Study Title: A Pilot Study in Feasibility and Safety: Point of Care testing with thromboelastography (TEG) for blood product transfusion and coagulation in patient's requiring extracorporeal membrane oxygenation (ECMO)

Principal Investigator: Stephen Esper, MD, MBA

Document: Informed Consent Form
Document Date: 29 AUG 2019

NCT #: NCT02887820
STUDY #: STUDY19070239

University of Pittsburgh

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: A Pilot Study in Feasibility and Safety: Point of Care testing with thromboelastography (TEG) for blood product transfusion and coagulation in patient's requiring extracorporeal membrane oxygenation (ECMO)

Principal Investigator: **Stephen A. Esper, MD, MBA, Assistant Professor of Anesthesiology**
Department of Anesthesiology, C-Wing
200 Lothrop Street
Pittsburgh, PA 15213
Cell: 412-592-2511
Office: 412-647-4723
Fax: 412-647-6290

Co-Investigator and Mentor: Darrell Triulzi, MD, Director of the Division of Transfusion Medicine, Department of Pathology and Medical Director, Institute for Transfusion Medicine

Co-Investigators:
Arthur Boujoukos, MD (Department of Critical Care Medicine)
John H. Waters, MD (Chief, Magee Women's Hospital, Department of Anesthesiology, Professor of Anesthesiology)
Penny Sappington, MD (Assistant Professor of Critical Care Medicine, Medical Director of Surgical ICU)
Kathirvel Subramaniam, MD, MPH (Associate Professor of Anesthesiology)
Jonathan D'Chuna, MD (Surgical Director Lung Transplantation, Vice Chairman Academic Affairs and Education)
Robert L. Kormos, MD (Professor of Surgery)
Michael Boisen, MD (Assistant Professor of Anesthesiology)
JW Awori Hayanga, MD, MPH (Surgical Director of Lung Transplant Outcomes Research)
Luigi Lagazzi-Garros, MD (Cardiothoracic Surgeon)

SOURCE OF SUPPORT: American Heart Association

WHAT IS THE PURPOSE OF THE STUDY?
You have been asked to participate in this research study because you have been placed on extracorporeal membrane oxygenation (ECMO) for medical necessity. The purpose of the study is to determine if an alternative coagulation test called the thromboelastogram (TEG) has an improved ability to assess bleeding risk during treatment with ECMO when used with other tests traditionally used to test coagulation. Given the nature of the ECMO circuit, heparin, a blood thinner, must be given during its use in order to prevent life threatening blood clots (also known as thrombosis). However, bleeding can result from excessive doses of heparin and this is the most common complication from ECMO. Therefore, it is necessary to closely monitor the coagulation system with blood tests to avoid both bleeding and blood clots. The TEG is a blood test that can quickly assess multiple parameters of the coagulation system and thus we believe the TEG may an effective measure of bleeding risk than the coagulation studies commonly used in most critical care units today. This study plans to enroll 50 research subjects on ECMO 18 years and older.

WHAT WILL BE THE COURSE OF THE STUDY?
Upon initiation of ECMO, a TEG algorithm will be used in conjunction with traditional laboratory tests both intraoperatively and post operatively to manage hemostasis. Intra-operatively, TEG results will be used in addition to standard laboratory tests to determine transfusion requirements. Postoperatively, TEG results will be used in addition to standard laboratory coagulation tests to determine rate of heparin administration in order to prevent thrombosis. Each TEG test will require an additional 1 milliliter of blood drawn from the arterial line. These TEGs will continue to be performed at assigned intervals throughout your time on ECMO. Based on the results of these tests, management decisions will be made according to predetermined guidelines and clinical appropriateness. Interventions undertaken by critical care physicians may include changing the dose of heparin administered, giving blood transfusions, performing additional laboratory studies, and consulting with other specialists.

Each participant in the study will be continuously monitored in the intensive care unit throughout their time on ECMO. Parameters that will be monitored and recorded will include vital signs (age, height, weight, blood pressure, heart rate, pulse oximetry, central venous pressure, temperature, urine output, and possibly pulmonary artery pressure monitoring), estimated blood loss (such as through chest tube output), transfusion requirements, laboratory values, heparin dosages, and other mediations given.

Any identifying data about you as the patient will be removed to insure that your privacy is not compromised. You may also choose to end your participation in the study at any time for any reason.

WHAT ARE THE POSSIBLE RISKS, SIDE EFFECTS, AND DISCOMFORTS OF THIS RESEARCH STUDY?

