https://www.cirbi.net/CIRBI/sd/Rooms/DisplayPages/LayoutInitial?Container=com.webridge.entity.Entity[OID[AC482809EC03C442A46F2C8EEC4D75D3]] **INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION**

Sponsor / Study Title:	**University of Maryland, Baltimore / "Cooling to Help Injured Lungs (CHILL) Phase IIB Randomized Control Trial of Therapeutic Hypothermia in Patients with ARDS"**
Protocol Number:	**CHILL**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

This form is for use in a research study that may involve participants who may or may not have the capacity to consent to take part in the study. When the participant cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the participant rather than the person (legally authorized representative) who is signing and dating this form for the participant. In cases where the participant's representative gives consent, the participant should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the participant regains the capacity to consent, informed consent will be obtained from the participant and the participant offered the ability to leave the study if desired.

KEY INFORMATION

You are invited to take part in a research study of a possible new treatment for people with a type of lung injury called acute respiratory distress syndrome (ARDS), which can be a complication of pneumonia, viral infections including influenza and COVID-19, severe trauma, and other severe infections. This research study, sponsored by the Department of Defense, is designed to determine whether whole body cooling by 2-3°C (3.6°-5.4°F) for 48 hours along with medication to prevent shivering will be beneficial in ARDS.

To be eligible for this study, you will have already been placed on a mechanical breathing machine. If you agree to be in this study, you will be randomly assigned to either the cooling study treatment or usual standard of care study treatment for ARDS. You will have a 50% chance of being assigned to each group. If you are assigned to the cooling group, you will be deeply sedated and given a neuromuscular blockade, a type of medication that prevents shivering by relaxing your muscles. This is effect is reversible and these medications are used frequently in the usual care of people with ARDS. You will be cooled using cooling blankets or cooling pads for 48 hours, then rewarmed slowly and the medications to prevent shivering will be stopped. We will monitor how well your lungs and other organs are working by

following your physical exam and laboratory results and we will collect 12 cc. of blood (2 teaspoons) at six times over the first week. After the first week, we will follow how you are doing by reviewing your medical record. You will be given a test of your thinking ability when you leave the ICU and when you leave the hospital. We will contact you 60 and 90 days after you start the study to see how you are doing.

People with ARDS are at high risk for death and ARDS survivors are at high risk for long-lasting disabilities. Studies in cells in the test tube and in animals suggest that cooling may reduce the lung injury that occurs in ARDS, including ARDS that is caused by COVID-19. If you are assigned to the cooling study treatment group, the cooling may reduce your lung injury.

The word "you" in this form refers to adult on the breathing machine who will be in the study. Your legally authorized representative (LAR) will be asked to read, sign and date this consent form to give permission for you to participate, if you are not able to sign and date for yourself. This form gives you important information. Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like, including any possible risks to you. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

BACKGROUND AND PURPOSE OF STUDY

We are asking you to join this research study because you have moderate to severe ARDS, which can threaten your life. About 40% of people with ARDS like yours die. ARDS causes fluid to fill your lungs and makes it hard for you to breathe and to get enough oxygen. Your regular doctors are using a breathing machine to help you breathe and get more oxygen.

The purpose for this study is to see if decreasing your body temperature from 37°C (98.6°F) to 34°-35°C (93.2°-95°) for 48 hours helps decrease lung injury. There is information from studies in test tubes and animals and small studies in humans to suggest that cooling by 2°C (4.5°F) might reduce lung injury. Cooling may help people with ARDS by slowing their metabolism and the need for oxygen and by reducing inflammation. If you are assigned to the cooling group your body temperature will be reduced from 37°C (98.6°F) to 34°-35°C (93.2°-95°) for 48 hours using cooling blankets or pads already approved by the Food and Drug Administration (FDA). Since cooling causes shivering, which greatly increases your need for oxygen, we will also give you FDA-approved muscle relaxant medication to prevent shivering. We will measure oxygen levels in your blood, the time that you need to remain on a breathing machine, time spent in the intensive care unit, your blood levels of glucose, ions, and how your lung, kidney and liver get on while you are ill.

