SIREN Informed Consent Forms

The Sponsor/Investigator of P-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 P-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 P-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 P-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 picecap-contact@umich.edu.

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

INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

For studies conducted in compliance with the revised Common Rule

Study Title / Sponsor:	**P-ICECAP: Pediatric Influence of Cooling duration on Efficacy in Cardiac Arrest Patient / National Institutes of Health**
Protocol Number:	**Protocol Number**
Principal Investigator:	**«PiFullName»**
(Study Doctor)	
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 participant. 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

Your child is eligible to participate in a research study involving children who have had a cardiac arrest. A cardiac arrest occurs when a child's heart stops for a period of time. Children often do not wake up right away after their hearts are restarted. This is because of injury to the brain during cardiac arrest.

The goal of this study is to find out if cooling children's bodies for longer durations than are used in clinical practice can help the brain recover after cardiac arrest. Doctors do not yet know how best, or how long, to control temperatures in children after cardiac arrest. Current guidelines recommend controlling temperature for 3-5 days. The guidelines also say that controlling temperature may involve cooling or just preventing fever for the first two days.

This study compares cooling children for shorter or longer lengths of time to try to learn what duration is best. In this study children are cooled for different lengths of time or their temperature is kept normal to prevent fever. The length of cooling for each child is chosen by a computer mostly by chance, like flipping a coin. Except for the management of body temperature, children in this study will get the same care for cardiac arrest as children not in the study. All children who have had cardiac arrest are treated in the pediatric intensive care unit (PICU).

If your child participates in this study, the study will assign your child a length of cooling or fever prevention in the PICU. The temperature and duration your child is assigned may be different from what your child's doctor would do if your child was not in this study. While in the hospital, the study team will follow along with the PICU doctors and nurses caring for your child. Information about your child will be collected from the medical record. Many children with cardiac arrest survive and recover. Sadly, some do not. While some children who survive get all better, others are not able to do all the things that other children their age can do. The study team will contact you from time to time over a year to see how well your child is doing. We also ask that children have a follow up visit with the study team after about one year. At this visit we will ask more questions about life at home and your child's recovery. A neurologist will examine your child. You and your child are done with the study after the one year visit.

This study may help us learn how to better treat other children like yours in the future. Your child may or may not benefit from being in the study. Cooling for a longer or shorter duration or fever prevention in the study may be better, the same, or worse than how body temperature is controlled in children who are not in the study. Participation in this study also has risks. Longer or shorter durations of cooling assigned in the study may be safer or less safe. Prolonged cooling may be safer or less safe than keeping your child at a normal temperature. Children getting different durations of cooling may have more or fewer problems. The problems may include infections, bleeding, blood transfusions, abnormal heart rhythms, changes in blood sugar or electrolyte tests, or discomfort. Study participation could involve accidental release of private information. There may be additional risks that are unknown or unexpected. Also, some of the questions we ask you during the hospitalization or follow up visits may be upsetting.

Participation in the study is voluntary. If your child is not in the study, your child's doctors will choose how to control your child's temperature and for how long. There is no penalty for choosing not to participate. If your child is not in the study there will be no loss of benefits that they otherwise would have been entitled to. Being in the study will not limit your child's access to other treatments. You can remove your child from the study at any time.

The study is funded by the National Institutes of Health. About 900 children will be enrolled at about 40 hospitals. A regulatory review of safety data on the first 40 children is needed for the study to continue. Safety data is carefully reviewed throughout the study. There is no cost to participate in the study. Charges for all routine medical care will be billed the same way whether or not someone is in the study. There is no payment for being in the study.

The rest of this form and the study researchers will give you more detailed information about the study. This information will help you decide whether or not you want to let your child be in the study. The study team can explain words or information that you do not understand. Please read this form and ask any questions to help you decide. If you consent to participation, please sign and date the form.

MORE DETAILED INFORMATION

What is cardiac arrest?