As with any research study, there may be adverse events or side effects that are currently unknown and it is possible that some of these unknown risks could be permanent, serious or life-threatening. Many of these risks are inherent to treatment with ECMO.

Risk to you: Each TEG test will require 1 milliliter of blood, drawn from a pre-existing arterial line. The average patient will require approximately 15 TEG tests over the course of study participation. Since the arterial line is already in place per standard of care, the risks associated with venipuncture are not applicable to this study.

Risk of breach of confidentiality: In rare cases, people not associated with this research study may inadvertently see the identifiable research results. The study staff will attempt to prevent this from happening by keeping all research records in locked files, and by identifying medical information by a research record number, rather than by name or social security number. The code book containing the name and number will be kept secure by the primary investigator.

WHAT ARE THE BENEFITS OF THE STUDY?
You are not expected to experience any direct benefit from participating in this study but your participation may help improve care for future patients.

WHAT TREATMENTS OR PROCEDURES ARE AVAILABLE IF I DECIDE NOT TO TAKE PART IN THIS RESEARCH STUDY?
If you chose not to participate in the study, you will receive standard monitoring and testing that is currently used in the cardiothoracic intensive care unit at UPMC Presbyterian Hospital during treatment with ECMO. This includes monitoring of vital signs, signs of bleeding or thrombosis, serial PT, PTT, Anti-Xa, platelet count, and fibrinogen measurements, heparin dosing, transfusions as dictated by laboratory testing and clinical evidence, and other medications needed to maintain hemodynamic stability. If you chose to be in the study, these same medications will also be available to you.

WILL I BE PAID FOR BEING IN THIS STUDY?
You will not be paid for participating in this study.

IF I AGREE TO TAKE PART IN THIS RESEARCH STUDY, WILL I BE TOLD OF ANY NEW RISKS THAT MAY BE FOUND DURING THE COURSE OF THE STUDY?
You will be promptly notified if any new information develops during the course of this study and you may change your mind about continuing to participate in this study at any time.

WILL MY INSURANCE PROVIDER OR I BE CHARGED FOR THE COSTS OF ANY PROCEDURES PERFORMED AS PART OF THIS RESEARCH STUDY?
The standard services will be billed to you or your insurance carrier. You are still responsible for any applicable co pays, coinsurances and/or deductibles that are associated with your surgery, treatment and hospitalization. You will not be charged for the additional TEG testing associated with this study.

WILL THIS RESEARCH STUDY INVOLVE THE USE OR DISCLOSURE OF MY IDENTIFIABLE MEDICAL INFORMATION?
This research study will involve the recording of current and future identifiable medical information from your hospital records. The information that will be recorded will be limited to information concerning the purpose of this study which includes evaluation of coagulation dysfunction during ECMO. The identifiable information that will be included in your medical record may include age, sex, height, weight, preexisting and future medical conditions, vital signs (including blood pressure, heart rate, respiratory rate, pulse oximetry, central venous pressure, and pulmonary artery pressures), blood loss, serial laboratory tests (including complete blood count, metabolic panels, PT, PTT, anti-Xa, platelet count, fibrinogen, and TEG measurements), radiological testing, heparin dosing, blood transfusions, and other medications needed to maintain hemodynamic stability. This identifiable information will be kept confidential in your medical record at UPMC Presbyterian Hospital and research records will be kept secure by the primary investigator of this study.

WHO WILL PAY IF I AM INJURED AS A RESULT OF TAKING PART IN THIS STUDY?
University of Pittsburgh researchers and UPMC medical providers understand the importance of your voluntary participation in this research study. These individuals and their associates will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research. If you

believe that you are injured as a result of the research procedures being performed you should immediately contact the Principal Investigator or one of the Co-investigators listed on the first page of this form.

Emergency medical treatment for injuries directly related to your participation in this research study will be provided to you by the hospitals of UPMC. It is possible that UPMC may bill your insurance provider for the costs of this emergency treatment. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care unless otherwise specifically stated below. At this time, there is no plan for any additional financial compensation.

WHO WILL KNOW ABOUT MY PARTICIPATION IN THIS RESEARCH STUDY?
Any information obtained from this research will be kept confidential. All records related to your involvement in this research study will be stored in a locked file cabinet by the Primary Investigator. Your identity in such records will be indicated by a case number rather than by your name or other identifiable information. The information linking these case numbers with your identity will be kept separate from the research records and again in a locked file cabinet. You will not be identified by name in any publication of the research results.

