University of California, San Diego
Parent Consent for Child to Act as a Research Subject

Omega-3 LCPUFA Supplementation in Very Low Birth Weight Infants for the Prevention of Retinopathy of Prematurity: Proposal for a Prospective Randomized Controlled Masked Clinical Trial with Lipidomic and Transcriptomic Analyses

The purpose of this form is to give you information about the research study. If you decide that you would like your infant to take part in the study, you will be asked to sign this form. By signing this form, you are giving your permission for your infant to take part in the study and become a study participant. This form describes the purpose, procedures, benefits, risks, discomforts and precautions of the research study. Take time to read the following information carefully and discuss it if you wish with a friend, relatives, and/or with your personal doctor. You may refuse and not allow your infant to take part or you may withdraw your infant from this study at any time without this decision affecting your infant's care at UCSD. Before you decide and agree to have your infant to take part, it is important for you to know why the research study is being done and what it will involve. Ask as many questions as needed. You should not sign this form if you have any questions that have not been answered to your satisfaction.

Who is conducting the study, why your child been asked to participate, how your child was selected, and what is the approximate number of participants in the study?

Dr. Shira Robbins and her research staff are conducting a research study to learn more about how omega-3 fatty acid supplementation in low birth weight infants changes the blood profile of infants that receive this nutritional treatment.

For many very low birth weight infants or infants born at 30 weeks gestation or less, it is necessary to give them additional nutrition through the vein (intravenous) to promote growth and development. This nutrition consists of a mixture of supplements, including fatty acids, and is routinely given to infants as a part of their standard of care.

Approximately 517,000 infants are born prematurely every year and as low birth weight and premature infants are surviving longer, they are at risk of developing severe retinopathy of prematurity (ROP). ROP is a disease of the eye affecting prematurely-born babies. It is thought to be caused by the abnormal growth of retinal blood vessels which may result in scarring and retinal detachment. ROP can be mild and may resolve spontaneously, but it may lead to blindness in serious cases. ROP is the leading cause of irreversible childhood blindness in the United States. As such, all preterm babies are at risk for ROP, and very low birth weight is an additional risk factor.

Recent research suggests that omega-3 fatty acids may act as protective factors in diseases

affecting retinal blood vessels. Omega-3 fatty acids make compounds that protect against the growth of abnormal blood vessels by preventing inflammation.

For this study, the researchers will add the Omega-3 fatty acid to the nutritional feedings that are routinely given to low birthweight infants receiving nutritional supplements for their growth. The addition of the Omega-3 fatty acid is the experimental part of this study. Omega-3 fatty acids have been used in a recent international and US based studies where 140 infants received the drug and no adverse (bad) events were reported. If your baby had been born at full term (not born early), then he/she would have received higher doses of Omega-3 fatty acids naturally as this fatty acid is provided by the mother's body while still inside the womb.

You are being asked to allow your infant to participate in this study because your infant was born at 30 weeks gestation or less or he/she weighed less than 1,500 grams (3.3 lbs) at birth and will be receiving nutritional supplements during their stay in the hospital. There will be approximately 120 participants (60 infants and up to 60 mothers) enrolled in this study at UCSD Medical Center Hillcrest and Jacobs Medical Center.

This study is being funded by several grants including those provided by UC San Diego and the Hartwell Foundation.

HOW LONG WILL YOUR INFANT BE IN THE STUDY?
Your infant will be enrolled until he/she is full term or until their retinal blood vessels have completely developed (shortly after term). We may continue to follow your infant for at least until 5 years of age. This will depend on your infant's progress over the years by standard clinical eye exam in our outpatient clinic.

WHAT IS INVOLVED IN THE STUDY?
If you agree to have your infant participate in this study, you will be asked to sign this consent form.

Your infant will be randomized (selected by chance) to one of two groups. Your infant will have a 50/50 chance of being placed in either group one or two.

If your infant is randomized to group one, he/she will receive the standard nutrition supplements. For this group, there will be no changes to the standard nutrition your child would receive regardless of their participation in this study.

If your infant is randomized to group two, he/she will receive the standard nutrition plus omega-3 fatty acids (also known as Omegaven). Your infant will receive the additional fatty acid supplementation of Carlson's baby fish oil in a split dose with their standard nutrition. This fatty acid supplementation will continue until the baby is full term (40 adjusted weeks of age). If your infant is discharged before he/she is full-term, your infant will be sent home with a bottle of the fatty acid supplementation for you to continue daily until he/she is full-term (40 weeks of age).

