you are able to father children and your partner is a woman who could possibly become pregnant (she has not completed menopause, or has not had a hysterectomy and/or both tubes and/or both ovaries removed), you must agree to either abstain completely from vaginal intercourse for the duration of the study and for [X time] after your last dose of study drug, or use a condom every time you have vaginal intercourse, even if you have had a vasectomy (because vasectomy does not prevent transmission of drug in semen). If your partner is currently pregnant, breastfeeding, or becomes pregnant during the study, you must use a condom for all types of intercourse to prevent transmission.
  + You should not donate sperm for the duration of the study and for [X time**]** after your last dose of study drug.
* **Men, Concern about Seminal Transmission to Partner: Sample Language**
  + The study drug may be transmitted to a partner during sex, which could possibly have bad effects for your partner. Therefore, you must agree to use a condom every time you have any type of intercourse, even if you have had a vasectomy (because vasectomy does not prevent transmission of drug in semen), your partner is a woman who cannot possibly become pregnant, or your partner is a man.
  + You should not donate sperm for the duration of the study and for [X time**]** after your last dose of study drug.

**IV) Description of Actions Taken in Event of Pregnancy**

* Description should include
  + Specific actions (stopping drug, study withdrawal, etc.)
  + Any follow-up of pregnancy in either subject or subjects’ partner
* **Women, Sample Language:**
  + If you do become pregnant during the study, your study doctor will stop the study drug, withdraw you from the study, and notify the sponsor. You will be followed for the duration of the pregnancy to better understand the potential effects of the study drug on pregnancy outcomes.
* **Men, Sample Language:**
  + You should notify your partner about your participation in this study, and the potential risks to pregnancies that begin while you are taking the study drug. If she does become pregnant during the study, you should notify your study doctor, and she should notify her doctor. She will be asked for permission to collect information about the pregnancy to better understand the potential effects of the study drug on pregnancy outcomes.

**V) Description of Any Known or Suspected Potential Risks to Future Fertility (if appropriate)**

* Description should include
  + Whether risks are known or unknown
  + Discussion of options for fertility preservation, if available
* **Women, Sample Language** 
  + The study drugs used in this study may affect your ability to become pregnant in the future. There may be fertility preservation options available, which your study doctor will discuss with you.
* **Men, Sample Language**
  + The study drug used in this study may affect your ability to father children in the future. There may be fertility preservation options available, which your study doctor will discuss with you.

**EXAMPLE**

**REPRODUCTIVE RISKS**

**For Women:** The effect of [study drug] on the risk of birth defects, miscarriage, or other bad outcomes when taken during pregnancy or while breastfeeding is unknown. To reduce the risk of any harmful effects, women who are pregnant, trying to become pregnant, or breastfeeding are not allowed to participate in studies using [study drug].

If you are a woman who could possibly become pregnant (you have not had a hysterectomy and/or both tubes and/or both ovaries removed) and you have a partner who is able to father children, a blood pregnancy test will be performed, and it must be negative to continue in the study. In women 40 years old and older, blood pregnancy tests may sometimes give a false positive or “indeterminate” result, and additional testing may be required to confirm your eligibility for the study. You will also have additional urine pregnancy tests at some study visits, as described above, and they also must be negative for you to continue in the study.

You and your partner must agree to either abstain completely from vaginal intercourse for the duration of the study and for 30 days after your last dose of study drug or use a highly effective method of contraception for the same length of time. Highly effective methods include (a) partner vasectomy, (b) bilateral tubal ligation, (c) intrauterine devices (IUDs), (d) hormonal implants (such as Implanon), or (e) other hormonal methods (birth control pills, injections, patches, vaginal rings). If you and your partner are not currently using one of these methods your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness required for this study. Because no birth control method is 100% effective, you should notify your study doctor immediately if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test.

If you do become pregnant during the study, your study doctor will stop the study drug, withdraw you from the study, and notify the sponsor. You will be followed for the duration of the pregnancy to better understand the potential effects of the study drug on pregnancy outcomes.

**For Men**

It is unknown whether pregnancies that began while the father was taking the study drug are at increased risk for birth defects, miscarriages, or other bad outcomes. To reduce the risk of any harmful effects, men who are trying to become fathers are not allowed to participate in studies using the study drug.

If you are able to father children and your partner is a woman who could possibly become pregnant (she has not completed menopause, or has not had a hysterectomy and/or both tubes and/or both ovaries removed, you and your partner must agree to either abstain completely from vaginal intercourse for the duration of the study and for 90 days after the last dose of study drug, or use a highly effective method of contraception for the same length of time. Highly effective methods include (a) vasectomy, (b) bilateral tubal ligation, (c) intrauterine devices (IUDs), (d) hormonal implants (such as Implanon), or (e) other hormonal methods (birth control pills, injections, patches, vaginal rings). If you and your partner are not currently using one of these methods your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness required for this study.

You should not donate sperm for the duration of the study and for 90 days after the last dose of study drug.