**University of New Mexico Health Sciences Center**
**Consent to Participate In Research**

Mild Encephalopathy in the Newborn treated with Darbepoetin
The **MEND** Study
**Version 12/4/2018**

## PURPOSE AND BACKGROUND

You are being asked to consider whether you would like your infant to participate in a research study. The following information describes the study and your infant's role as a possible participant. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. The study is being conducted by Dr. Tara Zamora, as principal investigator at the University of New Mexico, in conjunction with investigators at the University of Utah, University of Texas Southwestern, and by those assistants as she may need. Approximately 15-20 infants will take part in this study at the University of New Mexico, and a total of 80 infants will take part at all the sites combined. The study will take approximately 2 years to complete enrollment and analysis. Please read this information carefully and do not hesitate to ask any questions about the study information provided below.

Your infant qualifies to be in this research study because he/she has been diagnosed to have a condition called neonatal encephalopathy (NE). Neonatal encephalopathy results from decreased blood flow and oxygen to all the organs in the body, including the brain. Your infant's history and physical examination shows that he/she has a mild form of NE. In this hospital and in many others, infants with this condition are monitored for several days, often in a Neonatal Intensive Care Unit. There is currently no medical therapy available to infants with mild NE. However, some babies with mild NE go on to develop problems with their development, as they grow older. Development refers to how well babies learn move their bodies, handle their emotions, learning ability, self-control, and memory. These skills usually grow as a child grows, but sometimes they develop more slowly or don't fully develop. In cases where these skills develop more slowly, or don't develop, we refer to that as developmental disability.

We are researching a medication called 'Darbepoetin' that may help to improve developmental outcomes by protecting the brain. The use of Darbepoetin in this study is investigational, meaning it has not been approved by the Food and Drug Administration (FDA) to be used this way. Darbepoetin (Darbe) helps the body to produce more red blood cells, which are the cells that carry oxygen around the body. In addition to increasing red cell growth, Darbe has been shown to provide brain protection and to improve developmental outcomes following brain injury in small clinical trials for babies with more severe forms of encephalopathy.

This study will help us to learn if Darbe will help improve developmental outcomes in infants with mild NE. We hope that in the future the use of this medication may improve the developmental outcomes of babies with mild NE, and also lessen the risk of long-term disabilities.

The study will be carried out at the University of New Mexico Hospital newborn intensive care unit (NICU) and other sites as listed above.

In this study, infants with mild NE will be placed in one of two study groups before 24 hours of age: Darbe group, or placebo group (placebo means no actual medicine will be given, only the fluid the medicine is mixed in will be given). The doctors and nurses will not know if your baby received Darbe or placebo. All infants will be monitored very closely and will receive all the usual care of the Newborn Intensive Care Unit (NICU) for this condition. Your infant's participation in the study will last for 12 months. The medication will be given, one time, within 24 hours of birth and you will then receive a phone call at 4 months of age asking you about your child's development, and a formal in person developmental assessment will be done when your baby is 8-12 months old. After all the infants have been tested we will check to see which babies received Darbe and which ones received the placebo, this will take about 4 years.

**STUDY PROCEDURES**

**What will happen if I decide to let me infant participate?**

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

1. **Receive one dose of the study drug, (10 µg/kg) Darbe through an IV that your baby already has, within 24 hours of birth.**

2. **Receive placebo (salt water) as an IV within 24 hours of birth.**

Your infant will be followed closely and important clinical information will be collected for the study such as blood tests, breathing support, infections, nutrition, as well as the results of any tests such as head ultrasounds and magnetic resonance imaging (MRI) that are ordered by your infant's doctor as part of your infant's NICU care. We will also collect information from your baby's chart about his or her family, specifically: mom's age, mom's education level, race, and ethnicity.

If your baby has blood tests done as part of his or her normal care then we will save the leftover blood of all of those samples for up to 3 years. These samples will be used to check how much of the study drug is in your baby's blood and may be used to check how your baby's blood reacted to the study drug.

**Optional Baseline Sample for Drug level testing:**

Additionally, we would like to take an additional four drops of blood (less than $1/10^{th}$ of a teaspoon or 0.3 mL) from a blood sample obtained before the study drug is given. This will ensure that we have enough blood to test for the change in drug level before and after the medication is given. We will try to draw this blood sample with one that is being drawn for your baby's routine care, such as checking his or her sugar (glucose) level, but we may need to poke your baby to obtain this sample, if there is not a scheduled lab prior to administration of the study drug.

