HRP 580 – HRPP COM Consent Form Template (v.08/30/2021)

This template is for research conducted at Penn State Health and the Penn State College of Medicine only.

Researchers at other Penn State locations should use the "HRPP" templates in CATS IRB Library.

Note: Additional consent form information is available in the following documents on the IRB website on the Infonet under Departments/Research/IRB-HSPO/Resources/Forms https://infonet.pennstatehershey.net/web/irb/resources/forms

- Consent Form - Suggested Consent Wording
- Consent Form - Genomic Studies Required Language

Use low-literacy techniques to the extent possible throughout the consent form.

- Explain medical terms and complex words in lay terms and simple language.
- Avoid long sentences and paragraphs.
- Use bulleted lists and incorporate white space, where appropriate.

Delete all instructions before printing your final form. Instructions are included in italics or shaded boxes.

CONSENT FOR RESEARCH
Penn State College of Medicine
Penn State Health

Title of Project:	Pilot study examining the pharmacokinetics of 0.35mg norethindrone vs 5mg norethindrone acetate
Principal Investigator:	Sarah Horvath, MD
Address:	35 Hope Drive, Hershey PA 17033
Telephone Numbers:	Weekdays: 8:00 a.m. to 5:00 p.m. (717) 531-3503.

Subject's Printed Name: _____

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you, and there will be no penalty or loss of benefits to which you are entitled.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

Key Information Instructions:

- The revised Common Rule human subjects regulations require subjects be given a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent, as well as the entire document, must be organized and presented in a way that facilitates comprehension.
- This section is required for studies approved by the PSCOM IRB on or after 01/21/2019. This section is optional for studies whose initial IRB approval was granted before 01/21/2019.
- **You may DELETE this section if the consent document without this section and without the signature lines is less than 2,000 words (approximately 5 pages, single-spaced, 1-inch margins)**
- This Key Information section should, for most studies, be **≤ 2 pages long**.
- Check with the HRPP if you are unsure if this section is needed.
- Federal agencies expect that, in general, the Key Information section will include a concise explanation of the following: (1) That consent is being sought for research and that participation is voluntary; (2) A brief summary of the purpose of the study; (3) Duration of participation; (4) A brief description of the procedures to be followed in the research; (5) A summary of the most important risks; and (6) Appropriate alternative procedures or courses of treatment, if any that might be advantageous to the potential subject.
- However, federal agencies have stressed the key information should be meaningful within the context of the study and have therefore avoided strictly defining what information should be included.

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this research. More detailed information is provided later in this form. If you have any questions, be sure to ask the study team.

Why am I being invited to take part in this research study?

We are asking you to take part in this voluntary research study because you are a healthy, premenopausal woman with regular menstrual cycles and are not currently taking a hormonal type of birth control.

What is the purpose of this research study?

The purpose of this voluntary research study is to assess the relative bioavailability of norethindrone at different times in individuals taking 0.35mg norethindrone vs 5mg norethindrone acetate. This knowledge will demonstrate that it is safe to prescribe norethindrone acetate as contraception and will allow for future studies.

How long will the research study last?

This study will require a total of 19 visits including screening and take approximately 2-3 months (two complete menstrual cycles) to complete.

What will I need to do?

There are 2 phases to this study which will cover two consecutive menstrual cycles. Starting day 1-3 of your first menstrual cycle after signing the consent form, you will take one of two study medications, either 0.35mg norethindrone or 5mg norethindrone acetate as your first, Phase 1 therapy. You will take your first therapy once a day for a total of 7 consecutive days at the same time in the morning between 6:30 and 8:00am. On each of those 7 days you will report to the Hershey Medical Center approximately one hour

after taking your study medication for a single blood draw to measure the level of norethindrone and other hormones in your blood. . On day 8 you will stop taking your study medication and will report to the Clinical Research Center (CRC) at the Hershey Medical Center by 7:15am for an 8 hour pharmacokinetic (PK) test. PK testing measures the amount of the study drug in your blood and tells the researchers how much time it takes for the study drug to be absorbed into your body and how long it stays in your body .
You will have an IV placed in your arm, and will have one tube of blood drawn every hour starting at 8am and ending at 4pm. On Day 21 of your cycle you will report to the Hershey Medical Center for a single blood draw to assess your hormone and norethindrone levels.
For Phase 2 at the start of your very next menstrual cycle you will repeat the same procedures as in Phase 1 with the study medication that you did not take in Phase 1.

Each evening, you will be asked to complete a symptom diary to document any symptoms (i.e. abnormal bleeding) and overall satisfaction with your therapy.

