PARENTAL CONSENT - CLINICAL BIOMEDICAL
Version 1.0

Title of this Research Study
Compassionate Use of an Intravenous Fish Oil Lipid Emulsion (Omegaven®) for the Treatment of Intestinal Failure Associated Liver Disease in Children

Invitation
You are invited to allow your child to take part in this research study. You have a copy of the following, which is meant to help you decide whether or not to allow your child to take part:

- Informed consent form
- "What Do I need to Know Before Being in a Research Study?"
- The Rights of Research Subjects

Why is your child being asked to be in this research study?
You are being asked to allow your child to be in this research study because your child has been diagnosed with parenteral nutrition associated liver disease (PNALD) and is receiving treatment at Children's Hospital & Medical Center. Your child's doctors have used standard therapies to try to prevent the progression of this liver disease, but despite this, the liver disease is still present.

If your child is pregnant, nursing an infant, or plans to become pregnant during this study, she may not be in this study.

What is the reason for doing this research study?
Children unable to tolerate adequate oral or enteral feedings require nutrition be given by vein (called IV parenteral nutrition). Although this solution is necessary and life sustaining, it can result in severe liver disease. Experimental data has shown that the IV fat mixture we currently use may be contributing to this liver disease.

We have an alternative form of IV fat mixture, called Omegaven® that could be used in place of the IV fat mixture currently used. Omegaven® contains 10% fish oil which is different than the current IV fat mixture that contains soybean oils. Omegaven® is investigational and is not FDA approved. It is available at Children's Hospital & Medical Center as part of a research study.

What will be done during this research study?
Omegaven® will be given at a goal dose of 1 gram/kg/day and will be infused over 24 hours. Omegaven® will be infused intravenously through either a central or peripheral

catheter alone or with solutions containing dextrose (sugar) or amino acids (protein). Your child will remain on Omegaven® until weaned from parenteral nutrition, or your child/family requests the research to be stopped. We will collect information from your child's medical record to evaluate the effectiveness and safety of Omegaven®. The information we will collect will include medical history and birth history, laboratory results, procedures and outcomes, as well as physical exam findings, medications, and feeding history.

What are the possible risks of being in this research study?
The manufacturer has indicated that there may be increased risk of an allergic reaction to this product in patients with egg or shellfish allergies. Its use is not recommended for patients with impaired fat metabolism, severe bleeding disorders, or unstable diabetes.

Due to lack of experience in certain life threatening situations, the manufacturer does not recommend the use of this product in patients with severe liver or kidney problems. The risk associated with the use of this product in your child, given that he/she has severe liver injury, is not known. Omegaven® may be associated with essential fatty acid deficiency. To minimize the potential for deficiency, we will monitor your child's levels of essential fatty acids. The long term side effects are unknown and there is a potential risk of bleeding, or infection.

There are possible side effects that can be seen during infusion of fat emulsions, including Omegaven®: slight rise in temperature, flushing, chills, lack of appetite, nausea/vomiting, trouble breathing, headache, chest pain, increase/decrease in blood pressure, allergic reaction. Additional risks associated with Omegaven®use include allergic reaction, bleeding problems, and problems with clotting.

There is a slight risk of loss of confidentiality. It is possible that other rare side effects could occur, which are not described in this consent form. It is also possible that your child could have a side effect that has not occurred before.

What are the possible benefits to your child?
Omegaven® may be effective in stabilizing or reversing liver injury associated with the use of parenteral nutrition. Your child may not get any benefit from being in this research study.

What are the possible benefits to other people?
The results of this study may help to inform how best to use Omegaven® for the treatment of children with parenteral nutrition associated liver disease.

What are the alternatives to being in this research study?
The alternative to receiving Omegaven® is to continue to receive the IV fat mixture that your child is currently receiving. The investigators will discuss with you the risks and benefits of this alternative.

What will allowing your child to be in this research study cost you?
There is no cost to you for your child to be in this research study.

Will you or your child be paid for being in this research study?
Neither you nor your child will be paid to be in this research study.

Who is paying for this research?
This research is being paid for by Children's Hospital & Medical Center.

