A Multi-Center Randomized Trial of Laparotomy vs Drain as the Initial Therapy for ELBW Infants with Necrotizing Enterocolitis (NEC) or Isolated Intestinal Perforation (IP): Outcomes at 18-22 Months Adjusted Age

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APPENDIX B:
SAMPLE CONSENT FORM FOR RANDOMIZATION

A Multi-Center Randomized Trial of Laparotomy vs Drain as the Initial Therapy for ELBW Infants with Necrotizing Enterocolitis (NEC) or Isolated Intestinal Perforation (IP): Outcomes at 18-22 Months Adjusted Age

A Trial for the NICHD Neonatal Research Network

INVITATION TO TAKE PART

You are being invited to enter your infant into a research study called "A Multi-Center Randomized Trial of Laparotomy vs Drain as the Initial Therapy for ELBW Infants with Necrotizing Enterocolitis (NEC) or Isolated Intestinal Perforation (IP)". This study has been designed by Dr. Martin Blakely, a pediatric surgeon, and the study's lead investigator from Le Bonheur Children's Medical Center which is associated with the University of Tennessee in partnership with the investigators in the Neonatal Network for the National Institute of Child Health and Human Development (NICHD). Dr. Kevin Lally (pediatric surgeon) and Dr. Kathleen Kennedy (neonatologist- specializing in the care of sick newborns) and their research staff are responsible for the study's conduct here at the University of Texas Health Science Center and Children's Memorial Hermann Hospital (CMHH). This study will evaluate whether a laparotomy or a peritoneal drain should be the initial treatment for infants that are diagnosed with either NEC or IP (or both). Refusal to take part in this study or withdrawal at a later date will not affect the care given to your infant by his/her physician or any other health professional with the University of Texas Health Science Center and Children's Memorial Hermann Hospital. This study (CPHS # HSC-MS-09-____) has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston, an independent committee to help assure that research studies are safely and properly performed.

DESCRIPTION OF THE RESEARCH

Purpose

Your infant has been diagnosed as possibly having NEC, IP or perhaps, both. Necrotizing Enterocolitis (NEC) is a serious infection of the intestines. An Isolated Perforation (IP) is a hole in the wall of the small or large intestine. Both of these problems are life-threatening. Infants that have NEC or IP often do very poorly. Over 50% of them die and many of the infants that live will have long term problems. At this time we have two treatments that the pediatric surgeons perform for infants with possible NEC or IP. One is a peritoneal drain and the other is a laparotomy. Both of these treatments are widely accepted and commonly used however there has not been a study to show which one is better.

The Pediatric Surgeons have been asked by your infant's doctor to evaluate your infant and they have determined that your infant may need to be treated for this problem. They have also agreed that your infant could be a good patient to take part in this study as they are unable to decide which therapy (peritoneal drain or laparotomy) would be the best for your infant.

The purpose of this research study is to determine which treatment (laparotomy or peritoneal drain) is the best first treatment for premature infants with NEC and/or IP. The investigators of this study want to know which of the treatments improves survival and which improves survival with as few as possible long term disabilities. Long term disabilities will be determined at 18-22 months adjusted age.

Procedure

If you decide to have your infant take part in this study, he/she will be randomly assigned (like a flip of the coin) to receive either a peritoneal drain or laparotomy. Your infant has an equal chance of being in either group. If your infant is randomized to a peritoneal drain the surgeon will create a small opening in the lower abdomen and insert a rubber tube which will be secured with stitches to the abdomen. The purpose of the drain is to relieve the pressure when the abdomen is full and "tight" and to drain fluids and feces from the abdomen if the infant has an IP. It <u>does not</u> allow the surgeon to look at the bowel (small and large intestines) or determine if the infant has NEC. Peritoneal drains are done with local anesthesia

and sedation (pain medication). If your infant is randomized to a laparotomy the surgeon will surgically open the abdomen to expose the abdominal contents so that they can do a thorough inspection of the bowel, remove any diseased/dead bowel, repair a perforation (if there is one), and perform other procedures that he/she feels are necessary. A laparotomy is performed under general anesthesia in the NICU or the operating room.