For both groups, the infants' nutritional needs will be carefully monitored by their doctor and a nutritionist.

To monitor the amount of nutrition getting into your infant's blood, we will collect samples of blood and perform tests. As much as possible, we will coordinate the study collection of blood to occur at the same time as the standard of care blood draws routinely done to monitor your infant's health. We will collect 1.3 milliliters (about ¼ teaspoon) of blood at 4 different times spread apart while your infant is in the hospital. We will collect a total of about 1 teaspoonful of blood.

This blood will be used for looking at what new genes (mRNA) that your infant is making and to check how many fatty acids your infant has in the blood. Before testing, the blood will be stored in a storage facility at the UCSD and labelled with a barcode without your infants' personal information. This is not your infant's DNA, and no DNA will be isolated or tested. Samples will be stored for 10 years. After this time point, all samples will be destroyed if not used by that time. If you decide to withdraw your consent the blood samples that were already drawn will be destroyed, however, any data we obtained from testing the samples will be kept.

For both groups, we will examine your infant's eyes according to the standard NICU guidelines and protocols. We will also examine your infant's eyes in our eye clinic after discharge over time as we do for all premature infants to support your infant's visual development.

WHAT ARE THE RISKS OF THE STUDY?

Blood Drawing:

Risks of drawing blood from your infant may include bruising or bleeding at the site where the blood will be drawn. Your infant may have mild pain, irritation of the vein, and swelling. There may also be a possibility of infection. This will be minimized by making your infant experience the minimum number of separate blood draws. The blood draws will usually occur as part of routine NICU care so your infant will already be having a blood draw.

Many preterm infants require blood transfusion. Since this study involves removing a small amount of blood (1/4 teaspoon at a time), the risk of anemia and blood transfusion is slightly higher. The change of blood volume in very low birth weight infants can lead to changes in blood pressure. If a transfusion is needed there is the risk of exposure to blood products including the risk of a negative reaction to the blood transfusion in the organs and tissues in the body

You should report any problems to the baby's neonatal doctor. For more information about these risks, ask your infant's study doctor.

Because this is an investigational study there may be some unknown risks that are currently unforeseeable. You will be informed of any new significant new findings.

There is a risk of a loss of confidentiality if information on the study is lost or stolen. Every measure will be taken to ensure confidentiality.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
We will monitor your infant's liver for problems that we would not normally check for soon after birth. It is possible that the omega-3 nutrition your infant receives may decrease the risk of your infant needing laser treatment for retinopathy of prematurity and gallbladder problems, based on previous studies done if randomized to group two. It is also possible that your infant will not benefit by being in this study. We hope the information learned from this study will benefit other premature infants in the future.

WHAT OTHER OPTIONS ARE THERE?
The alternative is to not participate.

INVOLUNTARY REMOVAL FROM THE STUDY:
The study doctors may decide to take your infant out of this study if your infant's condition gets worse or if your infant has a serious side effect or needs treatment not allowed in the study. The study doctors may also take your infant out of the study if they decide it is no longer in your infant's best interest to continue. If this occurs, you will be told and your study doctor will talk to you about other options.

WHAT ABOUT CONFIDENTIALITY?
Study records that identify your infant will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, your infant will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of UCSD Medical Center. For records disclosed outside of UCSD Medical Center, we will assign a unique code number. The key to the code will be kept in a locked drawer or on a password protected computer in the study's research office.

Every effort will be made to maintain your confidentiality or the confidentiality of your infant's medical records, however, this cannot be guaranteed. There is the potential risk of loss of confidentiality. Certain offices and people other than the researchers may look at your infant's medical charts and study records. These include people from:

- The Food and Drug Administration (FDA), (because they oversee the use of new drugs in the U.S).
- The Department of Health and Human Services (DHHS)
- The University San Diego, California's (UCSD) Institutional Review Board

Your infant's records will not be used for any purpose other than learning about the purpose of the study or shared with anyone else without your permission. The results from this study may be published; however, you infant will not be mentioned by name or any other personal identifiers.

Study records will be retained for 10 years after the end of the study or per local/state regulations or until participants reach 21 years of age, whichever is longer. Study information in your infant's medical records will be kept forever.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the sharing of such records, including information that may identify your infant. This is very unlikely, but if sharing the information is ever required, UCSD's Institutional Review Board will take steps allowable by law to protect the privacy of personal information.

A copy of this permission form will go into your infant's medical record.

