PARENTAL PERMISSION TO PARTICIPATE IN A RESEARCH STUDY AT THE CHILDREN'S MERCY HOSPITALS

PILOT RANDOMIZED CONTROL TRIAL OF NECROTIZING ENTEROCOLITIS SCREENING BY EVALUATING FECAL CALPROTECTIN LEVELS, AND BY USING EITHER ABDOMINAL RADIOGRAPH, OR BOWEL ULTRASOUND AND ABDOMINAL RADIOGRAPH IN PREMATURE NEONATES

WHO IS DOING THIS STUDY?

A study team led by Dr. Erin Opfer is doing this study. Other health care professionals may help them.

We are asking your child to be a part of this research study. Please read the information below and ask questions about anything that you do not understand before you make a choice.

WHY IS THIS STUDY BEING DONE?

Necrotizing enterocolitis (NEC) is the most common bowel disease in premature and low birth weight infants. It is defined by the loss of bowel wall structure allowing bacteria and other toxins to leak into the bowel causing infection and sometimes death of bowel tissue. Treatment of NEC is based upon clinical evaluation of your son/daughter, blood work, and the results of an abdomen x-ray.

Recent studies have shown that the use of a bowel ultrasound may be useful to diagnose NEC due to its ability to look at how the bowel is moving and receiving blood flow. Ultrasound images are created by using sound waves that are sent through the body to create a picture of the bowel and internal organs and evaluate how they are functioning. Ultrasound does not involve radiation and has no known adverse effects.

Fecal calprotectin is a calcium-binding protein which is found in the stool during times of inflammation. Several studies have shown an increase of this protein in premature babies that develop NEC; however, there is not enough data on baseline levels in infants. Testing the stool of premature babies for this protein may be an effective screening tool for the detection of early NEC.

The purpose of this research study is to test different imaging strategies and to evaluate fecal calprotectin levels in infants with suspected NEC. The study will assess whether imaging techniques and calprotectin levels provide an accurate and early diagnoses of NEC and examine how it affects patient outcomes, such as patient length of stay in the hospital. We will be comparing patient outcomes between two groups: those who get an abdomen x-ray (Arm A) versus patients who get an abdomen x-ray plus a bowel ultrasound (Arm B). All participants will have their stool evaluated for calprotectin levels.

WHO CAN BE IN THIS STUDY?

We are asking your child to be a part of this research study because he or she was born prior to or at 32 weeks gestation.

Up to 160 children, ages 0 to 4 months, will be asked to be in this study at The Children's Mercy Hospitals.

WHAT WILL HAPPEN TO MY CHILD IN THIS STUDY?

While we take steps to reduce risks, there are certain risks (the possibility that something bad or unpleasant can happen) that could occur if your child participates in this research. **Please review carefully** the study procedures described below and their associated risks.

If you agree for your child to be in this study, he/she will be enrolled until discharge or transfer from Children's Mercy.

If you decide for your child to be in this study, the following things will happen if your child is suspected to have NEC:

- Your child will be placed into one of the following two groups:
  - Group A: Patients in Group A will receive an abdominal x-ray when their doctor suspects NEC. This is the standard of care that we use for helping to diagnose NEC today.
  - Group B: Patients in Group B will receive an abdominal x-ray as well as a bowel ultrasound when their doctor suspects NEC.
- The group to which your child will be assigned will be decided randomly, like tossing a coin. There is an equal chance of your child being assigned to either group. You or your child's doctor cannot decide which group your child will be assigned to. Your child should take part in this study only if you agree that your child will be in any of the study groups.
- This study is "open-label," which means that both you and your child's study doctor will know which group your child is assigned to.
- Calprotectin levels in the stool will be measured at enrollment, after week five of life (if on full feeds), and at three, separate consecutive times for those children suspected of NEC.

Optional Use of Samples for Future Research: In addition to the main study already described, there is more research in which your child can take part. We would like to use any left-over stool samples from the study for future research. These samples will be used to learn more about bowel diseases in premature babies. No additional risks are expected because the sample(s) are already being collected.

- You can choose to have your child be only in the main study.
- If you say no to this additional research, the left-over samples will be destroyed once all study procedures are completed. Your decision will not affect your child's care in any way.
- Once the stool is collected, it will be stored at Children's Mercy Hospital for use in the Premature Infant Stool Biorepository. Stool that is collected could be stored indefinitely.
- Stool stored will be stored so that it contains none of your child's identifiable information. Only the study team will be able to link your child's information to their stool stored. The study team will not share the link between your child's stool and their identifiable information with researchers doing future studies to reduce the risk of loss of confidentiality.
- Your child's samples will be used only for research and will not be sold. You should know that research sometimes results in discoveries that may one day have commercial value. For example, discoveries could eventually lead to new tests, drugs, or other products. Development of new products relies on the study of samples from hundreds or thousands of people, not on any one person. If this happens, neither you nor your child would share in any financial recovery. You and your child will not receive money or other compensation for use of these samples. You will not be informed about future use or results.
- Stool stored will be stored so that it contains none of your child's identifiable information. Only the study team will be able to link your child's information to their stool stored. The study team

will not share the link between your child's stool and their identifiable information with researchers doing future studies to reduce the risk of loss of confidentiality.

