OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

IRB#: 16291

Clinical Research Consent Summary

TITLE: **Improving the effectiveness of orally dosed emergency contraceptives in women of varying weights/BMIs – Part 2. UPA EC, BMI > or = 30mg/k^2 and weight > or =80kg and curtailed PK sampling**

PRINCIPAL INVESTIGATOR: Alison Edelman, MD, MPH 503-418-2585

You are being asked to join a research study. You do not have to join the study. Even if you decide to join now, you can change your mind later.

1. The purpose of this research study is to determine how well an emergency contraceptive pill containing ulipristal acetate works in women of higher weight and body mass index (BMI) as compared to women of lower weight and body mass index. This type of emergency contraceptive is currently available only with a prescription. It is the most effective form of oral emergency contraception. There is concern that it may be less effective in women of higher weights and BMI. We want to learn more about the drug level differences and how the ovary responds in women of differing BMI and weight. The overall goal of this research is to improve the effectiveness of contraception for women, no matter their weight or BMI.

2. The study drug is a tablet taken once by mouth.

3. The study drug is approved by the U.S. Food and Drug administration (FDA)

4. The National Institutes of Health is paying for the research study.

5. If you agree to be a part of this study, your participation will last 5 months. This will include up to 33 visits to the clinic at Oregon Health & Science University (OHSU). The majority of these visits will include a blood draw as well as a vaginal ultrasound and will last approximately 30 minutes but two visits will last longer (2 hours).

6. Samples and information collected during the study may be saved for future research.

CO1450

OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

IRB#: 16291

Clinical Research Consent and Authorization Form

TITLE: **Improving the effectiveness of orally dosed emergency contraceptives in women of varying weights/BMIs – Part 2. UPA EC, BMI > or = 30mg/k^2 and weight > or =80kg and full PK sampling**

PRINCIPAL INVESTIGATOR:	Alison Edelman, MD, MPH	503-418-2585
CO-INVESTIGATORS:	Paula Bednarek, MD, MPH	503-418-2585
	Mark Nichols, MD	503-418-2585
	Jeffrey Jensen, MD, MPH	503-418-2585
	Maureen Baldwin, MD	503-418-2585
	Eva Patil, MD	503-494-2685
	Leo Han, MD	503-494-2685
	Marci Messerle Forbes, FNP	503-494-6151
	Andrea O'Donnell, FNP	503-494-3131
	Maria Rodriguez, MD	503-494-2685
	Jacqueline Lamme, MD	503-494-2685
	Alyssa Colwill, MD	503-494-2685

FUNDED BY: National Institutes of Health

CONFLICT OF INTEREST: The investigators involved in this study have no conflict of interests related to this research.

PURPOSE: The purpose of this research study is to determine the differences in drug level and ovulation in women of varying weight and body mass index (BMI) using an emergency contraceptive pill containing ulipristal acetate.

This type of emergency contraceptive is currently available only with a prescription. It is the most effective form of oral emergency contraception. There is concern that it may be less effective in higher weights and BMI. We want to learn more about the drug level differences and how the ovary responds in women of differing BMI and weight. The overall goal of this research is to improve the effectiveness of contraception for women, no matter their weight or BMI.

CO1450

You have been invited to be in this research study because:

1) You are between the ages of 18 and 35
2) You are in good general health, have a body mass index (BMI) ≥30 and a weight ≥176 lbs and the study medication are safe for you to take.
3) You have regular menstrual cycles (between 21 and 35 days)
4) You have been proven to be ovulatory

5) You are willing to use condoms (if you are sexually active with a male partner), you are willing to not have sex with men during the study, or you have had a tubal ligation (or have a partner who has had a vasectomy) or you have a copper IUD.

If you agree to be a part of this study, your participation will last 5 months. This will include up to 33 visits to the clinic at Oregon Health & Science University (OHSU). The majority of these visits will include a blood draw as well as a vaginal ultrasound and will last approximately 30 minutes but two visits will last longer and will include a series of blood sampling (2 hours).

You will also be given information about being involved in another part of this study. If you agree to be involved in Part 1, you will be asked to sign a separate consent form. Your participation in Part 1 would include up to 13 additional visits over an additional 1 month of participation. Your total participation in both parts of the study would last approximately 6 months and included up to 46 visit.

You do not have to join the study. Even if you decide to join now, you can change your mind later.

We may have left over blood samples from you. We are asking your permission to store these samples indefinitely in a blood and data bank (also called a repository) so that they may be used and disclose in the future for research. We will not be performing genetic research on these samples.

