PROTOCOL: Compassionate Use of Omegaven® IV Fat Emulsion

Background

In the United States, patients dependent upon parenteral nutrition (PN) receive parenteral fat emulsions composed of soybean oils. Lipids are necessary in PN dependent patients due to their high caloric value and essential fatty acid content. However, intravenous lipid emulsions have been implicated in predisposing patients to PN associated liver disease. Phytosterols such as those contained in soybean oils are thought to have a deleterious effect on biliary secretion. Accumulation of lipids in the hepatic Kupffer cells may further impair liver function.

Although the currently available omega-6 fatty acid emulsions prevent fatty acid deficiency, it is thought that they are not cleared in a manner similar to enteral chylomicrons and therefore accumulate in the liver and resulting in steatotic liver injury (neonatal cholestasis). It is hypothesized that a fat emulsion comprised of omega-3 fatty acids (i.e., fish oil), such as Omegaven,® would be beneficial in the management of steatotic liver injuiry by its inhibition of de novo lipogenesis, the reduction of arachidonic acid-derived inflammatory mediators, prevention of essential fatty acid deficiency through the presence of small amounts of arachidonic acid, and improved clearance of lipids from the serum. Animal studies have shown that IV fat emulsions such as fish oil that are high in eicosapentaenic and docosahexaenoic acid reduce impairment of bile flow which is seen in cholestasis caused by conventional fat emulsions. Furthermore, intravenous omega-3 fatty acids are well tolerated and might reduce the inflammatory effect in the liver of prolonged PN exposure and, potentially, reverse steatotic hepatic dysfunction. By administering Omegaven® in place of conventional phytosterol/soybean fat emulsion, the progression of PN-associated cholestasis can be prevented or reversed.

Specific Objectives

The following is a compassionate use protocol designed to treat selected infants and children, in the inpatient and/or outpatient settings, with parenteral nutrition-associated liver disease (PNALD) to reverse cholestasis (elevated serum transaminases and direct bilirubin) with Omegaven® Fat Emulsion. This protocol will end if the product is approved for use in the United States or if an FDA clinical trial proves Omegaven® treatment to be ineffective.

Preliminary Studies

Preliminary Safety and Efficacy Data for Use of Omegaven® in Infants. A recent study in Boston reported the experience of using Omegaven® in 18 former premature infants with a variety of GI surgical conditions resulting in short-bowel syndrome (Gura et al, 2008). Infants receiving Omegaven® normalized their serum bilirubin by 9 weeks compared with 44 weeks in historical controls. There were more deaths and transplantations in the historical control group. There was no association between the use of Omegaven® and essential fatty acid deficiency, hypertriglyceridemia, coagulopathy, infection, or growth delay. The study reported no safety issues with fish-oil use.

Boston Children's Hospital has seen improvement in over 50 infants who have received Omegaven® long-term (in the hospital and at home) without negative effects (Gura et al, 2008). Use in this long-term fashion may delay or prevent the need to perform a transplant related to ongoing liver failure (Gura et al, 2006).

There is no minimum or maximum length of time for the subject to receive the Omegaven®. Boston Children's Hospital is currently following several children who have received Omegaven® for over 2 years and one child who has received it for almost 5 years.

The following details a protocol for hospital and home use of intravenous Omegaven® fat emulsion in selected infants and children with parenteral nutrition-associated liver disease (PNALD).

Methods

Design

The following is a compassionate use protocol designed to treat selected infants and children, in the inpatient and/or outpatient settings, with parenteral nutrition-associated liver disease (PNALD) to reverse cholestasis (elevated serum transaminases and direct bilirubin) with Omegaven® Fat Emulsion. This protocol will end if the product is approved for use in the United States or if an FDA clinical trial proves Omegaven® treatment to be ineffective.

Patient Selection and Inclusion/Exclusion Criteria

To receive Omegaven® in the hospital or at home, subjects will first be required to satisfy inclusion criteria including: a diagnosis of PNALD (defined as two consecutive direct bilirubin levels of 2 mg/dl or more) in a parenteral nutrition-dependent infant or child. Other causes of liver disease will have been excluded using standard clinical criteria without the mandatory need for a liver biopsy. The patient must have utilized standard therapies to prevent the progression of the cholestasis including reduction/removal of copper and manganese from daily PN, trial of enteral feedings if possible, and the use of ursodiol and/or phenobarbital.