You are eligible to enroll in this study because you met at least some of the criteria for ARDS, but you will not be assigned to begin study treatment (cooling vs. no-cooling) unless the level of oxygen in your blood drops low enough to qualify.

We will ask as many as 340 people with ARDS to join this over a 4-year period.

WHAT WILL HAPPEN DURING THE STUDY

Your total participation in this study will last 90 days. Your active participation in this study will last one week. Active study treatment will last approximately 54 hours, including the time required for cooling and rewarming. Blood samples will be collected up through study day 7. We will follow your medical record to see how you are doing, give you a test to evaluate your thinking ability when you leave the ICU and when you leave the hospital, and check with you after 60 and 90 days to see how you are doing.

<u>Study Treatment</u>:

You will have a 1-in-2 (50%) chance (like flipping a coin) of getting one of the following study treatments:

1. Cooled to 34°-35°C (93.2°-95°F) for 48 hours using cooling blankets or other external cooling devices while receiving medications to keep you asleep and to prevent shivering by relaxing your muscles; or

2. Standard of care study treatment, which may include warming to keep body temperature close to 37°C (98.6°F) and treatment of fever over 38°C (100.4°F) using medications and cooling blankets.

Neither you nor the study doctor will choose what study treatment you get. You will not be told which study treatment you are getting, however your study doctor will know.

If you agree to be in this study and are assigned to the cooling group, we will make sure right away that you are deeply sedated, start a muscle relaxant medication (to block shivering) and place cooling blankets or cooling pads on you to begin cooling until your body temperature reaches 34°-35°C (93.2°-95°F), and keep you at this temperature for 48 hours while you are receiving medications to keep you asleep and prevent shivering in the ICU. Normal body temperature is 37°C (98.6°F). The dose of muscle paralysis medication will be adjusted the lowest level needed by measuring your muscle responses.

We will adjust the muscle relaxant medication dose to the lowest level needed to prevent shivering by monitoring the depth of relaxation. Treatment with sedation and temporary muscle paralysis is often used to help patients breathe more safely and effectively while on a breathing machine. The effects of the muscle paralysis are temporary. Deep sedation will block feelings of paralysis and cooling. Following the 48 hour cooling period, you will be re-warmed over 3 to 6 hours. Once you are rewarmed to at least 36°C (96.8°F), the temporary paralysis will be stopped. After you are back to normal temperature you will get standard care. We will continue to follow you to see when you no longer need to be on a breathing machine, no longer need to be in the ICU, and no longer need to be in the hospital. The same type of cooling that we are studying for ARDS in this study is standard of care in patients after cardiac arrest because it reduces brain injury. It is not yet known whether similar cooling treatment will reduce lung injury in ARDS although work in the test tube and in animal models of ARDS suggest it may. In order to learn more about whether cooling will help people like you we have to study it.

If you are selected to be in the usual standard of care study treatment group we may administer acetaminophen (the drug in Tylenol) to treat fever and use cooling or warming blankets/pads to maintain your body temperature between 36°C (96.8°F) and 38°C (100.4°F). You may receive sedation and paralyzing medications at the discretion of your ICU care team.

Blood Collection:
We will collect 12 cc of blood (about two teaspoons) when you first enter the study and at five other times over the next week for a total of 72 cc (14 teaspoons) over one week, which is about one sixteenth the volume as a typical blood donation.

Data Collection:
We will record measurements from your breathing machine. We will also collect information from your medical record while you are in the hospital. This information includes things like blood pressure, heart rate, temperature, your study treatments, blood test results, and results of tests for infection or failure of your organs. We will collect data from the medical record about how you are doing at 28, 60, and 90 days after starting the study. If you are no longer in the hospital, we may call you or a person who is close to you and agrees to help us find out how you are doing, or your healthcare provider after 60 or 90 days. Your information collected during this study may be used for future research studies or distributed to another researcher for future research studies once any identifier linking the information/specimen to you has been removed.

Blood Storage: We will freeze some parts of your blood samples and store them for up to six years after completion of the entire study. Your biospecimens collected during this study may be used for future research studies or distributed to another researcher for future research studies once any identifier linking the information/specimen to you has been removed.