A member of the study team will send a text message reminder at 7:30AM to remind you to go to the Clinical Research Center each day to get your blood drawn and complete your daily symptom diary in the evening

What are the main risks of taking part in the study?
For this study, the main risks to know about are side effects from the study drug and a potential for loss of confidentiality

What are the possible benefits to me that may reasonably be expected from being in the research?
There are no benefits to you from taking part in this research. Results of the study may benefit other people in the future by helping us learn whether we can prescribe a new type of birth control that may also benefit future patients who suffer from abnormal bleeding, pelvic pain, or endometriosis.

What happens if I do not want to be in this research?
Participation in research is completely voluntary. You can decide to participate or you may choose not to participate.

DETAILED INFORMATION
The following is more detailed information about this study in addition to the information listed above.

1. Why is this research study being done?

Instructions: Include the following information when applicable:
- Briefly summarize the purpose, e.g., "this research study is being done to …".
- Indicate the FDA status of any drugs or devices that are being tested in the research, and specify "investigational" when applicable.
- Indicate the approximate overall enrollment unless these numbers are not important to a decision to take part in the research.

This research is being done to determine the pharmacokinetics(PK) of 0.35mg norethindrone and 5mg of norethindrone acetate and the potential to use norethindrone acetate as a form of birth control.

The norethindrone medication being used in this study has been approved by the FDA as a standard of care use for women with endometriosis and as a form of birth control. The norethindrone acetate medication being used in this study has been approved by the FDA as a standard of care use for women with endometriosis but is not approved as a form of birth control and is experimental in this study.

Approximately 6 people will take part in this research study at Penn State Health.

2. What will happen in this research study?

Instructions: Include the following information when applicable:

- Outline the procedures in lay terms and in order of occurrence and how often they will be performed.
- Be sure to include:
  - screening procedures that occur after signing the consent form
  - treatment assignment/randomization
  - procedures during treatment
  - final visit and follow-up
- **Use lists, tables or flow charts whenever possible.** If practical, prepare a time line chart or schematic to accompany description of procedures and test for research that requires more than 1 or 2 steps/visits.
- Identify all drugs or biologics (dose, frequency, and route of administration), devices, and procedures that are experimental or that are used in an experimental manner.
- Indicate which are standard procedures (standard of care) versus research procedures. Identify any procedures which are experimental. Identify what procedures are part of regular medical care that will be done even if the subject does not take part in the research.
- Indicate whether the research will include any hospitalizations or outpatient clinic visits or telephone or written follow-up.
- Include the length and duration of visits and procedures.
- If the research involves blood collection, indicate the amount [in English units, teaspoons/tablespoons] and how often and if any special preparation is required (e.g., fasting). Common blood and urine tests should be described as “common blood tests to determine your health status.” List any tests that are out of the ordinary for the specific condition being studied in the research.
- Indicate with whom the subject will interact, where the research will be done and when the research will be done.
- If applicable, describe in lay terms randomization procedures, probability for random assignment to each treatment, double-blinds, emergency unblinding, and use of placebo. Include the following for a clinical trial that involves randomization. “You will be randomly assigned to receive one of the [number] study treatments. This means whichever study treatment you receive will be determined purely by chance. You will have a [give the odds of being in any study group, e.g., equal chance, 1 out of 3, etc.]. [For double-blind studies] Neither you nor the research team will know which study treatment you are receiving, but the research team will be able to get this information quickly if it is needed to ensure your safety. [For single blind research studies] You will not be told which treatment you are getting, however your study doctor will know.”
- If the study involves surveys or questionnaires, include a statement that the subject is free to skip any questions that he/she would prefer not to answer.
- If the research involves a screening visit and includes tests or procedures that would not be done for clinical purposes, then consent must be obtained prior to the screening visit. Avoid

wording such as "After the screening visit, if you are eligible to **participate** in the study, you will …" Rather, use wording such as "After the screening visit, if you are eligible to **continue** in the research, you will …" or "…if you are eligible to **receive** the research treatment, you will …"
- Include what will happen to any research specimens once the research is completed.
- When applicable indicate that the subject may be contacted for future research.

To participate in this research you must first sign the consent form.

The study consists of two phases covering two full menstrual periods as shown in the summary table below.

You will receive two different study therapies over 2 consecutive menstrual cycles. The therapies being examined in this study are 0.35mg norethindrone oral pill daily for 7 days and 5mg norethindrone acetate oral pill daily for 7 days. Norethindrone is FDA approved for endometriosis and as a form of birth control. Norethindrone acetate is FDA approved for endometriosis but is not FDA approved as a form of birth control.

