SIREN Informed Consent Forms

The Sponsor/Investigator of [TRIAL] does not allow edits to this central IRB approved main consent form for this multicenter trial. This is to ensure equity of the language across the enrolling sites. Your site may add site-specific content in a single contained section below the universal text if necessary. This section is limited to information that pertains specifically to your local institution.

Please note the process for submitting informed consent forms for [TRIAL] as sites submit ceding applications to local IRBs. All SIREN informed consent forms are approved by the Advarra Central IRB (ER-CIRB) with the parent protocol. The informed consent form is a completely locked down form, to be used consistently across [TRIAL] sites. Please submit this form to your local IRB as is, without making any site specific changes. The current ER-CIRB approved form to be used is located in the [TRIAL] Toolbox and the Getting Started page.

Where local site and study team contact information needs to be included, this will populate directly into the form after the site application is submitted to and approved by the ER-CIRB. In very limited circumstances, when institutionally required language is requested by the IRB, there is potential to add a separate site specific section at the end of the form prior to the signature page. However, for the time being, please submit the form as is. Additions will only be considered per a request from the IRB, and will be discussed on a case by case basis. Should this request from the IRB be made, please provide at the earliest time the additional requested language in a separate document for review by the SIREN CCC. Please do not edit or insert language into the body of the trial-wide approved ICF.

Please note that while HIPAA language is already included in the body of the consent form, a separate local HIPAA form is acceptable for use, so long as it is signed and dated by subject/LAR.

We understand that this process differs from how the ICF review process has operated for other trials. We are happy to help as we move along with this process; please let us know if we can be of assistance. Please also note the below statement from Advarra regarding this process for SIREN trials.

As you know, Advarra is the single IRB for the SIREN network trials. If your organization has a negotiated process in place with Advarra specifically as it pertains to the Informed Consent language, please note that the established process that has been in place with your site and Advarra is suspended for the SIREN network's trials. SIREN has their own IC process which Advarra will follow for these specific trials. Any non-SIREN trials will follow the established process you already have in place with Advarra.

If you have any questions regarding this please contact BOOST-contact@umich.edu.

Thank you for your attention with this matter,
Best regards,
Advarra Institutional Services Team & SIREN

CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Study Title:	**"Biomarkers in the Brain Oxygen Optimization in Severe Traumatic Brain Injury - A multicenter, observational study of the effect of derangements in brain physiologic parameters on brain injury biomarker levels in patients with severe traumatic brain injury."**
Granting Agency:	**The Department of Defense, U.S. Army Medical Research and Materiel Command (USAMRMC)**
Protocol Number:	**Bio-BOOST**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

This form is for use in a research study that involves participants who are unconscious or in coma, and do not have the capacity to consent to take part in the study. You are the legally authorized representative of the patient. In cases where the participant's representative gives consent, the participant should be informed about the study to the extent possible if the participant regains consciousness. During the course of the study, if the subject regains the capacity to consent, informed consent will be obtained from the subject and the subject offered the ability to leave the study if desired.

This form provides information to help you decide whether or not to consent for participation in this study. More detailed information is provided in the following pages. If you have any questions, please ask the research team.

Summary of Key Information

Your family member (or a person you represent) has been diagnosed with a severe traumatic brain injury (TBI) and has already been enrolled in a study that is examining two ways of treating patients with brain injury.

The purpose of this additional optional research study is to examine the use of blood tests for monitoring changes that occur in the brain after severe TBI. Severe TBI patients are typically in a coma and that limits doctors' ability to monitor patients' recovery. There are currently no blood tests for monitoring recovery from severe TBI. For these reasons, it is difficult for doctors to adjust TBI treatment based on how well an individual patient responds to therapy.

Participation is voluntary and can be withdrawn at any time. There is no penalty for choosing not to participate.

Participation may include:	**Enrollment and 16 and 24 hours after injury**	**Every 12 hours on study days 2-5**	**Once a day on study days 7, 14 and at 6 months**	**Once, 2 hours after participant has decreased blood flow in the brain or decreased brain oxygen levels**
Blood collection *(~1Tablespoon/15ml)*	✔	✔	✔	✔
CSF collection, *if accessible through drain placed for clinical care--(5ml, about one teaspoon)*	✔	✔	**Not applicable**	**Not applicable**
Medical Record Review/data collection	*Ongoing*			

Benefit: Participants will not directly benefit from being in the study. Participation in the study may help doctors learn about how blood tests can be used to guide the treatment of TBI patients.

Since blood tests done on these samples will be for research purposes and we are not yet sure of the accuracy of these tests, you will not be given the results of this analysis. Accordingly, the test results will not be used in taking care of your family member (or a person you represent).