What should you do if your child is injured or has a medical problem during this research study?
Your child's welfare is the main concern of every member of the research team. If he/she is injured or has a medical problem or some other kind of problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at the Children's Hospital & Medical Center. If there is not sufficient time, you should seek care for your child from a local health care provider.

The Institution will provide required medical care if a medical problem arises as a direct result of being in this study. The Institution has no plans to provide other compensation if a medical problem arises as a direct result of being in this study. If your child has insurance, the insurance company may or may not pay the costs of medical treatment. If he/she does not have insurance, or if the insurance company refuses to pay, you will be expected to pay for the medical treatment.

Agreeing to this does not mean you have given up any of you or your child's legal rights.

How will information about your child be protected?
Your child has rights regarding the protection and privacy of his/her medical information collected before and during this research. This medical information is called "protected health information" (PHI). PHI used in this study may include his/her medical record number, address, birth date, medical history, the results of physical exams, blood tests, x-rays as well as the results of other diagnostic medical or research procedures. Only the minimum amount of PHI will be collected for this research. Your child's research and medical records will be maintained in a secure

manner.

Who will have access to information about your child?
By signing this consent form, you are allowing the research team to have access to your child's PHI. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at the Institution.

Your child's PHI will be used only for the purpose(s) described in the section "What is the reason for doing this research study?"

You are also allowing the research team to share his/her PHI, as necessary, with other people or groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- Federal law requires that your child's information may be shared with these groups:
    - The HHS Office of Human Research Protection (OHRP)
    - The Food and Drug Administration (FDA)

You are authorizing us to use and disclose your child's PHI for as long as the sponsor needs to obtain approval from the FDA.

You may cancel your authorization for further collection of your child's PHI for use in this research at any time by contacting the principal investigator. However, the PHI which is included in the research data obtained to date may still be used. If you cancel this authorization, your child will no longer be able to participate in this research.

How will results of the research be made available to you during and after the study is finished?
In most cases, the results of the research can be made available to you when the study is completed, and all the results are analyzed by the investigator or the sponsor of the research. The information from this study may be published in scientific journals or presented at scientific meetings, but your child's identity will be kept strictly confidential.

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator at the following address: 8200 Dodge Street, Omaha, NE 68114.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as

required by U.S. law. This website will not include information that can identify your child. At most, the website will include a summary of the results. You can search this website at any time.

What will happen if you decide not to give permission for your child to be in this research study?
You can decide not to give permission for your child to be in this research study. Deciding not to be in this research will not affect your child's medical care or his/her relationship with the investigator or the Institution. Your child's doctor will still take care of him/her. Your child will not lose any benefits to which he/she is entitled.

What will happen if you decide to stop your child's participation once it starts?
You can stop your child's participation in this research ("withdraw") at any time by contacting the Principal Investigator or other research personnel listed at the end of this consent form.

Deciding to withdraw will otherwise not affect your child's care or relationship with the investigator or this institution. Your child will not lose any benefits to which he/she is entitled.

For the safety of your child, please talk to the research team before you have him/her stop taking any study drugs or stop other related procedures. They will advise you how to withdraw your child safely. If you withdraw your child, you may be asked to allow your child to undergo some additional tests. You do NOT have to agree to have your child undergo these tests.

Your child may be taken off the study if he/she doesn't follow instructions of the investigator or the research team. Your child may also be taken off the study if:

- your child develops toxicity considered unacceptable by your child's physician.
- you request to discontinue treatment and/or observation of your child for any reason.
- the Principal Investigator decides that stopping treatment is in your child's best medical interest.
- the study team is unable to contact you or your child.

Any research data obtained to date may still be used in the research.

Will you be given any important information during the study?
You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want your child to continue being in the study.

What should you do if you have any questions about the study?

You have been given a copy of *"What Do I Need to Know Before Being in a Research Study?"* If you have any questions at any time about this study, you should contact the Principal Investigator or any of the study personnel listed on this consent form or any other documents that you have been given.

What are your child's rights as a research subject?