You will be asked to use non-hormonal birth control such as condoms during the study starting with your screening visit and until the end of Phase 2.

You will interact with Halina Yee, MD and Sarah Horvath, MD, who will send you daily text message reminders to present to the Clinical Research Center and/or 35 Hope Drive clinic for blood draws. You will interact with other members of the study team as well as nurses employed at the Clinical Research Center and 35 Hope Drive.

For your safety, you must tell the study doctor or nurse about all the prescription drugs, herbal products, over-the-counter drugs (OTC), vitamins and other supplements you are taking. Check with the study doctor before starting any new medicines (including prescription, OTC drugs, vitamins and herbal supplements) or changing doses of medications that you are already taking.

All of the procedures and tests done for this research are for experimental purposes only.

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Table of Visits Summary	**PHASE 1**					Break until next menstrual cycle	**PHASE 2**			
Procedures	Pre-Screening/ Screen Visit 1	P1 Day 1 (Start of menses day 1-3)	P1 Days 2,3,4, 5,6, 7	P1 Day 8	P1 Day 21		P2 Day 1 (Start of menses day 1-3)	P2 Days 2,3,4, 5,6, 7	P2 Day 8	P2 Day 21
Screening Criteria	X	X								

Informed Consent	X	X								
Urine Pregnancy Test	x									
Dispense study medication	X			X						
Return unused study medication				X					X	
Take study drug between 6:30-8:00am		X	X				X	X		
Complete symptom/satisfaction survey		X	X	X			X	X	X	
Return symptom/satisfaction surveys to site				X					X	
Urine pregnancy test?		X		X			X		X	
Blood draw (LH, FSH, Estradiol, Progesterone)	X			X	X				X	X
Single PK blood draw for norethindrone		X	X		X~~*~~		X	X		X
8 hour PK Testing				X					X	

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Study Visit Details

Screening

To participate in this research you must first sign this consent form.

Screening

- Once we have determined that you are eligible to participate in the study either at your clinic visit or by chart review of your medical history, and if you agree to participate, you will have a screening visit. Your screening visit may occur on the same day as your clinic visit or scheduled on another day if you are contacted by an investigator based on review of your ~~endometriosis~~ history.
- If you are in the clinic for a standard of care visit and are offered a chance to participate by one of the investigators, they will give you the information about the study. If you are interested in participating, you will receive a copy of this consent form to read. After you have read the consent form the investigator will review it with you and answer any questions you may have prior to obtaining your informed consent.
  If you agree to participate, consent will be obtained between you and the investigator in clinic and you will start your screening visit at this time.

- If you were contacted by the investigator for participation based on their review of your ~~endometriosis~~ history you will be given information about the study and if you are interested, the consent form will be emailed or mailed to you to read. If you are interested in participating, you should let the investigator know and you will be schedule for a separate screening visit or you can combine your screening and Day 1 visit.

- At the screening visit:
  - You will have a urine pregnancy test to confirm that you are not pregnant.
  - You will be asked to confirm that you will use non-hormonal contraception during the study.
  - You will be asked to confirm the date of your last menstrual period and to estimate ~~of~~ the start date of your next menstrual period for scheduling purposes. We will ask you to tentatively schedule your Day 1 visit to fall on either day 1, 2, or 3 of your upcoming menstrual cycle. This should occur on Monday through Friday so your Day 8 PK testing will not fall on the weekend. The investigator will assist you with estimating Day 1 and you will need to inform the investigator on the day your menses starts so you can be scheduled appropriately for your Day 1 visit. All Day 1 visits will occur at the Clinical Research Center in the Main Hospital.
  - You will receive your first supply of either 5 mg norethindrone or 0.35mg norethindrone acetate and specific instructions on taking it
  - You will receive a packet of daily surveys to take home with you and start on the evening o~~f~~ your Day 1 visit. You will document symptoms, including bleeding and pain, in your symptom diary each night while you are taking the medications. You may choose to not answer any component of the diary should you choose. Completion of your daily symptom diary should take approximately 10 minutes.
  - You will need to provide your cell phone number in order for the investigators to send you a daily text reminder to come to the site for your blood draw and to complete your daily symptom diary.

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Day 1- Phase 1 and 2

Day 1 will occur on day 1, 2, or 3 of your menstrual cycle (as instructed by the study team). Your Day 1 visit can only be scheduled Monday through Friday to avoid your Day 8 visit from occurring on the weekend.

