A Randomized Trial of Supplemental Parenteral Nutrition in

Under and Over Weight Critically Ill Patients:

The TOP UP Trial

Investigational Product Procedures Manual

Intended Audience: Research Cooridnators/Pharmacists

This study is registered at Clinicaltrials.gov.
Identification number NCT 01206166

Funded by:

Sponsor: Dr. Daren Heyland

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All questions related to study procedures should be directed to the Project Leader.

Study Synopsis

Hypothesis: Increased energy and protein delivery to underweight and overweight critically ill patients (Body Mass Index [BMI] <25 or ≥35) will result in improved 60 day survival compared to usual care.

Background: The optimal amount of energy and protein a given patient should receive to reduce morbidity and mortality is unclear and remains controversial. Our recent International multicenter observational study of 2772 ICU patients from 165 ICUs showed a significant inverse linear relationship between the odds of mortality and total daily calories received. Increased amounts of calories was most important for the BMI<20 group followed by the BMI 20-<25 group and BMI ≥35 group with no benefit of increased calorie intake for patients in the BMI 25-<35 group. Feeding an additional 1000 kcals almost halved the odds of 60-day mortality in patients with a BMI <25 or ≥35. Similar results were observed for feeding an additional 30 grams of protein per day. Thus, a prospective randomized trial is warranted to confirm our hypothesis that in patients with a BMI of <25 and those with a BMI ≥35 increasing the provision of more energy and protein can impact clinical outcomes.

Study Design: This pilot study is a multicenter, randomized trial of 160 critically ill patients. Patients will be randomized to one of 2 interventions: enteral nutrition (EN) alone or enteral nutrition plus parenteral nutrition (supplemental PN group). Patients will be stratified on the basis of admission BMI: <25 or ≥35, medical or surgical admission diagnosis, and by site.

Study Population & Setting: 160 critically ill adult patients (≥18 years old) with BMI <25 or ≥35 from 8-9 tertiary care ICU's in Canada, United States, and Europe.

Study Intervention: Patients will be randomized to receive EN only or EN plus PN (supplemental PN group). In both groups, we suggest the following dosing standards:

Guidelines for Dosing of Protein and Energy Based on BMI Category

	Minimum Energy	Minimum Protein
BMI <20	30 kcals/kg actual wt	1.5 g/kg actual wt
BMI 20 - <25	25 kcals/kg actual wt	1.5 g/kg actual wt
BMI>35	25 kcals/kg ABW*	1.5g/kg ABW*

* ABW=adjusted body weights. Weights in obese patients to be calculated according to the following formula: Obesity-adjusted Body weight= IBW + [actual weight – IBW] x 0.25, where IBW is ideal body weight is based on a BMI of 25

The EN only group to receive standard enteral nutrition therapy as per our Canadian Clinical Practice Guidelines with a minimum target of calories and protein developed for each stratum. Due to variability of clinical practice around the world, the targets are minimum requirements for energy and protein; each participating site will calculate requirements based upon best-evidence for the disease process for each individual patient. Patients in the EN only group will receive no additional PN in the first 7 days following randomization unless a contraindication to EN develops.

Supplemental PN group to receive the same prescription for calories and protein (in each stratum) and will receive EN via the same protocol as in the control group but in addition, they receive additional protein/energy via the parenteral route. We propose to use a 3-in-1 parenteral admixture solution containing an olive oil/soybean oil ratio of 80:20 and 9 gms nitrogen per litre (Olimel N9 with electrolytes, BE370946 {Belgium}, NL 33592 {France} or Olimel 5.7% E DIN 02352532 {Canada}, provided by Baxter). We propose to start the PN solution immediately after randomization at 25 ml/hr and increase by 25 ml/hr every 4 hours as needed and as tolerated (monitoring blood sugars and electrolytes regularly and triglycerides twice weekly until 100% of goal calories are reached). The relative amount of PN and EN will be monitored and adjusted daily to ensure that the patient receives 100% of prescribed calories daily. We will provide a feeding protocol to standardize the provision of enteral nutrition and study parenteral solutions.

The study PN solution will continue for 7 days. At 7 days post randomization, if the patient is in the ICU and requires feeding via the parenteral route, Olimel will be provided to both groups, as per recommendations from recent guidelines.

