A RandomizEd Trial of ENtERal Glutamine to minimiZE Thermal Injury

Study Procedures Manual

Intended Audience: Research Coordinators

This study is registered at Clinicaltrials.gov.
Identification number NCT00985205

09 February 2016
## Document History

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<th>Date</th>
<th>Superseded Version (Date)</th>
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<td>Version 1:</td>
<td>15 January 2016</td>
<td>Original version</td>
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The initiation of study intervention is independent of enteral nutrition, therefore there is no need to wait for enteral nutrition to be started.
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## Study Contacts

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<tr>
<th>Name</th>
<th>Role</th>
<th>Contact Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Daren Heyland</td>
<td>Principal Investigator, Coordinating Investigator</td>
<td><a href="mailto:dkh2@queensu.ca">dkh2@queensu.ca</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cell: +1403-915-5573</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fax: +1613-548-2428</td>
</tr>
<tr>
<td>Maureen Dansereau</td>
<td>Project Leader</td>
<td><a href="mailto:danserem@kgh.kari.net">danserem@kgh.kari.net</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>office: +1613-549-6666 ext. 6686</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cell: +1613-888-4320</td>
</tr>
<tr>
<td></td>
<td><strong>For urgent issues, if unable to reach PL or PI:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Janet Overvelde</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CERU Operations Manager</td>
</tr>
<tr>
<td></td>
<td></td>
<td><a href="mailto:overvelj@kgh.kari.net">overvelj@kgh.kari.net</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>office: +1613-549-6666 ext. 6241</td>
</tr>
<tr>
<td>Chris Gray, CCRP</td>
<td>Central Pharmacy Manager, Research Pharmacy Consultant</td>
<td><a href="mailto:Chris.gray@epipharm.com">Chris.gray@epipharm.com</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Office: 613-549-6666 ext. 3339</td>
</tr>
<tr>
<td>IT Help Desk</td>
<td></td>
<td><a href="http://www.ceru.ca/helpdesk/open.php">http://www.ceru.ca/helpdesk/open.php</a></td>
</tr>
</tbody>
</table>

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

PLEASE NOTE: the Project Leader is blinded. Please take care not to unblind the PL in your communications, written or verbal.

In the event you are unable to reach the Project Leader, please contact the Principal Investigator (PI). If you are unable to reach either the PL or PI, please contact the CERU Operations Manager.

Please direct all questions related to the investigational product, storage, shipping, or resupply to the Central Pharmacy Manager.
## Glossary

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACU</td>
<td>Acute Care Unit (ICU or Burn Unit)</td>
</tr>
<tr>
<td>ADL</td>
<td>Activities of Daily Living (index of independence)</td>
</tr>
<tr>
<td>AE</td>
<td>Adverse Event</td>
</tr>
<tr>
<td>APACHE</td>
<td>Acute Physiology and Chronic Health Evaluation classification system for severity of disease</td>
</tr>
<tr>
<td>CERU</td>
<td>Clinical Evaluation Research Unit at Kingston General Hospital (Methods Centre)</td>
</tr>
<tr>
<td>CRF/eCRF</td>
<td>Case Report Form/electronic Case Report Form</td>
</tr>
<tr>
<td>CRS</td>
<td>Central Randomization System</td>
</tr>
<tr>
<td>CTN</td>
<td>Clinical Trial Notification (Australia)</td>
</tr>
<tr>
<td>CTSI</td>
<td>Clinical Trial Site Information (Canada)</td>
</tr>
<tr>
<td>CV</td>
<td>Curriculum Vitae</td>
</tr>
<tr>
<td>DAL</td>
<td>Delegation of Authority Log</td>
</tr>
<tr>
<td>EDCS</td>
<td>Electronic Data Capture System</td>
</tr>
<tr>
<td>EN</td>
<td>Enteral Nutrition</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration (USA)</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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<tr>
<td>HC</td>
<td>Health Canada</td>
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<tr>
<td>hCG</td>
<td>Human Chorionic Gonadotropin (pregnancy indicator)</td>
</tr>
<tr>
<td>HOB</td>
<td>Head of Bed</td>
</tr>
<tr>
<td>IADL</td>
<td>Instrumental Activities of Daily Living (index of functioning)</td>
</tr>
<tr>
<td>ICF</td>
<td>Informed Consent Form</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
</tr>
<tr>
<td>IP</td>
<td>Investigational Product</td>
</tr>
<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
</tr>
<tr>
<td>LAR</td>
<td>Legally Acceptable Representative</td>
</tr>
<tr>
<td>NA</td>
<td>North America</td>
</tr>
<tr>
<td>NOK</td>
<td>Next of Kin</td>
</tr>
<tr>
<td>PL</td>
<td>Project Leader or delegate</td>
</tr>
<tr>
<td>PN</td>
<td>Parenteral Nutrition</td>
</tr>
<tr>
<td>po</td>
<td>orally, by mouth</td>
</tr>
<tr>
<td>QIUF</td>
<td>Qualified Investigator Undertaking Form (Canada)</td>
</tr>
<tr>
<td>RC</td>
<td>Research Coordinator</td>
</tr>
<tr>
<td>REB</td>
<td>Research Ethics Board</td>
</tr>
<tr>
<td>REBA</td>
<td>Research Ethics Board Attestation (Canada)</td>
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<tr>
<td>REDCap™</td>
<td>Research Electronic Data Capture system</td>
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<tr>
<td>SAE</td>
<td>Serious Adverse Event</td>
</tr>
<tr>
<td>SD</td>
<td>Study Day</td>
</tr>
<tr>
<td>SDM</td>
<td>Substitute Decision Maker</td>
</tr>
<tr>
<td>SF-36</td>
<td>Short Form 36 (quality of life survey)</td>
</tr>
<tr>
<td>SI</td>
<td>Site Investigator</td>
</tr>
<tr>
<td>SOFA</td>
<td>Sequential Organ Failure Assessment</td>
</tr>
<tr>
<td>SSSS</td>
<td>Site Staff Signature Sheet</td>
</tr>
<tr>
<td>Sub-I</td>
<td>Sub-Investigator</td>
</tr>
<tr>
<td>TBSA</td>
<td>Total Body Surface Area</td>
</tr>
<tr>
<td>ULN</td>
<td>Upper Limit of Normal</td>
</tr>
<tr>
<td>VS</td>
<td>Vital Signs</td>
</tr>
</tbody>
</table>
Study Synopsis

Overview
The primary purpose of this study is to determine the overall treatment effect and safety of enteral glutamine administration to severely burn injured patients in acute care units (ACUs). We assert that glutamine administration will decrease 6 month mortality, decrease hospital-acquired blood stream infections from Gram negative organisms, reduce acute care unit and hospital length of stay, and improve the physical function of surviving burn injured patients.

Study Design
A large, multicenter, double-blind, pragmatic, randomized controlled trial of 2700 patients with severe burns randomly allocated to receive enteral glutamine or placebo (maltodextrin).

Setting
Approximately 60 tertiary acute care burn centres in Canada, the United States, Australia and Europe.

Study Population
2700 adult patients with deep 2nd and/or 3rd degree burns requiring skin grafting. For patients age 18 – 59 years we require a TBSA (Total Body Surface Area) ≥ 20%, or in the presence of an inhalation injury, a minimum of 15 % TBSA is acceptable. For patients aged 60 years or older we require a TBSA ≥ 10%.

Study Intervention
Patients will receive glutamine or placebo (maltodextrin) through their feeding tube every 4 hours, or orally 3 – 4 times a day, for a total of 0.5 g/kg/day until 7 days after their last grafting operation, or discharge from the acute care unit, or 3 months after admission to the acute care unit, whichever comes first.

Outcomes
Primary outcome: 6-month mortality
Secondary outcome: Time to discharge alive

Tertiary outcomes: Health-related quality of life with particular focus on physical function
Incidence of acquired bacteremia due to Gram negative organisms
Hospital mortality
Duration of mechanical ventilation
Acute care unit length of stay
Hospital length of stay

Trial Duration
Study Recruitment Period
4 years - based on approximately 1 patient per site per month, as demonstrated in the pilot study.

Estimated Total Study Duration
We anticipate the total study duration to be 5 years, broken down as follows: 6 month Start-up period, 4-year recruitment period, and a 6-month follow-up period
Data processing and Statistical analysis
Data will be collected and managed by the Clinical Evaluation Research Unit, in Kingston, Ontario.