On Day 1 you will complete the following procedures:

- Start of your study medication
  - If you are assigned to take norethindrone for Phase 1, you will take one dose (one pill) of 5 mg norethindrone by mouth between the hours of 6:30 and 8:00am.
  - If you are assigned to take norethindrone acetate for Phase 1, you will take one dose (one pill) of 0.35 mg norethindrone acetate by mouth between 6:30 and 8:00am.
  - You must document the time that you took your study medication.
- You will report to the Clinical Research Center (located in suite 4500 of the main hospital) one hour after your take your study medication.
- You will have one tube of blood drawn for levels of norethindrone and other hormones. The volume of blood drawn is ½ tsp. No special preparation is necessary for this blood draw.
- You will be reminded to start your symptom diary in the evening of your Day 1 visit.

- You will be reminded to take your medication as described for the next 6 days (Day 2 through Day 7 of the study)

Day 2 thru Day 7- (Phases 1 and 2)

On Days 2,3,4,5,6, and 7 you will complete the following procedures:

- You will take your study medication between 6:30 and 8:00 am and document the time.
- You will need to report to the Hershey Medical Center one hour after taking your medication for a blood draw (one tube of blood approx. ½ tsp). You will report to one of two sites depending on the day of the week.:
    - Monday through Friday you will report to the Clinical Research Center in the Main Hospital for the blood draw
    - Saturday or Sunday you will report to 35 Hope Drive (suite 202) for your blood draw. You must time your study medication so that you can report to Hope Drive no later than 7:30am for blood draws on the weekend.
- You will complete your symptom diary each night
- Day 2 through Day 7 visits will take between 15 and 30 minutes to complete.

Day 8 – (Phases 1 and 2)

- On your Day 8 visit you will not take any study medication that morning but will report to the CRC promptly at 7:15am for the 8-hour PK testing. You will be required to remain on site for 8 hours to complete this test. You will have an IV (needle in your vein) inserted for this testing by one of the trained nurses at the CRC. This will involve only one needle stick at the beginning of the test. One tube of blood equivalent to ½ tsp will be drawn initially to measure the level of norethindrone, LH, FSH, Estradiol, and progesterone in your blood. One tube of blood will then be drawn through the IV every hour after that for a total of 8 hours. The total amount of blood drawn for the entire test (9 tubes) is approximately 4.5 tsp. The total time for this visit is 8.5 hours.
- You will need to return your symptom diary for Days 1-8 at this visit
- Phase 1 only: You will be asked to estimate the start date of your next menstrual cycle and will set up a tentative date for your Day 1 Phase 2 visit. You will be dispensed study medication for the start of Phase 2 at this visit.
- The Day 8 visit is required for continued participation. If you do not attend your Day 8 visit in either Phase 1 or Phase 2 you will not be able to continue in the study.

Day 21- (Phase 1 and 2)

On Day 21 of your current menstrual cycle you will need to:

- Report to the CRC (Monday-Friday) between 7:30 and 8:00am *or* 35 Hope Drive (Saturday or Sunday) by 7:30am for a single blood draw of approximately ½ tsp.
- Return your symptom diary
- Day 21 of Phase 1 is the completion of Phase 1 only. You will start Phase 2 on Day 1-3 of your very next menstrual cycle exactly as described above.
- Day 21 of Phase 2 will be your final visit for the study.

What are my responsibilities if I take part in this research?
If you take part in this research, your major responsibilities will include:

- Take your prescribed medication exactly as instructed by the study doctor
- Attend all your study visits at the time instructed
- Attend your Day 8 PK visits for both Phases in order to continue in the study
- Complete your daily symptom surveys and return them on Day 8 and Day 21
- Let the study doctor know about all of your medications and/or any changes to your medications or any changes to your health during your participation in the study.
- Use an acceptable form of non-hormonal contraception such as condoms during your participation in the study
- If you agree, you may be contacted for future research

3. What are the risks and possible discomforts from being in this research study?

Instructions: The information in this section should be limited to the risks and discomforts related to the procedures done for research purposes, and should not include those related to research subject's routine medical care. Include the following information when applicable:

- Describe each of the following risks, if appropriate: physical risks, psychological risks, privacy risks, legal risks, social risks, economic risks.
- If known, describe the probability and magnitude of the risk.
- Use lay terms for the risks and discomforts for each procedure and/or drug.
- If possible, group the risks into categories such as expected, occasional, or rare and quantify these categories (e.g., 5 of 100 people who receive the drug).
- Be sure to list all side effects.
- **The use of a list or a table is strongly recommended.**
- Include risks of procedures that are done as part of follow-up that are not standard of care.
- If addressing risks for standard-of-care procedures, identify these as "risks you would have with or without the research."
- If the risk profile or any research-related interventions is not well known or the research involves investigational drugs or devices, include a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or becomes pregnant) that are currently unknown or unforseeable.
- If relevant, address the potential risks and precautions related to becoming pregnant or fathering a child.
- If the research includes women of child bearing potential or pregnant women, and the risk profile of any research interventions or interactions on embryos and fetuses is not well known, include a statement that the particular treatment or procedure may involve risks to the embryo or fetus, if the subject is or becomes pregnant, which are currently unknown or unforeseeable.
- If the research involves the use of an investigational device, add device malfunction as a possible risk if appropriate.
- If the research involves randomization, add the risks of randomization. For example: "You will be assigned to a treatment program by chance. The treatment you receive may prove to be less effective or to have more side effects than the other research treatment(s) or other available treatments."