_____**Yes, I agree** to allow an extra sample of blood (less than $1/10^{th}$ of a teaspoon) to be taken from my baby
**INITIALS**

_____**No, I do not agree** to allow an extra two drops of blood to be taken from my baby's blood sample
**INITIALS**

No head ultrasounds or MRIs will be done just for the study, but your doctor may order these test so that he/she can better care for your baby.

After you go home, you will receive one phone call at 4 months of age asking you important questions about your child's development.

At 8-12 months of age, research data will be collected at your normally scheduled clinic visit at UNM which will include a formal developmental test and brief medical exam.

We will give your primary care doctor a letter stating that your baby is participating in this study and provide them with our contact information. If your baby has had his/her blood levels checked (hematocrit), we will contact your baby's primary care provider and ask your baby's medical history We will ask your doctor to allow us to document these results.

We will keep all data for up to 10 years.

**RISKS**

Darbe is currently approved for use in adults and children, but is considered an investigational drug in neonates. Repeated use of Darbe in adults can increase the risk of abnormal blood clot formation, convulsions (seizures), hypersensitivity (allergic reactions), increase red blood cell number, decrease white blood cell number (white blood cells help fight infections), increase blood pressure, heart attack, stroke, and death. Studies of Darbe use in adult cancer patients have shown increased cancer growth that rarely can result in death. To date, there is no information that these drugs would increase any such complications in infants. Infants are at a lower risk for these complications than adults. There may also be side effects and discomforts that are not yet known.

This study was evaluated by the FDA as an investigational new drug. They approved the study and would like us to monitor for a disease called Pure Red Blood Cell Aplasia (PRCA). This is a very rare (less than 1 per 10,000 people treated with Darbe) disease that causes low blood levels (anemia) in adults who use frequent injections of Darbe. None of these side effects have been documented in infants or children. If your baby has low blood levels (anemia), and we have appropriate samples of blood stored (from the leftover blood from the NICU), we will ask to get a blood sample at the follow up visit and we will send your baby's blood to a special lab to see if it is related to the Darbe that he/she was given, at no cost to you.

Your infant will be assigned to a treatment group by chance (similar to flipping a coin). The treatment your infant receives might be less effective, not effective, or have more side effects than another study treatment.

**BENEFITS**

There may or may not be a direct benefit to your infant being in the study. One possible benefit to your infant is that Darbe may help the brain recover from injury to a greater extent. Your baby will also receive extra developmental tests to see how they are developing. Additionally, the benefits seen in taking part in this study may help future infants with this condition.

**ALTERNATIVES TO PARTICIPATION**

Your infant will continue to receive the same standard of intensive care whether or not you decide to allow him or her to participate in this study. Currently, there is no FDA-approved drug in infants that is used to prevent brain injury.

**CONFIDENTIALITY**
Your infant's participation in research will involve a loss of privacy, but information about your infant will be handled as confidentially as possible. Representatives of the University of New Mexico Health Sciences Center (UNMHSC) Human Research Review Committee (HRRC) that oversees human research, the FDA, and study auditors will be permitted access to your infant's records. Also, your infant's participation in the study and information in your infant's study records may be disclosed to your infant's doctors and nurses, and may be disclosed as otherwise provided by law. Your infant's name will not be used in any published reports about this study. All information about your infant taking part in this research will be kept confidential, in a locked file inside a locked office at the hospital. A copy of this consent form will be placed in your infant's medical record.

**COST OF STUDY**
The study drug will be given to your infant at no charge and you will not be required to pay for any study procedures. The cost of the developmental assessments will be done at no charge to you but may be billed to a third party payer since it is part of standard care. The costs of your infant's NICU clinical care will not be covered by the study, and will be billed to you or a third party payer. Examples of third party payer's are insurance companies or Medicaid.

**EMERGENCY TREATMENT AND COMPENSATION**
If your infant is injured as a result of this study, the University of New Mexico Health Sciences Center (UNMHSC) will provide your infant with emergency treatment, at usual charge to you or a third-party payer. No commitment is made by the UNMHSC to provide free medical care or money for injuries to participants in this study. If you have any questions about these issues, or believe that you or your infant have been treated carelessly in the study, please contact the HRRC Office at the University of New Mexico Health Sciences Center, Albuquerque, New Mexico 87131, (505) 272-1129 for more information.