- You may change that decision at any time. If you change your mind, you should contact the Repository Manager, Dr. Venkatesh Sampath, at Children's Mercy Hospitals at 816-802-1177. However, if some of the research with your child's stool has already been completed, the information from that research may still be used.
- You will be asked to mark your choice at the end of this form.

RECORD REVIEW

Your child's participation will involve collecting information from his/her medical record that is obtained during normal clinical care by the research team.

The information collected will include the following:

- Age
- Medical Record Number
- Account Number
- Race/ethnicity
- Gender
- Laboratory/Medications/Vital Signs
- Height/Weight
- Information about your child's imaging results (abdomen x-ray and bowel ultrasound)
- Information regarding your child's medical history and current health.
- Calprotectin level in stool

WHAT ARE THE RISKS OF THE STUDY?

There are certain risks in this study. These risks may include:

- There is a slight risk of loss of confidentiality. Your child's confidentiality will be protected to the greatest extent possible.

- Ultrasound imaging has some theoretical risks. It introduces energy into the body, which can heat body tissues slightly. It also can produce small pockets of gas in body fluids or tissues. These theoretical risks are proportional to the strength of the ultrasound waves. In the study procedures, we will be using weak ultrasound waves that do not generate enough energy to be significant. A large WHO study of diagnostic ultrasound using similar energy showed that there were no harmful effects from ultrasound imaging.

If your child has any of these problems or changes in the way he or she feels, you should tell the investigator or other study personnel as soon as possible.

There may be risks we don't know about right now. We will tell you about any new information that might change your decision to keep your child in the study.

WHAT ARE THE BENEFITS OF BEING IN THIS STUDY?

There may be no direct benefit to your child from being in this research study. However, by being in this study, there is potential for earlier detection of NEC on bowel US, which can lead to quicker interventions and potential better outcomes for these patients.

WHAT ABOUT EXTRA COSTS?

- There are no extra costs to you or your child's insurance company from being in this study.

- Insurance will still be billed for routine standard care (abdomen x-ray, blood work, stool testing, etc). Although study funds may pay for certain study-related items and services, you or your child's insurance company will still be required to pay for all of your child's routine care that would have occurred if your child was not part of this research study. These charges may include an abdominal radiograph. If your child is randomized to arm B and receives an ultrasound as part of this research study, the study will cover the costs of the ultrasound. If your doctor orders an ultrasound outside of the study parameters, your insurance will be responsible. The study will also cover any stool calprotectin testing.

WHAT ABOUT CONFIDENTIALITY?

Your child has rights regarding the privacy and confidentiality of his or her health information. When health information includes identifiers (like names, addresses, phone numbers and social security numbers) that link it directly to an individual, it is called protected health information (PHI). Federal laws require that PHI be kept secure and private. In certain situations, federal law also requires that you approve how your child's PHI is used or disclosed. A research study is one of those situations.

By signing this permission form, you are permitting the following people to have access to your child's medical record and use your child's PHI for the research purposes described in this form. You are also permitting your child's PHI to be shared with everyone listed below:

- The research team, which includes the study personnel listed on this form and other persons involved in this study at The Children's Mercy Hospitals;
- The Institutional Review Board at The Children's Mercy Hospitals;
- Other researchers, hospitals, and institutions that are part of this study and their Institutional Review Boards;
- A group that oversees the data (study information) and safety of this research;
- People from organizations that provide independent accreditation and oversight of hospitals and research;
- Government/regulatory agencies (both US and international), such as the Office for Human Research Protections whose job it is to protect human subjects and oversee the conduct of research

By signing this permission form, you are allowing your child's health information to be recorded in the research record. The research record is separate from your child's medical record. Information about your child that is obtained during this study will be recorded in a research record and may also be recorded in your child's medical record. A research record will be created and kept in the Radiology research office. The research record may include documents that have your child's name, assigned study ID number, medical record number, date of birth, account numbers and dates of service. All research records will be maintained in a confidential manner.

There will be a separate database, in which all study information is collected. This database will be used to analyze the study information and find out the study results. Information in this database will include your child's assigned study ID number, date of birth, account number and dates of service.

By signing this permission form, you are allowing your child's health information to be recorded in the research record. You are also permitting your child's research record to be shared with everyone listed above.

Some people or groups who get your child's identifiable health information might not have to follow the same privacy rules that we follow. We will share your child's health information only when we must, will only share the information that is needed, and will ask anyone who receives it from us to protect your child's privacy. However, once your child's information is shared outside of The Children's Mercy Hospitals, we cannot promise that it will remain private.