Study Drug Risks:

Common side effects associated with norethindrone and norethindrone acetate:

- risk of unscheduled bleeding or spotting
- changes in menses
- increased prevalence of follicular ovarian cysts
- acne flare
- mood lability.

Rare but m~~M~~ore serious risks of norethindrone or norethindrone acetate include:

- cerebral embolism
- cerebral thrombosis
- Deep vein thrombosis, edema, pulmonary embolism
- Retinal thrombosis
- Depression
- Dizziness
- Fatigue
- Headache, migraine
- Insomnia (difficulty falling and /or staying asleep)
- Acne vulgaris, pruritis, urticaria, chloasma
- Hirsutism, hypermenorrhea
- Weight gain
- Nausea, vomiting
- Breakthrough bleeding
- Breast hypertrophy, decreased lactation, mastalgia
- Genital discharge
- Cholestatic jaundice, hepatitis, abnormal liver function tests
- Extremity pain, optic neuritis

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Allergic Reaction:

Even though it is an uncommon event, there is a risk of an allergic reaction to the study medications that may include hypersensitivity or anaphylaxis (hives, rash, swelling or difficulty breathing).
If you experience any of these symptoms stop taking your study medication and seek immediate medical help.

Risk of venipuncture (blood draws)

Blood draws may cause minor discomfort from a light pinch or pin prick when the sterile needle enters the skin. Occasionally, there will be pain, bleeding, and/or bruising at the site which will resolve itself in a few days. Also, on rare occasions, fainting will occur.
The risks of IV insertion include the risks of blood testing as described above and the chance of redness, soreness, or infection at the site of the IV insertion.

Unknown Risks:

In addition to the risks described above, there may be other unknown risks that we cannot predict associated with participating in this research.

Information for Women of Child Bearing Age:

There is risk of pregnancy if you are not using non-hormonal contraception during the study**.** If you should become pregnant at any time during your participation, you need to inform the study doctor right away. There is no adverse risk to the pregnancy with use of norethindrone or norethindrone acetate.

It is important that if you experience any side effects or other health issues during the study that you let the study doctors know immediately. If you are unsure about any of the study side effects, please ask the study doctor to explain them to you.

Risk of Loss of Confidentiality:

There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained as required by applicable law and to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

It is important that if you experience any side effects or other health issues during the study that you let the study doctors know immediately. If you are unsure about any of the study side effects, please ask the study doctor to explain them to you.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?

Instructions: Include the following information in this section:

- Reasonable expected benefits to the subject (if any)
- Do not overemphasize the benefits. Monetary reimbursement for participation is not a benefit.
- If benefits from participation may not continue after the research has ended, describe them here.
- Include the following for research involving prisoners: "Taking part in this research study will not improve your housing or correctional program assignments. Your taking part in this research study will not improve your chance of parole or release."
- If the research includes a placebo group, use the following text if appropriate, "There is no guarantee that you will benefit from this research. If you are assigned to the active study drug group, the possible benefits you may experience from this research study include <<list benefits>>. If you are assigned to the placebo group, you are not expected to benefit from this research."

You will not directly benefit from this research study.

4b. What are the possible benefits to others?

Instructions: Include the following information in this section:

- Address potential benefits to others (e.g., "The results of this research may guide the future treatment of… " or "Medical science may gain further understanding of… ").

The results of this research may guide the future development of a new form of birth control. Medical science may gain further understanding of the safety of using norethindrone acetate as birth control.

5. What other options are available instead of being in this research study?

Instructions: Include the following information in this section:

- Clarify that the potential subject may decline to participate in the research.
- Include any alternatives other than participating.
- For student subject pools, describe alternatives for course credit.
- For clinical trials, list alternative procedures or treatments, if any, that might be reasonable such as the standard of care and/or other research and/or the choice to receive supportive care. If applicable, include the important benefits and risks of these options.
- Indicate if the research treatment(s) can be obtained without enrolling in the research.