Diagram of Study Overview
Below is a diagrammatic representation of the RE-ENERGIZE Study. Refer to appropriate sections of this Study Procedures Manual for comprehensive instructions for study activities.
Roles & Responsibilities

CERU
CERU is responsible for the following:
- Providing procedures and tools for study implementation
- Providing training on procedures and tools
- Supplying a username and password for access to the Central Randomization System (CRS) and REDCap
- Providing ongoing support for research site activities
- Data validation and verification
- Distribution of data queries

Research Sites
The Site Investigator and any applicable delegates at the research site are responsible for the following:
- Supplying a computer with internet access for the CRS and REDCap
- Maintenance of local computer equipment
- Notifying CERU of any technical difficulties or malfunctions related to the CRS or REDCap
- Allowing only authorized study personnel to access the CRS or REDCap.
- Screening & enrolling eligible patients
- Informed Consent of potential research participants (or appointed substitute decision maker)
- Data collection
- Electronic Case Report Form (eCRF) completion on REDCAP™
- Data query resolution

Investigator Responsibilities

Per ICH GCP section 4, the Site Investigator is responsible for the conduct of the RE-ENERGIZE STUDY at the participating site. The list below represents an abbreviated version of some of the Site Investigator’s responsibilities (refer to ICH GCP for a comprehensive list of responsibilities):

- Full compliance with the requirements as set out in ICH GCP guidelines
- Protocol compliance
- Ensuring the rights, safety and welfare of the participant is protected
- Acknowledge and retain responsibility for study conduct
  - Personally conduct or supervise the clinical study
  - Ensure that all study staff are informed of their obligations
  - Maintain records of staff qualifications
  - Ensure that mechanisms are in place to ensure that site staff receive the appropriate information throughout the study
  - Ensure that appropriate medical coverage identified for any planned absences (holiday, attending a conference, etc.)
- Confirmation of Participant Eligibility
- SAE Identification and Assessment
• Investigator oversight and review of all study specific assessments and investigations.
• Allow monitoring, auditing & regulatory inspections
• Perform Severity of Burn and Grafting Assessments
  o The burn size must be determined by the attending surgeon/physician based on her/his clinical judgment using the Lund and Browder chart (see Appendix A) and documented as percentage of Total Body Surface Area (%TBSA) to confirm eligibility. This assessment must be confirmed by the SI or sub-I.
  o Initial Grafting Assessment
    After written consent has been obtained, the responsible surgeon/physician must assess the deep 2\textsuperscript{nd} and/or 3\textsuperscript{rd} degree burn using the Lund and Browder chart (see Appendix A) to determine the %TBSA expected to require grafting. This assessment must be confirmed by the SI or sub-I.
  o Final Grafting Assessment
    At the end of the study period, defined as 10 days post last successful graft, using the Lund and Browder chart (see Appendix A) the surgeon/physician must assess the %TBSA that actually required grafting. This assessment must be confirmed by the SI or sub-I.

Training
Each member of the site research team should be qualified by education, training and experience to assume responsibility for the proper conduct of the trial. The Site Investigator is responsible for ensuring that s/he and the local staff are adequately trained in GCP (GCP 4.1.1) and applicable regulations (e.g. Division 5 training for Canadian sites).

Each Site Investigator and study team member (i.e. Research Coordinator, Dietitian, Pharmacist) must have documented training on the RE-ENERGIZE study prior to initiation of any study procedure, or in the case of new staff joining the study mid-stream, before they initiate any study related duties and/or tasks. Study specific training will be provided by CERU Staff and conducted either in person or via webinar, a corresponding training record will be provided. In instances where members of the research team conducts internal team training related to the study, they should document the training in accordance with their local SOPs (e.g. training record, attendance sheet, etc).

Study Preparation

Required Documentation
Prior to site activation (i.e. the initiation of participant recruitment activities) each site must ensure the appropriate regulatory documentation has been completed and is in place. Required regulatory documentation includes, but is not limited to:
• Signed Protocol Signature Page
• Fully-executed Site Agreement
• Ethics Board (REB/IRB) approval
• Ethics approval of Informed Consent Forms (ICFs)
  o Country specific regulatory forms
  o Canada: REBA, CTSI, and QIUF
• Regionally: Local requirements
• CVs & medical licenses for the Site Investigator and sub-Investigators
• Signed Delegation of Authority Logs
Delegation of Authority

The Site Investigator at each site must provide CERU with a completed site Delegation of Authority Log (See Appendix B). The purpose of this log is to delineate the key delegated tasks assigned to appropriately qualified individuals on the RE-ENERGIZE Study research team. The site Delegation of Authority Log should be completed as follows:

i. Identify each individual that is involved in the conduct of the RE-ENERGIZE Study and to whom the Site Investigator (SI) has delegated key tasks.

ii. Each individual assigned to the study should complete the log including the effective start date of their activities. (The end date will be the time when the individual no longer has any association with the study).

iii. Refer to the sample key delegated tasks below. If you are in agreement with this list of tasks you may use this to record the various responsibilities of your site personnel.

iv. Update this log during the course of the study.

v. Scan/Fax this log, including any updated versions, to the Project Leader at danserem@kgh.kari.net / (613) 548-2428.
<table>
<thead>
<tr>
<th>Sample Key Delegated Tasks for the RE-ENERGIZE Study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screening subjects for eligibility</strong></td>
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<tr>
<td><strong>Conducting informed consent discussions for eligible patients</strong></td>
</tr>
<tr>
<td><strong>Obtaining written informed consent</strong></td>
</tr>
<tr>
<td><strong>Patient enrollment/randomization and follow-up</strong></td>
</tr>
<tr>
<td><strong>Daily monitoring of patient health, safety and study compliance</strong></td>
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<tr>
<td><strong>Data collection, including:</strong></td>
</tr>
<tr>
<td>• Electronic Case Report Form entries</td>
</tr>
<tr>
<td>• Electronic Case Report Form corrections</td>
</tr>
<tr>
<td>• Data query resolution</td>
</tr>
<tr>
<td><strong>Source documentation maintenance, including:</strong></td>
</tr>
<tr>
<td>• Study worksheets, checklists, monitoring sheets</td>
</tr>
<tr>
<td>• Data from electronic &amp; hard copy medical chart</td>
</tr>
<tr>
<td><strong>Reporting of Protocol Violations/Unanticipated Problems involving risk</strong></td>
</tr>
<tr>
<td><strong>Identification of Serious Adverse Events and documentation</strong></td>
</tr>
<tr>
<td><strong>Maintenance of Regulatory Documents</strong></td>
</tr>
<tr>
<td><strong>REB submissions and communications</strong></td>
</tr>
<tr>
<td><strong>Perform study specific training</strong></td>
</tr>
<tr>
<td><strong>Performing clinical assessments including burn outcomes and SAEs</strong></td>
</tr>
<tr>
<td><strong>Confirmation of completeness and accuracy of data collected</strong></td>
</tr>
<tr>
<td><strong>Optimizing delivery of nutrition and compliance with Clinical Practice Guidelines</strong></td>
</tr>
<tr>
<td><strong>Maintenance of IP inventory</strong></td>
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<tr>
<td><strong>Checking of treatment assignment online</strong></td>
</tr>
<tr>
<td><strong>IP dispensing &amp; accountability, including maintenance of logs</strong></td>
</tr>
<tr>
<td><strong>Drawing of blood samples</strong></td>
</tr>
<tr>
<td><strong>Processing and Storage of blood supplies</strong></td>
</tr>
<tr>
<td><strong>Batch shipping of frozen samples</strong></td>
</tr>
</tbody>
</table>
Clinical Supplies
Glutamine (Investigational Product)
Glutamine is the ‘active’ arm of treatment for the study. Glutamine is an amino acid produced normally by the body. It has important functions in regulation of gastrointestinal cell growth, function, and regeneration. Under normal conditions, glutamine concentration is maintained in the body by dietary intake and synthesis from endogenous glutamate. Data from clinical studies indicate that the role of and nutritional requirements for glutamine during burns, catabolic illness, trauma, and infection may differ significantly from the role of and nutritional requirements for glutamine in healthy individuals. Glutamine concentrations decrease and tissue glutamine metabolism increases during many catabolic disease states, and thus burn-injured patients are thought to be ‘deficient’ in glutamine or benefit from supplemental glutamine.

Nutrestore™ (L Glutamine)
Nutrestore™ is an amino acid (L Glutamine) powder that is approved for oral use in short bowel syndrome by the FDA. Refer to product Information sheet (monograph) for more details (Appendix C).

This product is pre-packaged in 5g individual packets.

This will be shipped to you from a central location in North America.

STORAGE: NutreStore™ (L-glutamine powder for oral solution) should be stored at 25°C (77°F) with excursions allowed to 15° - 30°C (59° - 86°F). [See USP Controlled Room Temperature]
**Maltodextrin (placebo)**
Maltodextrin is the ‘control’ arm of the treatment for the study. The ‘control’ has the same visual appearance and taste as the ‘active’ glutamine product used in this study. Maltodextrins are bland, low sweetness, pharmaceutical grade, white carbohydrate powders that are Generally Recognized As Safe (GRAS) as direct human food ingredients at levels consistent with current good manufacturing practices. They are prepared as a white powder by partial hydrolysis of corn starch with safe and suitable acids and/or enzymes. Maltodextrin is a source of carbohydrate commonly found in standard enteral nutrition and has no metabolic effects other than serving as a source of additional energy. The maltodextrin used in this study contains approximately 19 calories per 5g packet.

**Maltrin® M100 maltodextrin**
The MALTRIN® M100 maltodextrin is produced by Grain Processing Corporation (GPC) and then packaged by Anderson Packaging for the trial. Refer to product Information sheet (monograph) for more details (Appendix D).

This product is pre-packaged in 5g individual packets.

This will be shipped to you from a central location in North America.

**STORAGE:** Store under ambient conditions; protect from excessive heat and excessive humidity for extended periods of time.

