Institutional Review Board
3800 Spruce St., First Floor Suite 151
Philadelphia, PA 19104
Phone: 215-573-2540
(Federalwide Assurance # 00004028)

DATE: 18-Dec-2018
TO: Carrie Sims
CC: Diamond, Carrie A
Srinivasan, Kavitha
Balian, Steve

RE:

IRB PROTOCOL#: 826515
PROTOCOL TITLE: Trauma Induced Coagulapathy and Inflammation

SPONSOR: NO SPONSOR NUMBER
REVIEW BOARD: IRB #4

IRB CONTINUING REVIEW: NOTICE OF APPROVAL

Dear Dr. Sims,

The above referenced protocol was reviewed and re-approved by the Institutional Review Board using the expedited procedure set forth in 45 CFR 46.110 on 18-Dec-2018. This study has been determined to be eligible for expedited review category(ies) 9.

This approval is for the period 18-Dec-2018 to 17-Dec-2019.

The documents included with the application noted below are approved:

-HSERA Continuing Review, confirmation code: chiiedad, submitted 12/03/2018

ONGOING REQUIREMENTS:

- You must obtain IRB review and approval under 45 CFR 46 if you make any changes to the protocol, consent form, or any other study documents subject to IRB review requirements. Implementation of any changes cannot occur until IRB approval has been given.
- Reportable event, such as serious adverse events, deviations, potential unanticipated problems, and reports of non-compliance must be reported to the IRB in accordance with Penn IRB SOP RR 404.
- 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.

COMMITTEE APPROVALS: You are responsible for assuring and maintaining other relevant committee approvals. This human subjects research protocol should not commence until all relevant committee approvals have been obtained.

If your study is funded by an external agency, please retain this letter as documentation of the IRB's determination regarding your proposal.

If you have any questions about the information in this letter, please contact the IRB administrative staff. A full listing of staff members and contact information can be found on our website: http://www.irb.upenn.edu

***This letter constitutes official University of Pennsylvania IRB correspondence. ***

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UNIVERSITY OF PENNSYLVANIA RESEARCH SUBJECT INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	TrICI Trial Trauma Induced Coagulopathy and Inflammation Trial
Principal Investigator:	Carrie Sims, MD, MS Trauma Center at Penn Presbyterian 1St Floor Medical Office Building 51 N. 39th Street Philadelphia, PA 19104
Emergency Contact:	Carrie Sims, MD 215-588-5154

Why am I being asked to volunteer?

You (or your family member acting on your behalf) are being invited to participate in a research study that will investigate how the body responds to injury and bleeding. 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 investigator and/or the research team about this form. If you decide to participate, you will be asked to sign this form. Your doctor may be an investigator in this research study. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may want to ask for a second opinion about your care from another doctor who is not an investigator in this study. You do not have to participate in any research study offered by your doctor.

IRB Approval From: 12/18/2018 to 12/17/2019

If you are a family member, we are asking you to make a decision about this study on behalf of your family member because their injuries or current clinical condition make it impossible for them to understand the risks and benefits of this study. When they are better and able to understand risks and benefits, we will ask them as well.

What is the purpose of this research study?

During trauma, there are a number of events that occur to stop bleeding and limit injury. The normal blood clotting processes depends on the interactions between various proteins and cells within the blood. For most people, these events occur in coordinated fashion. For seriously injured patients, however, the levels of important clotting proteins can be too low and the body's natural response to injury can be exaggerated. These events can lead to problems with bleeding, inflammation, and eventually organ failure. Unfortunately, we cannot tell which people will do well and which people will do poorly when they arrive to the trauma bay. This study will help us develop a computer mathematical model and point-of-care tests that can predict which patients are at risk for worse outcomes. Specifically, by looking at an injured patients blood pressure, heart rate, temperature, clotting parameters and proteins, and inflammatory cells, we hope to develop a way of predicting which patients are at increased risk for bleeding and organ dysfunction. In order to develop this computer model, each patient's clinical data will be analyzed using math. A computer model that predicts which patients are at risk for bleeding could help the doctors intervene earlier. We will also use blood samples to develop a blood test using a small chip that recreates the body's small blood vessels. We will test if this point of care test can be used to evaluate each patient's ability to clot blood and whether or not the interventions, such as blood products and pressure medications, are being helpful. This study is purely observational. You will not be required to take any medication and you will not need to do anything differently than what your trauma surgeon would want you to do if you were not in this study.