You may choose not to be in this research study and may decline to participate in the research study.

Before you decide if you want to be in this research, we will discuss the other choices that are available to you. We will tell you about the possible benefits and risks of these choices.

The therapy offered in this research is available to you for endometriosis without taking part in this research study

6. How long will I take part in this research study?

Instructions: Include the following information in this section:
- Explain the time commitment to complete this research study, e.g., "It will take you about 14 months to complete this research study. During this time, we will ask you to make 14 study visits."

If you agree to take part, it will take you about 3 months to complete this research study. During this time, we will ask you to make 19 study visits (including this visit) to complete this research study. This study will require approximately 30 hours of time commitment.

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

7a. What happens to the information collected for the research?

Instructions: Include the following information in this section:
- Explain how research data and/or tissue samples will be labeled and stored at PSH/PSU, and at any outside entities or institution.
- Include information about a Certificate of Confidentiality if applicable.
- Explain how any videos, audio recordings or photographs are labeled and secured, who has access to these materials and when they will be destroyed.
- Describe any limitations on confidentiality based on possible legal issues. For example, if the research team is likely to uncover abuse, neglect, or reportable diseases, explain that this information may be disclosed to appropriate authorities. For example, "We will use and disclose your research records when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. *{Include the following statement if the study does not have a Certificate of Confidentiality.}* Your research records can be opened by court order. Your records also may be provided in response to a subpoena or a legal request for the production of documents."

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed, and there may be situations where disclosure is required by law.

Your research records can be opened by court order. Your records also may be provided in response to a subpoena or a legal request for the production of documents.

In our research files at Penn State Health (PSH) and Penn State College of Medicine (PSU) we will include these identifiers: Your name, phone number, address, date of birth, medical record number, and study ID number

- Your research records will be labeled with your: study ID number, your initials, and dates of visits, and will be kept in a locked file in Dr. Sarah Horvath's research office.
- A list that matches your name with your code number will be kept in a locked file in Dr. Horvath's research office.
- Your research samples will be labeled with your study ID number, study phase, study visit number, and date the sample was collected. Your samples will be stored in secure freezers in the Clinical Research Center freezers in the locked and passcode protected Ob/Gyn research lab, C3607.
- A copy of this signed consent form will be included in your PSH medical record. This means that other PSH healthcare providers will know you are in this study.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

We will do our best to keep your participation in this research study confidential to the extent permitted by law. However, the following people/groups may check and copy records about this research.

- The Office for Human Research Protections in the U. S. Department of Health and Human Services
- The PSH/PSU Institutional Review Board (a committee that reviews and approves research studies) and
- The PSH/PSU Human Subjects Protection Office
- The PSH/PSU Research Quality Assurance Office
- The PSH/PSU Investigational Drug Services Pharmacy

7b. What will happen to my research information and/or samples after the study is completed?

- If data or specimens will be retained after the study for future research, explain where the data or specimens will be stored, who will have access to the data or specimens, and how long the data or specimens will be retained.
- If data will be submitted to central databases for use in future research studies, include this information in this section.
- If applicable, explain if clinically relevant research results will be disclosed to subjects and, if so, under what conditions.

Your information or samples that are collected as part of this research will not be used or distributed for future research studies, even if all of your identifiers are removed. Your samples that are collected for this research will not be retained and will be destroyed at the completion of their analysis.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will contact you to let you know what they have found.

7c. How will my identifiable health information be used?

Instructions: Include the following information in this section:

- Section 7c is mandatory if the research creates, obtains, uses, and/or discloses **protected health information** (PHI) about the research subjects.
- Do **not** include any part of Section 7c unless the research fits the above criteria.
- If the research involves prisoners, add the following statement: "If you are a prisoner, your medical records may also be given to officials and agencies within the criminal justice system when necessary and permitted by law."
- If applicable, describe any limitations on confidentiality based on possible legal issues. For example, if the research team is likely to uncover abuse, neglect, or reportable diseases, explain that this information may be disclosed to appropriate authorities. For example, "As with information contained in research records generally, we will use and disclose your identifiable health information when we are required to do so by law, such as for laws that require us to report child abuse or abuse of elderly or disabled adults. Additionally, unless this study is covered by a Certificate of Confidentiality, we will also comply with legal request or orders that require us to disclose your identifiable health information."

If you give your consent, health information that can be traced to you will be collected for this research study. In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so. We will use and disclose your information only as described in this form and in the PSH Privacy Notice.