Cardiac arrest means that the heart stopped beating. When this happens, the brain can be injured because the heart is not pumping blood with oxygen to the brain. Your child is now in a coma or comatose. A coma means someone is unconscious and cannot respond much or at all to voice or touch. Your child may be able to be in this research study about possibly decreasing brain injury after a cardiac arrest. Brain injury due to a cardiac arrest may prevent a child from waking up or doing the things they were able to do before the arrest. Brain injury may cause a child to have slower development and/or loss of previous skills controlled by the brain, such as talking, feeding themselves, thinking, and walking. Brain injury causing coma after cardiac arrest can also cause a child to die.

Why are you asking me to have my child in this study?

You are being asked to have your child participate in a research study because your child has survived a cardiac arrest. We understand this is a difficult time. Your child is eligible because they received CPR with chest compressions for over two minutes, now have a breathing tube in with a machine breathing for them and are not acting normally. In younger children, this means they are not moving normally and in older children this means they aren't able to follow commands. Your child's doctors will test them if they could be pregnant. If your child is pregnant, they cannot be in the study.

Why are we doing this study?

Cooling a person a few degrees below normal temperature is called therapeutic hypothermia. This is done to try to improve a child's chances of recovering brain function. We don't know if this cooling helps or how long we should cool to give the best chance of brain recovery. It may be that cooling is not better than keeping your child at a normal body temperature. Longer cooling durations may put your child at higher risks for medical problems.

This is a special kind of research study called a clinical trial. In a clinical trial, children are given different treatments so the study team can figure out what works best. In this case, the different treatments we are studying are different lengths of cooling, including no additional cooling at all.

Children who can be in this study have already begun regular medical treatment with a temperature control device to keep the temperature somewhere between 33°-37°C (91.4°-98.6°F). This hospital uses temperature control for children in a coma after a cardiac arrest, whether they are in this research study or not. The temperature control device uses a blanket or pads that keep an eye on and can change your child's temperature. There is already a thermometer monitoring your child's temperature that is connected to the device, so the device knows what your child's temperature is at all times. Right now, your child's intensive care doctors have started with a temperature target somewhere in the 33°-37°C (91.4°-98.6°F) range for your child.

What is involved in the study?

If enrolled in the study, your child will be assigned to be cooled to 33°C (91.4°F) for a specific period of time, up to 96 hours (4 days), and then be kept at a normal temperature 36.8°C (98.2°F) until the end of the 5th day or assigned to be kept at a normal temperature for the whole 5 days.

If your child's temperature is above what is assigned by the study, your child will be cooled to the assigned temperature of 33°C (91.4°F) or 36.8°C (98.2°F). If your child's temperature is below what is assigned by the study, your child will be warmed to the assigned temperature of initially cool, 33°C (91.4°F), or normal, 36.8 °C (98.2°F).

The temperature and duration your child is assigned may be different from what your child's doctor would do if your child was not in this study. All other treatments your child will receive are the usual intensive care treatments they would receive whether enrolled in the study or not.

How long will my child be cooled?

In this study, the length of cooling is assigned by chance, like by rolling dice. The first 150 children in the study have the same chance to be cooled for 24, 48 or 72 hours. After 150 children are in the study, children may be assigned by chance to 12, 18, 24, 36, 48, 60, 72, 84 or 96 hours of cooling or no additional cooling. After your child has been cooled for the length of time the study assigned, they will be rewarmed to normal temperature (36.8°C or 98.2°F)) slowly, over about a day (unless they were in the no additional cooling group). We will

then keep them at this normal temperature until the end of the fifth day (120 hours). If your child is assigned to the 0 hour group, your child will be kept at a normal temperature of 36.8°C (98.2°F) for 120 hours. While receiving the study treatment they will get medicine to keep them comfortable and to prevent shivering. If at any time your child's doctor no longer believes cooling to be in your child's best interest, the doctor can rewarm your child to normal temperature temporarily or permanently.

What information will be collected?

The study team will check on your child frequently while your child is in the hospital. They will collect information about your child's medical care. After the 5 day temperature control time period is over, there are no additional study related treatments. However, there will be follow-up telephone calls and one return visit in one year. In the hospital and on the calls, we will also ask a number of questions about how your child is doing.