Paitents will be excluded if they have other documented causes of chronic liver disease (i.e., Hepatitis C, cystic fibrosis, biliary atresia, alpha-1-anti-trypsin deficiency), or already have signs of proven severe advanced liver disease including cirrhosis on biopsy, varices, ascites. Additional exclusion criteria: an allergy to any seafood product, egg protein, and/or previous

allergy to Omegaven,® active coagulopathy characterized by ongoing bleeding or by a requirement for clotting factor replacement (e.g. fresh frozen plasma or cryoprecipitate) to maintain homeostasis, inpaired lipid metabolism or severe hyperlipidemia with or without pancreatitis, unstable diabetes mellitus or hyperglycemia, stroke, embolism, collapse and shock, recent MI, cholestasis due to any reason other than PNAC {PNALD}, active new infection at time of initiation of Omegaven,® or hemodynamic instability. The patient may not be enrolled in any other clinical trial involving an investigational agent (unless approved by the designated physicians on the multidisciplinary team) and the parent or guardian must be willing to provide consent.

Included will be infants and children from birth to 5 years of age who reside in the NICUs, general pediatric units or PICUs at Staten Island University Hospital. For home administration, patients may be admitted (if not already in-patients) to the medical unit appropriate for their medical status at Staten Island University Hospital for 72 hours to initiate the administration of the Omegaven®. This will allow time for observation of any unexpected side effects and for parents to be provided education on home TPN and Omegaven®. The patient will be admitted to the neonatal intensive care unit (NICU) if they have been transferred from a referral hospital's NICU. If a patient is receiving parenteral nutrition (not containing Omegaven®) at home, they would be admitted to the general pediatrics medical floor for this observational period. If a patient has already received Omegaven® either at Staten Island University Hospital or at another hospital, they will not be required to be admitted for the 72 hour inpatient admission prior to starting Omegaven® at home. If home care is necessary, parental training will occur during the hospital admission and will continue with home health agency nurses provided through home care agencies arranged by the Division of Neonatology at Staten Island University Hospital.

Details of Omegaven® Administration

After baseline labs are obtained (Tables 2 and 3), therapy with Omegaven® will be initiated at the goal dose of 0.5 gram/kg/day infused over 24 hours for 1-2 days, and then advanced to 1 gram/kg/day. This is a maximum dose and may be decreased at the discretion of the investigators. Omegaven® will be infused intravenously through either a central or peripheral catheter alone or in conjunction with parenteral nutrition. If additional fat calories are needed, if possible, they will be provided via the enteral route. The same standards of care provided to all patients receiving parenteral nutrition solution will be followed. Routine nutritional monitoring is described in Table 3.

In the event that a patient is unable to achieve adequate calories parenterally, and is unable to tolerate enteral feeds, it may be necessary to evaluate whether or not the patient should continue the therapy with Omegaven® as monotherapy or resume therapy with conventional fat emulsions so that additional parenteral fat calories can be given. The clinical team, in conjunction with the patient's primary physician, will determine if the patient should be removed from the protocol.

In-patient administration:

Orders for Omegaven® will contain the following data elements: body weight, total daily dose (ml), and hourly infusion rate (ml/hour). Prior to the administration of each Omegaven® dose, two nurses will check the dose dispensed against the physician's orders and verify that the

infusion pump settings (hourly rate, volume to be infused) are correct before the infusion is started.

As previously mentioned, Omegaven® may be infused in the same manner as conventional fat emulsions through either a central or peripheral line. The emulsion is isotonic. It is compatible with parenteral nutrition solutions and may be co-infused with TPN via y-site. The product may be infused through a 1.2 micron inline filter.

Outpatient Monitoring and Administration for patients on home therapy
After the initial evaluation by the Division of Neonatology, patients will return to the clinic for routine follow-up. Subjects will be asked to return to the clinic every 2 weeks for the first 2 months of treatment. Thereafter, patients will return to the clinic on a monthly basis, or as directed by the Division faculty. It will be explained to the parent/legal guardian that these follow up visits are important and that the study physicians reserve the right to drop the subject for non-compliance if safety measures cannot be adequately monitored.