We plan to enroll up to 80 women in the study at OHSU. By signing this consent form, you are consenting to the 2 longer two hour visits. Additionally, if you have not already participated in Part 1 of this study, you may be eligible to do so but will need to sign the Part 1 consent form.

PROCEDURES:

If you agree to be in this study, you will be asked to give your consent by signing this form. Participation in this study will consist of up to 30 visits. The details of these visits are described below. Participation in this study involves a time commitment so please consider whether this will fit into your schedule. Some study visits may need occur on weekends or holidays depending on your cycle.

At each of your study visits, study staff will review information regarding your last menstrual period, any medical concerns, and any medications you take as well as taking your vital signs. Your weight will be obtained at the beginning and end of the study. Prior to taking the study medication (UPA), a urine pregnancy test will be performed.

At the majority of your study visits, you will have a blood sample taken and undergo a vaginal probe ultrasound to monitor your ovarian activity, specifically the development of a follicle (a normal occurring cyst) and ovulation (the release of the egg). Starting on cycle day 7-8, you will have visits every other day until you are given the study medication. The medication will be given to you based on the size of your follicle (approximately cycle day 10). On the day you are given the medication, you will undergo more frequent blood sampling and must stay at the research unit for approximately 2 hours. Following this, you will have daily study visits for 7 days unless evidence of ovulation occurs earlier. You will have no visits for the remainder of this menstrual cycle but will be in contact with the study staff to notify them when your menstrual period starts. This will be the end of your study participation.

V0 Screening visit (Luteal phase)
At this visit, study staff will go over the consent form with you. You will have time to ask any questions you may have. After you have agreed to be in the study, study staff will take your complete medical and gynecologic history, including smoking history, documentation of

menstrual cycle history, current sexual activity and contraceptive method with dates of use, and information about pregnancies and childbirths. Study staff will also ask questions about your education, ethnicity/race, marital status, and alcohol or drug use. Expect the screening visit to take approximately 2 hours.

- A general physical examination (including height, weight and body mass index, a ratio of your weight to height) will be performed. Blood pressure (BP) and pulse will be measured.
- Blood will be drawn from a vein in your arm (about 2 teaspoons) to check your hormone (progesterone) levels. This blood test should occur between days 18-25 of your menstrual cycle. If this visit does not fall within that window, we will ask you to return to the clinic for this blood draw.

Of note, if you already participated in Part 1 of this study, then you do not need to repeat this visit unless more than 12 months have passed.

Cycle 1 V1-V6 (Control cycle)
Starting on day 7-8 of your menstrual cycle, you will be seen every other day until documentation of an enlarged follicle where you will then be followed daily for 7 days unless evidence of ovulation occurs earlier or no development of an ovulatory follicle occurs. You will receive no study drug in this cycle, we are only monitoring how your normal cycle acts. If no evidence of an ovulatory follicle occurs, this will be the end of your study participation.

At these visits, study staff will:

- Take vital signs
- Get urine for a pregnancy test (only at the visit where you receive study drug)
- Update your medical and gynecological history, medications and allergies
- Take blood samples to test your hormone levels. A total of 2 tablespoons of blood will be collected at each visit.
- Perform a transvaginal ultrasound (TVUS) to examine your ovaries and monitor signs of ovulation. Before the procedure, you will be asked to empty your bladder. For the vaginal ultrasound, the tip of a small, thin ultrasound instrument (probe) is lubricated with a small amount of gel and inserted in your vagina. Only two to three inches of the instrument are inserted into the vagina. Ultrasound imaging uses sound waves to produce pictures of the inside of the uterus and ovaries. The ultrasound pictures will be shown on a computer monitor. The provider will be looking at the thickness of the endometrium (lining of the womb), number of ovarian follicles (fluid filled sacs located just beneath the ovary's surface that contain the immature eggs), and whether you have ovulated recently or are about to ovulate (release an egg).

Each study visit will take approximately 30 minutes to complete.

Cycle 2 V1-V13 (Treatment cycle)
Starting on day 7-8 of your menstrual cycle, you will be seen every other day until documentation of an enlarged follicle where you will then take study drug. You will be followed daily for 7 days from the time you take the study drug unless evidence of ovulation occurs earlier or no development of an ovulatory follicle occurs. If no evidence of an ovulatory follicle occurs, this will be the end of your study participation.

Expect these visits to take approximately 30 minutes. At these visits, study staff will:

- Take vital signs
- Get urine for a pregnancy test (only at the visit where you receive study drug)
- Update your medical and gynecological history, medications and allergies

- Take blood samples to test your hormone levels that help determine ovulation. At total of 2 tablespoon of blood will be collected at each visit.
- Perform a transvaginal ultrasound (TVUS) to examine your ovaries and monitor signs of ovulation.