Outcomes: The primary outcome for the definitive study is 60 day mortality. Secondary outcomes include 28 day mortality, hospital mortality, duration of stay (ICU and hospital), multiple organ dysfunction (SOFA and PODS), duration of mechanical ventilation, development of ICU-acquired infections, functional status at hospital discharge, and 3 and 6 month survival and health-related quality of life.

Specific Aims: The specific aim of the proposed study is to conduct a pilot study involving 160 critically-ill lean and obese patients enrolled at 9 sites in order to:

1. To confirm that we can achieve a clinically significant difference in calorie and protein intake between the two intervention groups.
2. To estimate recruitment rate i.e. number of eligible and enrolled patients per month per site.
3. To evaluate the safety, tolerance, and logistics around providing supplemental PN in the study population in the context of a multicenter trial, e.g.
    a. To ensure adequate glycemic control in both groups
    b. To ensure that the other metabolic consequences of the feeding strategies are minimized.
    c. To establish adequate compliance with study protocols and completion of case report forms.

A secondary aim of this pilot study will be:

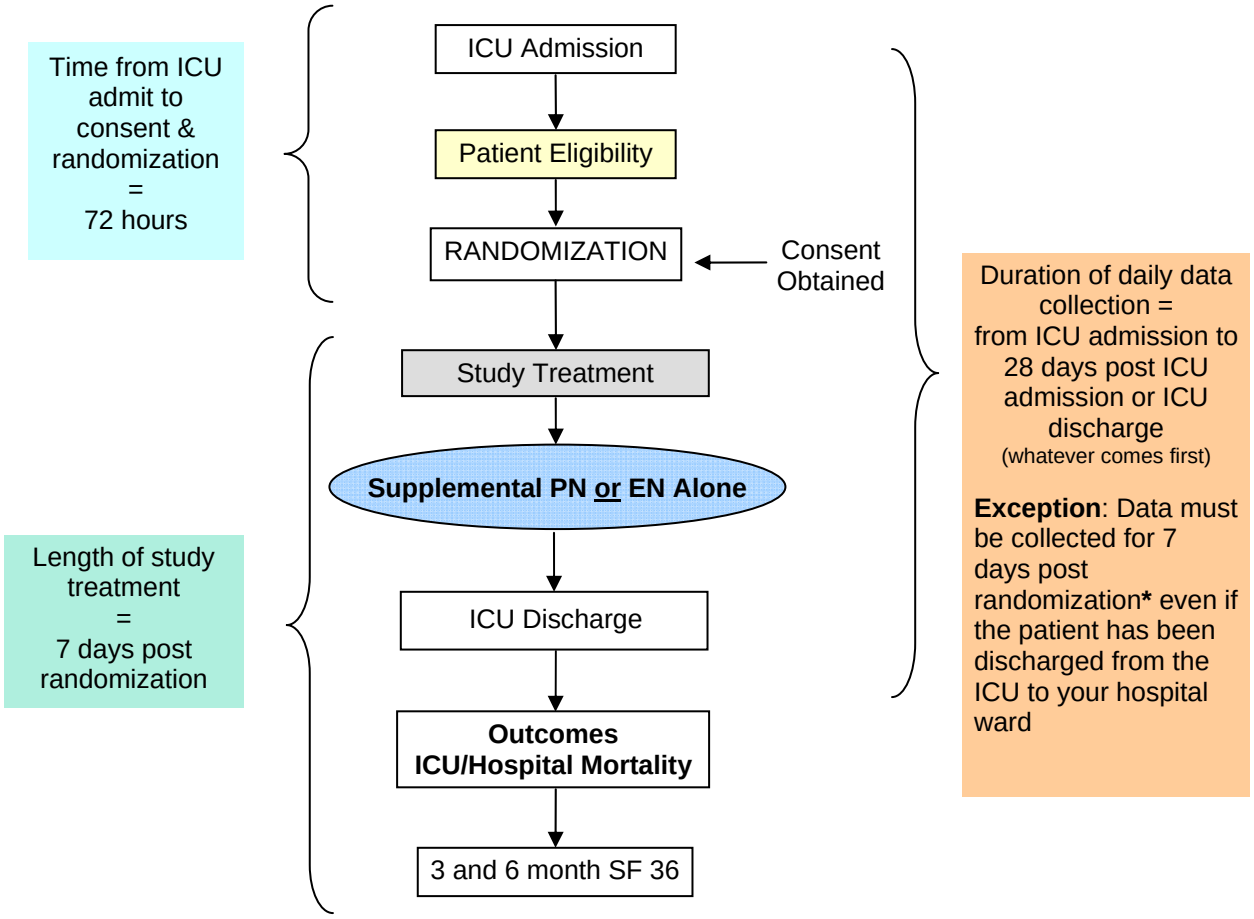
1. To explore the effect of differential rates of calorie/protein provision on muscle mass and muscle function.