Orders for home use of Omegaven® will be signed by the Division of Neonatology physicians, ensuring that subjects are compliant with study parameters while receiving the treatment drug. Orders for the Omegaven® will include: body weight measurement, total daily dose (ml), and hourly infusion rate (ml/hr). Prior to each Omegaven® dose, the nurse and/or parent will check the dose dispensed against the physician's orders and verify that the infusion pump settings (hourly rate, volume to be infused) are correct before the infusion is started.

Routine monitoring done at outpatient appointments and at home (through collaboration with the necessary home care agencies) will be recorded. No blood work will be done for study purposes only. Anthropometrics, new diagnoses, surgical procedures, medications, hospital readmissions, infections, feeding plans (e.g., volume, caloric density, and name of enteral formulas), and other pertinent data will also be recorded. The Team physicians will monitor clinically for signs of an essential fatty acid deficiency and adjust the nutrition strategy as needed.

Baseline laboratory monitoring (Table 2 and 3)recorded within 10 days of enrollment will include: BUN, CO_2, creatinine, glucose, serum chloride, potassium, sodium, calcium, phosphorus, magnesium, triglycerides, white blood cell count (WBC or leukocyte count), WBC differential count, red blood cell count (RBC or erythrocyte count), hematocrit (Hct), hemoglobin (Hgb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet count, and mean platelet volume (MPV), liver panel [alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), albumin, total protein, direct bilirubin (conjugated), total bilirubin, lactic acid dehydrogenase (LDH)], essential fatty acid (EFA) profile, prothrombin time (PT), partial thromboplastin time (PTT), and INR. The above lab monitoring, with the exception of the EFA profile, will typically be done approximately every month at home or at each clinic visit. Routine evaluations done through the home health service will be continued as usual.

Dose Modification

Lipid Intolerance. If lipid intolerance develops (defined as serum triglyceride levels > 200 mg/dl), the following will be considered prior to reducing the dose: a) if the level was obtained while the patient was receiving a continuous 24 hour infusion of Omegaven®, the total dose should be infused over 20 hours, and a repeat serum triglyceride level obtained prior to resuming the infusion 4 hours later, b) other sources of lipid intolerance should be considered and addressed (drugs, renal disease). If the triglycerides continue to remain high despite the aforementioned interventions, a dosage reduction of 25% of the current dose will be considered. If subsequent triglyceride levels are elevated the dosage will continue to be reduced, and then Omegaven will be discontinued if there is no effect of dose reduction. Subsequent levels will be monitored and adjustments made. After a week, if triglyceride levels are in an appropriate range, Omegaven will be reintroduced.

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Duration of Therapy. Patients will remain on Omegaven® until weaned from PN. Patients may continue monotherapy with Omegaven® as an additional source of calories after the dextrose/protein portion of PN is discontinued. Omegaven may be restarted within seven days of discontinuing therapy. After seven days, and meeting inclusion criteria, Omegaven can resume at the initial dose of 0.5 grams/kg/day, advancing to 1 gm/kg/day

Adverse Event Criteria and Reporting Procedures

Adverse events (AEs) and serious adverse events (SAEs) will be assessed and reported from the time of the first Omegaven® infusion until Omegaven completion and resolution of event(s). This is a very high risk population so adverse events are not uncommon. However, events such as death, blood stream infection, the development or worsening of respiratory distress, or hemodynamic instability; electrolyte abnormalities, catheter malfunction, bowel obstruction, and urinary tract infection will be reported. Any serious or unexpected adverse events will be reported to the SIUH IRB within 48 hours, and the FDA within 7 days. In particular, the patient will be observed during and shortly after Omegaven® administration for the occurrence of anaphylactic or allergic reactions. As inpatients, those experiencing adverse events that are moderate or severe in nature and that may be related to Omegaven® will have their treatment temporarily halted until the adverse event has resolved. Dose modifications will occur as described above. Patients receiving Omegaven® at home will be observed by their parent or caregiver. If adverse events that are moderate or severe in nature as an outpatient, parents will be told to report to the Emergency Department at Staten Island University Hospital for evaluation and possible hospital admission for their child. If a dose reduction is made for adverse events later considered to be unrelated to Omegaven,® the Omegaven® dose will be increased back to the dose prescribed prior to the dose reduction. Patients with anaphylactic or allergic reactions will not continue treatment.
Adverse events and serious adverse events will be collected and reviewed monthly for emerging patterns.

