

APPENDIX D. SAMPLE CONSENT

Informed consent statement for:

Darbepoetin in Preterm Infants

You are being asked to allow your infant to be part of a research study. This study will look at a medication called darbepoetin alfa (Darbe). Darbe is a medication which can help to make new red blood cells in the body, and may also protect the brain and help with brain growth.

This study will include infants who are 23 to 28 weeks at birth and who are less than 24 hours of age. The doctors will look at the effects of Darbe on new red blood cell growth, the number of blood transfusions needed while in the hospital and developmental outcomes at about 2 years of age.

You are being asked to let your infant be in this study because your infant was born very prematurely and is at risk for complications of prematurity. Not all infants born this early survive, and some who do survive may develop serious medical problems related to the brain, lung, intestine, eyes, and other organs. Whether you agree to have your infant participate in this study will not change the medical problems associated with prematurity. Your infant's doctors have discussed your infant's extreme prematurity with you already, and will keep you up to date on your infant's progress.

It is important for you to understand why we are doing this research study and what it means if you allow your child to join this study. You must understand the information in this consent. You may discuss it with relatives, friends and others if you wish. Please know that you must give consent by the time your infant is 24 hours old. If you have any questions about this research, please ask us.

The *Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)* is paying for this study. The *NICHD* is part of the National Institutes of Health (NIH) in the federal government. This study is being done at XXXX by XXXX (*name of site and PI*).

Investigator: Dr. Robin Ohls

Location: University of Utah

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Protocol Title

A randomized, masked, placebo controlled study of darbepoetin alfa administered to preterm infants to improve red cell mass and neurodevelopmental outcome

Why is this study being done?

Drugs like Darbe that help the body make red blood cells may also protect the brain and help the brain grow. This study will test learning and development at 2 years of age in infants getting Darbe, compared to infants who did not get Darbe.

Red blood cells are very important because they carry oxygen to the all areas in the body. Infants born early often have low red blood cell counts. They may need red blood cell transfusion to make the red blood cell levels higher. This study will also help us find out if Darbe can help premature infants make new red blood cells. We will also keep track of blood transfusions to see if fewer transfusions are needed.

Darbe is approved by the Food and Drug Administration (FDA) for adults with low red cell counts (anemia) and is being studied in children with anemia. It has been measured as a treatment in premature infants in about 10 studies.

What will happen if I decide to participate?

If you agree to this study, these things will happen:

- Your infant will receive Study Medication during the time he/she is part of this study.
- Your infant will be assigned by chance (like picking a number out of a hat) to get Study Medication which is either Darbe **or** a placebo. A placebo is a saline or sugar water solution that does not contain the Darbe medication. There is an equal chance (fifty-fifty) of being in one of the two groups. Neither you nor the doctor or nurses or research staff will know which group your infant is in. However, if there is a medical emergency, the researchers may be told which group your infant is in.

Study Medication- Darbe group:

- The study medication will be given through an intravenous line (IV), or as a small injection just under the skin if your infant does not have an IV.
- If study medication is given as an injection, the person giving the injection will cover the spot so that no one can tell whether your infant got the injection or not.
- The study medication will be given once a week for up to 13 weeks (13 doses).

Study Medication- Placebo group:

- The study medication will be given through an intravenous line (IV), or as a **sham** injection. Giving a **sham** injection means the person will pretend to give the injection, but no injection will happen. The spot will be covered so no one can tell if an injection was given or not.
- The study medication or **sham** injection will be given once a week for a total of up to 13 times.

Both groups:

- Your infant will get extra iron which may also help to make new red blood cells. Infants in our unit usually get extra iron as part of standard care. Your infant may receive iron via the IV route, *<add if this applies: which may be different than the usual route iron is given in our NICU>*
- Your infant may get a red blood cell transfusion if his/her red blood cell counts fall below levels that are part of the study. These levels are the same as how we usually decide to give blood transfusions in our unit *<replace with your site's transfusion guideline if different>*.
- Your infant's doctors may also give a red blood cell transfusion if your infant needs blood in an emergency.
- We will collect blood samples from your infant to see what effect Darbe may have on
 - the growth of new red blood cells
 - blood levels of Darbe and other factors involved in brain injury and recovery
 - iron levels
- Blood will be drawn up to four times (maximum 4 mL, a little less than 1 teaspoon)

- before the first dose of study medication (this may be from the umbilical cord, not from your infant)
- when your infant is 2 weeks old (two samples will be drawn)
- when your infant is 6 weeks old (one sample will be drawn)

Additional blood draws may be necessary to check your infant's iron levels if they are too low or too high. There will be no more than 2 extra blood draws in this case and the total amount of blood drawn including all the labs above will not be more than about 1 teaspoon.