Future Plans: If the results of this pilot study are positive, then we will proceed to a large scale trial of 2000 patients across approximately 40 ICUs to determine the efficacy of the proposed nutritional strategy.

Study Overview

Below is a diagrammatic representation of the TOP-UP Study. Refer to appropriate sections of the Implementation Manual for further details concerning specific activities.

Diagram 1: Overview of the TOP-UP Study



***7 days post randomization = the day of randomization PLUS an additional 7 FULL days.**

Investigational Product Administration

Patients randomized to the TOP-UP Study will receive one of the following:

Name of Group	Intervention
Supplemental PN	**EN & Olimel N9E/5.7%E**
EN Only	**EN**

Both EN only and Supplemental PN groups

Dosing
Both the supplemental PN and the EN only group will receive the exact same prescription for calories and protein (within each BMI stratum). The proposed target dose of protein and energy based on BMI category for both groups is as follows:

Guidelines for Dosing of Protein and Energy Based on BMI Category

	Minimum Energy	Minimum Protein
BMI <20	30 kcals/kg actual wt	1.5 g/kg actual wt
BMI 20 - <25	25 kcals/kg actual wt	1.5 g/kg actual wt
BMI>35	25 kcals/kg ABW*	1.5g/kg ABW*

* ABW=adjusted body weights. Weights in obese patients to be calculated according to the following formula: Obesity-adjusted Body weight= IBW + [actual weight – IBW] x 0.25, where IBW is ideal body weight is based on a BMI of 25

Enteral Nutrition
Timing of initiation
Once the patient is stabilized (adequate volume status and on stable or decreasing doses of vasopressors) and there is a nasogastric tube or feeding tube in place, EN should be started within 24-48 hrs of admission to ICU in both groups.

Type of enteral formula
The enteral nutrition formula choice will be made by the site as per standard care. The type of enteral formula will be selected by the dietitian following their nutritional assessment. A standard enteral solution with 1.2 ± 0.2 kcal/ml will be used according to standard practice and the following will **not** be allowed:

- Hypercaloric entera formulas (>1.4 kcal/ml)
- Protein supplements in the first 7 days post randomization
- Glutamine supplements (IV or EN) in the first 7 days post randomization
- Pre/probiotics in the first 7 days post randomization

Administration of enteral formula
Enteral nutrition should be initiated at 25 ml/hr and increased by 25ml/hr increments every 4 hours as tolerated until goal rate is reached.

A bedside enteral feeding protocol to aid the nurses in initiating and progressing the rate of EN will be provided. This algorithm will include strategies to optimize delivery of EN such as monitoring gastric residual volumes, use of motility agents or small bowel feeding in patients with high gastric residual volumes and elevating the head of the bed to 45 degrees.

Patients in both groups will be fed according to the Canadian Critical Care Nutrition clinical practice guidelines

Duration of administration
Patients in both groups will receive enteral nutrition until the feeding tube is removed.

Supplementation with trace elements and multivitamins
In the event that a patient does not receive enteral nutrition and is dependant on parenteral nutrition for >48 hrs, the use of intravenous trace elements and multivitamins is recommended (not to be added to the bag but to be given via IV). Standard doses of multivitamins and the following ranges of trace elements are a suggested, as a guideline: 5 mg zinc, 1 mg copper, 0.5 mg manganese, 10 mg chromium and 60mcg selenium. Participating sites will use commercially available trace element solutions that are consistent with these above mentioned guidelines and their standard of care. At the end of this study period, clinicians can prescribe open label supplements as clinically indicated in both groups.