Your child has rights as a research subject. These rights have been explained in this consent form and in The Rights of Research Subjects that you have been given. If you have any questions concerning his/her rights or complaints about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
    - Telephone: (402) 559-6463.
    - Email: IRBORA@unmc.edu
    - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
- Research Subject Advocate
    - Telephone: (402) 559-6941
    - Email: unmcrsa@unmc.edu

Documentation of informed consent

You are freely making a decision whether to give permission for your child to be in this research study. Signing this form means that:

- You have read and understood this consent form.
- You have had the consent form explained to you.
- You have been given a copy of The Rights of Research Subjects
- You have had your questions answered.
- You have decided to permit your child to be in the research study.
- If you have any questions during the study, you have been directed to talk to one of the investigators listed below on this consent form.
- You will be given a signed and dated copy of this consent form to keep.

Signature of Parent/Guardian _____
Date _____

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the parent(s)/guardian(s) of the subject. In my judgment, the parent(s)/guardian(s) possesses the legal capacity to give informed consent for the subject to participate in this research and is voluntarily and knowingly

giving informed consent.

Signature of Person obtaining consent _____
Date _____

Authorized Study Personnel
Principal
* Jones, Brian
phone: 402-955-7400
degree: MD

Secondary
* Cusick, Robert (Bob)
phone: 402-955-7400
alt #: 402-955-7404
degree: MD

Participating Personnel
Brester, Michelle
alt #: 402-955-7404
degree: NP

Infantino, Benjamin
alt #: 402-955-5700
degree: MD

* Raynor, Stephen
phone: 402-955-7411
alt #: 402-955-7404
degree: MD

Lead Coordinator
Dawson, Machelle
alt #: 402-559-5698
degree: RN, BSN, MEd

Other Coordinator
Jones, Sara (Sara)
phone: 402-559-1747
alt #: 402-559-1747
degree: RD, LMNT

What Do I Need To Know Before Being In A Research Study?

You have been invited to be in a **research study**. Research studies are also called "clinical trials" or "protocols." **Research** is an organized plan designed to get new knowledge about a disease or the normal function of the body. The people who are in the research are called **research subjects**. The **investigator** is the person who is running the research study. You will get information from the investigator and the research team, and then you will be asked to give your **consent** to be in the research.

This sheet will help you think of questions to ask the investigator or his/her staff. You should know all these answers before you decide about being in the research.

What is the **purpose** of the research? Why is the investigator doing the research?

What are the **risks** of the research? What bad things could happen?

What are the possible **benefits** of the research? How might this help me?

How is this research different than the care or treatment I would get if I wasn t in the research? Are there other treatments I could get?

Does **everyone** in this research study get the same treatment?

Will being in the research **cost** me anything extra?

Do I have to be in this research study? Will the doctor still take care of me if I say **no**?

Can I **stop** being in the research once I ve started? How?

Who will look at my **records**?

How do I reach the investigator if I have more **questions**?

Who do I call if I have questions about being a **research subject**?

Make sure all your questions are answered before you decide whether or not to be in this research.

Academic Research & Services Building 3000 / 987830 Nebraska Medical Center / Omaha NE 68198-7830
402-559-6463 / FAX 402-559-3300 / Email: irbora@unmc.edu / http://www.unmc.edu/irb

THE RIGHTS OF RESEARCH SUBJECTS
AS A RESEARCH SUBJECT YOU HAVE THE RIGHT

to be told everything you need to know about the research before you are asked to decide whether or not to take part in the research study. The research will be explained to you in a way that assures you understand enough to decide whether or not to take part.

to freely decide whether or not to take part in the research.

to decide not to be in the research, or to stop participating in the research at any time. This will not affect your medical care or your relationship with the investigator or the Nebraska Medical Center. Your doctor will still take care of you.

to ask questions about the research at any time. The investigator will answer your questions honestly and completely.

to know that your safety and welfare will always come first. The investigator will display the highest possible degree of skill and care throughout this research. Any risks or discomforts will be minimized as much as possible.

to privacy and confidentiality. The investigator will treat information about you carefully, and will respect your privacy.

... to keep all the legal rights you have now. You are not giving up any of your legal rights by taking part in this research study.

to be treated with dignity and respect at all times

The Institutional Review Board is responsible for assuring that your rights and welfare are protected. If you have any questions about your rights, contact the Institutional Review Board at (402) 559-6463.