Some of your infant's blood samples will be sent to the University of New Mexico in Albuquerque, New Mexico to measure levels of Darbe and other factors involved in brain injury and recovery. Leftover blood samples may be saved for testing of antibodies (substances in the bloodstream that can attach to the medicine and prevent it from working). If this testing is needed, the blood will be sent to AMGEN, a company where testing can be done. Leftover samples will be saved until the end of the study (about 3 years) and then will be thrown away.

We will let your infant's doctor know about any abnormal lab results.

- We will look at your medical record to collect information about your pregnancy and delivery. We will look at your infant's medical record to get information about his/her hospital stay.
- You will be asked to come back for one visit when your infant reaches 22-26 months corrected age (from the time of his/her due date which is about 2 years of age) to see what effect Darbe has on brain development.
- At this visit we will weigh and measure your infant. We will ask you for health information about your infant. A developmental test (Bayley test) will be done. You, your child and the Bayley examiner (a person specially trained to give the Bayley test) will be in a room with different types of toys such as picture books and blocks. The examiner will use these toys to test your child's development. The test will take about 60 minutes. You will get a complete report about your infant's development after the test.

How many infants will take part in this study?

A total of 650 infants will be enrolled in this study. We plan to enroll <N> infants from <institution>.

How long will the study last?

Your infant will be part of the study until he/she reaches 35 completed weeks gestation (4 weeks before their due date), are discharged, or are sent to another hospital, whichever comes first. Your infant will finish the entire study by coming back for the developmental test when your infant reaches 22-26 months corrected age (from the time of his/her due date which is about 2 years of age).

What are the risks and possible discomforts from being in this research study?

Known side effects of Darbe and other drugs like Darbe **in adults** include high blood pressure, aches and pains, rash, and rarely, blood clots and seizures. High blood pressure and/or seizures have been seen in a few premature infants getting Darbe. However, the same number of infants who did not get Darbe had high blood pressure and/or seizures. If any of the following occurs in your infant, the study medicine will be stopped:

- blood clots are found during your infant's care

- if your infant receives high blood pressure medicine and their high blood pressure continues
- if your infant receives seizure medicine and their seizures continue

Your infant's iron levels will be monitored during the study, and the dose of iron they receive will be decreased if their iron levels are high, or increased if their iron levels are low.

Your infant will also be monitored for sepsis (infection in the blood) during this study. There is no reason to believe the risks for infection are higher in one group than another or that the medication being given would cause infection. However, it is possible that the injections or blood draws may increase the risk of infection.

In addition, information will be collected from your infant's clinically scheduled eye exams which are performed to monitor for a specific type of eye disease in preterm infants called retinopathy of prematurity (ROP). One previous study reported increased ROP in preterm infants receiving erythropoietin (a short acting red cell growth factor). The most recent studies show no difference in the risk of ROP between infants receiving Darbe and those not receiving Darbe. An extremely rare event seen only in adults is the formation of antibodies against the medicine. For those adults, the medicine was stopped and they were treated with red cell transfusions and medicines to decrease the antibodies. This has never been reported in infants.

There may also be side effects and discomforts that are not yet known.

Your infant will be in one of the two groups (Darbe group or placebo group) by chance. One group may not be helped as much, or have more side effects than the other, but we do not know that now.

The risks of drawing blood from a vein or giving a shot under the skin include possible bruising and swelling around the site of the injection, and, rarely, an infection. These procedures may be uncomfortable due to pain at the time of the needle stick when giving the injection or during the time blood is drawn.

Your infant may become tired, fussy or bored during the developmental test.

Another risk of this study is loss of confidentiality or other people might find out some information. We will try to keep your infant's medical record secure. You and your infant will be given a study ID number. There will be no names or other identifiable information about you or your infant in any study report that may be published after the study is complete. Measures taken to protect your and your infant's identity are described in the confidentiality section of this form.

What are the benefits of taking part in this study?

There may be no benefit if your infant joins in this study. Potential benefits of the study medicine in preterm infants include improved brain development and higher cognitive scores at 2 years of age, decreased transfusions, and decreased exposure to blood donors. Information from this study may help other preterm infants in the future.

There is a chance that the developmental test (Bayley test) may find that your child has a developmental problem that you and your child's doctor were not aware of.

What other choices do I have if I do not allow my infant to take part in this study?

If you decide to not have your infant join this study, he/she will continue to get usual neonatal care.