The research team may use the following health information:

- Past, present, and future medical records, including identifiable information
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

The following people/groups may see, use, and share your identifiable health information:

- PSH/PSU research staff involved in this study
- The PSH/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare
- The PSH/PSU Human Research Protection Program (HRPP)
- The PSH/PSU Research Quality Assurance Office
- THe PSH/PSU Investigational Drug Services Pharmacy
- Non-research staff within PSH/PSU who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- Federal and state agencies (such as the U.S. Food and Drug Administration, the Office for Human Research Protections, the Department of Health and Human Services, the National Institutes of Health, and other U.S. or foreign government bodies that oversee or review research)
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Organizations that provide independent accreditation and oversight of hospitals and research

- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)

These groups may also review and/or copy your original PSH/PSU records while looking at the results of the research study. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information. We share your information only when we must, and we ask anyone who receives it from us to protect your privacy.

We may remove identifying information from your protected health information. Once we do this, the remaining information will not be subject to the privacy laws. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Because research is an ongoing process, your permission for the use, storage and sharing of your health information will continue indefinitely.

Your privacy rights:

- You have the right to refuse to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you will not be able to take part in this research study.
- You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing using the address on the front of this form. Once permission is withdrawn, you cannot continue to take part in the study.
- If you withdraw your permission, we will stop collecting health information about you for this study; we may continue to use and share your health information that we already have if it is necessary for safety and scientific soundness of the research study; and we will not be able to take back information that has already been used or shared with others.
- You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. However, you may not be allowed to see or copy certain health information that is a part of this research study. This is only for the period of the study. You will be allowed to see that information when the entire research study is complete.

8. What are the costs of taking part in this research study?

8a. What will I have to pay for if I take part in this research study?

Instructions: Include the following information in this section:

- If there are costs to the subject that may result from participation in the research, include a statement describing any additional costs associated with study participation.
- If applicable clarify that subjects will incur no extra expense for participation or clearly describe any costs to the subject, e.g., "There is no cost to you for taking part in this study."
- Explain how costs will be covered.
- If research tests/procedures are conducted in a clinical setting, provide specific information about which tests/procedures would be the responsibility of the subject and/or his/her insurance carrier and which tests/procedures are covered by the research study.
- If the sponsor is not paying for research tests or study treatments, add a sentence instructing subjects to check with their insurance carrier prior to deciding whether or not to participate.
- Include the following statements for research involving prisoners where there may be a need for follow-up examination or care after the end of participation. "If you are a prisoner and are released from jail before you finish this research study, you should take steps to get insurance or

Medicaid coverage. Regular office visits and standard treatment will be billed to you or your health insurance. You may continue in the research study after your release from prison. If you move out of the area, we will help you make arrangements to be followed by a physician."

For costs of tests and procedures that are only being done for the research study:

- You or your insurance provider will not have to pay for the study medications norethindrone acetate or norethindrone, while you take part in this study. You or your insurance provider will be responsible for the cost of your non hormonal birth control supplies.
- You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition.
- Examples of research-related tests and procedures that may be provided at no cost to you may include: allresearch blood draws for hormone and norethindrone levels. Talk to the study team about which items and procedures this includes.

For costs of medical services for care you would receive even if you were not in this research study:

- You and/or your insurance company will be responsible for the cost of your non-hormonal contraceptive supplies and any tests or procedures that you would receive even if you were not in this research.
- You and/or your insurance company will be billed for the costs of these routine tests and procedures in the usual manner.
- You will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage.
- You will be responsible for any charges not reimbursed by your insurance company.
- Some insurance companies may not pay for routine costs for people taking part in research studies. Before deciding to be in this research you should check with your insurance company to find out what they will pay for.

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?

Instructions: Include the following information in this section:

- Include the PSH mandatory wording for treatment for injury (see below).
- If the sponsor will cover costs of research-related injuries, add a statement regarding the sponsor's compensation for research-related injuries. This paragraph must be consistent with the subject-injury language in the sponsor contract.
- If there is no risk of injury to the subject, omit this section.

It is possible that you could develop complications or injuries as a result of being in this research study. If you experience a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If you experience a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and the principal investigator will arrange for medical treatment. You should also let any health care provider who treats you know that you are in a research study.

PSH/PSU compensation for injury

- There are no plans for PSH/PSU to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your insurance carrier or to you.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility.

When you sign this form you are not giving up any legal right to seek compensation for injury.