Known risks from study participation include discomfort, bruising and bleeding from the blood draw site and accidental release of your information.

There is no payment or compensation for being in the study. There is no cost to being in the study. Charges for all standard medical care will be billed the same way whether or not someone is in the study.

If you consent, you will be asked to sign and date this form.

MORE DETAILED INFORMATION

What is the purpose of this research study?

The purpose of the research study is to better understand how blood tests can be used for monitoring changes that occur in the brain after severe TBI.

Why is this an important question to study?

Severe TBI patients are typically in a coma and that limits doctors' ability to accurately monitor patients' recovery. There are currently no approved blood tests for monitoring severe TBI. For these reasons, it is difficult for doctors to adjust TBI treatment based on how well a patient responds to therapy. If it turns out that blood tests accurately reflect changes in the brain that occur in the brain after TBI, then they may be useful for guiding TBI treatment decisions made by doctors in the future.

How long will the participant be in the study? How many people will be in the study?

Participants are in the study for about 6 months. About 300 participants with an adequate number of blood draws will be enrolled at about 15 hospitals.

What happens in this study?

We will collect one tablespoon (15 ml) of blood and one teaspoon (5 ml) of cerebrospinal fluid (CSF) (the fluid that circulates around the brain and the spinal cord) from each participant at the following time points:

1. At enrollment and at 16 and 24 hours following injury.
2. Every 12 hours on study days 2 - 5;
3. Once a day on study days 7 and 14 and at 6 months (at days 7, 14 and 6 months, only a blood sample will be collected).
4. If such an event occurs: Once, 2 hours after the participant has a prolonged period of decreased blood flow in the brain or decreased brain oxygen levels

Given the need to collect blood and CSF sample as soon as possible, the enrollment, 16 and 24 hours following injury blood samples may be collected prior to obtaining your consent. However, if you do not consent to being in the study, those blood samples will be destroyed.

CSF will only be collected if an external ventricular drain is placed by the participant's doctors in the participant's brain so they can measure intracranial (inside the head) pressure (ICP) as part of clinical care

Blood will be processed into blood components (serum and plasma) and genetic material (DNA, mRNA). Analyses may include whole genome sequencing (determining all of your genetic information in one measurement). In addition, as described above, the blood and CSF specimens will be tested for levels of special proteins associated with brain injury.

After temporary storage at the local hospital, biological samples (serum, plasma, DNA, mRNA, CSF) will be sent to the TBI Biorepository at the University of Pittsburgh for indefinite long-term

storage. Only a unique participant number will be used to identify the participant's information and biological sample. The biological samples may be provided to researchers at academic institutions, hospitals, national repository and biotechnology/pharmaceutical companies. De-identified (all identifying information has been removed) clinical and genetic data may be provided to the researchers requesting biological samples. These researchers may perform analysis of the biological samples provided by the participant. As this is done for research purposes, no results will be given.

The biological samples provide genetic material, which could be used for studies designed to identify the genes that affect recovery from TBI. In addition, the data and samples may also be used to study other diseases.

What risks may participants experience?

Risks from sample collection:
Blood sampling may be obtained from a pre-existing tube inserted in your artery or vein (similar to an IV tube) that is standard of care. A rare risk is infection of this catheter from sampling (occurs in less than 1% or less than 1 out of 100 patients). If a catheter is not available, a venipuncture may be performed. A venipuncture can cause slight discomfort, bruising and infection at the site. Fainting is an infrequent risk from blood drawn by venipuncture. There is a rare risk of infection from collecting the CSF sample. Best clinical practice guidelines will be performed by trained professionals to minimize this risk.

Risks to confidentiality:
When biological samples and information are sent to the University of Pittsburgh Biorepository, a unique participant number is assigned to this information. A unique participant number is a combination of numbers and/or letters that do not correspond to any information you have provided to us (for example, birth date, age, name) and which is different for each person who participates in this study. The biorepository uses a secure computer system. There is a slight risk that there could be a breach of the security of this computer system resulting in the access of information about the participant or medical history. Safeguards (including the use of password protected computers and restricted access to study data) are in place to minimize this risk. Information about the participant will not be released to anyone, unless you request it.

Risks of Genetic Testing:
A possible risk from participation in this study involves loss of privacy as a result of providing biological samples for research. Although genetic information is unique to the participant, some genetic information is shared with children, parents, brothers, sisters, other blood relatives, and members of your ethnic group. Consequently, it may be possible that genetic information from them could be used to help identify the participant. Similarly, it may be possible that genetic information from the participant could be used to help identify them. While information traditionally used for identification will not be released (for example, name, date of birth, address, telephone number), people may develop ways in the future that would allow someone to link genetic or medical information back to the participant.