Currently, there is no FDA-approved drug that is used in infants to protect the brain, or prevent transfusions. *<Insert current unit standard for use of erythro stimulating agents, if they are used>*. Your infant cannot get Darbe if he/she is not in the study.

Will my infant's medical information be kept private/confidential?

<Insert standard institutional language about confidentiality. Following is a sample>

Information about your infant will be kept as private as possible. However, being in a study means some loss of privacy. People from the University of New Mexico Health Sciences Center Human Research Review Committee (HRRC) that supervise human research, the FDA, and study auditors will be allowed to see your infant's records if they ask. Your infant's part in the study and information in your infant's study records may be shared as provided by law. Your infant's name will not be used in any published reports about this study. A copy of this consent form will be placed in your infant's medical record.

All information about your infant for this study will be kept in a locked file inside a locked room at the hospital. Coded information that is only seen by the research staff is kept in password-protected computers in the same office. Coded information will be sent to the NICHD Neonatal Research Network's Data Coordinating Center at Research Triangle Institute (RTI) in Research Triangle Park, North Carolina.

Results of the levels of Darbe in your baby's blood will be shared with researchers at the University of Iowa to study how Darbe is used in the body. Information from this research study will be kept by *<Local Research Institution>* and RTI International and may be shared for future research in accordance with the NIH Public Access Policy. Information released under this policy will not identify your baby or his/her participation in this research study.

A description of this study is available at [ClinicalTrials.gov](https://clinicaltrials.gov), ID number NCT03169881, as required by U.S. Law. This website will not include information that can identify you or your infant. At most, the website will include a summary of the results of this study. You can search this website at any time.

What are the costs of being in this research study?

You will not have to pay for the study drug or any study procedures. The costs of your infant's clinical care will be billed to you or your insurance. This is not paid for by the study.

What happens if my child is injured as a result of taking part in this research study?

In the event of physical injury to your infant as a result of them being in this research, necessary medical treatment will be given to your infant and billed as part of their medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to find out the extent of your infant's health care coverage. There is no program in place for other monetary compensation for such injuries. However, you and your infant are not giving up any legal rights or benefits to which you are otherwise entitled.

Will I be paid for taking part in this research study?

You will not get any payment for your infant's participation in this study. The cost of the neonatal follow-up clinic visit at 22-26 months corrected age will be covered by the study. You may be paid for

the cost of travel for the study follow-up visit if you live more than 50 miles from the clinic. We will arrange for an overnight stay at a local hotel for families living at a distance where it's not reasonable for return travel in one day.

New Information

You will be told about any new information that could cause you to change your mind about your infant staying in the study. You will also be told of anything that could affect your infant's health or safety.

Can I take my infant out of the study later?

Your permission for your infant to be part of this study is voluntary. You may stop your infant from being in the study at any time during the study without affecting your infant's health care or other services your infant will receive. If you decide you do not want your infant to be in the study, we would like to do a physical examination of your infant for safety purposes. *<or use institution-specific language.>*

Your infant's doctor or the study doctor may also stop your infant from receiving the study drug if there are concerns about it being safe for your infant. As listed above in the risks section, reasons for stopping the study drug include presence of blood clots, high blood pressure not responding to medicine, or seizures not responding to medicine.

If I have questions or concerns about this research, whom can I contact?

<Use institution-specific language. The following is an example>

If you have any questions or concerns at any time about the research study, you can contact *<Name(s)>* or their associates Monday through Friday 8am to 5 pm at XXX-XXX-XXXX or by *<Institution specific paging instructions, if appropriate>* If you think your infant may have been hurt by this study, you can contact the same people. For research-related injuries or emergencies after hours, please call XXX-XXX-XXXX. For research-related injuries or emergencies during regular business hours, you should call XXX-XXX-XXXX.

If you would like to speak with someone other than the research team, you may call the *<name>* at XXX-XXX-XXXX. You may also call this number if you have questions about your rights as a research subject. For more information, you may also access *<name>* website at [*<web address>*](#).

CONSENT

<Use institution-specific language. The following is an example.>

I confirm that I have read this parental Informed Consent document and have had the chance to ask questions. I will be given a signed copy of this form to keep.

I agree to allow my child to be in this research study and allow you to use and disclose health information about my child for this study, as you have explained in this document.

Name of Subject (type or print)

Name of Parent/Legal Guardian Signature of Parent/Legal Guardian

Date/Time

I have explained the research to the subject or his/her legal representative, and answered all of his/her questions. I believe that he/she understands the information described in the consent form and freely consents to participate.

Name of Investigator/Research Team Member (type or print)

Signature of Investigator/Research Team Member

Date/Time