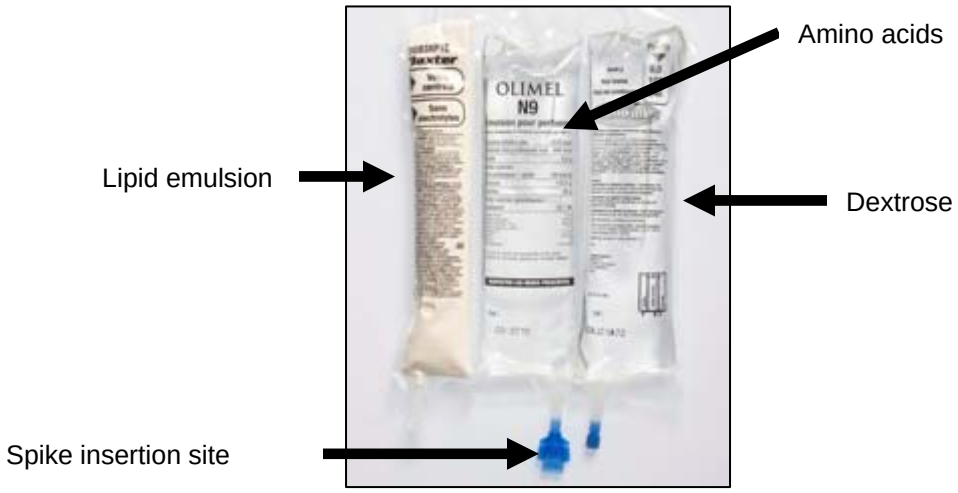
Co-Interventions
To reduce the effect of varying nutritional practices as confounding factors on the outcomes of The TOP-UP trial, it is important to standardize, *as much as possible*, nutrition practices. All sites are encouraged to follow Clinical Practice Guidelines for Nutrition Support and to follow a similar approach to weaning patients from mechanical ventilation. Implementation of daily sedation vacations, and sepsis management guidelines will be recommended. In addition, daily trials of spontaneous breathing in patients meeting the criteria specified by evidence based guidelines for weaning will be recommended. A glycemic control protocol will be used in both groups to maintain blood sugars less than 10 mmol/l (180 mg/dL) or at lower ranges specified per local protocol as long as tight glycemic control is not being practiced. The literature on early physiotherapy and mobilization is just emerging and there are no specific guidelines on this topic. Rather than standardize such practices across all participating units, we will collect data on these rehabilitation practices to be able to describe them.

Supplemental PN group (Intervention)
In addition to receiving EN as described above, the supplemental group will also receive the study parenteral solution (ie Olimel) to achieve the target hourly prescribed rate of infusion.

Olimel
The study parenteral solution is a 3-in-1 parenteral admixture solution containing an olive oil/soybean oil ratio of 80:20 and 9 gms nitrogen per litre called Olimel 5.7% E DIN 02352532 {Canada}, IND # 112,014 in US, provided by Baxter. It is also referred to as Olimel N9 E (with electrolytes) {BE370946 in Belgium, NL 33592 in France}. This product will be similar in caloric density to the standard EN solutions (1-1.4 kcals/ml).

The olive oil contains significant amount of alpha-tocopherol which, combined with a moderate PUFA intake, contributes to improve vitamin E status and to reduce lipid peroxidation. The amino acids solution contains 17 L series amino acids (including 8 essential amino acids), which are indispensable for protein synthesis. The protein and energy content of Olimel N9E enables the maintenance of an adequate nitrogen/energy balance in critically ill patients.

Olimel will be provided in 1 liter bags (see picture below).



Content of Olimel 5.7% E (N9E) 1000 ml bags

27.5 % Glucose solution (corresponding to 27.5 g/100 ml)	400 ml
14.2 % Amino acid solution (corresponding to 14.2 g/100 ml)	400 ml
20 % Lipid emulsion (corresponding to 20 g/100 ml)	200 ml

For more details about the composition of the reconstituted emulsion after mixing the content of the 3 compartments, refer to the Product Monograph.

After the Olimel has been reconstituted, the mixture will be a homogeneous emulsion with a milky appearance. Due to its high osmolarity, Olimel N9E can **only** be administered through a dedicated central vein. Since the compatibility issues are unknown, the infusion should not be piggybacked with other lines. Refer to Investigational Product for more details or call the project Leader for questions related to infusions with insulin etc

The pharmacy at each site will receive an initial shipment of Olimel from Baxter before enrollment starts and after regulatory documents have been obtained by the Methods Centre. Since the study is unblinded, each site will request subsequent product by emailing the Project Leader. Additional Olimel will be provided to the sites for patients needing prolonged parenteral nutrition i.e. beyond 7 days post randomization (study intervention duration).