A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or an individual's family members. These health insurers or health plan providers also are prohibited from using such information for decisions regarding coverage, rates, or preexisting conditions. GINA also prohibits employers from using genetic information

for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment. Furthermore, the researchers have adopted strict privacy and confidentiality procedures for maintaining genetic information as described in this consent form. You should be aware, though, that if the participant's genetic information were accidentally released to the wrong source, federal law does not protect against genetic discrimination by companies that sell life insurance, disability insurance, long-term care insurance, or by adoption agencies.

The researchers have taken steps to minimize these risks. The study team will monitor closely for these possible risks and complications will be treated if needed. As with any research study, there may be additional risks that are unknown or unexpected.

What is the possible benefit?

There are no direct benefits to the participant for being in this study. However, participation will contribute towards improving medical care for future patients with TBI.

What is the alternative to participating in this study?

This study is for research purposes only. Your alternative is to not participate.

Is withdrawal allowed?

Taking part in this study is voluntary. You may choose to take part or may refuse to participate in the study at any time. Leaving the study will not result in any penalty. If you do withdraw from the study, then you may request that any unused sample be destroyed. However, data and samples that have already been distributed to approved researchers will not be retrieved. After the study is completed (the study will last a total of about two and half years), it will not be possible to remove samples.

The Investigator can stop your participation at any time without your consent if it is in your best interest or if the study is canceled.

What if new information becomes available?

We will provide any new information that may affect a participant's willingness to continue in the study. Participants may be contacted about future available studies. We may also contact participants with periodic updates about the study.

AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

How will personal information be protected?

The study investigator and his/her collaborators will consider the participants' personal information confidential to the extent permitted by law. "Personal Information" means

information that can be used to identify the participant or health information about the participant. This includes name or initials, date of birth, gender, ethnic origin and medical and health-related information such as blood tests, diagnostic imaging and results, the results of physical examinations, medical history and hospital records, and information directly observed in the study.

Information about the participant collected for the study may be stored electronically or on paper. The information stored on the computer is kept in password protected files that are maintained on password protected computers. The information stored on paper is stored in a locked file cabinet in a locked office. Only the members of the study team and the persons and groups listed below will have access to the participants' medical information for this study.

The government agencies responsible for making sure that studies are conducted and handled correctly, and other organizations involved in this research study may look at the participant's study records in order to perform their duties. These include: the Department of Defense, the US National Institutes of Health (NIH), the US Office for Human Research Protections, the US Food and Drug Administration (FDA), researchers from the University of Pennsylvania and the University of Pittsburgh, representatives from The Strategies to Innovate Emergency Care Clinical Trials Network (SIREN) Clinical Coordinating Center at the University of Michigan, representatives from the Data Coordination Unit at the Medical University of South Carolina, the Central Institutional Review Board, and/or other agents of the study who will be bound by the same provisions of confidentiality. Information from this study may be submitted to the U.S. government, including the U.S. Food and Drug Administration (FDA).

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

. The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the Department of Defense which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Although every effort will be made to maintain confidentiality of the participant's medical and health records, absolute confidentiality cannot be guaranteed. We will use a unique participant number rather than the participant's name on study records where we can. The participant's name and other facts that might point to the participant will not appear when we present this study or publish its results. Viewing or storing this electronic informed consent form on a personal electronic device may allow information provided on this form (such as names and email addresses) to be inadvertently shared with others if the device is lost, hacked, or otherwise compromised.

We will keep any records that we produce private to the extent we are allowed or required by law. The participant's records may be kept indefinitely.

The study doctor and treating institution are required by law to protect the study participants' health information. With this form, you authorize the study doctor to use and disclose the participant's health information, as described in this section, in order to conduct this research study. You have the right to revoke this authorization, at any time, and can do so by writing to the study doctor at the address on the first page. Even if you revoke the authorization, the study doctor and/or sponsor may still use health information they have collected about the study participant, if necessary for the conduct of the study. However, no new information will be collected.

Your authorization does not have an expiration date unless indicated elsewhere. You do not have to sign and date this information and consent form, but if you do not, the person you represent will not be able to take part in this research study. Those persons who receive the participant's health information may not be required by US Federal privacy laws (such as the Privacy Rule) to protect it and may share the information with others without your permission, if permitted by laws governing them.

