SIREN Informed Consent Forms

The Sponsor/Investigator of ICECAP 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 ICECAP 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 ICECAP 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 ICECAP 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 icecap-contact@umich.edu.

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

NIH SIREN
Emergency
Trials
Network

ICECAP

CONSENT FOR CLINICAL RESEARCH STUDY
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Sponsor / Study Title:	**The National Heart, Lung, and Blood Institute (NHLBI) and The National Institute of Neurological Disorders and Stroke (NINDS) / "ICECAP: Influence of Cooling duration on Efficacy in Cardiac Arrest Patients"**
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 a 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 participant regains the capacity to consent, informed consent will be obtained from the participant and the participant will be offered the ability to leave the study if desired.

SUMMARY OF KEY INFORMATION

A person that you represent has survived a cardiac arrest. He or she is now in a coma (comatose). He or she may be eligible to participate in a research study. Brain injury causing coma after cardiac arrest can be fatal or prevent patients from recovering. We are doing a study to learn more about a way to possibly lessen brain injury after cardiac arrest. Therapeutic hypothermia (cooling the body and the brain a few degrees below normal temperature) is a

standard treatment in which comatose patients are rapidly cooled. This is done to try to improve their chances of recovering to normal. Standard practice is to cool patients for about a day. However, the best length of time of cooling is not known. Longer or shorter durations of cooling may improve, worsen, or have no effect on chances of recovery from cardiac arrest.

The goal of this study is to learn whether different lengths of time for body cooling affect recovery.

Participants in this study must have already begun standard, non-study medical treatment with cooling.

In this study, different participants are cooled for different durations. Durations are assigned mostly by chance, like by flipping a coin, using a computer program from a few possible lengths of time. The durations being studied range from less than a full day to three days.

After study treatment, we will contact participants or their caregivers about once per month to see how participants are doing. We ask that participants who survive their cardiac arrest follow-up in the research clinic in about 3 months. This visit involves questions and puzzle-like exercises to see how well the brain may be functioning. Participation in the study ends after three months. The study team will review the participant's medical records while they are in the study as needed. About 1,800 participants will be enrolled at about 50 hospitals.

Being part of the study will help doctors learn how long to cool future victims of cardiac arrest. It will also help doctors learn whether to cool patients at all. There may or may not be direct benefit from being in the study. Some participants may benefit directly if recovery turns out to be more likely with the duration of cooling they receive, while others may have a worse outcome.

Participation may also have risks. Known risks from study participation include accidental release of private information. Longer or shorter durations of cooling may be safer or less safe than standard care. Participants may have more or fewer infections, bleeding, blood clots, abnormal heart rhythms, or discomfort because of their cooling duration. There may be additional risks that are unknown or unexpected.

Participation in the study is voluntary. The alternative to being a part of this study is usual care. Usual care is most often cooling for about one day. There is no penalty for choosing not to participate. A participant can quit the study at any time.

Medical records and data collected in the study will remain as private as possible. Records may be viewed by the study team here or from the study coordinating centers. Records may also be seen by those who review the safety and conduct of the study. Review is done by this hospital and by government regulators and funders.

There is no payment 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.

Please contact us for any questions about the research, participants' rights, or other concerns.

- Please carefully read this form. Additional detail about each item just described is found below.
- Please listen to the study team. They will explain the study and this form to you.
- Please ask questions about anything that is not clear.

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

MORE DETAILED INFORMATION

Why is my family member (or the person I represent) being asked to participate?

You are being asked whether the person that you represent would wish to participate in a research study. Patients are eligible to be in this study if they survived a cardiac arrest but are now comatose, and have begun standard medical treatment involving cooling of the body to try to help preserve brain function. Coma after a cardiac arrest is a very serious medical condition. Many patients with this condition do not survive to leave the hospital, and many others can have mild to severe long-term problems. We are conducting a study of investigational interventions of longer or shorter durations of hypothermia as treatment for these patients.