On the day that you take the study drug, you will need to stay at the research unit for 2 hours to obtain a series of blood draws. At this visit, study staff will:

- Take vital signs
- Get urine for a pregnancy test (only at the visit where you receive study drug)
- Update your medical and gynecological history, medications and allergies
- Perform a transvaginal ultrasound (TVUS) to examine your ovaries and monitor signs of ovulation.
- Place an I.V. (intravenous access). You may also choose "single stick" venipuncture for each blood draw.
- Provide you with study drug to take.

Draw blood to test for study drug levels at 0.5, 1, 1.5, 24, 48, 72, 96, and 120 hours after the study drug has been taken. A total of 4 tablespoons of blood will be collected in total.

Cycle 3 Washout cycle

No study visits will occur during this menstrual cycle but you will remain in contact with study staff, likely 1-2 times, by telephone or email for scheduling purposes and to discuss any health changes you are experiencing.

Cycle 4 V1-V13 (Treatment cycle)

Starting on day 7-8 of your menstrual cycle, you will be seen every other day until documentation of an enlarged follicle where you will then take study drug. You will be followed daily for 7 days from the time you take the study drug unless evidence of ovulation occurs earlier or no development of an ovulatory follicle occurs. If no evidence of an ovulatory follicle occurs, this will be the end of your study participation.

Expect these visits to take approximately 30 minutes. At these visits, study staff will:

- Take vital signs
- Get urine for a pregnancy test (only at the visit where you receive study drug)
- Update your medical and gynecological history, medications and allergies
- Take blood samples to test your hormone levels that help determine ovulation. At total of 2 tablespoon of blood will be collected at each visit.
- Perform a transvaginal ultrasound (TVUS) to examine your ovaries and monitor signs of ovulation.

On the day that you take the study drug, you will need to stay at the research unit for 2 hours to obtain a series of blood draws. At this visit, study staff will:

- Take vital signs
- Get urine for a pregnancy test (only at the visit where you receive study drug)
- Update your medical and gynecological history, medications and allergies
- Perform a transvaginal ultrasound (TVUS) to examine your ovaries and monitor signs of ovulation.
- Place an I.V. (intravenous access). You may also choose "single stick" venipuncture for each blood draw.
- Provide you with study drug to take.

Draw blood to test for study drug levels at **0.5, 1, 1.5, 24, 48, 72, 96, and 120** hours after the study drug has been taken. A total of 4 tablespoons of blood will be collected in total.

	Screening Visit 0	Control Cycle Starting Cycle 1 day 7-8	Treatment Cycle Starting Cycle 2 day 7-8	Washout Cycle 3	Treatment Cycle Starting Cycle 4 day 7-8
Consent, Screening tests and medical history	X				
Phone or email contact				X	
Blood draw	X	X	X		X
Ultrasound		X	X		X
Study Medication & urine pregnancy test			X*		X*
Longer series of blood draws (over 5 hours)			X**		X**
Total time	1 hour	30min/visit	30 min/visit for all but 1 visit which will be 2 hours		30 min/visit for all but 1 visit which will be 2 hours

*Visit number study medication will be taken depends on ultrasound findings.
**The study visit on the day the study medication is taken will last 1 hours

In the future, your blood sample and/or information may be used by the investigators in this research for other research studies. The samples and information will be labeled as described in the **CONFIDENTIALITY** section.

ACCESS TO YOUR TEST RESULTS

We do not plan to share your research test results with you or your primary care provider. However, if we discover information that is important for your health care, either in this study or in the future, we will contact you and ask if you want to know the results. If you choose to receive the results, you may need to have the test repeated in a non-research laboratory. You may learn information about your health that is upsetting or that impacts your future birth control choices or your future fertility.

RISKS AND DISCOMFORTS:

Ulipristal Acetate (UPA)

All medicines may cause side effects, but many people have no side effects or minor side effects. The use of study drug (UPA) can affect the timing and length of your next menstrual period. Other less common side effects include:

- Headache (18%)
- Nausea (13%)
- Abdominal Pain (8-15%)
- Menstrual cramping (7-13%)
- Bleeding/spotting between period (9%)
- Fatigue (6%)
- Dizziness (5%)

As with any drug, allergic reactions may occur due to the study drug. These may range from mild to severe, can be life-threatening/fatal and include hives, difficulty breathing, and swelling of your face, lips, tongue, or throat. You should seek emergency medical treatment should you experience an allergic reaction.