Infants that are randomized to receive a drain as their first treatment may go on to require a laparotomy if the surgeon thinks it is necessary. Likewise, those infants that are randomized to receive a laparotomy as their first treatment may go on to have additional laparotomies if the surgeon thinks it is necessary. After the first randomized treatment the surgeons and your infant's doctor will decide which other treatments your infant should have, if any.

If your infant does have a laparotomy and it is necessary to surgically remove some of the bowel, the bowel that is removed will be sent to the laboratory for analysis. We would like your permission to share the results of that analysis with the other investigators of the study, our data center, and the NICHD as it may give us some important information about NEC.

Your infant's hospital course will be followed closely and important information will be gathered such as ventilator (breathing machine) and oxygen requirements, infections, heart problems, feeding difficulties, brain problems and of course any other surgeries. Information will be collected from the chart prior to enrollment as well as after enrollment until your infant comes to the clinic for his/her 18-22 months visit. We are especially interested in any surgeries that your infant may have after discharge and before the 18-22 month visit. We would also like your permission to collect surgery information after discharge even if the surgery is not in one of the Memorial Hermann hospitals.

TIME COMMITMENT

This study begins with your agreement to allow your infant to take part. Your infant will be followed in the hospital through discharge and during that time there will be no time commitment asked of you. After discharge we will ask to see your infant in the High Risk Infant Clinic (across the street from CMHH) around 2 months, 6 months and 12 months and at 18 – 22 months. The 18-22 month visit that is most important. At 18-22 months your infant will undergo a complete examination and evaluation. He/she will receive an assessment of growth, a physical exam as well as neurological (brain examination) and developmental (brain and motor) testing. This follow-up will take about 2-4 hours. Currently the 18-22 month visit is the end point of the study however we would like your permission to continue to keep in contact with you and your infant beyond this time in case the study analysis shows a need for continued follow-up.

BENEFITS

There may be no benefit to your infants for taking part in this study. Infant's in the future will most likely benefit from his/her taking part. Nevertheless, whether or not your infant receives an initial drain or laparotomy he/she might benefit from the extra monitoring in the neonatal care unit or from early discovery of and treatment of any developmental problems during follow-up.

RISKS, AND/DISCOMFORTS

NEC and IP are serious, life-threatening conditions which may require immediate intervention. All abdominal surgeries have risks including bleeding, infection of the abdominal cavity and or the abdominal wound, injury to abdominal organs and complications from anesthesia. These risks are the same risks your infant would have even if you decided not to take part.

ALTERNATIVES

This study is voluntary. You have the alternative to not allow your infant to take part in the study. If you choose not to have your infant take part, he/she will receive the therapy that the medical or surgical team decides.

STUDY WITHDRAWAL

You may withdraw your infant from the study at any time by contacting one of the Research Team at [redacted]. Although unlikely, your infant's doctor also has the right to withdraw your infant from the study if he/she feels your infant may be harmed if he/she continues to take part.

IN CASE OF INJURY

If your infant suffers an injury as a result of taking part in this research study, please understand that nothing has been arranged to provide free treatment of the injury or any other type of payment. However, all needed facilities, emergency treatment, and professional services will be available to your infant, just as they are to the community in general. You should report any injury to Dr. Kathleen Kennedy at [redacted] and to the Committee for the Protection of Human Subjects at [redacted].

COSTS, REIMBURSEMENT AND COMPENSATION

There will be no additional costs to you or your infant for taking part in this research study.

