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INSTITUTIONAL REVIEW BOARD
(Federalwide Assurance # 00004028)

04-Apr-2012

Kurt Barnhart
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HUP
3400 Spruce St
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Attn: Alka Shaunik
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PRINCIPAL INVESTIGATOR : Kurt Barnhart
TITLE : Serum and Plasma Bank for the Development of Novel Ectopic Pregnancy Biomarkers
SPONSORING AGENCY : National Institutes of Health
PROTOCOL # : 806587
REVIEW BOARD : IRB #2

Dear Dr. Kurt Barnhart:

The above referenced protocol was reviewed and re-approved by Dr. Emma Meagher, Executive Chair of the IRB (or her authorized designee), using the expedited procedure set forth in 45 CFR 46.110(b) (9), on 04-Apr-2012.

Approval by the IRB does not necessarily constitute authorization to initiate the conduct of a human subject research study. You are responsible for obtaining any relevant committee approvals.

This approval is for the period 04-Apr-2012 to 03-Apr-2013.

The following documents were included in this review:

- IRB Continuing Review Form, signed and dated 03/28/12
- Cover Letter, dated 03/28/12

In addition, the documents noted below were submitted as a modification to the above-referenced protocol and were reviewed by Dr. Emma Meagher, Executive Chair of the IRB (or her authorized designee) using the expedited procedure set forth in 45 CFR 46.110 and approved on 04-Apr-2012.

- Revised Combined Informed Consent & HIPAA Authorization Form, Version 3, dated 03/28/12
- Summary of Changes, dated 03/28/12
- Revised Study Protocol, Amended: 03/28/12
- Revised IRB Protocol Summary, dated 02/07/08

When enrolling subjects at a site covered by the University of Pennsylvania's IRB, a copy of the IRB approved informed consent form with the IRB approved from/to stamp must be used unless a waiver of written documentation of consent has been granted.

If you have any questions about the information in this letter, please contact the IRB administrative staff. Contact information is available at our website: <http://www.upenn.edu/regulatoryaffairs>.

Thank you for your cooperation.

Sincerely,

IRB Administrator

Research Subject Informed Consent and HIPAA Authorization Form

Protocol Title:	Serum and Plasma Bank for the Development of Novel Ectopic Pregnancy Biomarkers
Principal Investigator:	Kurt T. Barnhart, MD, MSCE 3701 Market St., Suite 810, Philadelphia, PA 19104-5509 215-662-7727
Emergency Contact:	Infertility Fellow on Call 215-662-6100

If you are reading this document to decide whether your child should participate in this study, the terms “you/your” refer to your child.

Why am I being asked to volunteer?

You are being invited to participate in a research study because you are pregnant and are having pain and/or bleeding. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

The purpose of this research is to take and store blood and urine samples from women who come to a doctor with pain and/or bleeding in early pregnancy. These symptoms may indicate that there is a problem with the pregnancy, but can also occur in a pregnancy that is healthy and growing. When a woman has these symptoms, doctors do many tests (including blood tests and ultrasounds) to try to determine how far along the pregnancy is, whether it is healthy, and most importantly whether the pregnancy is growing in the right place. It can take several visits and tests for the doctors to make this diagnosis. If the pregnancy is growing outside the uterus (called an “ectopic pregnancy” or a “tubal pregnancy”) it is dangerous for the mother and doctors need to treat it right away. It can be treated with a surgery to remove the ectopic pregnancy (salpingostomy), surgery to remove the fallopian tube the ectopic pregnancy is in (salpingectomy), or with a drug called methotrexate.

The doctors running this research project are trying to see if there are substances (biomarkers) in the blood or urine of a pregnant woman that can tell whether the pregnancy is an ectopic pregnancy or not. To do this, they need to study blood and urine from women who have an ectopic pregnancy, women who are having a miscarriage, and women with a healthy growing pregnancy. The doctors are also trying to see if there are any biomarkers that can tell whether a woman with an ectopic pregnancy is a good candidate to be treated with methotrexate, rather than surgery.

How long will I be in the study? How many other people will be in the study?

If you participate only in the main study, your participation will only involve taking blood and urine samples today. If you choose to participate in the substudy, your participation will last until the doctors taking care of you have determined whether you have an ectopic pregnancy, a miscarriage, or a healthy growing pregnancy. If you have an ectopic pregnancy and you and your doctor decide to treat it with methotrexate, your participation may continue until your treatment is over.

Women will be approached for samples over a three-year period. However, the samples will be stored and tested for much longer.

Women total will have their blood taken and urine collected for the main study across the three participating medical centers..

What am I being asked to do?

Today you will have two tubes of blood (about 12ml or 2½ teaspoons) drawn and will donate a urine specimen for the study. We will try to have this blood drawn at the same time as you have having blood drawn for other tests related to your clinical care. However, this may not be possible in every case. We may also take some blood that is left over from the blood that was drawn for tests related to your clinical care. This blood is left over and would have been discarded; your participation in this study will not affect the tests your doctor has ordered for your clinical care.

You may also be asked to participate in a substudy. To be eligible to participate in the substudy, you must need to come back for one or more visits for further tests so that your doctor can determine whether you have an ectopic pregnancy, a miscarriage, or a healthy growing pregnancy; or if you were treated with methotrexate, for further tests to determine whether it is working. For the substudy we will draw two extra tubes of blood and collect urine each time you come back for a visit, and may collect leftover blood as explained above along with a urine specimen. If you are not scheduled to come back for a visit for more than 7 days, we may ask you to make a separate visit to draw blood and collect urine for the study. If you are asked to make a separate visit for the study, we will draw two tubes of blood (about 12ml or 2½ teaspoons) at each of those visits.