- **While in the hospital:** We will ask about how your child was doing before the cardiac arrest. This includes a quality of life survey. We will also ask you for a brief survey about you and your child's family life and your household information. This should take less than one hour.
- **Phone calls at three months and 12 months after the cardiac arrest**: We will call you at 3 and 12 months. We will ask about how you and your child have been doing since leaving the hospital. There will be questions about your child's quality of life as well as your child's behavior. These calls should take between 30 minutes and 1 hour.
- **Visit at 12 months:** At this visit, your child will see a pediatric neurologist who is an expert in brain functioning. The neurologist will examine your child to assess how the brain is functioning. The visit will take less than two hours.

What can I expect from the researchers?

If researchers or doctors taking care of your child find out about unexpected risks or dangers to your child or others in the study, they will inform you and may remove your child from the study if needed. As described earlier, your child's doctor can change how long your child is cooled or what the target temperature is set at for care, if needed.

What are the possible benefits of the study?

Your child may or may not directly benefit from being in the study. Your child may have better brain function after their cardiac arrest if the temperature management they are assigned to results in better outcomes than the other temperature management assignments. However, your child may not benefit if a much different length of cooling turns out to result in better outcomes, or if maintaining bodies at a normal temperature turns out to be better. Being part of this study may help children in the future.

What are the possible risks and discomfort of the study?

This study has risks. The study team and your doctors will watch closely for any problems and your child will be treated if needed. As with any research study, there may be additional risks that are unknown or unexpected.

The length of cooling varies from no further cooling after starting the study to 96 hours of cooling. Both cool and normal temperatures have risks, and these may be different based on how long or short the cooling lasts. Cooling more than 48 hours has not been studied in this age group. Risks that might be related to temperature control duration include:

- Bleeding: cooling might lower blood counts and affect how well the body can create clots.
- Infection: infections in the ICU are common. Cooling might affect how well the body can fight infection
- Fever: shorter durations of cooling may not prevent fever as well as longer durations.
- Cardiac arrhythmias and cardiac arrest: the heart might not beat regularly when cool and the heart might stop again.
- Electrolyte levels and blood sugar may change when being cooled or being rewarmed
- Seizures and worsening brain damage occur a lot after cardiac arrest. We don't know if cooling makes this better or worse.
- Pain or shivering from cooling or the devices may happen.
- Skin problems are rare, but sometimes redness and swelling can be seen from cooling devices.

Your child will be watched closely no matter how long they are cooled or if at all. Varying body temperatures has the risk of contributing to the problems listed above. It is standard of care to monitor for bleeding, infection, abnormal heart rhythms, electrolyte shifts, shivering and skin problems in any child who has had a cardiac arrest. Treatments depend on the problem. In the ICU, it is common to receive blood products, antibiotics, pain medicines and sedatives. Your child may need CPR or medications for another cardiac arrest or abnormal heart rhythm. Skin problems may require movement or removal of a cooling device. Your child may need more or less of these treatments based on how long and if they are cooled. In a prior study, children cooled for two days had similar risks compared to those maintained in a normal temperature range. The cooled group appeared to recover better and more survived, but the study may not have been large enough to know for sure. That study only looked at two days of cooling. It did not look at longer or shorter durations. In that study there was also no difference in risks between those cooled for two days and those kept at normal temperatures. About 1 in 10 had abnormal heart rhythms in both groups. About half got blood transfusion in both groups. And about half got antibiotics for infection in both groups.

You may be distressed by answering some follow up questions about you or your child. You can always ask for more time or decide not to answer any questions you don't want to.

There may also be other risks that are unknown.

What are the alternatives to participation?

Study participation is not required for care. Being in the study is voluntary. If you choose not to have your child in this study, they will receive standard intensive care in this hospital. Temperature control is part of standard intensive care, but the choice of temperature at which a child is maintained and for how long varies by local practice in different hospitals and by the preferences of different doctors. National practice guidelines for standard critical care suggest keeping temperatures between 33-37°C (91.4 - 98.6°F) for about 3-5 days. At many hospitals participating in this study, the common practice is keeping temperatures around 36°C (96.8°F). The study team or your child's doctor can tell you exactly what temperature control strategy will be pursued for your child if you decide not to be in the study.

What if my child is injured as a result of being in this study?

If your child becomes ill or injured from being 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.