For storage of Olimel, refer to the “Product dispensing for supplemental PN group” section.

Timing of initiation

The study PN should be started as soon as central line access is available, preferably within 2 hours of randomization. Given that the sooner the PN is started, the more likely it will have a treatment effect, any delays in initiation should be minimized.

Administration of Study PN: Paired Feeding

The hourly rate of study PN to be infused is dependent upon the hourly rate of EN and should be adjusted up or down to ensure that the target hourly rate is obtained, This target rate is the rate that will provide 100% calories or protein, as determined by the dietitian/MD.

The study PN should be started at a rate of 25 ml/hr (or at a higher rate if no concerns about hyperglycemia or electrolytes) and increased by 25 ml increments at least every 4 hours (or faster if as tolerated monitoring blood glucose every 4 hours and electrolytes as needed) till 100% of goal calories/rate is reached.

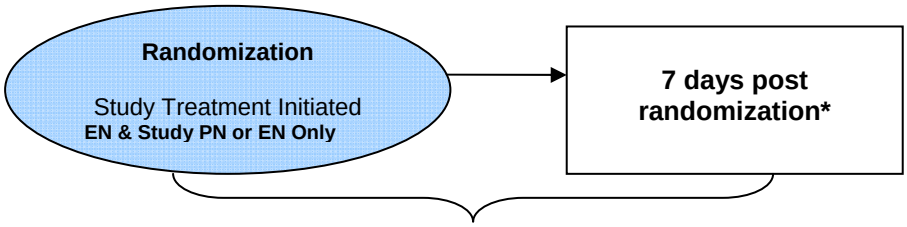
The relative amount of PN and EN received **must** be monitored every hour and adjusted hourly to ensure that the patient receives 100% of their target goal rate. If there is an interruption of EN for any reason, PN will be restarted to maintain the hourly target rate.

The target is to reach the combined rate by EN plus PN or PN alone within 24 hrs from randomization

There is no routine blood testing for the study however, blood glucose, insulin and electrolytes should be monitored frequently (whenever they are drawn for clinical reasons). **In the event that glucose, phosphate, potassium or magnesium levels are critically out of range and levels are becoming more abnormal (ranges as specified at your local site), EN or PN should not be advanced.**

Both enteral and parenteral solutions will be provided continuously over a 24 hour period.
Do not stop parenteral study infusion for procedures or surgery. We do not encourage doubling up infusion rates to make up for missed hours.

Duration of administration
The study PN will be continued for 7 days post randomization* or until death, whichever comes first. This means that the study PN should be given until 23:59 hrs on study day 7, unless central line access is an issue.



Duration of Study Intervention

In the event that the patient is discharged from ICU prior to 7 days post randomization*:
The study PN must be continued in the hospital ward at 50% goal (no hourly titration) until 7 days post randomization OR until the patient is tolerating adequate amounts of oral nutrition, whatever happens first. If the patient becomes or is NPO, the study PN can be continued at full target rate until 7 days post randomization*.

In the event that after 7 days post randomization*, PN is clinically indicated:
- if the patient is still in the ICU: use study PN (Olimel) until study day 28 or until PN is not needed, whatever occurs first.
- if the patient has been discharged from ICU to the hospital ward, use standard PN solution.

In the supplemental group, the use of non-study PN within 7 days post randomization* will be considered a protocol violation.
Please refer to the Protocol Violation section.

Enteral Nutrition only group

The enteral nutrition only group will receive EN only as described in the section titled "Enteral Nutrition".

In the event that within 7 days post randomization*, PN is clinically indicated:

- The enteral nutrition only group MUST not receive any parenteral nutrition in the first 7 days post randomization*. If the patient develops an **absolute** contraindication to enteral nutrition, and parenteral nutrition is clinically indicated, Olimel should be used if in the ICU. However this is to be reported as a Protocol Violation (refer to protocol violation section).

In the event that after 7 days post randomization*, PN is clinically indicated:

- if the patient is still in the ICU: use study PN (Olimel) until study day 28 or until PN is not needed, whatever occurs first.
- if the patient has been discharged from ICU to the hospital ward, use standard PN solution.

