UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

PALEOLITHIC VS HEALTHY ADA DIETS FOR TREATMENT OF POLYCYSTIC OVARIAN SYNDROME (PCOS)

This is a medical research study. Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctors, Heather Huddleston, Umesh Masharani or Lynda Frassetto, M.D. You are being asked to take part in this study because you are a nonsmoking woman with PCOS, taking no medications, and you are between the ages of 18-40 years old.

Why is this study being done?

PCOS is a syndrome, which includes elevated androgen levels, irregular menstrual cycles and insulin resistance. Standard treatments, which include weight loss and medications to improve insulin secretion are only partly successful, and may require that young women take medications for decades.

The study investigators have been evaluating the effects of specific diets on insulin resistance in healthy volunteers and subjects with type 2 diabetes, and have found that subjects with insulin resistance seem to respond particularly well to these diet regimens.

Volunteers with PCOS are being asked to participate to see if following these diets can help regularize your menstrual cycles. The results of this study may help improve fertility treatments for women with PCOS.

Who pays for this study?

This study will be funded by donations to the project. None of the study investigators have financial interests related to the study.

How many people will take part in this study?

About 32 people will take part in this study.

What will happen if you take part in this research study?

Study locations: PCOS clinic at UCSF Mission Bay campus, and the Clinical Research Centers (CRC) at 400 Parnassus Ave at the Parnassus campus.

Before you begin the main part of the study...

You will need to have an appointment to be evaluated at the PCOS clinic at UCSF Mission Bay campus. Dr. Huddleston or one of her colleagues will discuss the study with you. You will need to sign the informed consent before you can be part of the study. You may take the consent form home and send it back to us by mail if you want or complete it online via Docusign. The address to send it back to is:

Heather Huddleston, MD
UCSF campus box 0916
499 Illinois St, San Francisco CA 94158

As part of the routine evaluation, you will have:

- **Medical History:** You will have a medical history taken, similar to those done for regular medical care. You will also be asked about ongoing alcohol and illegal drug use.
- **Physical exam:** You will have a physical examination, similar to those done for regular medical care.
- **Urine sample:** You will be asked to give a urine sample for laboratory tests.
- **Blood drawing (venipuncture):** You will be asked to give a blood sample for laboratory tests. Approximately 3 tablespoons of blood will be drawn by inserting a needle into a vein in your arm for these tests.
- **Pregnancy:** If you are already pregnant, you may not participate in this study.
- **Ovarian ultrasound:** A baseline vaginal ultrasound to count the number and size of follicles in the ovaries. If you have had an ultrasound in the previous 4 months before this study, and can bring the results to Dr. Huddleston, that would also be acceptable.

During the main part of the study...

If the screening history, exams and tests show that you can continue to be in the study, and you choose to take part, then you will be started on a Healthy ADA diet for 2 weeks. After the two weeks, you will be randomized to either a Paleolithic diet or a Healthy ADA diet.

Diets:

A. Healthy ADA diet: The Healthy ADA recommended diet includes meat, fish, low fat dairy, whole grains, legumes, fruits and vegetables. There is no restriction on caffeine intake. There is no specific limitation on calories. Artificial sweeteners are allowed.
B. Paleolithic type diet: The Paleo diet includes meat, fish, fruits, vegetables and nuts. There is no restriction on caffeine intake. The only sugars that are allowed are honey and artificial sweeteners. This diet excludes all dairy products, all grains, and legumes. It also excludes any foods that must be cooked to be safely edible, e.g., potatoes, cassava root, red kidney beans. There is no calorie limitation.

You will be randomized to either the Healthy ADA diet or the Paleo diet for 4 months. At the end of the 4 months, you can choose to continue your participation further or stop your participation in the study. If you are interested in continuing your participation in the study and on the ADA diet, you can be switched over to the Paleo diet. If you decide to do this, you will be on the Paleo diet for 4 months. If you are already on the Paleo diet, you have the option of continuing another 4 months.

Nutrition help:

Diet information: You will get a lot of information about your diet. This will include written materials about allowable foods, websites with specific information, recipes, grocery stores and restaurants in the Bay area that can

Diet coaches: Our study assistants have received college level training in nutrition, and will be helping you adapt your eating habits to the diets. This will include giving advice about foods, how to follow meal plans, where to go grocery shopping, eating out, and answering any questions you have. At the beginning of each diet phase, you will get calls at least every 1-2 days to see how you are doing, and work out any problems you may be having with the diet. As the study progresses, the assistants will contact you at least once a week.