You may choose not to sign this permission form and not have your child be in the study. You may cancel your permission to use and share your child's PHI at any time by contacting the study personnel listed on this form. You may also contact The Children's Mercy Hospitals Health Information Management (HIM) in writing. If you cancel your permission, your child may no longer participate in this study. Your child's PHI that has already been collected for the study may still be used; however, no new information will be collected except information related to adverse events or other safety issues.

If you do not cancel your permission, your child's PHI may continue to be recorded until the entire study is finished. Some information about the study may be included in your child's medical record. Any study information recorded in your child's medical record will be kept forever. Unless stated elsewhere in this form, you may not have access to your child's research record or research test results.

Results of this study may be made public. If made public, your child will not be identified in any publications or presentations.

WHAT ARE THE ALTERNATIVES TO BEING IN THIS STUDY?

Instead of being in this study, you may choose for your child not to participate.

WHAT ARE MY CHILD'S RIGHTS AS A STUDY PARTICIPANT?

Being in a research study is voluntary. Your child does not have to be in this study to receive medical care. If you choose not to have your child participate, there will be no penalty or loss of benefits to which your child is otherwise entitled.

You may withdraw your child from the study at any time without penalty or loss of benefits to which your child is otherwise entitled. We will inform you of any new information that develops during this study. This information may affect your decision to keep your child in the study. If you choose to withdraw your child from the study or if you are asked by your child's personal doctor to withdraw your child from the study, you must tell the study team as soon as possible.

Dr. Erin Opfer or the Institutional Review Board [IRB] may stop the study at any time. The investigator(s), your child's doctor, or the IRB may remove your child from the study at any time without your permission.

If you withdraw your child from the study early for any reason, the information that already has been collected will be kept in the research study and included in the data analysis. No further information will be collected for

the study. The information that already has been collected will be de-identified and cannot be traced back to your child.

WHO SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

Dr. Erin Opfer is in charge of this research study. You may call Dr. Opfer at 816-234-3273 with questions at any time during the study. You may also call Maura Sien, study coordinator, at 816-302-6065 with any questions you may have.

You should call Dr. Opfer if you believe that your child has suffered injury of any kind or is sicker as a result of being in this research study.

You may also call The Children's Mercy Hospital Pediatric Institutional Review Board (IRB) at (816) 701-4358 with questions or complaints about this study. The IRB is a committee of physicians, statisticians, researchers, community advocates, and others that ensures that a research study is ethical and that the rights of study participants are protected.

SPONSOR AND INSTITUTIONAL RESPONSIBILITIES

In the case of illness or injury resulting from this study, treatment is available at The Children's Mercy Hospitals, but will be provided at the usual charge. Payment for this treatment will be your responsibility. The hospital may not bill insurance or other third-party payers for this care. The Children's Mercy Hospitals does not have funds set aside to pay research participants if the research results in injury. By signing this form, you, or your child, are not giving up any legal rights to seek compensation for injury.

MAKING YOUR CHOICE FOR OPTIONAL FUTURE RESEARCH

Please read each sentence below and think carefully about your choice. After reading each sentence, circle "Yes" or "No" and initial each item.

I agree that my child's stool can be used by other researchers in the future to study bowel diseases in premature infants.

Yes No _____ Initials

I agree that my child's stool sample collected for this study may be stored at Children's Mercy Hospitals for an indefinite amount of time and may be used in future research studies regarding bowel diseases in premature infants. I understand that the sample that is stored still contains information that may identify me.

Yes No _____ Initials

_____ _____ _____

Signature of Parent/Legally Authorized Representative Date Relationship to Participant

PERMISSION OF PARENT OR LEGALLY AUTHORIZED REPRESENTATIVE

The purposes, procedures, and risks of this research study have been explained to me. I have had a chance to read this form and ask questions about the study. Any questions I had have been answered to my satisfaction. I give permission for _____ to participate in this research study. A copy of this signed form will be given to me.

_____	_____	_____
Signature of Parent/Legally Authorized Representative	Date	Relationship to Participant

STUDY PERSONNEL

I have explained the purposes, procedures, and risks involved in this study in detail to:

_____
Print name(s) of Parents/ Legally Authorized Representative

_____	_____	_____
Signature of Person Obtaining Permission/Assent	Date	Time

Print Name of Person Obtaining Permission/Assent _____

WITNESS

Witness signature is only required in the following circumstances:

- Permission/assent obtained via telephone/telemedicine;
- Enrolling non-English speaking participant via the short form method;
- Subject or LAR cannot read or write or is visually impaired; OR
- IRB has required a witness or patient advocate to be present.

I have witnessed the permission/assent process and signature(s) for this research study:

_____	_____
Signature of Witness	Date

Print Name of Witness_____

INTERPRETER

☐ Interpreter Used ☐ Qualified Bilingual Study Staff Used
I was present and provided interpretation services during the signing of this document.

_____	_____
Signature of Interpreter	Date

Printed Name of Interpreter: _____