Non study parenteral solutions are not recommended during the study intervention period as their use may add a confounding variable in the EN only group.

In the EN only group, the use of any PN (study or non-study) within 7 days post randomization* will be considered a protocol violation. *Please refer to the Protocol Violation section.*

***7 days post randomization = the day of randomization PLUS an additional 7 FULL days.**

Study Orders for EN only group

After randomization, the Research Coordinator is responsible for facilitating/writing the Physician's Orders for the TOP UP Study in the medical chart. See Sample below for patients randomized to the EN only group.

Sample Medical Orders

This patient is enrolled in _____IRB study ID#, 'A Randomized Trial of Supplemental Parenteral Nutrition in Under and Over Weight Critically Ill Patients' (The TOP-UP study).

Hourly target rate of EN is __ ml/hr

- Start standard enteral solution of 1.2 ± 0.2 kcal/ml within 24-48 hrs of ICU admission at 25 ml/hr.
- Advance rate by 25 ml every 4 hrs until target rate has been achieved.
- Follow Enteral Nutrition Algorithm to minimize interruptions i.e.
  - monitor gastric residual volumes q 4 hrs
  - consider use of motility agents & small bowel feeding if gastric residual volumes repeatedly > 250 mls
  - elevate the head of the bed to 45 degrees
- Blood work: as per usual practice
- Record all hourly EN infusions in medical chart

Product Dispensing for Supplemental PN Group

After the patient has been randomized on the Central Randomization System to the supplemental PN Group, the Research Coordinator/pharmacy/delegate is to proceed with the following:

1. **For day 1**: obtain enough 1 litre bags of the investigational product (IP) to last one day, according to the dietitian/MDs determination of hourly rate.

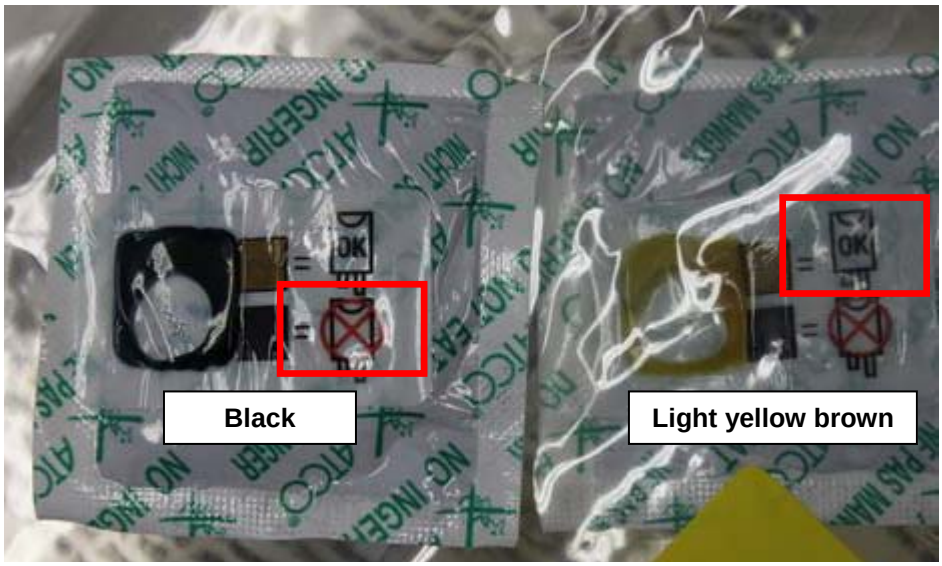
   Example: if the dietitian has determined the hourly rate is 65 ml/hr, the total volume needed for 1 day would be 65 X 24 = 1536 mls. The Research Coordinator/pharmacy/delegate is to obtain 2 X 1 Litre bags of the product.

   In order to prevent running out of product before the bag change time, you may need to supply 2 X 1 litre bags on day 1.

2. **For Subsequent days:** determine how much enteral nutrition the patient is anticipated to tolerate and will prepare enough IP accordingly.

