Appendix C: Sample Consent Form

Parental Permission/Research Informed Consent

Title of Study: Optimizing Cooling Strategies at < 6 Hours of Age for Neonatal Hypoxic-Ischemic Encephalopathy (HIE)

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Funding Source: *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)

Purpose

You are being asked to allow your child to be in a research study examining the beneficial effects of brain cooling because your infant has been evaluated and diagnosed with a condition called Hypoxic Ischemic Encephalopathy (HIE). HIE results from decreased blood flow and oxygen to all the organs in the body including the brain. Certain signs noted on your child's physical examination show that your child has encephalopathy. In this hospital and in many others, infants diagnosed with HIE at less than six hours of age are given a standard treatment of whole body cooling, decreasing their body temperature to 33.5 degrees Centigrade (92.3 degrees Fahrenheit) for a period 72 hours using a cooling blanket. This mild decreasing of infants' body temperatures (body cooling) appears to be the most promising treatment available to infants with moderate to severe HIE, protecting their brains therefore reducing the rate of death and improving outcomes at 18 months of age

This study of Optimizing Cooling will be examining the potential of greater positive effects of cooling at a lower temperature, 32.0 degrees Centigrade (89.6 degrees Fahrenheit) and/or a longer duration of time, for a period of 120 hours. This study is being conducted at Hutzel Women's Hospital and Children's Hospital of Michigan at Wayne State University and at other university medical centers across the United States through the National Institute of Child Health and Human Development (NICHD) sponsored Neonatal Research Network. The estimated number of study participants to be enrolled at Wayne State University is about 50 as part of about 726 throughout the country.

Please read this form and ask any questions you may have before agreeing to be in the study.

In this research study, infants with HIE and eligible for cooling before 6 hours of age will be placed in one of four cooling groups, be monitored closely and receive the care of the Newborn Intensive Care Unit (NICU). Investigators in this study want to know which of the four cooling management groups may improve infants' survival and improve survival with as few as possible long-term problems. Study assessment of long-term outcomes will be done at a clinic follow-up visit at 18-22 months.

Study Procedures

If you agree to have your child take part in this research study, he/she will be randomly assigned to one of four study groups. Random assignment (like a flip of a coin) means your child has a one in four chance of being placed in any of the following cooling groups:

1. **a temperature of 33.5°C (92.3°F) for a period of 72 hours—the control group as this is our usual care for infants with moderate to severe HIE**
2. **a temperature of 33.5°C (92.3°F) for a period of 120 hours**
3. **a temperature of 32.0°C (89.6°F) for a period of 72 hours**
4. **a temperature of 32.0°C (89.6°F) for a period of 120 hours**

To provide body cooling, infants are placed on a blanket system designed to provide cooling and warming as needed. This blanket is used in children's hospitals in the NICU, in operating rooms during surgeries, and to cool children with high fevers. Your child will be cooled according to the study group assigned. During cooling your child's temperature will be very closely monitored by continuous esophageal temperature readings. This will be done by placing a soft, narrow, flexible plastic tube into your child's nose and down to just above the stomach (the esophagus). Skin temperatures will also be monitored closely. At the end of the assigned period of cooling, your child will be slowly re-warmed until a normal body temperature of 36.5 to 37.0°C (97.7 to 98.6°C) is reached. Re-warming will be started before the end of the assigned cooling period if there are any complications related to the lower than normal temperature or if your child should need more support to the heart and lungs by a procedure called ECMO.

Your child's care will otherwise continue as the usual standard clinical care in the nursery. Your child's hospital stay will be followed closely and important information will be collected such as ventilator (breathing machine) and oxygen requirements, assessment of body systems including the brain and heart, any infections and nutrition progress. Results of standard clinical tests performed on infants with HIE, head ultrasound and magnetic resonance imaging (MRI) will be documented.

When your child is 18-22 months old, he/she will be seen at the Developmental Assessment Clinic or Children's Research Center at Children's Hospital of Michigan. During this 2-3 hour follow-up visit, you will be asked questions about how your child is doing (approximately 30 minutes), a pediatrician will examine your child (approximately 30 minutes) and his/her development also will be checked. Your child will undergo developmental testing by a trained psychologist or tester (lasting about 1 hour).

In order to contact you following your child's hospital stay, we will ask for your contact information including home address, home and cell phone numbers, email address, and your permission to use public internet social and search pages. The 18-22 month visit is the end point of the study; we would however like your permission to continue to keep in contact with you and your child beyond this time in case the study analysis shows a need/opportunity for additional follow-up.