Please review and sign the attached HIPAA form to complete your authorization for use and disclosure of your infant's personal health information.

WHAT ARE THE COSTS?
There will be no additional costs to you as a result of your infant being in this study. However, routine medical care for your infant's condition (care your infant would have received whether or not in this study) will be charged to you or your insurance company.

You will not be responsible to cover the costs of the study nutritional drug, omega-3. That will be the study doctor's responsibility.

WHAT IF YOUR CHILD IS INJURED IN THE STUDY?
If your infant is injured as a direct result of participation in this research, The University of California, San Diego, will provide any medical care needed to treat those injuries. The University of California, San Diego, will not provide any other form of compensation to you if your infant is injured. You may call the Human Research Protections Program Office at (858) 246-4777 for more information about this, to inquire about your infant's rights as a research participant or to report research-related problems.

WILL YOU OR YOUR CHILD BE COMPENSATED?
You or your infant will not receive any compensation for participation in this research study.

WHO DO YOU CALL IF YOU OR YOUR CHILD HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, contact the study doctors at:

Shira Robbins, MD (858) 822-4333

WHAT ARE YOUR INFANT'S RIGHTS AS A PARTICIPANT?
Taking part in this study is voluntary. You may choose not to let your infant take part or you may choose to leave the study at any time. Your decision will not result in any penalty or loss of benefits to which your infant is entitled. If you have questions about your infant's rights you may call:

University of California, San Diego
Human Research Protections Program
(858) 246-4777

You will be told about any new information that may affect your infant's health, welfare, or willingness to stay in this study. You may choose for your infant not to be in the study, or, if you agree to be in the study, you may withdraw your infant from the study at any time. If you withdraw your infant from the study, no new data about your infant will be collected for study purposes other than data needed to keep track of your withdrawal.

Your decision not to participate or to withdraw your infant from the study will not involve any penalty or loss of benefits to which you or your infant is entitled, and will not affect your or your infant's access to health care at University of California, San Diego. If you do decide to withdraw your infant, we ask that you contact Dr. Robbins in one of the following ways: in writing, telephone call, or tell her that you are withdrawing your infant from the study. Dr. Robbins' telephone number is (858) 822-4333 and her mailing address is 9415 Campus Point Dr, La Jolla CA 92093-0946. Blood samples that have already been collected cannot be withdrawn. We may decide to take your infant off this study if your infant's condition gets worse, or we determine that it is no longer in your infant's best interest to continue.

SIGNATURE AND CONSENT TO BE IN THE STUDY:
Your signature below means that you have read the above information about this study and have had a chance to ask questions to help you understand what your infant will do in this study and how your infant's information will be used.

You can change your mind later if you want to. You will be given a copy of this signed consent form and a copy of the Participant's Bill of Rights. By signing this consent form you are not giving up any of your or your infant's legal rights. You agree to allow your infant to participate in this research study.

_____ _____
NAME OF PARTICIPANT AGE

_____
NAME OF PARENT OR GUARDIAN

_____ _____
SIGNATURE OF PARENT OR GUARDIAN DATE/TIME

PERSON PROVIDING THE EXPLANATION OF INFORMED CONSENT:

Person's Name: (Please Print): _____

Person's Signature, Date: _____

PARTICIPANT'S BILL OF RIGHTS

It is important that the purpose and procedures of the research study are fully understood and that consent is offered willingly. A participant in a research study or someone, who is asked to give consent on behalf of another person for such participation, has the right to the following:

1. Be informed of the nature and purpose of the research.

2. Be given an explanation of all procedures to be followed and of any drug or device to be used.

3. Be given a description of any risks or discomforts, which can be reasonably expected to result from this research study.

4. Be given an explanation of any benefits, which can be reasonably expected to the participant as a result of this research study.

5. Be informed of any appropriate alternative procedures, drugs, or devices that may be advantageous and of their relative risks and discomforts.

6. Be informed of any medical treatment, which will be made available to the participant if complications should arise from this research.

7. Be given an opportunity and encouraged to ask any questions concerning the study or the procedures involved in this research.

8. Be made aware that consent to participate in the research may be withdrawn and that participation may be discontinued at any time without affecting continuity or quality of medical care.

9. Be given a copy of the signed and dated written consent form.

10. Not be subjected to any element of force, fraud, deceit, duress, coercion, or any influence in reaching the decision to consent or to not consent to participate in the research.

If you have any further questions or concerns about your child's rights as a research participant, please contact your research doctor or the UCSD Human Research Protections Program at (858) 246-4777