   Example: if the patient is anticipated to tolerate 25 ml/hr of enteral nutrition and the goal rate is 65 ml/hr, prepare enough IP for the remaining volume i.e. 40 ml/hr X 24 = 960 mls = 1 X 1 litre bag

3. **Re-constitution of Olimel:**
   To open the Olimel, remove the protective overpouch.
   a. Check the oxygen absorber / oxygen indicator sachet:
      - If the tip of the indicator is **"light yellowish brown"**, this means the protective overpouch has been sealed properly and the product can be used.
      - If the indicator is **"black"**, this means the protective overpouch has **not** been sealed properly that the bag **must not** be used.



   b. Confirm the integrity of the bag and of the non-permanent seals. Use only if the bag is not damaged, if the non-permanent seals are intact (i.e. no mixture of the contents of the three compartments), if the amino acids solution and the glucose solution are clear, colourless, practically free of visible particles, and if the lipid emulsion is a homogeneous liquid with a milky appearance.
      - The timing of OLIMEL administration should be considered once the product is removed from the overwrap. Per the approved label, OLIMEL can be stored for up to 24 hours under refrigeration after overwrap has been removed and followed by 24 hour administration. "

c. Ensure that the product is at room temperature when breaking the non-permanent seals.
d. Manually roll the bag onto itself, starting at the top of the bag (hanger end). The non-permanent seals will disappear from the side near the inlets. Continue to roll until the seals are open along approximately half of their length.
e. Mix by inverting the bag at least 3 times
f. After reconstitution, the mixture is a homogeneous emulsion with a milky appearance.

Refer to Training Slides for Reconstitution of Olimel for pictures

4. Generate and attach one label (appx 3 X 5") with the following patient ID details and attach to the outside of each reconstituted Olimel bag

Label Template

Study: The TOP-UP Study
ID #: NCT01206166
Olimel N9E

PARENTERAL USE ONLY

Canadian Sponsor: Dr. Daren Heyland
Clinical Evaluation Research Unit, Kingston General Hospital,
76 Stuart St, Kingston, ON K7L 2V7

Randomization #: _____
Patient ID: _____
Patient Name: _____

Directions: Run at maximum goal rate of XX ml/hr and titrate down as enteral feeds increase.

Storage: Room temperature between 15-30° C
Expiration: 24 hrs

5. Complete the Investigational Product Accountability/Dispensing Logs (amount received, destroyed, batch #, expiry, quantity dispensed, patient details, balance of product, etc) (see **Appendix A**) and keep these in the Inventory study files.

6. Repeat steps 3-7 daily for duration of intervention = 7 days post randomization, or death/discharge, whichever occurs first.

7. Destroy all expired products as per local procedures after recording this on the Investigational Accountability Log.

8. Research Coordinator/pharmacy/delegate to send the following to CERU monthly:
   Temperature logs for Olimel (unopened, unmixed bags at 15°C to 30°C). Refer to **Appendix B** for Sample Temperature Log.

Due to the unpredictability of EN interruptions, supplemental PN will need to be readily available for the bedside nurses, even in the absence of the Research Coordinator.
The Research Coordinator must ensure that the bedside nurses are trained on the procedures related to the reconstitution of the Olimel.

Study Orders for Supplemental PN group

After randomization, the Research Coordinator is responsible for facilitating/writing the Physician's Orders for the TOP UP Study in the medical chart. See Sample below for patients randomized to the supplemental group (EN + Olimel).

Sample Medical Orders

This patient is enrolled in _____IRB study ID#, 'A Randomized Trial of Supplemental Parenteral Nutrition in Under and Over Weight Critically Ill Patients' (The TOP-UP study).

Hourly target rate of EN or PN (i.e. Olimel) or combined EN + PN is 80 ml/hr

- If not on EN, start Olimel at 25 ml/hr (or higher) and advance by 25 ml (or faster) every 4 hrs until target rate has been achieved.
- If EN is started while patient is on Olimel, start standard enteral solution of 1.2 ± 0.2 kcal/ml at 25 ml/hr (or higher) and advance by 25 ml q 4 hrs (or faster) so that EN + PN = hourly target rate (80 ml/hr).
- Adjust PN hourly so that EN + PN = 80 mls/hr.
- Check blood glucose q4h; insulin drip to maintain blood glucose (BG) at <10 mmol/l (180 mg/dL) or according to acceptable local ranges. Do not advance EN or PN until BG within the desired range.
- Maintain EN+PN total at target rate (80 ml/hr) for 7 days from randomization.
- Follow Paired Feeding Algorithm to minimize interruptions i.e.
    - monitor gastric residual volumes q 4 hrs
    - consider use of motility agents & small bowel feeding if gastric residual volumes repeatedly > 250 mls
    - elevate the head of the bed to 45 degrees
- Record all EN and PN infusions given on the Medication Administration Record as "TOP UP supplement" as mls/hour.