Serum and plasma (parts of the blood) will be separated from the blood, and will be frozen and stored for later analysis. These samples will be sent to the Laboratory of David Speicher (Wistar Institute, Philadelphia PA) for analysis. The serum and plasma can be stored this way indefinitely.

Certain information about you will be collected as well: your age, race and ethnicity, the number of ectopic pregnancies you have had in the past, the results of an hCG (human chorionic gonadotropin, the “pregnancy hormone”) test that was done as part of your clinical care, how far along your doctor thinks your pregnancy is, your diagnosis (ectopic pregnancy, miscarriage, or healthy growing pregnancy) once known, and how your doctor made the diagnosis. If you choose to participate in the substudy, we will also track the number of days in between each sample that you give.

What are the possible risks or discomforts?

The risks of having your blood drawn include pain, bruising or infection at the site of the needle puncture. Rarely, some people may get dizzy or faint. We will try to reduce the risks by collecting the samples for the research at the same time you are having your blood drawn as part of your clinical care. The risks of having repeated blood draws are small, because the volume of blood being drawn each time (12ml or 2½ teaspoons) is small, and because you were going to have blood drawn as part of your clinical care. It is not anticipated that there will be any additional risks from donating a urine specimen.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You are not expected to benefit from your participation in this study. **It is important for you to know that the blood or urine collected for this study is not going to be tested immediately. The results of the tests will not be given to your doctor, and will not be used as part of your clinical care.** While the doctors conducting this study hope that the information learned may help other women in the future, by developing a new test, they do not know enough now about what any results mean.

What other choices do I have if I do not participate?

You do not have to participate in this study. You can have your blood drawn for your clinical care only and not used for research.

Will I be paid for being in this study?

There is no compensation for your participation.

Will I have to pay for anything?

You do not have to pay to have your blood drawn for this study, for the storage of the samples, or for the tests to be done for the research.

You and/or your health insurance will be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study. This includes the clinical tests to determine whether you have an ectopic pregnancy, a miscarriage, or a growing pregnancy, and any treatments for your condition once diagnosed.

What happens if I am injured or hurt during the study?

If you have a medical emergency during the study you should go to the nearest emergency room. You may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event that you are hurt or injured as a result of participation in this research study, please contact the investigator listed on page one of this form.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise offered from the University of Pennsylvania. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, or the study Sponsor, without your consent because:

- Your doctor feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, or the study Principal Investigator, has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records.

Please refer to the separate "HIPAA Privacy Authorization" document that explains more specifically how your personal information will be protected.

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

What personal health information is collected and used in this study, and might also be disclosed?

The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name, address, telephone number, date of birth
- Personal demographics and medical history
- Current and past medications or therapies
- Pregnancy hormone level(s), pregnancy outcome and method of diagnosis
- Results of tests and procedures you will undergo during this research study as described in the informed consent form.

Why is your personal contact and health information being used?

Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. In some situations, your personal health information might be used to help guide your medical treatment.

Which of our personnel may use or disclose your personal health information?

The following individuals may use or disclose your personal health information for this research study:

The Principal Investigator and the Investigator's study team
Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).

Who, outside of UPHS and the School of Medicine, might receive your personal health information?

As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

Individuals or organizations responsible for administering the study:

- Laboratory of David Speicher (Wistar Institute, Philadelphia PA) (facility that will analyze samples)
- The National Institutes of Health (the funding sponsor)

Regulatory and safety oversight organizations

- The Office of Human Research Protections

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations.

However, to protect your privacy, the samples you donate will be stored in vials labeled with your assigned study ID number, not your name or medical record number. The study database will also identify you with your study ID number, rather than your name or medical record number. A link does exist between your identifying information and the study database, but access to the link is locked and accessible only to authorized study personnel.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may UPHS and the School of Medicine be able to use or disclose your personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research repository (database). However, UPHS and the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

You have given written authorization to do so

The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place

As permitted by law

Will you be able to access your records?

During your participation in this study, you will be able to access your medical records, but not the study database. The Principal Investigator is not required to release research information to you that is not part of your medical record.

Can you change your mind?

Yes, at any time you may withdraw your approval to allow the use and disclosure of your personal health information as described here. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study.

If you withdraw your permission to use any blood or tissue obtained for the study, the Principal Investigator will ensure that these specimens are destroyed or will ensure that any information that could identify you is removed from these specimens.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. You will also be given the UPHS and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your personal health information.

By signing this document you are permitting the UPHS and the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form.

If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the University of Pennsylvania Institutional Review Board (a group of people who review the research to protect your rights) at (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this Informed Consent and HIPAA form will be given to you.

Main Study:

I consent to one-time blood sample collection.

Subject's Printed Name

Subject's Signature or Child Assent (if subject is less than 18 years of age) Date

Parent/Guardian Printed Name (if subject is less than 18 years of age)

Parent/Guardian Signature (if subject is less than 18 years of age) Date

Printed Name of Person Conducting Informed Consent
Discussion

Signature of Person Conducting Informed Consent Date
Discussion

Sub-Study:

I consent to blood sample collection at least weekly until diagnosis (healthy growing pregnancy or miscarriage) or treatment (ectopic pregnancy).

Subject's Printed Name

Subject's Signature or Child Assent (if subject is less than 18 years of age) Date

Parent/Guardian Printed Name (if subject is less than 18 years of age)

Parent/Guardian Signature (if subject is less than 18 years of age) Date

Printed Name of Person Conducting Informed Consent
Discussion

Signature of Person Conducting Informed Consent Date