Social media: We will be sending you E-questions, either by text or email (whichever you prefer), asking about adherence to the diets and food cravings. These will be sent to you once every 1-2 weeks. Our study assistants will also be communicating with you via your chosen form of communication. This can include texting, emails, twitter, facebook, or you may choose another format on which you and your study assistant can work together.

We will also offer a telephone sessions where the investigators and the diet coaches will answer questions, help with concerns and discuss how to better comply with the study requirements.

Menstrual cycles: You will be asked to keep track of your menstrual cycles for the entire duration of the study. This includes start and stop dates.

Ovarian ultrasounds: You will have an ovarian ultrasound at basline and 16 weeks during the study. This will allow us to follow follicle size and number during the study. If you decide to do the optional additional 4 months, you will have another ovarian ultrasound at 32 weeks.

Body composition: You will have measurements of body composition done during the study. This includes measuring your height and weight, hip and waist circumference, and the amount of fat and muscle, which is done by bioimpedance spectroscopy (BIS). To do the BIS test, you must be come in having not eaten overnight. The BIS test takes about 5 minutes, is not painful, and does not use radiation. These occur at baseline and 16 weeks, and if you opt for the additional 4 months, at 32 weeks.

Questionnaires: You will be asked to fill out eating related and psychological health and behavior questionnaires. These include food craving, stress and emotional eating surveys, and quality of life, depression, stress, physical activity and sleep questionnaires. You will fill out various questionnaires during the course of the study at weeks -2, 0, 4, 8, and 16. If you opt to do the additional 4 months, they will occur at weeks 24 and 32.

What amount of blood will you have collected in the study?

The total amount of blood drawn during the entire study is about 4 tablespoons at weeks 0, 8, and 16, for a total of about 200 mL of blood over the 16 week period. This is less blood than what you would lose by donating a unit of blood. If you opt to do the additional 4 months, you would have 4 tablespoons of blood drawn at weeks 24 and 32. The total amount of blood for the entire 32 week period is about 300 mL of blood.

How long will you be in the study?

Participation in the study will be over a 18 week period. The time required for this study will include approximately:

Study Time Commitment
Screening: at PCOS clinic (2-3 hours)
Prior to starting: questionnaires, blood draws, body composition measures, diet information/advice (about 2 hours)
First 2-3 weeks of starting one of the study diets: Daily to 2-3 times/week communications with study assistants for diet review and problem solving (5-10 minutes/episode)
Several times per week during first 4 weeks; every 2 weeks until week 16 (or possibly 32): E-questionnaires (1-2 minutes)
Monthly: review of menstrual cycle and weight measurements (5-10 minutes)
At week 8 (and possibly 24): blood draws, questionnaires (30-60 minutes)
At week 16 (and possibly 32): Ovarian ultrasound, body composition, blood draws, questionnaires (2 hours)

Can you stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can you expect from being in the study?

There are very few risks to being in this study. You should talk to your study doctor about any side effects you experience while taking part in the study.

Risk and side effects include…

- **Diets:** Both of these diets may be different from what you ate before. Changing diet habits can be stressful.
- **Ovarian ultrasounds:** Vaginal ultrasounds can be uncomfortable.
- **BIS:** You must come in fasting for the BIS.
- **Blood drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection.
- **Questionnaires:** Questionnaires ask about your personal life and behaviors. This may make you uncomfortable.
- **Inconvenience:** There is inconvenience to being in any study. This includes time spent coming in for study visits and doing study procedures.

What do we do to prevent risks from happening?

- **Diets:** You will receive individualized counseling from trained assistants to help you adapt to the study diets.

- **Ovarian ultrasounds:** These ultrasounds are done by highly trained personnel with many years of experience in a specialized clinic. You should tell the doctor or technician if the ultrasounds are uncomfortable.
- **BIS:** BIS does not use radiation, is not painful, and takes about 5 minutes.
- **Blood drawing (venipuncture) risks:** Blood draws are done by highly trained personnel with many years of experience.
- **Questionnaires:** All of the information is confidential, and protected by the university IT systems.
- **Inconvenience:** There is inconvenience to being in any study. This includes time spent coming in for study visits and doing study procedures.

Are there benefits to taking part in the study?

There may be a benefit to you if the study interventions help improve menstrual cycle regularity or insulin resistance.

What other choices do I have if I do not take part in this study?

Participation in this study is entirely voluntary and subjects can choose not to participate. Subjects have the right to withdraw at any time.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record and all of the electronic communication information is kept private. Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible.