9. Will I be paid to take part in this research study?

Instructions: Include the following information in this section:

- Clearly describe any monetary compensation (total amount, average total amount, amount per visit, amount per hour, etc.) and whether payment is travel reimbursement, stipend, or a combination of the two.
- If subject is receiving reimbursement for travel only there is no need to collect SSN as this is not reported as income for tax purposes.
- If subject is paid by check the SSN must be collected. The consent form must state that the SSN will be collected and indicate that the SSN is needed for tax reporting purposes.
- Explain how compensation is pro-rated when a subject withdraws prior to completing the study. (This is mandatory to avoid possible undue influence associated with compensation.)
- If there is non-monetary compensation (e.g., small gift, gift certificate), describe that separately from the monetary compensation statement.
- Include the following statement for Department of Defense (DOD) research that targets military personnel where subjects will be paid. "Military personnel should check with their supervisor before accepting payment for participation in this research."

You will receive payment for your participation in this study based on the following schedule:

- $20 each for Days 1,2,3,4,5,6,7, and 21 for both phase 1 and 2
- $100 for each day 8 PK testing for both phase 1 and 2
- $20 extra for completing the entire study

You will receive a total of $540 at the completion of the entire study, both phase 1 and 2.

If you do not complete the study for any reason, you will be paid for only the visits you have completed. The payment will be provided by a Greenphire Clincard.

Greenphire Clincard

This reimbursement will be issued by an external company called Greenphire, which will issue your reimbursement. You will be issued a ClinCard, which is a debit card that your funds are loaded onto and can be used at your discretion. The research team will give Greenphire some personal information about you, as described below. Greenphire will only use your personal information to process this reimbursement and will not share it with anyone for any other purpose. Details of the debit card system are explained on an additional sheet. If you lose the card, you may be responsible for the replacement fee.

When a visit is completed, funds will be approved and loaded onto your card. The funds will be available within 2-3 business days. In order to assign a ClinCard to you and load funds onto

the ClinCard, Greenphire will need your Study/Subject ID, Name, Address, date of birth, and social security number

You will have the option to receive updates related to payment alerts via text message and/or email message. Standard text messaging rates will apply. In order to send you messages Greenphire will need your Mobile Phone Number and/or E-mail Address.

Payment received as compensation for participation in research is considered taxable income. If payments from Greenphire exceed $600 in any one calendar year, you will be required to provide your social security number so that Greenphire can file a 1099 (Miscellaneous Income) form on behalf of Penn State. Payment totals are calculated across all research participation at Penn State if you participate in multiple studies.

10. Who is paying for this research study?

Instructions: Include the following information in this section:
- Funding disclosure: Disclose what grantors, institution(s) (e.g., NIH) or companies are involved in the research through funding or grants. If none, say so.
- Conflict of Interest: Include information about any consultative relationships with the sponsor or financial or business interests the investigators may have related to this research.

Funds from the Department of Obstetrics and Gynecology at the Penn State College of Medicine will be used to support this research.

11. What are my rights if I take part in this research study?

Instructions: Include the following information in this section:
- If there are anticipated circumstances under which the subject's participation will be terminated by the investigator without regard to the subject's consent, include the anticipated circumstances under which participation may be terminated by the investigator without the subject's consent.
- If there are adverse consequences (physical, social, economic, legal, or psychological) of a subject's decision to withdraw from the research, include a statement describing the consequences of a subject's decision to withdraw from the research.
- If there are adverse consequences (physical, social, economic, legal, or psychological) of a subject's decision to withdraw from the research, explain procedures for the orderly termination of the research.
- For clinical studies, include a statement that any significant new findings that develop during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject, unless it is unlikely that there will be significant new findings during the course of the research which may relate to the subject's willingness to continue participation.
- Describe what will happen to data if a subject withdraws. For FDA-regulated research, see template text below.

Taking part in this research study is voluntary.
- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.

- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?

Instructions: Include the following information in this section:
- Clarify the subject's right to have questions answered.
- Indicate the person to contact in case of further questions about the research or to report a research-related injury.
- Indicate the person to contact for questions about subject rights and privacy issues.

Please call the head of the research study (principal investigator), Dr. Sarah Horvath at (717) 531-3503 if you:
- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the research protection advocate in the PSU Human Research Protection Program (HRPP) at (814) 865-1775 if you:
- Have questions regarding your rights as a person in a research study.
- Have concerns, complaints or general questions about the research.
- Have questions about your privacy and the use of your personal health information.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the Penn State College of Medicine's Clinical Research web site at http://med.psu.edu/clinical-research/faqs for:
- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the HRPP at (814) 865-1775.

A description of this clinical trial will be available on https://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative, provided the subject or subject representative an opportunity to discuss and consider whether or not to participate in the research, and have answered any questions about the research.

_____ _____ _____ _____

Signature of person who explained this research Date Time Printed Name
(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization
Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and authorize your information to be used and shared as described above.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name