Will we have to pay anything to be in the study?

There is no cost to participate. The study will not pay for the standard medical care that your child receives during participation. Temperature control is part of standard medical care and is used whether or not your child participates in the study. These costs will be billed to you or your insurance. Charges for temperature control are not different with different assigned durations or temperatures. There are no additional medical tests or procedures performed for research purposes in this study.

Will we be paid for being in the study?

No, you will not be paid for having your child in this study.

Future research studies

Information that identifies your child will be removed from the other information collected during this study. This study information, which cannot be linked back to your child, could then be used for future research

studies, or given to another investigator for future research studies without additional informed consent. Researchers might also contact you about your child being in future studies.

How is our contact information stored?

Contact information for your child, you, your family members, close friends, and associates will be collected to make sure that we can follow up to determine your child'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.

AUTHORIZATION TO COLLECT HEALTH INFORMATION

The study investigator and his/her collaborators will consider your child's personal information confidential to the extent permitted by law. "Personal Information" means information that can be used to identify your child or health information about your child. 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 your child 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 your child's 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 your child'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 your child'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 your child 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 consent to do so is provided 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 your child has consented to the disclosure, including for your child's medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research participants.

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 your child from voluntarily releasing information about themselves or their involvement in this research. If your child wants research information released to someone, your child 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 your child's medical and health records, absolute confidentiality cannot be guaranteed. We will use a study number rather than your child's name on study records where we can. Your child's name and other facts that might point to your child 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 your child may be discharged to a rehabilitation or nursing facility. Your child 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 12 months your child 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. Your child'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 your child's health information. With this form, you authorize the study doctor to use and disclose your child'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 your child'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 your child's information as described above. State law or the enrolling institution may require an additional separate form on which you can authorize sharing of your child's health information. If so, you will have to sign and date both forms for your authorization to be valid.

Who can you contact about this study?

Please contact the Investigator at the telephone number listed on the first page of this consent document if the participant experiences any medical problems, suffers a research-related injury, or if you have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Reimbursements for future study visits, if any;
- Responsibilities as a research participant;
- Eligibility to participate in the study;
- The Investigator's or study site's decision to exclude your child from participation;
- Results of tests and/or procedures;

If the participant seeks emergency care, or hospitalization is required, alert the treating physician that the participant is 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, 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: Pro00061683.

VOLUNTARY PARTICIPATION / WITHDRAWAL

You are free to have your child return to routine medical care at any time. If your child has been cooled, your doctors could rewarm them. You would be able to continue in the study and have the other follow up visits and assessments if you wanted. Also, if there are specific questions or surveys that you do not want to answer, you are always free to do only the parts of the study follow up that you are comfortable doing. You could also choose to stop all study activities and withdraw completely from the study. If you either choose not to have your child in the study or withdraw from the study, there will be no penalty to you or your child, and you will not lose any benefits to which you or your child may otherwise be entitled.

If you choose to tell the researchers why you are leaving the study, your reasons for leaving will be kept as part of the study record. If you decide to leave the study before participation is finished, please notify the research team. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from 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 this Web site at any time.

ADDITIONAL SITE SPECIFIC INFORMATION

Any additional information provided by this site is included in the following box.

CONSENT

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 have my child 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. If it is possible in the future, depending on your child's age and recovery, we will also ask your child if they agree to continue in the study.

SIGNATURES

_____

Printed Name of Participant

_____

Printed Name of Parent or Legally Authorized Representative

_____ _____/_____

Signature of Parent or Legally Authorized Representative Date & Time

_____

Authority of Legally Authorized Representative to act on behalf of Participant (usually parent or guardian)

_____

Printed Name of the Principal Investigator or Designee

_____ _____/_____

Signature of the Principal Investigator or Designee Date & Time

CONSENT TO CONTINUE PARTICIPATION AFTER REACHING THE AGE OF MAJORITY

I understand that I was enrolled in this research study with the consent of my parents or legally authorized representative when I was a child. Subsequently, I have reached the age of majority and am an adult. I am now being asked to consent to continue participation in this research. 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 continue participating 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.

_____

Printed Name of Participant

_____ _____/_____

Participant's Signature Date & Time