CONFIDENTIALITY

You, or your infant, will not be personally identified in any reports or publications that may result from this study. Any personal information about your infant that is gathered during this study will remain confidential to every extent or the law. A special number will be used to identify your infant in the study and only the investigator(s) at UT Medical School and Memorial Hermann Children's Hospital will know your infant's name. Please understand however, that representatives of the Food and Drug Administration (FDA), the National Institute of Health (NIH), the RTI International (RTI); our data center, the Committee for the Protection of Human Subjects (CPHS), and/or the investigators for this research study (NICHD, Dr. Blakely, his designee , or sub-investigators including Pediatric Surgeons) may want to review your infant's research and/or medical records for the purposes of verifying research data. There is a separate authorization form that you will be asked to sign which details the use and disclosure of your infant's protected health information.

NEW INFORMATION

You will be notified if significant new findings are discovered during the study that might affect your willingness to allow your infant to continue taking part.

QUESTIONS

You are making a decision whether or not to voluntarily take part in this research study. You should not sign until you understand all the information presented in the previous pages and until all your questions about the research have been answered to your satisfaction. If you have any additional questions regarding this study Dr. Kevin Lally, Dr. Kathleen Kennedy or one of the research team will be available to answer them for you at any time. You may contact them at [redacted] or [redacted].

SIGNATURES

Sign below only if you understand the information given to you about the research and choose to take part. Make sure that any questions have been answered and that you understand the study. If you have any questions or concerns about your rights as a research subject, call the Committee for the Protection of Human Subjects at [redacted]. If you decide to allow your infant to take part in this research study, a copy of this document will be given to you.

_____	_____	_____
Parent/guardian signature	Date	Time

_____
Printed name of Parent/guardian

_____	_____	_____
Person obtaining consent	Date	Time

_____
Printed name of person obtaining consent

_____	_____	_____
Witness	Date	Time

CPHS STATEMENT
This study (HSC-MS-09-____) has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston. For any questions about research subject's right, or to report a research-related injury, call the CPHS at [redacted].

APPENDIX C:
SAMPLE CONSENT FORM FOR PREFERENCE COHORT

A Multi-Center Randomized Trial of Laparotomy vs Drain as the Initial Therapy for ELBW Infants with Necrotizing Enterocolitis (NEC) or Isolated Intestinal Perforation (IP): Outcomes at 18-22 Months Adjusted Age

A Trial for the NICHD Neonatal Research Network
"Preference Consent"

INVITATION TO TAKE PART

You are being invited to enter your infant into a research study called "A Multi-Center Randomized Trial of Laparotomy vs Drain as the Initial Therapy for ELBW Infants with Necrotizing Enterocolitis (NEC) or Isolated Intestinal Perforation (IP)". This study has been designed by Dr. Martin Blakely, a pediatric surgeon, and the study's lead investigator from Le Bonheur Children's Medical Center which is associated with the University of Tennessee in partnership with the investigators in the Neonatal Network for the National Institute of Child Health and Human Development (NICHD). Dr. Kevin Lally (pediatric surgeon) and Dr. Kathleen Kennedy (neonatologist- specializing in the care of sick newborns) and their research staff are responsible for the study's conduct here at the University of Texas Health Science Center and Children's Memorial Hermann Hospital (CMHH). This study will evaluate whether a laparotomy or a peritoneal drain should be the initial treatment for infants that are diagnosed with either NEC or IP (or both). Refusal to take part in this study or withdrawal at a later date will not affect the care given to your infant by his/her physician or any other health professional with the University of Texas Health Science Center and Children's Memorial Hermann Hospital. This study (CPHS # HSC-MS-09-____) has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston, an independent committee to help assure that research studies are safely and properly performed.

DESCRIPTION OF THE RESEARCH

Purpose

Your infant has been diagnosed as possibly having NEC, IP or perhaps, both. Necrotizing Enterocolitis (NEC) is a serious infection of the intestines. An Isolated Perforation (IP) is a hole in the wall of the small or large intestine. Both of these problems are life-threatening. Infants that have NEC or IP often do very poorly. Over 50% of them die and many of the infants that live will have long term problems. At this time we have two treatments that the pediatric surgeons perform for infants with possible NEC or IP. One is a peritoneal drain and the other is a laparotomy. Both of these treatments are widely accepted and commonly used however there has not been a study to show which one is better.