**PAYMENT FOR PARTICIPATION**
You will not receive payment for your infant's participation in this study.

**NEW FINDINGS**
You will be informed of any significant new findings that become available during the course of the study, such as changes in the risks or benefits resulting from your infant's participation in the research, or new alternatives to participation that might change your mind about your infant participating. Your contact information (phone, address) will be kept in a locked file so that we can inform you which treatment your child received when the study is fully completed, if you choose.

**WITHDRAWAL**
Your permission for your infant to participate in this study is voluntary. You may refuse this permission or may stop your infant's participation at any time during the study without penalty or loss of benefits to which you are otherwise entitled. If you end your infant's participation, he or she will continue to receive standard treatment and will be able to receive medical care as usual

or participate in future research studies. In addition, your infant's participation may be stopped by the neonatology attending physician or the study doctor without regard to your consent if your infant has a study-related injury, or if there are administrative reasons. If you withdraw permission for your infant to participate, we would like to perform a final examination of your infant for safety purposes, and to collect clinical information from any follow up visits scheduled to monitor your infant's recovery. If you would like to withdraw your permission for your infant to participate and have all of his or her data removed from our database please inform the study team. You will be given a copy of this signed and dated information sheet.

A description of this study 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 results. You can search this website at any time."

**HIPAA Authorization for Use of Your Protected Health Information (HIPAA)**

As part of this study, we will be collecting health information about you and your child. This information is "protected" because it is identifiable or "linked" to your child.

**Protected Health Information (PHI)**

By signing this Consent Document, you are allowing the investigators and other authorized personnel to use your protected health information for the purposes of this study. This information may include: your education level, medical history, and growth parameters. We will be contacting your primary care provider and asking them about information from your child's appointment, such as weight, height, and head size.

In addition to researchers and staff at UNMHSC and other groups listed in this form, there is a chance that your health information may be shared (re-disclosed) outside of the research study and no longer be protected by federal privacy laws. Examples of this include disclosures for law enforcement, judicial proceeding, health oversight activities and public health measures.

**Right to Withdraw Your Authorization**

Your authorization for the use of your health information for this study shall not expire unless you cancel this authorization. Your health information will be used as long as it is needed for this study, up to 10 years. However, you may withdraw your authorization at any time provided you notify the UNM investigators in writing. To do this, please send a letter notifying them of your withdrawal to:

Tara G. Zamora
MSC10 5590
1 University of New Mexico
Albuquerque New Mexico 87131

Please be aware that the research team will not be required to destroy or retrieve any of your health information that has already been used or shared before your withdrawal is received.

**Refusal to Sign**

If you choose not to sign this consent form and HIPAA Authorization, then your child will not be allowed to take part in this study. This will not affect the care your baby receives in the NICU.

**What if I have questions or complaints about this study?**
If you have any questions, concerns or complaints at any time about the research study, Tara Zamora, MD, or her associates will be glad to answer them at 505-272-0180, Monday – Friday, 8am-5pm. If you would like to speak with someone other than the research team, you may call the Human Research Review Committee (HRRC) at (505) 272-1129. The HRRC is a group of people from UNMHSC and the community who provide independent oversight of safety and ethical issues related to research involving human participants.

**What are my and my child's rights as a research participant?**
If you have questions regarding your rights as a research participant, you may call the Human Research Protection Office (HRPO) at (505) 272-1129 or visit the HRPO website at http://hsc.unm.edu/research/hrpo/

**Consent and Authorization**

You are making a decision whether to allow your baby to participate in this study. Your signature below indicates that you read the information provided (or the information was read to you). By signing this Consent Form, you are not waiving any of you or your child's legal rights as research participants.

I have had an opportunity to ask questions and all questions have been answered to my satisfaction. By signing this Consent Form, I agree to have my child participate in this study. A copy of this Consent Form will be provided to me.

X _____ X _____

Name of legal guardian/parent (print) Signature of Legal Guardian/Parent Date

I have explained the research to the participant's legal guardian/parent and answered all of his/her questions. I believe that he/she understands the information in this consent form and freely consents to participate.

X _____ X _____

Name of Research Team Member Signature of Research Team Member Date

X _____

Child's Name