Patients will be withdrawn from Omegaven® treatment for any of the following:

a) Parent/legal guardian requests to discontinue treatment and/or observation for any reason.

b) A suitable organ has been located and the patient is able to undergo a liver or liver/intestinal transplant.

c) Decision by the Principal Investigator that termination is in the patient's best medical interest.

d) Omegaven will be stopped if lipid intolerance persists despite therapeutic changes as described on page 3 of the protocol (see Dose Modification).

e) Omegaven will be stopped if essential fatty acid levels are below normal two serial measurements.

This protocol will end if the product is approved for use in the United States or if an FDA clinical trial proves Omegaven® treatment to be ineffective.

Omegaven® Acquisition, Storage, Drug Accountability, and Dispensing

Bottles containing 50 mL or 100 mL of 10% Omegaven® will be purchased from International Pharmacy of Hamburg, Germany or directly from the manufacturer. Omegaven® is formulated as an emulsion from fish oils and will be stored at room temperature below 30° C (not frozen). Containers should be shaken before use

Inpatient

In the event that third party coverage is not available, Staten Island University Hospital will cover all drug costs for patients enrolled in this protocol.

The pharmacy will prepare and dispense Omegaven® after the receipt of the daily TPN orders, as per the manufacurer's preparation procedures. Shipping documents, FDA IND drug inventory and accountability will be maintained by the Research Pharmacists at Staten Island University Hospital. Pharmacy dispensing records will be reviewed by the investigators to ensure adherence with procedures for shipping, receipt, acountability, and dispensing of Omegaven.® Accountability and shipping documents will include relevant dates, lot numbers, quantities received or dispensed, to whom dispensed, returned drug and drug lost or damaged. At the end of the protocol, all used and unused Omegaven® will be accounted for. An FDA Investigational Agent Accountability Record will be maintained. Expired medication will be disposed of as per the manufacturer's recommendation.

Outpatient

We will make arrangements with home care agencies to be providers for the Omegaven® in the home. The agencies will import the Omegaven® directly from Germany and provide it to the patient at home, working under our IND number since all the patients will be enrolled in this protocol.

Patients will be billed for the Omegaven® at home just as they are billed for it while hospitalized at Staten Island University Hospital. Thus far, we are not aware of any Medicaid rejections of Omegaven® in other patient populations around the country and anticipate that Medicaid will continue to cover the cost for home use. If Omegaven® is continued at home, the home health care agencies will maintain drug accountability and shipping documents including relevant dates,

lot numbers, quantities received or dispensed, to whom dispensed, returned drug and drug lost or damaged. An FDA Investigational Agent Accountability Record will be maintained. Expired medication will be disposed of as per the manufacturer's recommendation**.**

Informed Consent

After meeting entry criteria, the Investigator and/or Sub-investigators will be responsible for obtaining informed consent. Informed consent will be obtained from the infant's parents and/or legal guardians after a full explanation of the purpose of the protocol, the risks and discomforts involved, potential benefits, have been provided by the Investigator and/or Co-investigators, both verbally and in writing. The original of the signed consent will be maintained by the investigator and a copy will be placed in the patient's medical record. The person who signed the consent must also be given a copy of the signed consent form.

Patient Confidentiality

Individual patient medical information obtained as a result of the administration of Omegaven® is considered confidential and disclosure to third parties, other than those cited below, is prohibited. Data generated will be available for inspection, on request by various regulatory agencies. These shall include all protocol-relevant documentation, including medical histories to verify eligibility, laboratory test results, treatment and diagnostic reports, admission/discharge summaries for hospital admissions occurring while the patient is receiving Omegaven® and autopsy reports (if available) for deaths occurring during or in temporal proximity to the study. As part of the required content of the informed consent, patients must be informed that their records may be reviewed by various regulatory agencies.

Risks and Discomforts

Omegaven® has been studied in animal pre-clinical models as well as Phase I, II, III, and post marketing human trials in both Europe and Asia. Prolonged bleeding time and an inhibited platelet aggregation can occur. It should not be administered to patients known to be allergic to fish or egg protein.

Contraindications to Omegaven® include the following: impaired lipid metabolism, severe hemorrhagic disorders, unstable diabetes mellitus, hemodynamic instability, stroke/embolism.