The purpose of this research study is to determine which treatment (laparotomy or peritoneal drain) is the best first treatment for premature infants with NEC and/or IP. The investigators of this study want to know which of the treatments improves survival with as few as possible long term disabilities. Long term disabilities will be determined at 18-22 months adjusted age.

Your infant has already had either a laparotomy or peritoneal drain or you have decided that you want the medical team to decide which treatment (laparotomy or peritoneal drain) your infant will receive. In either case we are still very interested in how your infant does with the treatment that the medical team has decided upon and would like to follow your infant throughout his/her hospitalization and first years of life. We are calling this part of the study the "preference study" as your doctors will pick which treatment they "prefer" for your infant.

Procedure

If you decide to have your infant take part in this "preference" study, he/she will have no procedures performed. The study will be data collected only. Your infant's hospital course will be followed closely and important information will be gathered such as ventilator (breathing machine) and oxygen requirements, infections, heart problems, feeding difficulties, brain problems and of course any other surgeries/complications. Information will be collected from the chart prior to enrollment as well as after enrollment in the "preference study" until your infant comes to the clinic for his/her 18-22 months visit. We

are especially interested in any surgeries that your infant may have after discharge and before the 18-22 month visit. We would also like your permission to collect surgery information after discharge even if the surgery is not in one of the Memorial Hermann hospitals.
If at any time your infant does have a laparotomy and it is necessary to surgically remove some of the bowel, the bowel that is removed will be sent to the laboratory for analysis. We would like your permission to share the results of that analysis with the other investigators of the study, our data center, and the NICHD as it may give us some important information about NEC.

TIME COMMITMENT

This study begins with your agreement to allow your infant to take part. Your infant will be followed in the hospital through discharge and during that time there will be no time commitment asked of you. After discharge we will ask to see your infant in the High Risk Infant Clinic (across the street from CMHH) around 2 months, 6 months and 12 months and at 18 – 22 months. The 18-22 month visit that is most important. At 18-22 months your infant will undergo a complete examination and evaluation. He/she will receive an assessment of growth, a physical exam as well as neurological (brain examination) and developmental (brain and motor) testing. This follow-up will take about 2-4 hours. Currently the 18-22 month visit is the end point of the study however we would like your permission to continue to keep in contact with you and your infant beyond this time in case the study analysis shows a need for continued follow-up.

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ALTERNATIVES

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IN CASE OF INJURY

If your infant suffers an injury as a result of taking part in this research study, please understand that nothing has been arranged to provide free treatment of the injury or any other type of payment. However, all needed facilities, emergency treatment, and professional services will be available to your infant, just as they are to the community in general. You should report any injury to Dr. Kathleen Kennedy at [redacted] and to the Committee for the Protection of Human Subjects at [redacted].

COSTS, REIMBURSEMENT AND COMPENSATION

There will be no additional costs to you or your infant for taking part in this research study.

CONFIDENTIALITY

You, or your infant, will not be personally identified in any reports or publications that may result from this study. Any personal information about your infant that is gathered during this study will remain confidential to every extent or the law. A special number will be used to identify your infant in the study and only the investigator(s) at UT Medical School and Memorial Hermann Children's Hospital will know your infant's name. Please understand however, that representatives of the Food and Drug

Administration (FDA), the National Institute of Health (NIH), the RTI International (RTI); our data center, the Committee for the Protection of Human Subjects (CPHS), and/or the investigators for this research study (NICHD, Dr. Blakely, his designee , or sub-investigators including Pediatric Surgeons) may want to review your infant's research and/or medical records for the purposes of verifying research data. There is a separate authorization form that you will be asked to sign which details the use and disclosure of your infant's protected health information.

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_____	_____	_____
Parent/guardian signature	Date	Time
_____		
Printed name of Parent/guardian		
_____	_____	_____
Person obtaining consent	Date	Time
_____		
Printed name of person obtaining consent		
_____	_____	_____
Witness	Date	Time

CPHS STATEMENT

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