Protein & Energy Dosing and Nutritional Assessment

Both groups

The Research Coordinator is to work with the dietitian/MD in the unit to ensure that she/he is trained on the type of nutrition data that needs to be collected and the timing. While the dietitian/MD will collect the data on worksheets, the Coordinator will record the data on to the Electronic Case Report Form.

Since the dose of the intervention is to be determined according to the prescribed energy, the dietitian/MD MUST determine the following asap after randomization

1. Minimum Protein and Energy needs
2. Prescribed Protein and Energy needs
3. Prescribed Volume for EN (or PN or combined EN + PN)
4. Hourly Infusion rate for EN, PN or both combined EN + PN

The following documents should be forwarded to the dietitian/MD to assist with the calculations for Protein/Energy Dosing and daily nutrition monitoring

- Protein and Energy Dosing Excel Worksheet
- Nutrition Timing mock eCRF (for instructions on data collection)
- Daily Monitoring mock eCRF (for instructions for data collection)
- Concomitant Medications mock eCRF (for instructions for data collection)

Nursing Procedures

The Research Coordinator is to train the bedside RNs in the unit on the following procedures:

- **EN group only procedures**
  - Start EN within 24-48 hrs of ICU admission is preferred but this can be delayed according to standard practice.
  - Type of enteral nutrition formula
  - Start @ 25 ml/hr and increase by 25 mls q 4 hrs as tolerated.
  - Do NOT supplement with parenteral nutrition within 7 days of post randomization. If the patient develops an **absolute** contraindication to enteral nutrition, and parenteral nutrition is clinically indicated, Olimel should be used if in the ICU as described under "Enteral Nutrition only group" section.

- **Supplemental PN Group procedures:**
  - Product Dispensing (as the RN will need to reconstitute the Olimel). Refer to Training slides for Reconstitution of Olimel.
  - Administration of Study PN: Paired Feeding
    - Start Olimel @ 25 ml/hr (or higher rate) and increase by 25 mls q 4 hrs (or faster) according to blood work.
    - Adjust study PN hourly so that EN + PN = target hourly rate
    - If EN interrupted, increase PN accordingly to meet target hourly rate
    - Inform the Research Coordinator of any interruptions in the target infusion rate (if EN + PN < target rate).

- Record all hourly EN and Study PN infusions for both groups administered on the Medication Administration Record as "TOP UP supplement" in mls/hour.

Refer to the "Enteral Nutrition only group" and "Supplemental PN Group" sections for more details

Investigational Product Dispensing/Accountability Log

Olimel 9E (Supplemental PN Group)

Site:

Page ____ of ____

The Investigational Product Accountability Log should be completed by the Research Coordinator/Pharmacist/delegate

Date IP received at site	# Olimel 1000ml bags received	#Olimel 1000ml bags destroyed	Lot #	Lot Expiration date	Subject number and initials	# 1000 ml bags dispensed	Date dispensed	Initials*	# 1000 ml bags returned	Initials†

*of site staff dispensing the investigational product – signature must be on delegation log

†of site staff acknowledging return of investigational product – signature must be on delegation log

Monthly Site Temperature Log

Store unmixed Olimel in overpouch between 15-30° C. Do not freeze.

Name of Site: _____ Research Coordinator/Pharmacist:_____ Month: _____Year: 20_____

Date	Temperature Low	Temperature Current	Temperature High	Date	Temperature Low	Temperature Current	Temperature High
01				16			
02				17			
03				18			
04				19			
05				20			
06				21			
07				22			
08				23			
09				24			
10				25			
11				26			
12				27			
13				28			
14				29			
15				30			
				31			

Signature of person submitting log: _____

Fax completed form to: (613) 548-2428
Attention: CERU TOP UP Study (613) 549-6666 ext 3830

To be filled out by Site daily and faxed to Clinical Evaluation Research Unit (CERU) monthly.

Appendix B: Sample Temperature Log