Side effects
The infusion of Omegaven® can lead to a prolonged bleeding time and an inhibited platelet aggregation. In rare cases, patients may experience a fishy taste. The administration of Omegaven® should be stopped or reduced if there is a marked increased in blood glucose levels during the Omegaven® infusion. Undesirable effects that are seen during the infusion of Omegaven® that may also occur with conventional fat emulsions (i.e., Intralipid®) include slight rise in body temperature, flushing or cyanosis, vomiting, changes in blood pressure, erythema, anaphylactic reactions.

Overdose:
In the event of an overdose of Omegaven® there is a risk of developing fat overload syndrome that may occur when the triglyceride level rises >200 mg/dL acutely as a result of too rapid a rate of infusion, or chronically at high infusion rates in associated with a change in the patient's clinical condition (e.g., renal dysfunction, sepsis). In such cases, the infusion should be stopped or, if necessary, continued at a reduced dose. Metabolic acidosis has occurred in patients receiving Omegaven® at excessive doses without simultaneous administration of dextrose.

Potential Benefit of Omegaven® Treatment

Omegaven® may be effective in stabilizing or reversing hepatic injury associated with the use of parenteral nutrition. It may allow the patient to continue to receive the majority of his/her caloric intake from parenteral nutrition while advancing on enteral nutrition or awaiting liver or liver/intestinal transplant.

Outcome Variables
Laboratory measurements, growth indices and trends will be reviewed as per the suggested monitoring schedule during Omegaven therapy. Desired endpoint to support effectiveness will be evidenced by a decline in serum direct bilirubin levels below 2 on two serial measures.

Potential Risks of No Treatment

Since Omegaven® will only be offered to those patients for whom no standard therapy is likely to be safe and effective, the risks of not being treated are those allowing for the natural history of their disease and associated clinical manifestations to progress. These include fulminate liver failure and death.

Data Safety and Monitoring Plan

The principal investigator will be responsible for monitoring the safety of the study. The Principal Investigator and study team will monitor data quality, adverse events and protocol deviations through protocol deviation logs. They will notify the IRB if there are any adverse event trends that could qualify as unanticipated problems.

References
1. Mullick FG, Moran CA, Ishak KG. Total parenteral nutrition: a histopathologic analysis of the liver changes in 20 children. Mod Pathol 1994;7:190-4.
2. Freund HR. Abnormalities of liver function and hepatic damage associated with total parenteral nutrition. Nutrition 1991;7:1-5; discussion 5-6.
3. Beath SV, Davies P, Papadopoulou A, Khan AR, Buick RG, Corkery JJ, Gornall P, Booth IW. Parenteral nutrition-related cholestasis in postsurgical neonates: multivariate analysis of risk factors. J Pediatr Surg 1996;31:604-6.
4. Greenberg GR, Wolman SL, Christofides ND, Bloom SR, Jeejeebhoy KN. Effect of total parenteral nutrition on gut hormone release in humans. Gastroenterology 1981;80:988-93.