Your blood specimens will not be used to make cell lines.

Your biospecimens collected during this study may be used for commercial profit (even if identifiers are removed) and you will not share in this profit.

Research results that are clinically relevant, including individual research results, will not be disclosed to you.

Researchers can look closely at large amounts of your genetic information by sequencing, or "reading," every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research will not include whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

The study doctor may remove you from the study if it is best for you.

EXPECTATIONS

If you take part in this research, you will be responsible to: (1) accept either study treatment – cooling with sedation and paralytic agent for up to 48 hours or usual care; (2) have blood drawn up to 6 times for a total of 72 cc or 14 teaspoons; and (3) let us know how you are doing 28, 60, and 90 days after joining the study.

POTENTIAL RISKS/ SIDE EFFECTS AND/OR DISCOMFORTS:

1. The muscle relaxant medications used (including *cisatracurium, atracruium, and rocuronium*) are approved by the Food and Drug Administration (FDA) for patients on a breathing machine. Rare (less than 1 in 200 people having these) side effects are a slow heart rate and allergic reaction. Many critically ill patients will become somewhat weak during their stay in the ICU; participants in the muscle relaxant group may develop moderate to severe weakness that may last for a longer time after the muscle relaxant is stopped. We will monitor for weakness while you are in the hospital. No increased weakness was seen in two recent ARDS studies, a 1006 participant study conducted in the U.S.A. and a 340 participant ARDS study conducted in France.
2. If you are in the group that receives cooling and muscle relaxants, the medicines used by your treating doctor to keep you very sleepy while you receive muscle relaxant may result in you being asleep and on the ventilator longer than if you did not get the muscle relaxant.
3. Mild hypothermia (cooling by 2° to 3°C or 3.6° to 5.4°F) may theoretically reduce the ability of your blood to clot normally, but several large studies have shown that cooling to this degree does not increase the chances of bleeding.
4. Mild to moderate abnormalities in blood electrolytes and glucose commonly occur during therapeutic hypothermia, but these will be closely monitored and corrected as needed.
5. Mild hypothermia can increase risk of infections but the risk depends on how long the cooling period lasts. Infection is uncommon when cooling for only 48 hours as we will do in this study.
6. Through all stages of sample and data collection, storage, sharing, and analysis, your privacy and confidentiality will be protected. The databases developed for this project will not contain any information that can identify you such as your name, address, telephone number, or social security

number. The information linking you to your data will be kept in a separate secure location. However there is still a chance of unauthorized access to your study data, but the risk of loss of this is very low.

7. The risk of 14 teaspoons of blood drawn over one week is in keeping with similar studies, but may rarely contribute to low blood count in participants who already have significant blood loss. Your blood counts will be followed as part of the clinical management of your illness.

UNFORESEEN RISKS

Since the intervention of longer or shorter durations of hypothermia as a study treatment for people with ARDs is investigational, there may be other risks that are unknown.

You can tell the study doctor if you feel that you are experiencing any side effects or have any questions regarding potential risks.

BIRTH CONTROL RESTRICTIONS

Since the risks of 48 hours of hypothermia in pregnant women or their unborn baby are not definitely known, you cannot participate in this study. If there is a possibility of your being pregnant, we will perform a pregnancy test to evaluate.

ALTERNATIVES TO PARTICIPATION

Taking part in this study is voluntary. If you decide not to be in this study your regular doctor will decide whether or not you should receive cooling as part of your care. The nurses, doctors, and other clinicians will do their best to give you the care you need for your illness, whether you join or do not join the study.

POTENTIAL BENEFITS

You may or may not benefit from cooling if in the cooling group. The purpose of the study is to find out whether cooling is beneficial in people with ARDS. The knowledge obtained from this study will help doctors learn whether cooling can help other people with lung injury.

COSTS TO PARTICIPANTS

It will not cost you anything to take part in this study. You will have the costs normally associated with your care. The addition of cooling to your current level of care will not add to the total cost of your care.

COMPENSATION FOR PARTICIPATION

«Compensation»

You will not be paid for participating in this study.