A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

E-questions via text message or email address are sent from a secure e-messaging system created by Michael Cohn, PhD, a researcher at the UCSF Osher Center for Integrative Medicine. This program sends links to the survey questions at pre-planned times phone and/or computer. The data is identified by a randomly-generated code that cannot be used to obtain your study ID or any identifying information. Data will be identifiable only by study ID number after a response has been received and transferred to our secure server. The website on which you respond does not request or display any identifying information. Communication with the website is protected with a 2048-bit Secure Sockets Layer (SSL) encryption, which is the industry standard for financial and medical data. Added data will be stored on a secure, encrypted server accessible only by study personnel.

In this study you will be asked about illegal drug use. The researchers will keep information about you as confidential as possible, but complete confidentiality cannot be guaranteed. On rare occasions, research records have been subpoenaed by a court.

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- UCSF's Committee on Human Research and
- The CTSI Clinical Research Center.

What are the costs of taking part in this study?

You will not be charged for any of the study activities or study medications.

Will I be paid for taking part in this study?

In return for your time and effort, the study will pay $10.00 for each blood draw visit and parking at UCSF Parnassus.

A check will be mailed to you about 6 weeks after your participation in the study has ended. You will have to provide your name, address and social security number in order to receive payment by check. As payments for research participation in excess of $600 per calendar year are reportable to the IRS, you will have to pay taxes on payments if you receive more than $600 in the year by participating in other research studies. If you drive and park in the UCSF Public Parking for your Screening Visit or Inpatient Study Days you may also receive parking vouchers to cover the cost of parking.

What happens if you are injured because you took part in this study?

It is important that you tell your study doctors, Dr. Heather Huddleston at 415 353-3040, Umesh Masharani at 415 353-2664 or Lynda Frassetto at 415 476-6143, if you feel that you have been injured because of taking part in this study.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, treatment will be available. The costs of the treatment may be covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

What are my rights if you take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer your questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctors, Dr. Heather Huddleston at 415 353-3040, Umesh Masharani at 415 353-2664 or Lynda Frassetto at 415 476-6143.

For questions about your rights while taking part in this study, call the office of the **Committee on Human Research**, UCSF's Institutional Review Board (a group of people who review the research to protect your rights) at **415-476-1814***.*

STORAGE OF BLOOD FOR FUTURE RESEARCH

Why is blood being stored?

By storing samples of your blood, the researchers will be able to perform future research that may help them understand the results of this study.

What will be done if you agree to have blood stored?

Several tablespoons of blood will be obtained at each of your study visits. The samples will be kept for research purposes only. The blood samples will be frozen and stored at the study doctor's laboratory. You will not be told the results of any testing or any future research.

What risks are involved with donating specimens for research?

Confidentiality: Donating specimens may involve a loss of privacy, but information about you will be handled as confidentially as possible. Your name will not be used in any published reports from research performed using your specimen. The researchers involved in this study will have access to information about you but they will not release any identifying information about you to researchers using your specimen. The UCSF Committee on Human Research and other University of California personnel also may see information about you to check on the stored specimens. Once your health information is disclosed to the research team it is not protected under the Health Information Portability and Accountability Act (HIPAA). The investigators of this study will continue to protect your personally identifiable health information as described in this consent form. The University of California complies with the requirements of HIPAA and its privacy regulations, and with all other applicable laws that protect the confidentiality of your health information.

What are the benefits of donating specimens for research?

There will be no direct benefit to you from allowing your specimen to be used for research. However, we hope we will learn something that will help in the treatment of future patients.

What financial issues should you consider before donating?

You will not be charged for donating and storing your specimen. You will not be paid for donating your specimen. If any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

How do we have your specimens removed from storage at a later time?

You may withdraw your consent to have your blood stored at any time by writing a letter to Dr. Lynda Frassetto (UCSF, campus box 0126, 505 Parnassus Ave, San Francisco, CA 94143.

What other choices do you have if you do not donate blood for storage?

Deciding to donate is your choice. You may choose either to take part or not to take part in this part of study. No matter what decision you make, there will be no penalty to you and you will still be able to take part in the main study.

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Consent for Storage of Blood

Please read the sentence below and think about your choice. After reading, put your initials in the "Yes" or "No" box.

No matter what you decide to do, it will not affect your care.

My urine may be taken and stored for future research.

YES	*NO*

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CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

Someone may contact me in the future to ask me to take part in more research.

YES	*NO*

If you wish to participate in this study, you should sign below. You will also be asked to sign a separate form authorizing access, use, creation and disclosure of health information about you.

_____ _____

Date Participant's Signature for Consent

_____ _____

Date Person Obtaining Consent