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**Site Activation**
Once the requisite regulatory documents (see page 10, Study Preparation/Required Documentation) and study specific training has been completed, and clinical supplies are onsite, the CERU PL will request access to the study electronic data capture systems (i.e. CRS and REDCap™) for all appropriate site research staff (e.g. research coordinators and pharmacists). At this point the site is considered activated and may initiate recruitment activities.
Patient Eligibility

Screening
Eligible patients may be admitted to either an Intensive Care Unit or a Burn unit. We shall hereafter refer to Acute Care Unit (ACU) to reflect either of these units. Sites should screen subjects admitted to their ACU daily for study eligibility. All of the patients who are screened and meet the Inclusion criteria should be documented using the Central Randomization System (CRS). This information is vital to both the site and CERU to facilitate ongoing discussion regarding recruitment efforts, successes and obstacles. Complete instructions on entry of data into the CRS can be found in the Electronic Data Capture Systems section later in this manual.

Patient eligibility and suitability must be confirmed by the Site Investigator/sub-I. Though any attending physician or surgeon may also be involved in confirming suitability of a patient for the study, it is the site investigator or sub-I that must confirm in writing that the subject is suitable.

Source documentation must be signed, including date and time.

Inclusion Criteria
Patients must meet all inclusion criteria to be eligible for the study.

1) Deep 2nd and/or deep 3rd degree burns requiring grafting
The presence of deep 2nd degree and/or deep 3rd degree burns requiring grafting is an assessment that must be made by the responsible surgeon/physician. This assessment made by the surgeon/physician must be confirmed by the SI.

The following burn injuries fulfill this criteria

<table>
<thead>
<tr>
<th>Thermal burn injuries:</th>
<th>The following burn injuries do NOT fulfill this criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scald</td>
<td>Do NOT include injuries from any of the following:</td>
</tr>
<tr>
<td>Fire (includes both Flame and Flash)</td>
<td>High voltage electrical contact (see exclusion #7.)</td>
</tr>
<tr>
<td>Radiation</td>
<td>Frostbite</td>
</tr>
<tr>
<td>Chemical</td>
<td>Stevens-Johnson Syndrome (SJS)</td>
</tr>
<tr>
<td>Unknown</td>
<td>Toxic Epidermal Necrolysis (TEN)</td>
</tr>
<tr>
<td>Other, specify_________________</td>
<td></td>
</tr>
</tbody>
</table>

If you have questions about the acceptability of a particular injury, please contact the PL or PI.

2) Patient meets one of the following 3 criteria:
   a. Patients 18 – 59 years of age with TBSA ≥ 20%
   b. Patients 18 – 59 years of age with TBSA ≥ 15% WITH inhalation injury (see table below for diagnosis of inhalation injury)
   c. Patients > 60 years of age with TBSA ≥ 10%
Diagnosis of inhalation injury requires both of the following 2 criteria:

<table>
<thead>
<tr>
<th>1) History of exposure to products of combustion;</th>
<th>2) Bronchoscopy confirming one of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a) carbonaceous material</td>
</tr>
<tr>
<td></td>
<td>b) edema or ulceration</td>
</tr>
</tbody>
</table>

If bronchoscopy is not clinically indicated, it should not be performed for the purposes of the study. The decision to perform a bronchoscopy must be driven by the clinical imperative to diagnosis an inhalation injury.

Exclusion Criteria
A patient is not eligible for the study if any one of the following exclusion criteria is present.

1) **72 hours from admission to Acute Care Unit (ACU) to time of consent**
   This refers to admission to your ACU. If a patient is transferred from another facility, the clock starts from the time of admission to your unit. For patients who are delayed in their presentation and transfer, please do not enroll if the arrival to your ICU is greater than 48 hrs from burn injury.
   The 72 hour window is determined from the time of ACU admission to time informed consent is obtained. While you have 72 hrs to enroll the patients, where possible, we would like to encourage you to enroll and randomize the patient as soon as possible as the beneficial effect of glutamine may be greater if started earlier.

   **NOTE:** Given that consent must occur before randomization, randomization may occur > 72 hours from the time of ACU admission.

2) **Patients younger than 18 years of age**
   There is no upper age limit for patients enrolled in the study.

3) **Patients with renal dysfunction will be excluded.** Renal Dysfunction – defined as:
   In patients **without known renal disease**, renal dysfunction defined as a serum creatinine >171 μmol/L or 1.93 mg/dL or a urine output of less than 500 mL/last 24 hours (or 80 mL/last 4 hours if a 24 hour period of observation is not available).

   In patients **with acute on chronic renal failure** (pre-dialysis), an absolute increase of >80 μmol/L or 0.9 mg/dL from baseline or pre-admission creatinine or a urine output of <500 mL/last 24 hours (or 80 mL/last 4 hours) will be required.

   Patients with **chronic renal failure on dialysis** will be excluded.

4) **Liver cirrhosis Child’s class C liver disease**
   The Child’s class C score is obtained by adding the points for all 5 criteria in the table below.

   Any patient with a score of 10 – 15 falls into Group C (severe hepatic impairment), which would be considered exclusion for this study.
Child-Pugh class C scoring table

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points assigned</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Total Bilirubin SI units</td>
<td>&lt; 2 mg/dL or &lt; 34 μmol/L</td>
</tr>
<tr>
<td>Serum Albumin SI units</td>
<td>&gt; 3.5 g/dL or &gt; 35 g/L</td>
</tr>
<tr>
<td>Prothrombin time or INR</td>
<td>&lt; 4 seconds or &lt; 1.7</td>
</tr>
<tr>
<td>Ascites*</td>
<td>Absent</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
</tr>
</tbody>
</table>

* Refer to ultrasound results. If ascites has been drained in the past, it should be considered Moderate.

5) Pregnancy (urine/blood tests for pregnancy will be done on all women of childbearing age by each site as part of standard of ACU practice)

6) Contraindication for EN: intestinal occlusion or perforation, intra-abdominal injury.
   This refers to an absolute contraindication for EN due to a medical/surgical condition. Being NPO for other reason, such a presumed intolerance to EN, is not considered a contraindication for Enteral Nutrition.

7) Patients with injuries from high voltage electrical contact.

   There has been extensive discussion by the steering committee regarding the inclusion or exclusion of patients with this type of injury. The determination has been made that burns form high voltage electrical contact are very different from thermal injuries and these patients must be excluded.

8) Patients who are moribund (not expected to survive the next 72 hours in the judgement of the Site Investigator or delegated doctor in charge).

   Note that an isolated DNR does not fulfil this criteria.

9) Patients with extreme body sizes: BMI < 18 or > 50 kg/m2

   When calculating BMI, the patient’s pre-burn dry weight should be used or estimated. Given that there may be some subjectivity involved in the determination of BMI, err on the side of including the patient. For example, if you estimate the weight and the BMI turns out to be 17 or 51, re-set the weight for the patient to be included.

10) Enrollment in another industry sponsored ICU intervention study

   (co-enrollment in all non-randomized academic studies will be approved. For academic randomized controlled trials, forward a synopsis or abstract of the study to the project leader to obtain pre-approval of the study to which you would like to co-enroll.)
11) Received glutamine supplement for > 24 hours prior to randomization.
   This refers to consistent administration of glutamine over the 24 hr period prior to randomization. If the patient received random or intermittent doses of open label glutamine, discontinue the glutamine prior to randomization. If they received glutamine for more than 24 hrs, they will have to be excluded.

12) Known allergy to maltodextrin, corn starch, corn, corn products or glutamine.
**Informed Consent**

“A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject’s decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.”

-ICH definition of informed consent

The Site Investigator is responsible for consent, even if the tasks associated with obtaining consent are delegated to other study staff.

Following the confirmation of subject eligibility, the site should seek consent. The nature of the RE-ENERGIZE study population is such that subjects are critically ill and often unconscious and in many cases will not be able to grant consent themselves.

Due to the acute care trial setting and the vulnerability of the patient population, informed consent will very often be requested from a third party; in most cases a legally acceptable representative (LAR) or if LAR does not exist, then other, non-legally appointed substitute decision maker (SDM; using a substitute decision maker hierarchy) as defined and permitted by local and state laws and regulations, and if approved by REB/IRB.

Substitute decision-makers are ranked in a hierarchy. The site investigator/research coordinator or delegate is expected to go down the list until a substitute who is available, capable and willing to make the incapable person’s decision is found. The order of hierarchy might differ from region to region, so every site should follow the SDM hierarchy that applies in their own region.

An example of hierarchy is found below:

1) A guardian appointed by the court if the court order authorizes the guardian to make health care decisions
2) A person with a “power of attorney for personal care” authorizing him or her to make health care decisions
3) A representative appointed by the Consent and Capacity Board (any person may apply to the board to be appointed as the substitute decision maker)
4) A spouse or partner
5) A child or parent (custodial parent if the patient is a minor)
6) A brother or sister
7) Any other relative

*No study procedure shall begin before written informed consent is obtained.*

All subjects must be consented to the study within 72 hours of Acute Care Unit admission. Before you approach for consent:

1) Familiarize yourself with the subject’s history.
2) Approach bedside nursing staff/medical staff for an update on the family’s involvement and their degree of knowledge of the subject’s condition.
3) Confirm subject eligibility and appropriateness of enrollment with the site investigator or sub-investigator.
Recommended Procedures for Obtaining Informed Consent
The following procedures should be followed when obtaining informed consent for a potential RE-ENERGIZE patient:

1) Prior to approaching the SDM to discuss participation in a research study, the attending doctor or delegate should provide an update of the patient’s condition.

2) If the doctor will not be discussing consent with the SDM, a member of the clinical team should introduce to the SDM the research team member who will be discussing consent with the SDM.