Participation is voluntary, which means you can choose whether or not you want the person that you represent to participate. If you choose not to have the patient participate, there will be no loss of benefits to which the patient is otherwise entitled. Before you make your decision, you will need to know what the study is about, the risks and possible benefits of being in this study, and what your family member (or the person that you represent) will have to do in this study. The research team is going to talk to you about the research study and this consent form. This form gives you important information about the study. Please take time to listen to this information carefully. You may find some of the medical information difficult to understand. Please talk to the study doctor and the research team about this form and ask them any questions you have. The study doctor is also called the principal investigator. You may also want to discuss it with your family or others. If you decide to consent for the person you represent to participate in the study, you will be asked to sign and date this form.

What is a cardiac arrest?

Sudden cardiac arrest occurs when the heart develops an abnormal heart rhythm that causes it to stop beating. The heart's pumping function is "arrested," or stopped. Without the heart

pumping, there is no blood flow to the brain, lungs and other organs. A person in cardiac arrest loses consciousness and has no pulse. Death occurs within minutes if the victim does not receive treatment. This is different than a heart attack, where the heart usually continues to beat but blood flow to the heart is partially blocked.

Survivors of cardiac arrest are often unconscious after their heart is restarted. This is from the brain not getting blood when the heart was not pumping. The heart and other organs may also be injured from the cardiac arrest. Medical care after a cardiac arrest is about allowing and helping the patient recover from these injuries. It is also about preventing it from happening again.

Why is this study being done?

The purpose of this study is to find out what durations of the study intervention are safe and most likely to result in the most complete neurological recovery. The study intervention is hypothermia. Hypothermia is the cooling of your body to a lower than normal temperature. Hypothermia is regularly used to treat patients who survive cardiac arrest, and **all participants in this study are already being treated with standard care hypothermia**. However, it is not known what duration of cooling is best for patients. There is information that suggests that cooling for longer than the time used in standard care may be better for patients. It is also possible that shorter durations are safer and equally effective.

Longer or shorter durations of hypothermia are an investigational intervention, which means that it has not yet been proven an effective treatment. It may be better, the same, or worse than cooling for the durations typically used. This type of research study is also called a clinical trial.

How many people will take part in the study?

This study will enroll up to 1800 people nationwide over approximately 4 years. All participating hospitals are in the United States. We expect to enroll an average of 36 people at each participating hospital. No person shall be excluded from participation based on gender, race, color, economic status, or national origin. All patients eligible for this trial are treated with routine hypothermia regardless of whether or not they participate in this study. Patients that do not participate in the study are typically treated with hypothermia for 24 hours. Those participating in the study may be treated for the same duration, or for shorter or longer durations.

What is involved in the study?

You are being asked to decide whether or not to consent on behalf of the patient eligible for this study. To consent on the patient's behalf, you must be a legally authorized representative, usually a spouse or other family member. To be included in this study, the patient must be at least 18 years of age, and must have had a cardiac arrest and have had cooling started within the past 6 hours. In addition, the patient needs to be cooled to 34 degrees Celsius or less (about 93 degrees F) within four hours of the time of cardiac arrest. If you consent, the participant will be treated with cooling for a duration ranging from less than a full day to three days.

Cooling will be performed by a device that manages the participant's temperature. The device will also be used to rewarm the participant slowly after the duration of cooling has ended. Rewarming usually occurs over 24 hours. After rewarming, the same device or other means will be used to try to keep body temperature around 36.5 degrees Celsius (about 98 degrees F) for the rest of the first 5 days. Our study team members will check on the participant daily for the first 5 days, and then periodically until hospital discharge.

The duration of cooling each participant receives is determined by a computer program. The duration picked is mostly at random from a set of possible choices of hours. As the study continues, patients are more likely to be randomized to durations of cooling where patients are doing better.

In addition to collecting information about your family member's (or person you represent) hospital stay, we will also access and record clinical information from the ambulance and emergency department, including care provided prior to now.

All other treatments and medical care for the participant's condition will be the same regardless of the duration of cooling.

