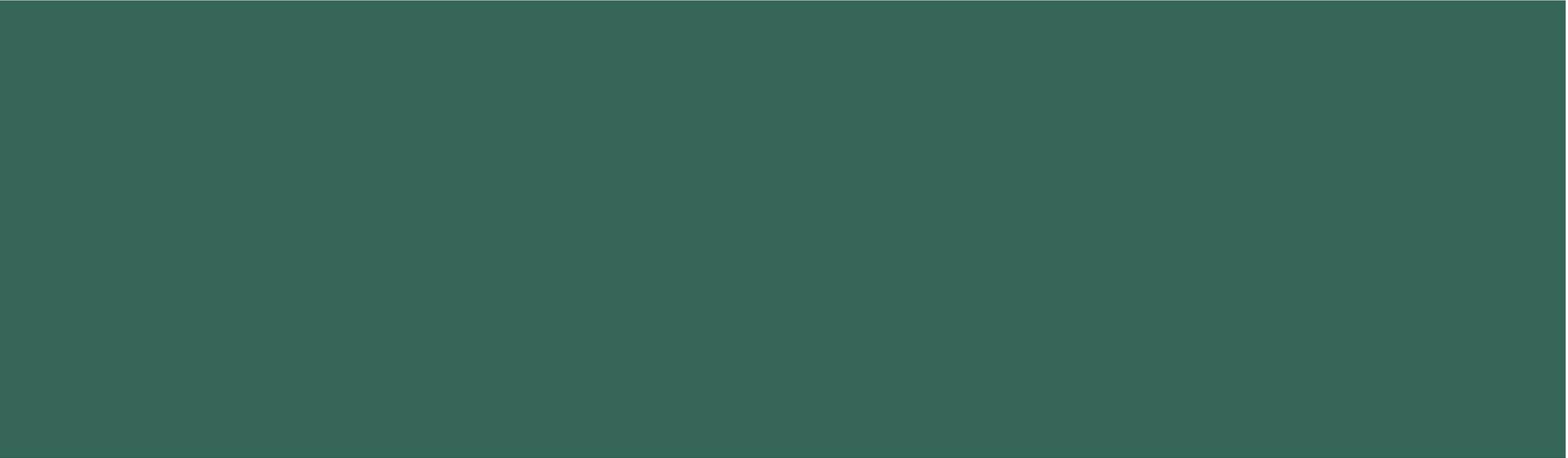


EXCLUSION OF PREGNANT WOMEN FROM RESEARCH

NOVEMBER 2017 IRB MEMBER TRAINING



INTRODUCTION

- Pregnant women have been historically underrepresented in research out of concerns about the liabilities associated with fetal harm and perceived inconvenience surrounding the regulations governing research involving pregnant women.
- This has resulted in gaps in knowledge about the health of pregnant women and how different drugs and devices impact this population.
- As noted in the March member training on the NIH's recent mandate to consider sex as a biological variable, women in general have been underrepresented in research.
- In recognition of the consequences of the broad exclusion of women and pregnant women, investigators are increasingly being prompted to include pregnant women in their studies when appropriate.

JUSTICE AND THE EQUITABILITY OF SUBJECT SELECTION

- This is fundamentally a matter of justice - subject selection should not disproportionately burden or benefit any particular population.
- Unjustified exclusions have resulted in similar under-representation of other populations such as:
 - HIV positive individuals
 - minorities and non-English speakers
 - economically disadvantaged and homeless people
- Exclusions should not be in place solely for convenience. This is not to say that every group should be represented in every study, but that eligibility criteria should be both *fair* and *relevant* to the research objectives.



IRB Considerations for studies from which pregnant women are excluded

RATIONALE

- What is the rationale for the exclusion? Does it make sense in terms of the risks and/or study objectives?
- Some common reasons for excluding pregnant women include:
 - the use of drugs, devices or procedures that pose safety concerns for the developing fetus, for nursing infants, or for pregnant women
 - research for which there is insufficient prior data needed to rule out serious risks to pregnant women and/or fetuses
 - confounding effects of physiological factors associated with pregnancy
 - research which does not apply to pregnant women or women of child-bearing potential (WOCBP)

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- Rationale for the exclusion should be clearly stated in the protocol and/or HS-ERA application.
 - The consent form should also include language explicitly informing prospective subjects that pregnant women will be excluded, along with a description of any risks underlying this exclusion.

PREGNANCY SCREENING

- If WOCBP may be included, is an adequate plan in place to establish pregnancy status at screening?
 - If pregnant women are excluded for safety reasons, the study should rely on pregnancy testing in lieu of self-report.
 - If the risks to pregnant women and/or fetuses are especially serious, the study team should consider relying on more sensitive methods of testing, e.g. serum instead of urine. The method of testing should be clear in the consent form.

OTHER CONSIDERATIONS

- In studies which involve several visits, the following additional concerns need to be addressed:
 - Is there a strategy to continuously monitor WOCBP for pregnancy?
 - Are there contraceptive requirements in place (i.e. for WOCBP, male subjects and/or female partners of male subjects)? Are these requirements reasonable in proportion to the reproductive risks?
 - Is there a wash-out period after completion of study activities during which pregnancy should continue to be avoided?
- The consent form should describe any requirements for ongoing testing and pregnancy avoidance along with a list of the acceptable forms of birth control.

INCIDENTAL PREGNANCIES

- The IRB should also consider how incidental pregnancies will be handled.
 - Will pregnant subjects be withdrawn from participation altogether or will they be permitted to continue to participate in minimal risk activities?*
 - The protocol should account for cases in which staying on study treatment may be in the best interest of the pregnant woman and/or the fetus. Withdrawing incidentally pregnant subjects shown to be benefiting needs to be balanced with risks to the pregnancy/fetus.
 - Will data be collected on pregnancy and birth outcomes (for both pregnant participants and female partners of male participants who become pregnant)**
 - If so, what elements of data will be collected?
 - How will the data be used in the context of the overall study objectives?
 - Are there plans for reporting the pregnancy to appropriate oversight agencies or any other clinical reporting responsibilities?
- The consent form should reflect any plans for incidental pregnancy follow-up.
- Where applicable, the study team should also supply a pregnant partner authorization form.

RESOURCES

- University of Pennsylvania IRB Guidance on Greater than Minimal Risk Research which Excludes Pregnancy
 - <http://www.upenn.edu/IRB/sites/default/files/Pregnancy-Contraception%20Guidance%20FINAL%20FOR%20RELEASE.pdf>
- OHRP Regulations Governing Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
 - <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#subpartb>
- NIH Office of Research on Women's Health
 - <https://orwh.od.nih.gov/>