3) The study team member obtaining consent is qualified to do so, and is knowledgeable in the study procedures.

4) Review the study details with the SDM in a quiet, private location.

5) Do not coerce or unduly influence the SDM for the patient to participate, or continue to participate in the study.

6) Fully inform the SDM of all pertinent aspects of research, in non-technical language that is easy to understand. If none of the patient’s SDMs speak/read the official language(s) in the study region (e.g. English or French in Canada), consent may be obtained via a translator if this service is available to the research team/hospital. If it is not possible to obtain consent due to “language barriers” this will be noted on the CRS as the reason why the patient’s SDM was not approached for consent.

7) Provide a copy of the consent form to the patient’s SDM and allow for ample time to read it and ask questions.

8) Ask the patient’s SDM questions to assess their comprehension of the material reviewed. Ensure she/he fully understands the information.

9) Ascertain the patient’s SDMs willingness to participate. Document the decision of any patient’s LAR/SDM who declines to participate.

10) Sign and record the date and time written informed consent was obtained:
    a. From the patient’s SDM
    b. By the person conducting the informed consent discussions

11) Document the consent process in the patient’s medical chart.

12) Provide the patient’s SDM with a copy of the signed document.

13) File the originally signed ICF with the study-related documentation. Place a copy in the patient’s medical chart.

Note: The research site should always follow local procedures pertaining to obtaining informed consent of patients in the ACU. If they conflict with what is stated above, follow local procedures.
Procedures for Faxed or Scanned or Emailed or Telephone Consent (where allowed by Ethics Board)

At those clinical sites where local laws and regulations allow and per Ethics Board approval, faxed or scanned or emailed or telephone consent, it is permitted. Ultimately, regardless of the method used to conduct and document the consent discussion, it is necessary to ensure there is written documentation of this process. Every effort should be made to have the consent properly executed in person, with SDM’s original signature obtained, as soon as possible after the fact.

Contact Information

It will be necessary to obtain extensive contact information for the patient, SDM, family and friends to ensure that you are able to reach the patient in 6 months to assess survival and conduct quality of life questionnaires. Refer to Appendix E for a patient/alternative contact person(s) information sheet. Additional information and tips can be found in the Follow-up Procedures document.

Remember to:

- Communicate any important new information that becomes available, and that may be relevant to the subject SDMs continuing consent
- Assess the subject through the duration of the study for competency to grant consent for her/himself
- Document the informed consent process in the source documents, including the following details:
  - SDMs comprehension of the material reviewed
  - SDM being given ample opportunity to review the ICF and decide whether or not to participate in the research
  - Adequate time being given to answer all questions satisfactorily
  - Informed consent having been obtained prior to initiating any study related procedures

Medical Chart Entry

The Research Coordinator will add an entry in the Medical Chart confirming that consent was obtained, from whom, time, eligibility assessed, patient randomized. See Sample entry below.

This patient is enrolled in IRB study ID#, ‘Randomized Trial of Enteral Glutamine to Minimize Thermal Injury’ (The RE-ENERGIZE study). Patient met all the inclusion criteria and none of the exclusion criteria as confirmed with Dr. ____________________.

Consent obtained from _______________ (relationship to patient) on dd/mmm/yyyy at time hrs. All questions & concerns addressed with patient/SDM at this time. Copy of consent was given to patient/SDM.

Date/time of entry: _______________________
Signature of Research Coordinator: _________________________

Patient enrolled to the RE-ENERGIZE study at time hrs on date. Patient met all the inclusion criteria and none of the exclusion criteria as
Investigational Product Handling and Administration

Duration of study treatment
Patients will receive the study intervention from randomization through 7 days post last successful graft, or ACU discharge, or 3 months from ACU admission, whichever comes first. IP will continue whether the patient is receiving enteral/parenteral nutrition or ventilation status. In the event that the patient is discharged to another facility before the 7 days after the last successful grafting operation, the intervention stops at discharge. Call the Project Leader if you have any questions about the duration of the study intervention.

We recognize that defining the end of study treatment phase by 7 days post last successful graft may not be very exact or precise. There may be unique features to some patients that make it difficult to define. As guidance, we generally mean when the patient is over the acute phase of their illness and either discharged from the acute care unit or entering in their rehabilitation phase.

If the patient requires an additional graft after the IP has been stopped per the duration or treatment defined above, do not restart the IP.

Determination of Dose
Patients will be randomized to receive investigational product (IP), either glutamine or placebo (maltodextrin), at the following dose:

a) Patients with a BMI <35 will receive 0.5 g/kg/day of IP based on pre-burn dry weight (actual or estimated).

b) Patients with a BMI >35 will receive 0.5 g/kg/day of IP based on the adjusted body weight, as per calculation below.

Adjusted Body Weight (ABW) = Ideal Body Weight (IBW) based on a BMI of 25 + [(pre-burn dry weight – IBW) x 0.25]

IP will be dosed in accordance with the patient’s pre-burn dry weight. By dry weight, we mean prior to resuscitation and it is likely consistent with the usual weight recorded on a prior chart or obtained from a family member.

IP Dosing Changes
As detailed above, the study intervention dose calculation is based on the patient’s pre-burn dry weight. All patients will remain on the initially calculated dosage of study intervention for the duration of their participation in the study with one noted exception.

EXCEPTION: If the patient has a change in body weight sufficient for the clinical team to alter dosage of clinical treatments, the study treatment should also be adjusted.

The trigger for the change in IP is the change, by the clinical team, in the weight used to dose clinical treatments. An example of events that may trigger such an event is amputation.

If there is a change in IP dosing during the study, the following should be documented in REDCap™:
• New dosing weight
• New IP prescription in # grams per day
• Date and Time IP dose changed

Initiation of IP Dosing
The IP (either glutamine or maltodextrin) should be started as soon as possible following randomization but no later than 2h from randomization. Research Coordinator must notify the pharmacy as soon as a patient is randomized to ensure IP is started within the 2h window.

The initiation of study intervention is independent of enteral nutrition, therefore there is no need to wait for enteral nutrition to be started.

Administration
A flow sheet of Nursing Procedures for administration of IP is attached as Appendix F.

Reconstitution of IP
The study intervention will be reconstituted by the nurse or RC at the patient’s bedside just prior to administration.

Each 5 grams of study intervention is to be mixed in 50 mL of sterile or tap water, per your standard procedure, in a clean container.

Administering IP via feeding tube
Once reconstituted, the IP is to be given as a bolus every 4 hours via the enteral route. Boluses are to be given via either a small bore feeding tube or a larger bore gastric/Levine tube. The boluses are to be given via a feeding tube once the latter has been inserted.

Exception to Dosing Schedule for Patients with a Weight <54kg
In the event the patient’s pre-burn dry weight is < 54 kg, the interval between some of the doses will be longer (i.e. up to 8 hrs). Refer to Appendix G (Dosing Weight Chart) for more details.

Administering IP when subject no longer needs a feeding tube
When the patient is tolerating oral feeds, the study intervention will be given TID or QID via the oral route according to the patient’s preference, as long as the patient receives the daily prescribed dose in grams.

When the intervention is administered orally, it may be mixed with any non-heated beverage (other than alcohol) or non-heated food such as:

- Yogurt
- Applesauce or Apple Juice
- Cereal
- Potatoes

Avoid mixing the IP with water when administering orally. Patients who participated in the pilot study reported disliking the taste when taking the IP orally when it was mixed with water.

NOTE: There should be no difference in the taste of the glutamine and the maltodextrin.
Mixing the IP with soda or highly acidic juices (such as grapefruit juice, orange juice or lemonade) is not recommended. The IP degrades or becomes unstable in an acidic medium.

**Interrupted or Missed Doses of IP**

While the enteral nutrition may be stopped for procedures and surgeries, you do NOT have to stop the study intervention for procedures or surgery. If possible, the study intervention should be continued as scheduled. In the event that an interruption or a missed dose does happen, the missed doses should be made up the same day by giving additional doses or doubling the scheduled dose, according to the following:

- Doses must be at least one hour apart
- Do not give more than double the scheduled dose at any one time

Feeding intolerance and high gastric residual volumes

High gastric residual volumes are a common occurrence in patients that are receiving enteral nutrition. The administration of the study intervention should continue despite high gastric residual volumes, unless there is an absolute need to stop the intervention i.e. severe vomiting, perforation or leak, bowel obstruction or a decision has been made by the SI/sub-I (i.e. Serious Adverse Event that is felt to be related to the study intervention).

To avoid interruptions in the delivery of the study intervention and enteral nutrition, ensure that strategies such as elevating the head of the bed, use of motility agents and small bowel feeding tubes, etc have been adopted. Refer to the Enteral Feeding Protocol (Appendix H and the Dietitian Manual for more details.

**IP adjustments in subjects with renal dysfunction**

In patients with renal dysfunction, who are not on dialysis, the Glutamine may contribute to elevated urea levels. We are uncertain about the safety of such a high urea level in the absence of dialysis. Some clinicians are comfortable with an isolated high urea; others are not. If the clinical team is uncomfortable with the level of the urea and the patient is not to be dialyzed on the same calendar day, the following guideline is suggested (but not absolutely required):

**Hold Intervention:** Urea/BUN >21.5 mmol/L or >60 mg/dL

At the discretion of the clinical team, study intervention may be restarted when blood urea is below the threshold for stopping. If the patient is on dialysis, regardless of the Urea or Cr levels, the study treatment should not be discontinued or held.
Study Treatment Allocation

Blinding
All site personnel (i.e. Investigator, sub-Is, coordinators, nurses, dietitians) as well as the central study team are blinded to subject treatment allocations.