Decisions About Withdrawal of Life Sustaining Treatments

Sometimes when patients are very sick, families decide that the patient would want to withdraw life-sustaining treatments within a few days. You should not choose participation in this study unless there is an intent to continue life-sustaining treatments for at least 5 days.

Decisions about continuing life-sustaining treatments for participants should be re-visited after 5 days when cooling and rewarming are completed. The doctors caring for the participant will discuss this with you if the person you represent remains unconscious. This is often the earliest time that doctors can make reasonable predictions about the likelihood of the participant's possible recovery. You should feel free to discuss the situation with others whom you think

will be of help, such as other family members and hospital clergy or counseling staff.

What Will Happen at the End of the Hospital Stay?

At the end of the hospital stay, a member of the study team will collect contact information for the participant, you, your family members, close friends, and associates. Someone from the study team will contact the participant every month after the cardiac arrest, for a total of 3 months. The study team may call, email, or text the participant or other provided contact. Contacts may tell us what they prefer. The purpose of these follow up contacts is to see how the participant is doing, to find out if there are any additional problems, and to see if any of your contact information has changed.

We will visit the participant during a scheduled clinic or therapy visit, or ask the participant to return to the study clinic one time about 3 months after the cardiac arrest. On this visit we will measure how well the recovery is going, and how the participant feels. During the visit, a study team member will ask questions about the participant's recovery. The study team member will not know how long the participant was cooled. There will be a questionnaire and some computerized and pencil and paper exercises. The exercises are like games or puzzles designed to measure different aspects of recovery. There are no risks anticipated from this visit. This visit will take about two hours. The questions and exercises may be audio or video recorded for quality monitoring purposes. If a visit is not possible, or we cannot ask all our questions during the visit, we may also call the participant to learn about the recovery. If possible, a telephone interview with the participant or caregiver will collect the same information as the visit except for the computerized and pencil and paper exercises. The phone call may take up to 1 hour.

How long does participation in the study last?

Participation in the study will last for approximately 3 months.

The participant will be checked to determine how they are responding to the study intervention. You (representing the participant) or the medical team may decide to stop the study intervention. Stopping the study intervention means cooling for a duration different than the duration chosen randomly for the participant. You may stop if there are serious side effects, or if you or the medical team decide that the study intervention is not in the participant's best interest. The study intervention may be stopped if the study leadership decides to stop the study. Even if the study intervention is stopped, the participant may still continue in the study. Information about how the participant is doing is still collected until 3

months from enrollment or until withdrawal of consent.

You, or the participant when able, may stop participation at any time by withdrawing consent. Stopping participation in the study means the study team stops collecting information about the participant. However, if you decide to stop participation in the study, we encourage you to talk to a doctor first. If you withdraw consent, only information already collected about the participant while in the study will be used in this study.

What are the risks of the study?

Because of the cardiac arrest, the patient is at risk for a number of complications regardless of participation in the study. Participating in the study may have additional risks. The study will determine if any of these risks is increased by the study intervention. Possible risks that may be increased by different durations of cooling may include:

- Abnormal heart rhythms (occur in about half of people after cardiac arrest)
- Infections in the lung (pneumonia), or other infections (occur in about half of people)
- Shifting or low blood electrolyte or glucose levels (occur in more than half of people)
- Neurological worsening (occurs in about 3-5 out of 10 people)
- Seizures (occurs in about 3 out of 10 people)
- Blood clots in the large veins in the leg (occur in about 1-2 out of 10 people)
- Bruising or bleeding (occur in about 1-2 out of 10 people)
- Skin problems related to cooling devices (occur in less than 1 in 10 people)
- Discomfort from cooling (since participants are comatose and sedated, this is very rare)

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.

Reproductive Risks: Cardiac arrest involves increased risk to a pregnancy. Cooling is not known to be dangerous in pregnancy. There may be unknown risks because cardiac arrest during pregnancy is rare.

Are there benefits to taking part in the study?