How long will I be in the study?

You will be asked to provide a blood and urine sample 7 times over the course of 5 days. Each collection will take about 15 minutes. We will also collect information about how you are recovering from your injury for up to 30 days after your admission.

What am I being asked to do?

You are being asked to provide a blood sample (15 ml or approximately 1 tablespoon) and urine sample (10ml) on admission to the trauma bay and then 3, 6, 12, 24, 48 hours and 5 days post admission. Although every effort will be made to take your blood sample from IV lines that you already have, sometimes this is impossible and we would need to use a needle to collect the sample from your vein. We will try to coordinate this with your clinical team in order to minimize the number of needle sticks. The urine samples will be collected either from a catheter (if one is in place) or through natural urinating.

You may also be asked for permission for us to use residual blood samples (blood that is left over from what was drawn as part of your clinical care). This blood is obtained from the clinical laboratory once it is no longer needed for your care.

The blood samples will be used for a variety of assays looking at blood clotting and inflammation. Specifically, we will look at clotting proteins, the time it takes for blood clots to form (and dissolve), how strong those clots are, and the activity of cells involved in clotting. We will also look at how the inflammatory cells are functioning, the proteins that promote or decrease inflammation, and the gene expression of proteins that might either increase or dampen clotting and inflammation. Residual blood samples will be studied for protein biomarker measurements and DNA analyses. The urine samples will be used to identify biomarkers for organ injury and dysfunction.

We are also asking to collect information your doctors are already monitoring. This is considered observational, meaning the research team will not direct your care, but rather simply observe what your doctors do and how your body responds. Specifically, we will record your vital signs (e.g. heart rate, blood pressure, respiratory rate, and temperature), the type/amount of medications you are given, the number blood transfusions or intravenous fluids you are given, the amount of blood loss that is experienced, and the amount of urine that is made. We will look at the values of any lab tests ordered by your doctor. We will also look at the development of any complications you experience within the first 30 days.

If you are discharged before all of the blood and urine samples are taken or you are discharged from the hospital before 30 days, that is fine. Your participation in this study will end at the time of your discharge from the hospital. No further samples or visits will be required for the purpose of this research study.

What are the possible risks or discomforts?

This research carries minimal risk to you. Over the 5 days, you will be asked to donate a total of 105 ml of blood (approximately 7 tablespoons) and 70 ml of urine (approximately 5 tablespoons). This is very well tolerated even after a trauma in which a patient has lost a large amount of blood. The risks associated with using a needle to take blood from a vein (“venipuncture”) include bruising, infection, redness, and fainting. These minor complications occur in approximately 12% of patients. The primary risk associated with taking blood from an existing intravenous or arterial line is infection. This risk is very low. As with any research, however, there may be risks that are currently unforeseeable.

This research includes genetic testing. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

There can be a risk in knowing genetic information. New health information about

inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. Webelieve the chance these things will happen is very small, but we cannot make guarantees.

A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

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. You will have an option to receive any results by email or postal mail at the end of the study.

What are the possible benefits of the study?

You will not get any direct benefit from being in this research study. Your participation, however, may help us understand how to improve the care of future trauma patients.

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

None, you can choose to participate or to decline. Your trauma care will not be impacted either way. Additionally, if you work or study at the University of Pennsylvania, your decision to participate or not participate in this study will have no influence on you standing with the University.

Will I be paid for being in this study?

No, there is not monetary compensation for this procedure. It is entirely voluntary.

Will I have to pay for anything?

No. However, you are still responsible for your surgical and hospital visit as well as any deductibles or applicable co-pays for routine office visits, scans and blood work.

What happens if I am injured from being in the study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

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

The study begins with your admission to the trauma bay and ends 30 days later. We will collect information from your medical chart during this time. We will collect a total of 7 blood and 7 urine samples during the first 5 days of your admission. You can leave the study at any time. If you decide after surgery that you do not wish to have your samples analyzed or your data collected, you can let us know and we will discard your samples and your data. You can also leave the study but choose to have any data/samples that have already been collected remain in the study, or allow us to continue collecting just data and no blood samples. Withdrawal will not interfere with your surgery or future care. Additionally, if for any reason your surgeon does not feel that you should participate, you will not be included in this study.