Unblinding
The investigational products used in the RE-ENERGIZE study are supplements to which there are no antidotes.

In the event of a serious adverse event or medical emergency involving a patient participating in the study, the treatment of the patient is not dependent on the knowledge of the study treatment code. If deemed necessary, the study intervention can be stopped, and no further action is required. If there are questions, contact the Study PI.

Randomization
All subjects will be randomized to study treatment using the Central Randomization System (CRS). Please see detailed electronic data capture system instructions in the following section.

Medical/Physician Orders
1) Following randomization and pharmacy notification, the Research Coordinator should prepare and/or facilitate the completion of study specific Medical/Physician Orders (see example in Appendix I)

2) File a copy of the completed RE-ENERGIZE Study Physician’s Orders in the medical chart with a copy in the study file.
Electronic Data Capture Systems

Each site will need to access two different electronic data capture systems for RE-ENERGIZE:

1. **Central Randomization System**

   The Central Randomization System (CRS) is a web-based system that will be used to screen and randomize eligible patients into the RE-ENERGIZE Study. The CRS may be accessed directly at: [https://ceru.hpcvl.queensu.ca/CRS/](https://ceru.hpcvl.queensu.ca/CRS/) or via: [http://www.criticalcarenutrition.com](http://www.criticalcarenutrition.com)

2. **REDCap**

   REDCap is a web-based electronic data capture system that will be used as the RE-ENERGIZE Study electronic Case Report Forms (eCRFs). REDCap may be accessed directly at: [https://ceru.hpcvl.queensu.ca/EDC/redcap/](https://ceru.hpcvl.queensu.ca/EDC/redcap/) or via: [http://www.criticalcarenutrition.com](http://www.criticalcarenutrition.com)

Granting CRS & REDCap Access

- Access to both the CRS and REDCAP will be granted to the Research Coordinator/delegate upon documentation of proper training of study procedures and receipt of Ethics Approval documentation and other essential documents.
- Research Coordinators that are granted access to the CRS and REDCAP must appear on the Delegation of Authority Log.

Central Randomization System

Screening & Randomization

All screening data should be entered into the Central Randomization System (CRS).

For eligible patients, the screening data must be entered onto the CRS in a timely manner in order to randomize the patient and start the study intervention as soon as possible.

Patient eligibility and suitability must be determined by the Site Investigator or sub-I. Sites are encouraged to use the Inclusion/Exclusion criteria eCRF worksheets to document screening and confirmation of eligibility by the SI/sub-I.
Types of Patients to be entered into the CRS
- All patients who meet the inclusion criteria must be entered into the CRS, including:
  - patients that do not meet any exclusion criteria and consent is obtained (Randomized patients)
  - patients that do not meet any exclusion criteria and consent is not obtained (Eligible but Not Randomized patients)
  - patients that meet an exclusion criteria (Not Eligible patients)

The table below provides several examples of the types of patients.

<table>
<thead>
<tr>
<th>Inclusion Criteria Present</th>
<th>Exclusion Criteria Present</th>
<th>Informed Consent Obtained</th>
<th>Enter into CRS</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
<td>Randomized</td>
</tr>
<tr>
<td>✓</td>
<td>×</td>
<td>×</td>
<td>✓</td>
<td>Eligible but Not Randomized</td>
</tr>
<tr>
<td>✓</td>
<td>✓</td>
<td>Exclusion criteria met - Do not approach for consent</td>
<td>✓</td>
<td>Not Eligible</td>
</tr>
<tr>
<td>×</td>
<td>×</td>
<td>Inclusion criteria Not met - Do not approach for consent</td>
<td>×</td>
<td>Do Not Enter into CRS</td>
</tr>
</tbody>
</table>

For each patient entered into the CRS, the system will issue a screening number. The screening numbers are assigned sequentially in an 8-digit format:

“Q” indicates the patient is being screened but not randomized

1002 - Q005

Site #  Patient #

If the patient is subsequently randomized, they will also be issued a randomization number. The enrollment numbers are assigned sequentially in an 8-digit format:

“R” indicates the patient has been randomized

1002 - R005

Site #  Patient #
Accessing & Entering a Patient in the CRS

URL: [https://ceru.hpcvl.queensu.ca/randomize](https://ceru.hpcvl.queensu.ca/randomize)

Once you have logged in successfully, you will be brought to the Home screen.

After selecting the “RE-ENERGIZE – Definitive” study from the Home page, you will be brought to the Site Status Page.

To enter data for a new patient, select the Add patient button on the bottom left of the screen.

Each patient entered in the CRS will also have a status associated with it. There are 4 status levels:

- **In progress**: inclusion data has been entered.
- **Not Eligible**: This patient was excluded.
- **Not Randomized**: This patient was eligible but consent was not obtained.
- **Randomized**: The patient was eligible, consent was obtained and the patient was enrolled into the study.
Inclusion Criteria
You will be brought to the Inclusion Criteria form. Complete the fields in the form as appropriate.

Note: Enter all patients into the Central Randomization System who meet the Inclusion Criteria. See the “inclusion criteria” section for more details.

Only patients who meet the inclusion criteria should be entered into the Central Randomization System (CRS). Eligibility must be confirmed by the Site Investigator/or sub-Investigator before randomization can occur.

Exclusion Criteria
Complete the exclusion criteria fields as appropriate. Choose all exclusion criteria that apply. If a patient meets any of the exclusion criteria, they are not eligible to participate in the study. See the “Exclusion criteria” section for more details.

Dates are to be entered in the DD-MMM-YYYY format.

All times should be recorded using the 24-hour (military) clock. All times must include a “:” (colon) to be saved. For example 1200 must be entered as 12:00.

Click SAVE.

Click on the radio buttons to select a “Yes” or “No” response for each criterion.

If you click “Yes” to any one criteria, this patient is not eligible for the study.

Click SAVE. No further data entry required.

If you click “No” to all criteria, this patient is eligible.

Click SAVE, then proceed to the Pre-Randomization Form.

To minimize any potential contamination, patients that have received glutamine for >24 hrs before randomization, should NOT be included.

For such patients, please enter them on to the Central Randomization System and add the reason for no consent as “received glutamine for > 24 hrs”
Remember:

- Patient eligibility must be confirmed by the Site Investigator/MD delegate
- **Only** enter patients who meet the inclusion criteria.
- You may want to use the eCRFs/Worksheets to document screening & eligibility

If a patient is found to meet an exclusion criterion after the patient is randomized into the study, please contact the Project Leader as soon as you become aware for direction on how to proceed.

**Pre-Randomization**

Pre-Randomization refers to the period of time between the determination of an eligible patient and randomization of a patient. The patient/next of kin **must** be approached for consent before you complete this form.

**Patient Eligibility Confirmed by MD**

Confirm eligibility of the patient with the site investigator or sub-investigator. Enter the name of the physician who confirmed patient eligibility. This individual should be listed on the Site Delegation of Authority Log.

**Consent**

Confirm if the SDM or patient was approached for consent.

- If the SDM/patient was not approached for consent, complete the following form as shown below.
Choose one of the following reasons for **NOT** obtaining consent:

<table>
<thead>
<tr>
<th>Reason</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Next of kin or substitute decision maker not available</td>
<td>The SDM or legally acceptable representative was not available for consent discussion within the required time frame.</td>
</tr>
<tr>
<td>Missed the patient</td>
<td>The patient was not identified by the site coordinator in time to approach for consent. <em>Example:</em> the patient was admitted over a long weekend.</td>
</tr>
<tr>
<td>Language Barriers</td>
<td>The SDM was not approached because of language barriers. A certified translator was not present.</td>
</tr>
<tr>
<td>Family dynamics</td>
<td>The SDM was not approached due to emotional stress or complicated family dynamics.</td>
</tr>
<tr>
<td>Pharmacy not available</td>
<td>The pharmacy not available to prepare the investigational product.</td>
</tr>
<tr>
<td>Recommendation of the clinical team</td>
<td>Clinical team does not recommend putting this patient on the study.</td>
</tr>
<tr>
<td>CRS Unavailable</td>
<td>The Central Randomization System (CRS) is unavailable.</td>
</tr>
<tr>
<td>Other (Please specify)</td>
<td>Specify the reason(s) for not obtaining consent that is not listed above. <em>Example:</em> patient received glutamine for &gt;24 hrs before randomization</td>
</tr>
</tbody>
</table>

If the SDM/patient was approached for consent, was consent obtained from the SDM/patient?
- If No, record the most important reason consent was not obtained and patient was not randomized
  - “Too Overwhelmed”, “Not interested”, “Did not respond (timed out)” or Other” and specify the reason.

If consent **IS** obtained, complete the following form as shown below.