If you are nursing an infant or you are pregnant now, you must not be in the study. The study medication does not harm a pregnancy or a nursing infant but both of these states could

adversely impact the main study outcomes. If you are at risk for pregnancy, the investigator will discuss what types of birth control are acceptable for use during this study. You will have to use contraception or not be at risk for pregnancy the entire time you are in this study. If you become pregnant during the research study, please tell the investigator and your doctor immediately.

There are several drugs (prescription and non-prescription) that may change the drug level of the study medication which would interfere with the purpose of this study. The investigator will carefully review all of the drugs you are taking before giving you the study drug. If any other health care provider prescribes any new drug(s), vitamins, or supplements for you while you are in this study, please tell the investigator before you take the new drug. You could also have that provider talk to the investigator before prescribing the new drug. Do not take any new over-the-counter drugs or supplements while you are in this study unless you first check with the investigator.

Blood Draws

Blood samples are taken at each visit to evaluate your hormone levels and at one of the visits, we plan to draw a series of blood samples. Blood draws will be performed through a single stick venipuncture at most visits except the visit where several blood draws are needed. At that visit, an IV will be used to draw your blood unless you prefer venipuncture. There is a small chance that the needle will cause bleeding, a bruise, an infection, or fainting. It is unlikely that this amount of blood removal at one time or over the period of the study will result in low blood levels or symptoms.

Transvaginal Ultrasound

There are no known harmful effects of a vaginal probe ultrasound. You may experience slight vaginal discomfort.

BENEFITS:

You will not benefit from being in this study. However, by serving as a subject, you may help us learn how to benefit patients in the future.

ALTERNATIVES:

You may choose not to be in this study.

CONFIDENTIALITY

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy.

We will create and collect health information about you as described in the Purpose and Procedures sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study and store in the Women's Health Research Unit repository (IRB# 6748) for possible future research.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The Food and Drug Administration
- The Office for Human Research Protections, a federal agency that oversees research involving humans
- The National Center for Research Resources
- Greenphire Clincard – debit card service

Those listed above may also be permitted to review and copy your records, including your medical records.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

Blood samples or information from this study may be shared with other investigators for future research studies. All identifying information about you will be removed from the samples before they are released to any other investigators.

We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

COMMERCIAL DEVELOPMENT:
Samples and information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

COSTS:
There will be no cost to you or your insurance company to participate in this study. You will be compensated up to $1720 depending on the number of study visits you complete. The compensation amounts are as follows:

- Screening visit (all participants): $20
- Routine study visits without serial blood draws: $50
- Study visit with serial blood draws: $100

Payment received as compensation for participation in research is considered taxable income for a research subject. If payments are more than $600 in any one calendar year, OHSU is required to report this information to the Internal Revenue Service (IRS). Research subject payments exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the research subject and a copy will be sent to the IRS.

You may receive payment via a debit card or check. If you receive payments using a debit card, details on how to use the card are detailed in the included card member agreement, as well as on a separate FAQ sheet. There may be fees (for example, if the card is inactive for more than six months), explained in those documents. Any fees will be deducted from the balance on your card.

We may request your social security number in order to process any payments for participation.

LIABILITY:
If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact Dr. Alison Edelman at 503-418-2585 or call 503-494-8311 and ask the operator to have the operator page her.

If you are injured or harmed by the study procedures or study drug you will be treated. OHSU and the funder do not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

PARTICIPATION:
If you have any questions, concerns, or complaints regarding this study now or in the future, contact Dr. Alison Edelman at 503-418-2585 or call 503-494-8311 and ask the operator to have the operator page her.

This research is being overseen by an Institutional Review Board ("IRB"). You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Alison Edelman, MD, MPH
3181 SW Sam Jackson, UHN 50
Portland, OR 97239
edelmana@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

If in the future you decide you no longer want to participate in this research, we will remove your name and any other identifiers from your samples and information, but the material will not be destroyed and we will continue to use it for research.

You may be removed from the study if investigator or funder stops the study, you become pregnant, you develop serious side effects or cannot tolerate the study medication, if we are unable to consistently perform the study procedures on you (e.g. cannot obtain blood), or you do not follow study instructions.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

A description of this clinical trial will be available on http://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.

The participation of OHSU students or employees in OHSU research is completely voluntary and you are free to choose not to serve as a research subject in this protocol for any reason. If you do elect to participate in this study, you may withdraw from the study at any time without affecting your relationship with OHSU, the investigator, the investigator's department, or your grade in any course.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

Subject Printed Name	Subject Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date