CONFIDENTIALITY AND ACCESS TO RECORDS AND BLOOD SAMPLES

This study will involve confidential information about your illness, but we will protect your privacy by removing your name and other personal information. Efforts will be made to limit your personal information, including research study and medical records, to people who have a need to review this

information. We cannot promise complete secrecy. The research study team, Advarra IRB, hospital staff, the study Data and Safety Monitor, the Food and Drug Administrator, and the Department of Defense (DoD) will have access to research records as a part of its human participants protection oversight activities. Only your study team in your hospital will know who you are and be able to tell which information and stored blood are yours. We think storing your blood for future studies has neither risks or benefits for you.

The data from the study will appear in medical journals. You will not be identified by name in any of these places. Everyone using study information will work to keep your personal information confidential. Your personal information will not be given out unless required by law.

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.

RIGHT TO WITHDRAW

Your participation in this study is voluntary. You do not have to take part in this research. You are free to withdraw your consent at any time. Refusal to take part or to stop taking part in the study will involve no penalty or loss of benefits to which you are otherwise entitled. If you decide to stop taking part, or if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the study doctor at the phone number listed on the first page of this document.

There will be no adverse consequences (physical, social, economic, legal, or psychological) of decisions to withdraw from the research.

If you decide to leave the study, the research team may ask you if you are willing to have some follow up care, tests, or contact with us. We will store blood samples already in freezers without links to you unless you give us a written request that they be destroyed. We will continue to collect data from your medical record without bother to you until you go home unless you specifically ask us not to.

We will give you any new information that may affect your decision to join or stay in this study.

UNIVERSITY STATEMENT CONCERNING RESEARCH RISKS

The University of Maryland, Baltimore (UMB) is committed to providing participants in its research the rights due them under State and federal law. You give up none of your legal rights by signing and dating this consent form or by participating in the research project.

Participating in research may result in an injury, as explained above. If you suffer an injury directly related to your participation in this project, UMB and/or one of its affiliated institutions or health care groups will help you obtain medical treatment for the specific injury and provide referrals to other health care facilities, as appropriate. UMB and/or its affiliated institutions or health care groups will not provide you with financial compensation or reimbursement for the cost of care provided to treat a research-related injury or for other expenses arising from a research-related injury. The institution or group providing medical treatment will charge your insurance carrier, you, or any other party responsible for your treatment costs. If you incur uninsured medical costs, they are your responsibility. The study staff can give you more information about this if you have a study injury.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

By signing and dating this Consent Form, you are not giving up any legal rights. If this research project is conducted in a negligent manner and you are injured as a direct result, you may be able to recover the costs of care and other damages from the individuals or organizations responsible for your injury.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- 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 the Study Subject Adviser: Pro00044486.

Signing and dating this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed and dated consent form.

If you agree to participate in this study, please sign and date your name below.

_____
Print Participant's Name

_____
Participant's Signature

Date:_____

_____
Investigator or Designee Obtaining Consent Signature

Date:_____

_____
Signature of Legally Authorized Representative

Relationship:_____

Date:_____

_____
Witness*

Date:_____

*Required for verbal consent

If returning a picture of the signed and dated signature page, please email to jhasday@som.umaryland.edu.
If FAXing the signed and dated signature page, please FAX to 410-328-0177

Consent form sent to LAR by:

- ☐ LAR unable to or declined transmission of consent form image and contents described over the phone
- ☐ FAXed
- ☐ emailed

Questions answered by:

- ☐ Phone
- ☐ FAX
- ☐ email

Consent given by:

- ☐ verbally over phone
- ☐ signature page FAXed
- ☐ signature page emailed

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of University of Maryland, Baltimore.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- US Department of Defense.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- A data safety monitoring board which oversees this study, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the investigational cooling study treatment works and is safe.
- To compare the investigational cooling study treatment to other the usual standard of care study treatment.

- For other research activities related to the investigational cooling study treatment.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

_____
Printed Name of Legally Authorized Representative

_____ _____
Signature of Legally Authorized Representative Date

_____
Authority of Legally Authorized Representative to act on behalf of Participant