Benefits

The possible benefits to your child for taking part in this research study are that body cooling at a lower temperature or a longer period of time than the current standard treatment for infants with HIE may show a greater reduction in brain injury and disabilities resulting from brain injuries. Additionally, the benefits seen in taking part in this study may help future infants with this condition.

The scheduled follow-up visit may lead to discovery of and treatment of any developmental problems.

Risks

By taking part in this study, your child may be at increased risk for disturbances of heart rhythm, abnormal blood clot formation or bleeding, or skin breakdown. These are problems that can occur with even standard of care body cooling but also without cooling because of a lack of blood supply to all the organ systems with HIE. Your child will be watched very closely and monitored for any side effects that can occur.

There may also be risks involved from taking part in this study that are not known to researchers at this time.

Alternatives

You have the choice to not allow your child to take part in the study. If you choose not to have your child take part, he/she will be evaluated by the medical team to receive the current standard cooling treatment for infants with HIE (33.5°C for a period of 72 hours)..

Study Costs

Participation in this study will be of no cost to you. Transportation, if needed, will be provided at the time of the follow-up visit.

Compensation

At the time of the 18-22 month follow-up visit, you will be compensated $50 (in the form of gift certificates) for your time and expenses of travel. In addition, your child may receive a small toy at the time of the visit.

Research Related Injuries

In the event that this research related activity results in an injury, treatment will be made available including first aid, emergency treatment, and follow-up care as needed. Care for such will be billed in the ordinary manner to you or your insurance company. No reimbursement, compensation, or free medical care is offered by Children's Hospital of Michigan, Hutzel Women's Hospital, Wayne State University (WSU), or the sponsor of this study NICHD. If you think that your child has suffered a research related injury, contact the PI right away at (313) 745-1436.

Confidentiality

All information collected about your child during the course of this study will be kept confidential to the extent permitted by law. Your child will be identified in the research records by a code name or number. Information that identifies your child personally will not be released without your written permission. However, the study sponsor NICHD, the data coordinating center at Research Triangle International (RTI), the Human Investigation Committee (HIC) at Wayne State University, or federal agencies with appropriate regulatory oversight [e.g., Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), Office of Civil Rights (OCR), etc.) may review your records.

When the results of this research are published or discussed in conferences, no information will be included that would reveal your child's identity.

Voluntary Participation/Withdrawal

Taking part in this study is voluntary. You have the right to choose not to allow your child to take part in this study. If you decide to allow your child to take part in the study you can later change your mind and withdraw from the study. You are free to only answer questions that you want to answer. You are free to withdraw your child from participation in this study at any time. Your decisions will not change any present or future relationship with Wayne State University or its affiliates, or other services you or your child are entitled to receive.

If you should decide to withdraw your child early during the cooling period, for reasons of safety your child will be re-warmed gradually to the standard of care body cooling temperature of 33.5°C or to a normal body temperature depending on the time of your early withdrawal.

Although unlikely, the PI may stop your child's participation in this study without your consent. If your child has any side effects that are very serious or if your child becomes ill during the course of the research study your child may have to drop out, even if you would like to continue. The PI will make the decision and let you know if it is not possible for your child to continue. The decision that is made is to protect your child's health and safety, or because it is part of the research plan that people who develop certain conditions or do not follow the instructions from the study doctor may not continue to participate.

While taking part in this study you will be told of any important new findings that may change your willingness to continue to take part in the research.

Questions

If you have any questions about this study now or in the future, you may contact Seetha Shankaran, MD or one of her research team members at the following phone number (313) 745-1436. If you have questions or concerns about you or your child's rights as a research participant, the Chair of the Human Investigation Committee can be contacted at (313) 577-1628. If you are unable to contact the research staff, or if you want to talk to someone other than the research staff, you may also call (313) 577-1628 to ask questions or voice concerns or complaints.

Consent to Participate in a Research Study:
To voluntarily agree to have your child take part in this study, you must sign on the line below. If you choose to have your child take part in this study, you may withdraw them at any time. You are not giving up any of your or your child's legal rights by signing this form. Your signature below indicates that you have read, or had read to you, this entire consent form, including the risks and benefits, and have had all of your questions answered. You will be given a copy of this consent form.