WHO WILL HAVE ACCESS TO IDENTIFIABLE INFORMATION RELATED TO MY PARTICIPATION IN THIS RESEARCH STUDY?
In addition to the investigators listed on the first page of this form and their associated research staff, the following individuals will or may have access to identifiable information related to your participation in this research study:

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research and medical information for the purpose of monitoring the appropriate conduct of this research study.

In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

Authorized representatives of the U.S. Food and Drug Administration (FDA) may review and/or obtain identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of monitoring the accuracy of the research data. While the FDA understands the importance of maintaining the confidentiality of your identifiable research and medical information, the University of Pittsburgh and UPMC cannot guarantee the confidentiality of this information after it has been obtained by the U.S. Food and Drug Administration.

Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).

FOR HOW LONG WILL THE INVESTIGATORS BE PERMITTED TO USE AND DISCLOSE IDENTIFIABLE INFORMATION RELATED TO MY PARTICIPATION IN THIS RESEARCH STUDY?

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical information) related to your participation in this research study for a minimum of six years after final reporting or publication of a project.

MAY I HAVE ACCESS TO MY MEDICAL INFORMATION THAT RESULTS FROM MY PARTICIPATION IN THIS RESEARCH STUDY?

In accordance with the UPMC Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider.

IS MY PARTICIPATION IN THIS RESEARCH STUDY VOLUNTARY?

Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary.

Your doctor is involved as an investigator in this research study. As both your doctor and a research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in a research study offered by your doctor.

YOUR RIGHT TO SEE YOU OWN MEDICAL INFORMATION

You are allowed to see any research information that becomes a part of your medical record. While your participation in the study is going on you are be able to see what treatments you are receiving. Although you will not know which group you are assigned to, you will have access to this information at the end of your participation in the study.

CAN I REFUSE TO GIVE PERMISSION TO RESEARCHER TO USE MY MEDICAL INFORMATION?

Permission to use your medical information for the purpose of this research study is voluntary. You do not have to let the researchers look at your medical information. However, if you do not give written permission for the researcher's use of your medical records, you will not be able to participate in this research study.

Whether or not you give permission for the researchers to use your medical records, your medical care at this and any other UPMC hospital or doctor's office will be the same.

MAY I WITHDRAW, AT A FUTURE DATE, MY CONSENT FOR PARTICIPATION IN THIS RESEARCH STUDY?

You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. Note, however, that if you withdraw your consent for the use and disclosure of your identifiable medical record information for the purposes described above, you will also be withdrawn, in general, from further participation in this research study. Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw your consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

Your decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

IF I AGREE TO TAKE PART IN THIS RESEARCH STUDY, CAN I BE REMOVED FROM THE STUDY WITHOUT MY CONSENT?

It is possible that you may be removed from the research study by the researchers if, for example, you are found to have a preexisting bleeding or clotting disorder or if you refuse to continue with the research study. If you are withdrawn from participation in this research study, you will continue to undergo the standard of care for any patient on ECMO.

VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study throughout the course of this study. Any questions will be answered by the researchers listed on the first page of this form. Any questions which I have about my rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).

By signing this form, I agree to participate in this research study. A copy of this consent form will be given to me.

_____ _____

Participant's Signature Date

_____

Participant's Name (Print)

PROXY CONSENT

_____ _____

Participant's Name (Print) Date

The above-named individual is unable to provide direct consent for study participation because

_____

Therefore, by signing this form, I give my consent for his/her participation in this research study.

_____ _____

Representative's Name (Print) Representative's Relationship to Participant

_____ _____

Representative's Signature Date

_____ _____

Witness Signature Date

VOLUNTARY ASSENT:

This research has been explained to me, and I agree to participate.

_____ _____

Participant's Signature **Date**

VERIFICATION OF EXPLANATION:

I certify that I have carefully explained the purpose and nature of this research study to the participant in appropriate language. He/she has had an opportunity to discuss it with me in detail. I have answered all his/her questions and he/she has provided affirmative agreement (i.e., assent) to participate in this study.

_____ _____

Investigator's Signature Date

_____

Role in Research Study

CONSENT FOR CONTINUED PARTICIPATION

I understand that I am currently participating in a research study. I further understand that consent for my participation in this research study was initially obtained from my authorized representative as a result of my inability to provide direct consent at the time that this initial consent was requested. I have now recovered to the point where it is felt that I am able to provide direct consent for continued participation in this research study.

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable. By signing this form I agree to participate in this research study.

By signing below, I agree to continue my participation in this research study. A copy of this consent form will be given to me.

_____ _____

Participant's Signature Date

CERTIFICATION of INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____

Printed Name of Person Obtaining Consent Role in Research Study

_____ _____

Signature of Person Obtaining Consent Date