**Pre-Randomization Form**

- Did you confirm eligibility of the subject with the site investigator, or sub-investigator? **Yes** □ **No** □
- Please indicate the name of the physician who confirmed subject eligibility: Dr. Jane Doe
- Was SDM/subject approached for consent? **Yes** □ **No** □
- Was consent obtained from the SDM/subject? **Yes** □ **No** □
- Consent Date: 2016-01-01 (YYYY-MM-DD)
- Consent Time: 09:24 (HH:MM 24hr)
- Height: 187 cm □ inches □
- How was height obtained? Measured □
- Weight: 186 kg □ lbs □
- How was weight obtained? Estimated □

**Dates are to be entered in the DD-MMM-YYYY format.**

**All times should be recorded using the 24-hour (military) clock. All times must include a colon (:) to be saved. For example 1200 must be entered as 12:00.**
• Record the consent date/time and the patient’s height, weight
• Use patient’s pre-burn weight to avoid fluctuations due to large fluid shifts.
• Indicate by placing a √ whether the weight is:
  • Measured (obtained by a weighing scale)
  • Estimated (obtained verbally from a healthcare professional or family)
• Record the height in cm and the weight in kg (to the nearest decimal point).

Once you click on the “Randomize” button, the patient will be randomized to the RE-ENERGIZE Study.

Randomization

Randomization must occur soon after consent so that the intervention can start as soon as possible (within 2 hrs from randomization)

You have successfully RANDOMIZED this subject to the REENERGIZE trial

Randomization #: 1001R050
Randomization Date: 2016-01-06 16:42 EST
Height: 187.00 cm
Weight: 186.00 lbs
BMI: 24.1
Dosing Weight: 84.4 kg

Contact your pharmacy to alert them of this new randomization!
Study treatment should begin within two hours of randomization

Note: Remember to make an entry in the subject’s medical chart to indicate they have been randomized to study treatment.

You may print a copy of the Randomization Form and file in the Patient Folder/Study files. Click “Save”
The Patient Status Page indicates that data entry for this patient is complete. If you do not click “Save” on the Randomization page, the Patient Status Page will continue to show Randomization as incomplete.

Note: All patient data collected following randomization can be entered on to the eCRF (REDCAP).

Click on the “Site Status” button to view all the patients screened and entered on the CRS.

You will note each patient entered into the CRS is issued a Screening Number. Those patients that are eligible and randomized are issued a Randomization Number.

To view a patient, click their enrolment number or their screening number,
You will then be brought to the Patient Status screen. It shows you each data entry form for the patient as well as the status of the form.

Each form has a status assigned:

<table>
<thead>
<tr>
<th>Status</th>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed</td>
<td>✔️</td>
<td>All data has been completed and saved.</td>
</tr>
<tr>
<td>Not Completed</td>
<td>❌</td>
<td>Data has not yet been entered on the form.</td>
</tr>
<tr>
<td>Locked</td>
<td>🕰️</td>
<td>The patient has been randomized and the data is no longer able to be edited by the site user.</td>
</tr>
</tbody>
</table>

Note: All subsequent data collection must be entered on to the eCRF (REDCAP) as described in the following pages.
REDCap Data Entry

The REDCap (Research Electronic Data Capture) is a web-based system used for the RE-ENERGIZE Study.

REDCap can be accessed at the REDCap login link https://ceru.hpcvl.queensu.ca/EDC/redcap/.

All authorized study personnel must log onto the web site using their own username and password prior to data entry.

Your user password can be changed at any time by clicking “My Profile” after logging into REDCap.
Navigating REDCap

My Databases

After you log into REDCap, you will be brought to the Home screen. Select the “My Databases” tab to see a list of the CERU studies you have access to.

Data Entry Field

The left side of the screen is the main navigation panel where you will see “Data Entry”. Select “Data Entry” to choose from a list of patients that are randomized and ready for data entry.
Event Grid Field

After you have selected a patient, you will be brought to the Event Grid. The Event Grid gives the user a snapshot of the data entry forms for the patient.

The type of data entry form is listed in the far left column of the table. The study day is listed on the top row of the table. Each dot on the table represents an individual data entry form. Each individual form can be accessed by clicking on the dot. As you can see below, the circled dot is the Daily Monitoring form for study day 3.

Each grid contains 30 study days. The buttons at the top of the grid represent each 30 day segment. To move to a specific set of study days/dates, click the corresponding button or click the ‘Next’ button to navigate to each sequential segment, click the ‘Previous’ button to return to the previous set of study days.
Slide the navigation scroll bar at the bottom of the table to reveal the right side of the Event Grid.

**Form Links**
You can navigate between forms on the same study day using the form links on the left side navigation menu.

**Form Status and Saving**
At the end of each form, you will be asked to specify the form status. This legend is to be used to assist you in remembering what data is either incomplete, unverified or complete. The
status is indicated on the Event Grid Field using the following convention:

<table>
<thead>
<tr>
<th>Status</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete</td>
<td>No data has been entered on a form. Blanks forms will automatically be set to incomplete.</td>
</tr>
<tr>
<td>Unverified</td>
<td>Data entry is partially completed on a form. The RC wants to double check data already entered on a form. Partially completed forms will automatically be set to unverified.</td>
</tr>
<tr>
<td>Complete</td>
<td>Data entry is complete on a form. Further changes to the data are not anticipated. Only forms manually set to complete will have this status.</td>
</tr>
<tr>
<td>Locked</td>
<td>Locked status will appear on all forms after all finalization checks are completed. Data on locked forms cannot be changed.</td>
</tr>
</tbody>
</table>

There may be up to 4 options at the end of each form to save your progress. The following example is for:

**Daily Monitoring - Study Day 1**

- **Save and go to Day 1 Daily Laboratory**: This option will save your progress and bring you to the next form on the same study day.
  
  *For example, if you are working on the Daily Monitoring form on Day 1, this option will save and bring you to the Daily Laboratory form on Day 1.*

- **Save and go to Day 2 Daily Monitoring**: This option will save your progress and bring you to the same form on the next study day.

- **Save and go to Grid**: This option will save your progress and return you to the Event Grid.

- **Save and Stay**: This option will save your progress and allow you to continue working on that form.

- **Clear Form**: This option will allow you to clear the entire form in case the entire form was completed in error.

- **Cancel**: This option will take you to the Event Grid screen. All newly entered data will be lost. Only the last saved version will remain.

**NOTE:** Always remember to “Save” before you navigate away from a form. Navigating from a form without saving will result in loss of data.

**Data Conventions in REDCap**

- Dates should be entered using the **YYYY - MM - DD** format i.e. 2010 - 07 - 24. A date picker calendar is available to enter dates. Single “click” on the icon and choose the appropriate month and year from the drop down boxes. Then “click” the appropriate day.
- Enter all times using the **HH:MM** 24-hour period format i.e. 22:37. The colon “:” must be entered. Use leading zeros where applicable i.e. 01:28.

- Midnight should be entered as **00:00**

- To access individual forms single click the corresponding “dot” on the event grid.

- To enter data directly into each field, **single click** on the left side of the mouse pointer and type information. Do NOT press enter after entering data into a field. This will cause the form to automatically save and bring you to a new screen that will allow you to return to the Event Grid.

- There should be NO blanks. If data is NOT available use the **“Not Done/Not Available”** checkbox options. This includes:
  - Data that is unavailable because the measure wasn’t taken or the test was not done.  
    *Example: T-Bilirubin was not done on a particular study day.*
  - Data that is not known. This assumes every effort has been made to find the data but it is missing from source documents.
    *Example: A particular data point was NOT entered in the medical chart. Or an ICU flow sheet has gone missing.*

- REDCap has an option for users to see the data entry history for each data field. By clicking on the **H**, a window will pop up listing the data entry history for the data field.
Stages of Data Entry
To help you determine the status of the patient data, we have designated different stages of data completion. Each stage marks the completion of a specific set of data. The diagram below summarizes the site responsibilities at these various stages.

1) Data Entry Stage
Enter data on REDCap and address blank field and range check errors

Once all the data is entered, select “Completed Data Entry” on the patient grid

2) Query Stage
Address complex data queries

Once all the queries are answered, the patient will automatically move to the next stage

3) Follow-up Stage
Complete 6 month Follow-up

Once all the queries are answered, the patient will automatically move to the next stage

4) Finalized
Patient chart closed
Investigator Confirmation Form Completed

Once all data has been completed up to and including hospital overview (6 month follow-up excepted), the user can proceed to the “Query Stage”. Simple queries such as missing fields and ranges The “Completed Data Entry” button is found at the bottom of the Grid.
Investigator Confirmation

Once the “Completed Data Entry” button has been selected, REDCap will run front-end logic and edit checks. If any data discrepancies are identified the user will see them listed on a new screen.

Each error identified must be addressed before you can “Lock” the patient.

There is an individual link to the relevant form to address each error noted.

Once all errors have been addressed by the site and patient is locked, the patient will be in the “Follow-up Stage”

Once a patient is “locked” the site will NOT be able to modify the data. Contact the Project Leader if modifications to the data are required.

After the completion of all data entry (i.e. Status of “Finalized”), the Investigator Confirmation form must be completed and forwarded to the Project Leader.

To access the Investigator Confirmation form, select the link from the Resources section on the left side menu.
The form will automatically be populated with the site name and patient enrollment number. Print this form and have the site Investigator sign and date.

By signing, the site Investigator is attesting to the following:

- The data collection and entry was conducted under his/her supervision and in accordance with study procedures.
- The data and statement, including newly acquired hospital infection adjudication are complete and accurate to the best of his/her knowledge.

Forward a scan or fax (613-548-2428) of the signed Investigator Confirmation form. File the original in your study files.
**Study Implementation and Data Collection Procedures**

The following procedures and associated instructions are also provided in the eCRF worksheets.