5. Yeh SL, Chen WJ, Huang PC. Effects of L-glutamine on induced hepatosteatosis in rats receiving total parenteral nutrition. J Formos Med Assoc 1995;94:593-9.
6. Kubota A, Yonekura T, Hoki M, Oyanagi H, Kawahara H, Yagi M, Imura K, Iiboshi Y, Wasa K, Kamata S, Okada A. Total parenteral nutrition-associated intrahepatic cholestasis in infants: 25 years' experience. J Pediatr Surg 2000;35:1049-51.
7. Moss RL, Das JB, Ansari G, Raffensperger JG. Hepatobiliary dysfunction during total parenteral nutrition is caused by infusate, not the route of administration. J Pediatr Surg 1993;28:391-6; discussion 396-7.
8. Helms RA, Christensen ML, Mauer EC, Storm MC. Comparison of a pediatric versus standard amino acid formulation in preterm neonates requiring parenteral nutrition. J Pediatr 1987;110:466-70.
9. Moss RL, Haynes AL, Pastuszyn A, Glew RH. Methionine infusion reproduces liver injury of parenteral nutrition cholestasis. Pediatr Res 1999;45:664-8.
10. Meehan JJ, Georgeson KE. Prevention of liver failure in parenteral nutrition-dependent children with short bowel syndrome. J Pediatr Surg 1997;32:473-5.
11. Whalen GF, Shamberger RC, Perez-Atayde A, Folkman J. A proposed cause for the hepatic dysfunction associated with parenteral nutrition. J Pediatr Surg 1990;25:622-6.
12. Zamir O, Nussbaum MS, Bhadra S, Subbiah MT, Rafferty JF, Fischer JE. Effect of enteral feeding on hepatic steatosis induced by total parenteral nutrition. JPEN J Parenter Enteral Nutr 1994;18:20-5.
13. Kaminski DL, Adams A, Jellinek M. The effect of hyperalimentation on hepatic lipid content and lipogenic enzyme activity in rats and man. Surgery 1980;88:93-100.
14. Hultin M, Carneheim C, Rosenqvist K, Olivecrona T. Intravenous lipid emulsions: removal mechanisms as compared to chylomicrons. J Lipid Res 1995;36:2174-84.
15. Qi K, Al-Haideri M, Seo T, Carpentier YA, Deckelbaum RJ. Effects of particle size on blood clearance and tissue uptake of lipid emulsions with different triglyceride compositions. JPEN J Parenter Enteral Nutr 2003;27:58-64.
16. Nestel PJ. Effects of N-3 fatty acids on lipid metabolism. Annu Rev Nutr 1990;10:149-67.
17. Chen W. Effects of fat emulsions with different fatty acid composition on plasma and hepatic lipids in rats receiving total parenteral nutrition. Clinical Nutrition 1996;15:24.
18. Yeh S. Effects of fish oil and safflower oil emulsions on diet-induced hepatic steatosis in rats receiving total parenteral nutrition. Clinical Nutrition 1996;15:80.
19. Gura KM, Lee S, Valim C, Zhou J, Kim S, Modi BP, Arsenault DA, Strijbosch RAM, Lopes S, Duggan C, Puder M. Safety and efficacy of a fish-oil-based fat emulsion in the treatment of parenteral nutrition-associated liver disease. Pediatrics 2008; 121:e678-e686.
20. Gura KM, Duggan CP, Collier SB, Jennings RW, Folkman J, Bistrian BR, Puder M. Reversal of parenteral nutrition-associated liver disease in two infants with short bowel syndrome using parenteral fish oil: implications for future management. Pediatrics. 2006 Jul;118(1):e197-201

Appendix Materials

Table 1

Comparison of Parenteral Fat Emulsions

	Intralipid® 20%	**Liposyn® II** 20%	**Omegaven®** 10%
Soybean oil	100%	50%	
Safflower oil		50%	
Fish oil			100%

% of Total Fat:

Linoleic acid	50	65	0.1 – 0.7
α-Linolenic acid	9	4	0.2
EPA			1.25 - 2.82
DHA			1.44 - 3.09
Arachidonic acid			0.1 - 0.4
Glycerol	2.3	2.5	2.5
Egg Phospholipid	1.2	1.2	1.2
Total kcals per ml	2.0	2.0	1.12
Available in the U. S.	Yes	Yes	No

Table 2: Schedule for Required Safety Monitoring for Omegaven® Therapy

(To be done baseline pre-Omegaven® therapy and serially as indicated until direct bilirubin <2.0 mg/dL on two serial measurements)

Parameter	Baseline	Every 2 wk to every month
Essential Fatty Acid Profile	X	X (month)
PT	X	X
PTT	X	X
INR	X	X

Table 3: **Suggested** Monitoring Schedule for Omegaven® Therapy

Parameter	Baseline (pre-therapy)	Daily	Every 2 wk to monthly
Body Weight	X	X	
Length; head circumference	X		X
Fluid intake	X	X	
Laboratory tests:			
Sodium, Potassium	X		X
Chloride, Bicarb.	X		X
Glucose	X		X
BUN/Creatinine	X		X
Triglycerides	X		X
Ca, P, Mg	X		X
Albumin	X		X
ALT (SGPT)/AST	X		X
Alk phosphatase	X		X
Fractionated Bilirubin	X		X
GGT	X		X
Cholesterol	X		X
Hemoglobin/Hct	X		X
WBC	X		X
Platelets	X		X
PT	X		X
PTT	X		X
INR	X		X

***For safety purposes:** serum triglycerides, coagulation labs are obtained at baseline, then biweekly for 4 weeks, and monthly thereafter; fatty acid profile is obtained at baseline, then monthly thereafter. Dose reduction will occur if there is evidence of lipid intolerance (serum triglycerides > 200mg/dL) or evidence of bleeding. Growth indices include weight, length, and head circumference will be computed every 2 weeks. Infants receiving Omegaven for more than one month will have vitamin E and copper levels drawn.