Name of Participant	Date of Birth
Signature of Parent/ Legally Authorized Guardian	Date
Printed Name of Parent Authorized Guardian	Time
*Signature of Parent/ Legally Authorized Guardian	Date
*Printed Name of Parent Authorized Guardian	Time
**Signature of Witness (When applicable)	Date
Printed Name of Witness	Time
Oral Assent (children age 7-12) obtained by	Date
Signature of Person Obtaining Consent	Date
Printed Name of Person Obtaining Consent	Time
Signature of translator	Date
Printed name of translator	Time

*** Both parent's signatures should be obtained however both are required for level 3 studies**

**** Use when parent/guardian has had consent form read to them (i.e., illiterate, legally blind, translated into foreign language).**

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HIPAA Authorization

A federal regulation, known as the "Health Insurance Portability and Accountability Act (HIPAA)" gives you certain rights concerning the use and disclosure (sharing with others) of your Protected Health Information (PHI). This regulation provides safeguards for the privacy and security of your information. Your permission (authorization) is required for the use and sharing of any protected health information collected as part of this research study. If you are not willing to sign this authorization to use and/or disclose your PHI by the research team, you will not be eligible to take part in this research study.

The principal investigator (PI) and her research team will use your medical records and information created or collected as part of this research study. Your PHI is important for the PI and her research team in order to collect information about you during the study, to be able to contact you if needed, and to provide treatments to you during the study, if required. The PI may send out your study related health information to the sponsor or other entities involved in this study.

Your medical records, which may contain information that directly identifies you, may be reviewed by representatives from groups identified below. The purpose of these reviews is to assure the study is being conducted properly, that data is being obtained correctly or for other uses authorized by law. These reviews occur at the study site or in the PI's research office and can take place anytime during the study or after the study have ended.

The PHI that will be "USED" for this research includes the following: name, address (street address, city, state and zip code), elements of dates, telephone numbers, e-mail address, social security number, medical record number, and any unique identifying numbers or characteristics or code.

The PHI that will be "DISCLOSED" or shared with others for this research includes the following: first three digits of zip code, elements of dates, and any unique identifying numbers or characteristics or code.

Your study information may be **used** or **shared** with the following people or groups:

- The PI, co-investigators, and key personnel of WSU associated with the research project
- WSU's HIC and the Institutional Review Boards (IRB)
- Authorized members of WSU's workforce who may need to access your information in the performance of their duties.
- Other collaborating academic research institutions, which include:
  - Stanford University
  - Duke University
  - Emory University
  - Brown University
  - University of Texas, Houston
  - University of Texas, Southwestern
  - University of Utah
  - University of New Mexico
  - University of Alabama, Birmingham
  - Tufts University
  - University of Iowa
  - Case Western University
  - University of Cincinnati
  - Yale University
  - Indiana University
- The study Sponsor NICHD or representative, including companies it hires to provide study related services, which includes: the study data coordinating center Research Triangle International (RTI)
- Federal agencies with appropriate regulatory oversight (e.g., FDA, OHRP, OCR, etc.) may review your records.

Once your information has been released according to this Authorization, it could be released again and may no longer be protected by the HIPAA regulations.

This Authorization does not expire. The research team may need to correct it or provide missing information about you even after the study has ended, and your medical records may be needed to assist in this process.

During your participation in this study you will have access to your medical record and any study information that is part of that record. The PI is not required to release research information that is not part of your medical record.

You may withdraw (take back) your permission for the **use** and **disclosure** of your PHI for this research at anytime, by **writing** to the PI at the address on the first page of this form. Even if you withdraw your permission, the PI for the research project may still use your PHI that was collected prior to your written request if that information is necessary to the study. If you withdraw your permission for use of your PHI, you will also be withdrawn from the research project. Withdrawing your authorization **will not** affect the health care that will be provided by the Detroit Medical Center and/or the WSU School of Medicine Practice Plans.

Authorization to use and disclose PHI

- By signing this document, you are authorizing the PI to **use** and **disclose** PHI collected about you for the research purposes as described above.

Signature of participant _____ Date _____

Printed name of participant _____

- For participants unable to give Authorization, the following individual is acting on behalf of the research participant (e.g., children, mentally impaired, etc.).

Signature of authorized representative _____ Date _____

Printed name of authorized representative _____ Relationship to the participant _____

Signature of person obtaining Authorization _____ Date _____

Printed name of person obtaining Authorization _____