All study procedures will be recorded in REDCap™. The following instructions are presented as they appear in the REDCap database. Refer to the Electronic Data Capture System section of this Manual for specific instructions related to accessing and using the CRS & REDCap™.

**Source Documentation**

As per ICH GCP (1.51) source documents are original documents, data and records. Site must ensure source documents are available to verify all data collected for the RE-ENERGIZE study.

**Study Days**

Data for the RE-ENERGIZE study is collected and recorded per calendar day from 00:00 to 23:59 daily.

Study Day 1 is defined as **ACU admit date** (not randomization) until 23:59 the same day. Each 24 hour period (00:00 – 23:59) represents a subsequent study day, example below:

Example: A patient is admitted to the ACU on Sept 8th, 2015 at 4:00 PM (16:00).

The study days would be:

- Study Day 1 = 2015-09-08 from 16:00 to 2015-09-08 at 23:59
- Study Day 2 = 2015-09-09 from 00:00 to 2015-09-09 at 23:59

**Patient/Alternative Contact Person(s) Information form**

This contact information is obtained to ensure you are able to reach the patient, a family member, friend, or other individual to ascertain survival status and to complete the month 6 follow-up questionnaires. Try to obtain different contacts of the patient and proxies and record it on the patient/alternative contact person(s) information sheet (Appendix E). It is ideal to obtain a alternative contact person(s) that lives with the patient and at least 2 alternative contact person(s) that do not live with the patient. These data are to be collected once, at consent or baseline.

**Baseline form**

These data are to be collected once, at baseline, and recorded in REDCap™.

**Age**

Enter the age of the patient in years at the time of screening (patients must be > 18 years of age to be eligible to participate in The RE-ENERGIZE Study).

**Sex**

Check the appropriate box (male or female).

**Ethnic Group**

Choose the appropriate patient ethnicity from the following list:

- White
- Black or African American
- Hispanic
- Asian or Pacific Islander
• Native
• Other (please specify)

APACHE II
Go to the following website http://www.sfar.org/scores/apache2.php to calculate the APACHE II score. Record the calculated score. Reminder: only use variables within the first 24 hrs of this ACU admission. If variables are not available from the first 24 hrs, go outside the 24 hr window and use data closest to ACU admission.

NOTE: Ensure the units that you are using for serum sodium, potassium and white blood count are correct.

Does the patient have an inhalation injury?
Indicate if the patient has an inhalation injury by placing a check in the corresponding box “Yes” or “No.” Smoke inhalation injury is defined as: an injury below the glottis caused by products of combustion. Diagnosis of inhalation injury requires both of the following:
  1) History of exposure to products of combustion
  2) Bronchoscopy revealing one of the following below the glottis
     • Evidence of carbonaceous material
     • Signs of edema or ulceration

Burn Size expressed as % TBSA
Record the total burn size expressed as %TBSA as documented by the attending surgeon/physician and confirmed by the SI/sub-I. Record %TBSA in the nearest whole number rounding up from 0.5 and down from 0.4; i.e. if 26.5% is reported, record as 27% and if 26.4% is reported, record as 26%.

Is the patient co-enrolled in another academic ACU study?
Indicate if the patient is co-enrolled in another academic ACU study, Yes or No. If Yes, then enter the name(s) of the study(ies).

High Dose Vitamin C
Indicate whether the patient received high dose Vitamin C as part of her/his resuscitation protocol, Yes or No.
As a guide, high dose Vitamin C resuscitation is commonly considered approximately 66mg/kg/hr administered for the first 24 - 48 hours after ACU admission.

Tobacco use
Indicate whether the patient is a current smoker or uses tobacco, Yes or No. If you are not able to obtain this information, check the “Not Available” box.

Date and time of burn
Enter the date and time the burn injury trauma occurred. If the time of the burn is not available check the “No time available” box.

Type of burn
Select the type of burn that best describes the nature of the thermal burn injury from the list below (select only one). Frostbite is NOT considered a type of burn for this study.
  • Scald
• Fire (Includes both flame and flash burns)
• Chemical
• Radiation
• Unknown
• Other (please specify) ______________

Do NOT Include
• Electrical Burns
• Frost Bite
• Steven-Johnson Syndrome (SJS)
• Toxic Epidermal Necrolysis (TEN)

Hospital admit
Enter the date and time of hospitalization. This is the time of initial presentation to your emergency department or hospital ward, whichever is the earliest. If the patient is admitted directly to the ACU, this date and time becomes the Hospital admit date and time. If the admit time is not available, enter the time of the first documentation.

ACU admit
Enter the date and time of ACU admission. If the patient is admitted directly to the ACU, this date and time is the same as the Hospital admit date and time. If the admit time is not available, enter the time of the first documentation.

Comorbidities
Only record comorbidities listed on the Comorbidities list (see Appendix J).

• History of Alcohol abuse
  We would like to monitor the number of subjects that are enrolled in the study who have a history of alcohol abuse. As such, please note that we have added ‘alcohol abuse’ to the Comorbidities list in the CRF under the ‘miscellaneous’ conditions category. Therefore if a subject has a documented history of alcohol abuse in the medical chart, it should be recorded in the CRF.

Organ Dysfunction form
These data are collected once at baseline for calculation of modified SOFA.

MAP (lowest)
Enter the lowest MAP. If the MAP is not available you can calculate it using the formula:

\[
MAP = \frac{1}{3} \text{ lowest systolic BP} + \frac{2}{3} \text{ corresponding diastolic BP}
\]

Example: Lowest systolic B/P was 140/90
1/3 Systolic: 46.7
2/3 Diastolic: 60
MAP: 46.7 + 60 = 106.7

Or use the tool on the website: http://www.mdcalc.com/mean-arterial-pressure-map/
Urine output (mL)
Place a check in the appropriate volume range for urine output for the study day.

- <200 mL/day
- 200-500 mL/day
- >500 mL/day

Vasopressors/Inotropes
Record the highest hourly dose infused for each of the following vasopressor/inotropes received during the study day.

For the following use the units indicated:

- Dopamine (µg/kg/min) (Only record dopamine if ≥ 5 mcg received)
- Dobutamine (µg/kg/min)
- Vasopressin (units/min)

For the following indicate either µg/min or µg/kg/min by placing a check in the appropriate box.

- Norepinephrine
- Epinephrine
- Phenylephrine

Ventilation/RRT form
Mechanical Ventilation
If the patient receives mechanical ventilation during the study, record the associated stop and start dates/times in REDCap™.

Duration of Data Collection
These data are to be collected at start and stop of invasive mechanical.

Did the patient ever receive invasive mechanical ventilation?
Indicate if the patient ever received invasive mechanical ventilation, Yes or No.

Ventilation Event 1
Invasive Mechanical Ventilation #1 Start
If the patient received invasive mechanical ventilation, place a check in the Yes box and record the actual start date and time of invasive mechanical ventilation, even if this occurs at an external institution or in the field before admission to your unit. This may not be the same time that the patient was intubated, but should be the time invasive mechanical ventilation was started.

Do not record episodes of temporary ventilation (defined as <48 hrs i.e. needed for operating procedures, etc).

Invasive Mechanical Ventilation #1 Stop
Record the date and time the invasive mechanical ventilation episode was discontinued.

For patients that are on and off the ventilator, the patient is considered to be ventilator free if they are successfully breathing without mechanical ventilation for > 48 hours. In this event, record the date and time the ventilation was actually discontinued (i.e. in this instance, the start of the 48 hrs).
Patients will be considered breathing without mechanical ventilation in any of these instances:
- extubated and on face mask (nasal prong)
- intubated or breathing through a t-tube
- tracheostomy mask breathing.
- continuous positive airway pressure (CPAP) <=5cmH2O without pressure support or intermittent mandatory ventilation assistance.

If patient is transferred out of the ACU to another institution and is still receiving mechanical ventilation, record the transfer date and time as the mechanical ventilation discontinuation date and time.
If the patient expired while mechanically ventilated, check the box titled "Same as death date & time".
If the patient is still mechanically ventilated 3 months after ACU admission, check the box titled “Still vented at Day 90”.

Ventilation Event 2
Invasive Mechanical Ventilation #2 Start
In the event that the patient is restarted on invasive mechanical ventilation after being extubated successfully for 48 hrs, place a check in the Yes box. Do not record episodes of temporary ventilation (defined as <48 hrs).

Record the date and time invasive mechanical ventilation was restarted.

If patient never restarted invasive mechanical ventilation, then check the box titled “Did not restart invasive mechanical ventilation” and proceed to the dialysis section

Invasive Mechanical Ventilation #2 Stop
Record the date and time the invasive mechanical ventilation episode was discontinued.

Ventilation Event 3
Invasive Mechanical Ventilation #3
Follow the instructions as listed for Mechanical Ventilation start # 2 and stop # 2 for the third episode of mechanical ventilation, if applicable.

Renal Replacement Therapy
If the patient receives renal replacement therapy during the study, record the associated stop and start dates/times in REDCap™.

Duration of Data Collection
These data are to be collected at start and stop of renal replacement therapy (dialysis).

Did the patient receive renal replacement therapy (dialysis) during this ACU stay?
Indicate if the patient received renal replacement therapy (dialysis) during this ACU stay.

The first time renal replacement therapy (dialysis) was started, was it due to acute renal failure?
Indicate if the first time renal replacement therapy (dialysis) was started was due to acute renal failure. If Yes, continue to the next question. If No, the dialysis section is complete.