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 obtained during the course of this research study 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.
Your name, medical record number will be recorded and you will be assigned a study number. Using this study number, we will record your pre-existing medical conditions, medications, laboratory values, vital signs (heart rate, blood pressure, respiratory rate, temperature, etc), transfusions, intravenous fluids and complications (see below). This hard copy case report form will be kept in a locked cabinet in the Penn Acute Research Lab (3 Mutch, Penn Presbyterian Medical Center) until the conclusion of the study (anticipated 3 years). All data will be entered into REDCap, a password protected University maintained data

network. Only Dr. Sims and the IRB at the University of Pennsylvania will have access to both your name and subject number. Deidentified encrypted data will be shared with our Princeton collaborators in order to develop the computer mathematical model.

Moreover, the federal law, Genetic Information Non-Discrimination Act (GINA), helps reduce the risk from health insurance or employment discrimination with regards to an individual's genetic information. It includes the following protections:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums; and
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote or fire you or when setting the terms of your employment.

What information about me may be collected, used or shared with others?

- Name
- Date of birth
- Medical record number
- Personal and family medical history
- Medications
- Results from blood tests
- Vital signs like heart rate, blood pressure, breathing rate and oxygenation (intermittent and continuous data)
- Number of blood products transfused (red blood cells, fresh frozen plasma, and platelets
- Volume of fluids to include intravenous fluids such as normal saline, plasmalyte, lactated Ringer's solution, albumin and oral fluids.
- Outcomes such as development of respiratory failure, kidney failure, liver failure, blood clots in the veins, and death
- How your blood clots – research blood samples will be analyzed by thromboelastogram to look at how quickly blood clots form (and dissolve) and how strong these clots are. Blood clotting will also be evaluated using microfluidic chip assays
- Clotting and Inflammatory proteins and the gene expression of proteins that increase and decrease clotting and inflammation
- Amount of free nucleic acids, such as RNA and DNA, in the serum. RNA and DNA are normally contained within the cells. During trauma, injured cells can release nucleic acids
- Activity of white blood cells (neutrophils and peripheral blood mononuclear cells)

Your data will be collected and entered into a secure data base maintained by the University of Pennsylvania (REDCap). A study number will be assigned to your data and your personal information will be linked to this data. Your personal

information will not be accessible to anyone other than Dr. Sims. De-identified data will be encrypted and shared with our collaborators in order to develop the computer mathematical model.

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research,
- oversee the research,
- see if the research was done right, and
- evaluate and manage research functions.

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The investigators for the study
- Other authorized personnel at Penn, including offices that support research operations

Who, outside of the School of Medicine, might receive my information?

- The Food and Drug Administration
- The Office of Human Research Protections
- Researchers at Princeton will receive de-identified, encrypted data in order to create the computer mathematical model.
- The National Institutes of Health (NIH)

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

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 the School of Medicine use or disclose my 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 database. However, 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

- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

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

Electronic Medical Records and Research Results

What is an Electronic Medical Record and/or a Clinical Trial Management System?

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.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

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, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

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 information produced from your participation in 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). Information related to 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 or in the CTMS, your information may be 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.).

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 Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (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 consent form will be given to you.

If the patient is not consentable:

You are being asked to consent to this research on behalf of your loved one. This is a temporary consent. When the patient is awake and able to understand the risks and benefits of the study, we will ask them for their permission to continue enrollment. We will also ask their permission to analyze any blood samples, urine samples, or data that has already been collected.

Name of Patient Surrogate (Please Print)	Signature	Date

Relationship to Patient

Name of Person Obtaining Consent (Please Print)	Signature	Date

If obtaining consent by phone, name and signature of witness to consent:

Name of (Please Print)	Signature	Date

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IF/When the patient is consentable:

You are being asked to consent to this research and are informed that samples and data may have already been collected when you were not able to provide consent.

_____ _____ _____

Name of Subject (Please Print) Signature Date

_____ _____ _____

Name of Person Obtaining Consent (Please Print) Signature Date

If you only wish for certain information and samples to be collected, please indicate so here with your initials: _____ blood samples; _____ urine samples; _____ residual (left-over) blood samples;_____clinical data;
_____ keep only the samples and data that have already been collected

When this study is complete, I wish to have the results sent to me. YES / NO (circle one)

I wish to learn more about community participation in trauma research. YES / NO (circle one)

Email address: _____ @ _____

Home address: _____
Street Address Apt. No.

_____
City State Zip Code