By signing and dating this form, you authorize the collection, access, use and disclosure of the participant's information as described above. **State law or the enrolling institution may require an additional separate form on which you can authorize sharing of the participant's health information. If so, you will have to sign both forms for your authorization to be valid.**

How is the contact information stored?

Contact information for the participant, you, your family members, close friends, and associates will be collected to make sure that we can follow up to determine the participant's condition, return the results of the research after the study is over, and provide any new information and study updates. The information is stored in a secure computer system separate from other personal or health information collected in the study.

How may the participant's data and samples be shared?

The biological samples may be provided to researchers at academic institutions, hospitals, and biotechnology/pharmaceutical companies. Samples may be utilized for any research study. US Federal rules require that data be securely stored in the Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system where it can be accessed by researchers in a de-identified manner. For more information see the website http://fitbir.nih.gov. Successful research using your samples could result in a commercial or therapeutic project with significant

value, such as a product for the medical treatment of TBI. You will not share in any financial benefits of these uses. Samples may be kept indefinitely.

Will the participant be required to pay anything?

There is no additional cost to participate in the study. Charges for all standard medical care will be billed in the same manner regardless of study participation. Funds are not available to cover the costs of any ongoing medical care and participants remain responsible for the cost of non-research related care. For questions about the participant's medical bills relative to research participation, contact the study investigator listed on this form.

Will the participant be paid for being in the study?

No. There will not be any payment to the participant for being in this study.

What if the participant is injured as a result of being in this study?

If a participant is injured or becomes ill from participating in the study, medical treatment will be available at this institution or elsewhere consistent with the care provided for any medical problem. Payment for this care will be billed the same as any other care for any medical problem. If the hospital at which the participant was enrolled has any additional answers to this question, this information is found at the end of this form.

In the event that the participant suffers injury as a result of their participation in this research study, no compensation will be provided to the participant by the granting agency (Department of Defense), the treating institution, or the researchers. The participant still has all of their legal rights. Nothing said here about treatment or compensation in any way alters the participants' right to recover damages.

Is there anything else I need to know?

Doctors caring for the participant during this hospitalization may also be researchers in this study. If so, the doctors are interested both in the participant's medical care and in the conduct of this research. There is no obligation to participate in any research study just because it is offered by the participant's doctors.

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.

What if I have questions?

You or the participant may ask and will receive answers to any questions you have during the course of the study. For any questions regarding this study or if the participant experiences any side effects or medical problems, contact the site researcher listed on this form.

Advarra serves as the Central Institutional Review Board (CIRB) for this study. The CIRB is not part of the research or the research team. Please contact Advarra, if you or the participant have questions about your role and rights as a research participant; wish to obtain more information about clinical research in general; have concerns, complaints or general questions about the research, or wish to provide input about the research study.

You can do so in the following ways:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting Advarra: Pro00042151.

CONSENT STATEMENTS

PARTICIPANT'S CONSENT (should the participant become cognizant during the study)

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

_____
Participant's Printed Name

_____ ___/___/___
Participant's Signature Date

STATEMENT OF LEGALLY AUTHORIZED REPRESENTATIVE

You should feel that you have been told enough about this study to give your informed consent before signing this form. Signing and dating this form does not waive any legal rights to which you or the participant are entitled. You will receive a copy of this form after it is signed and dated.

I want my family member (or the person I represent) to participate in this study. ◯ Yes ◯ No

If you want your family member (or the person you represent) to participate in this study, please sign and date below.

_____
Participant Name

_____
Printed Name of Legally Authorized Representative (LAR)

Your relationship to Participant (Spouse, Child, Parent, Sibling, Other [if other, please describe]):

_____

_____ ____/____/____ _____:_____AM/PM
LAR Signature Date Time

_____ _____
Investigator/Designee Name Role in the study

_____ ____/____/____ _____:_____AM/PM
Investigator/Designee Signature Date Time

INFORMED REFUSAL OF FURTHER PARTICIPATION

You should feel that you have been told enough about this study to give your informed consent before signing and dating this form. Signing and dating this form does not waive any legal rights to which you or the person you represent are entitled. You will receive a copy of this form after it is signed.

If you DO NOT want your family member (or the person you represent) to continue to participate in this study, please sign below.

_____
Participant Name

_____
Printed Name of Legally Authorized Representative (LAR)

Your relationship to act on behalf of Participant (Spouse, Child, Parent, Sibling, Other [if other, please describe]):

_____

_____ ____/____/____ _____:_____AM/PM
LAR Signature Date Time

_____ _____
Investigator/Designee Name Title

_____ ____/____/____ _____:_____AM/PM
Investigator/Designee Signature Date Time