If you agree for the person you represent to participate in this study, there may or may not be direct medical benefit to the participant. There may be an improved recovery from being in this study, but this is not guaranteed. We hope the information learned in this study will

benefit other patients receiving therapy for brain injury after cardiac arrest in the future.

What other options are there?

Participation in this study is voluntary. The alternative to participating in the trial is usual care. Usual care will include cooling for a duration chosen by the patient's doctor. Most often this would be 24 hours. If not participating in the trial, the patient will continue to receive the best standard care possible. Your decision whether or not to have the person you represent participate in the study will not adversely affect current or future medical care. Please talk to the treating doctor or the study doctor about these options.

There is no penalty for choosing not to participate. The participant may withdraw from the study at any time, either by his/her choice or at the direction of the participant's legally authorized representative. Choosing not to participate, not to continue participation, or choosing to withdraw consent will not alter the usual care available. Nor does it alter or waive any legal rights or benefits.

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 physiological monitoring or tests, 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 US National Institutes of

Health (NIH), the US Office for Human Research Protections, the US Food and Drug Administration (FDA), 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 will be submitted to the US Food and Drug Administration (FDA).

To help us protect the participant's privacy, this research is covered by a Certificate of Confidentiality from the US National Institutes of Health. With this Certificate, the investigators may not disclose or use information, or documents that may identify the participant 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, in the US unless the participant has 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 (see below); if the participant has consented to the disclosure, including for the participant's medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the NIH or when required by the FDA. A Certificate of Confidentiality does not prevent the participant from voluntarily releasing information about themselves or their involvement in this research. If the participant wants research information released to someone, the participant 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 to which you have consented 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 study 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.

When ready to leave the hospital, typically well after the period of cooling is complete, the participant may be discharged to a rehabilitation or nursing facility. The participant might also be discharged home and then readmitted to another medical facility later. Your signature on this document authorizes those facilities to release medical records to the researchers and research staff of this study. Only medical records that refer to the 3 months the participant is in the study are included in this authorization.

We will keep any records that we produce private to the extent we are allowed or required by law. The participant's records will be kept for as long as necessary for purposes of the research study.

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 information and consent form, you consent to 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 and date 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.

Will the participant have 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 participation. Costs related to cooling are part of standard medical care. 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. You may receive some travel reimbursement for your scheduled study follow-up visit.

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 bottom 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 (National Institutes of Health), 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. You will not be giving up any of your or the participant's legal rights by signing and dating this consent form.

Who could profit or financially benefit from the study results?

None of the researchers involved in this project have any financial interests in the outcome of this study. Companies that make cooling devices may financially benefit from the study results.

What are the participant's rights?

Taking part in this study is voluntary. You may choose for the participant not to take part or leave the study at any time. Leaving the study, or choosing not to take part, will not result in any penalty or loss of benefits to which the participant is entitled.

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.

Future research studies

Identifiers might be removed from the participant's identifiable private information collected during this study and could then be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

Clinically relevant results

This study does not involve individual research results that are clinically relevant. Individual research results will not be disclosed to you or the participant.

Where can I get more information?

Visit the ICECAP Study Web site: ICECAPtrial.org

You will also get a copy of this form.

We will tell the participant or you about new information that may affect the participants' health, welfare, or willingness to stay in this study.

Participants may also be contacted about future available studies. We may also contact

participants with periodic updates about the study. We may also contact participants after the trial has been completed to share the overall results of the study.

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 the Web site at any time.

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
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call toll free: 877-992-4724
- or by email: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00041076.

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 and dating this consent document. I will receive a copy of this signed and dated consent document.

SIGNATURES

_____
Printed Name of Participant

_____ _____ at _____
Participant's Signature Date and Time

STATEMENT OF LEGALLY AUTHORIZED REPRESENTATIVE

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 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.

_____
Printed Name of Participant

_____
Printed name of Legally Authorized Representative

_____
Relationship to Participant

_____ _____ at _____
Signature of Legally Authorized Representative Date and Time

_____	_____
Principal Investigator/Designee Name	Title
_____	_____ at _____
Principal Investigator/Designee Signature	Date and Time