Renal Replacement Therapy (Dialysis) Stop
Record the date and time dialysis was permanently discontinued in the hospital. This may occur on the ward.

If patient is discharged from hospital or transferred out of the ACU to another institution and is still receiving renal replacement therapy (dialysis), check the box “Continued past hospital discharge”.

At 3 months if patient is still on renal replacement therapy (dialysis) in hospital, check the box “At 3 months still on renal replacement therapy (dialysis) in hospital”

Burn Grafting Assessment form
These data are collected twice for each patient, once at the beginning of the study and once at the end of the study period.

Initial Grafting Assessment

Date of initial assessment
Record the date the initial assessment was completed by the attending surgeon/delegate.

If the Grafting Assessment was completed when determining eligibility, record the date of that assessment.

Deep partial/full thickness burn (expected to require grafting) %
The responsible surgeon/physician must assess the deep 2nd and/or 3rd degree burn using the Lund and Browder chart (see Appendix A) to determine the percent Total Body Surface Area (%TBSA) expected to require grafting. This assessment must be confirmed by the SI or sub-I. Record the %TBSA expected to require grafting.

- Reminder: Deep 2nd and/or 3rd degree burn requiring grafting is an inclusion criteria. This should not be zero.

Final/Last Grafting Assessment
A Final/Last Burn assessment must be completed on all patients, even if they are still receiving grafts or expected to receive additional grafts at the time of the assessment.

Indicate if the patient was still receiving grafts at 3 months or at ACU discharge by answering “Yes” or “No” to the question, “Was the patient still receiving grafts at 3 months or at ACU discharge?”

Date of final/last assessment
Record the date the final/last assessment was completed by the attending surgeon/physician. The assessment must be done at the end of the study duration, defined as 10 days post last successful grafting, or ACU discharge, or 3 months from ACU admission, whichever occurs first.
Area that required grafting
At the end of the study period, using the Lund and Browder chart, the surgeon/physician must assess the %TBSA that required grafting. This assessment must be confirmed by the SI/sub-I.

Record the actual, or the total at the time of assessment, %TBSA that required grafting as determined by the surgeon/physician on the date of the final/last assessment.

The Final Assessment should be recorded as %TBSA, not a percentage of the Initial Assessment expected to require grafting.

Example: Initial Grafting Assessment expected to require grafting = 25% TBSA
Final Grafting Assessment - area that actually required grafting = 25% TBSA

Final Grafting Assessment is recorded as 25% TBSA.

*In the example above, do not record the final assessment as 100% TBSA*

Study Intervention form
Study intervention is to be started within 2 hours of randomization.

Duration of Data Collection
These data are to be collected when study supplements are first started and when study supplements are finally stopped. In addition, any prescription changes will be recorded on the Study Intervention form.

Study Intervention

Date and time the first dose of study intervention was administered
Enter the date and time study supplements were first started in the format yyyy-mm-dd and hh:mm

Was Study Intervention started > 2 hours after Randomization?
Indicate Yes or No by placing a check in the corresponding box.

If the intervention starts after 2 hrs from randomization, you must provide an explanation in the space provided.

Date and time the last dose of study intervention was administered
Enter the date and time study supplements were finally stopped in the format yyyy-mm-dd and hh:mm

The stop date should be at the end of the study period i.e. 7 days after the last successful grafting operation or at discharge from ACU or 3 months from ACU admission, whichever occurs first.

Study Intervention Prescription
What was the study intervention prescription?
Record the initial study intervention prescription in grams/day. Each packet contains 5 grams of study intervention. If 10 packets per day are to be given, enter 50 in the prescription box.

Did the study intervention prescription change?
If the study intervention prescription changes, record the new prescription and date/time the change occurred.
NOTE: IP prescription should not change except if the patient has a change in body weight sufficient for the clinical team to alter dosage of clinical treatments, the study treatment should also be adjusted.

Daily Monitoring of Study IP (Daily Monitoring form)
These data are collected to determine the compliance to the prescribed dose of the study intervention and to identify any dose related Protocol Violations.

Study intervention is to be started within 2 hours of randomization.

Duration of Data Collection
Given the material affect on the study, these data are to be collected daily as close to REAL TIME as possible and as follows:

- Study Intervention: from randomization to 7 days post last successful grafting operation, or until ACU discharge, or until 3 months from ACU admission, whichever comes first.
- Dose related Protocol Violations: for duration of study intervention administration.

NOTE: Duration of Study Intervention is from randomization to 7 days post last successful graft, or until ACU discharge, or until 3 months from ACU admission, whichever comes first.

Prescribed # grams per day
At the top of each page record the number of grams per day of investigational product (IP) the patient is to receive.

NOTE: This is to assist you in determining the daily percentage of IP received.

Date
Enter the date corresponding to the calendar day for the data being collected.

# Grams given
Record the # grams given at each interval as documented in the medical chart. Each packet of study intervention contains 5 grams. If dose is recorded in the medical chart as # of packets administered, multiply # of packets by 5 and enter the # of grams administered.

Route
Select the route by which the study intervention was administered at each interval:

- PO
- EN
- Not Given/Not Applicable
Was there a 7th administration of IP today?
If more than 6 administrations of IP are given during the study day, additional entry fields may be accessed by selecting the “Yes” box in response to the question regarding a 7th dose. You may enter as many as 10 IP administration times each study day using the same method.

Percentage of study intervention received
Divide the number of grams actually given by the number of grams prescribed per day (documented at the top of the page) to determine the percentage of study intervention received. Record the percentage in the space provided.

Was there a dose related Protocol Violation today? (IP dosing <80% over a 3 day average)
A protocol violation with the delivery of the study intervention occurs when the patient receives < 80% of the total prescribed daily dosage over a 3 day average.
Report a dose related protocol violation when both of the following are true:
- Dose received on the indicated day is < 80% prescribed
- Dose received over a 3 day average is < 80% prescribed

In the event that the patient does not receive at least 80% prescribed daily dosage over a 3 day average, a Protocol Violation Form must be completed in REDCap™ within 24 hours of becoming aware. Refer to the Protocol Violation instructions later in this section.

Laboratory Units form

Duration of Data Collection
These data are to be collected once, at baseline.

Laboratory Units
Indicate the units each laboratory test is reported in by placing a check in the appropriate box.

Laboratory form
If blood chemistry and/or hematology testing are conducted per standard of care. There is no protocolized blood work for this study but if the labs are available, we will enter in the data to help with the overall safety assessment of the study IP. The indicated results should be recorded in REDCap™ according to the following schedule:

Duration of Data Collection
These data are to be collected as follows:
- Daily for 2 weeks: From admission to the ACU through study day 14
- Weekly: From day 15 to 10 days post last successful graft, d/c from the ACU, or 3 mos. after admission, whichever comes first. Collect weekly lab data from a single day during that study week. If there is no value available on the specified date, record the value from an adjacent day. If there is no value available for that study week, record N/A.
  - Defined as +/- 24 hours from study day 21, 28, 35, 42, 49, 56, 63, 70, 77, 84 and 90.

Laboratory Values
Record the highest or lowest for the day as indicated below. Exception: record glucose taken closest to 8:00 AM:
Nutrition Assessment/Timing form
In the following section, the word dietitian refers to the team member responsible for assessing and monitoring the patients’ energy needs during the course of the study.

Nutrition Assessment
These data are collected to determine how well the patient is being fed i.e the nutritional adequacy (% calories and protein received/prescribed). Refer to the Dietitian Manual for detailed instructions for nutrition assessment.

Baseline Assessment
Record the date of the baseline prescription. Record the total calories prescribed (kcal) and the total protein prescribed (grams).

If the prescription changes for this patient, enter the date, total calories prescribed (kcal) and the total protein prescribed (grams) of the new prescription.

Prescribed Energy and Protein needs
Contact your dietitian to obtain this information. These will need to be calculated by the dietitian at baseline (ACU admission or at the first dietitian assessment) and thereafter.

Use pre-burn dry weight. For Obese patients, if your standard practice is to adjust for obesity, follow your standard practice. If you do not have an obesity adjustment practice, use the formula below:

Adjusted Body Weight (ABW) = Ideal Body Weight (IBW) based on a BMI of 25 + [(pre-burn dry weight – IBW) x 0.25]

Prescribed energy needs are to be calculated by using Indirect Calorimetry, a predictive equation, or a simple weight-based formula but on average, should not lead to a prescription of less than 30 kcal/kg.

Prescribed Protein needs are to be calculated by using the following:
- If > 50% burns, use 1.5g/kg/day to 2.5g/kg/day
- If < 50% burns, use 1.2 g/kg/day to 2g/kg/day
If the prescribed energy or prescribed protein intake changes from week to week, record this in the appropriate row (Assessment #2, #3, etc) and record the date the prescription changed. If there are no changes in the prescription from baseline, place a check in the “No change from baseline” box.

Note: Energy and protein requirements are independent of the formula prescribed. Do NOT change prescription to accommodate a formula change.

**Nutrition Timing**
These data are collected to determine the timing of initiation of nutrition.

**Enteral Nutrition**
Was EN received during this ACU admission?
Indicate if the patient received EN during this ACU admission or not, Yes or No.

**Date/Time**
If the patient received EN, record the following:
- the start date and time of EN.
- the stop date and time of EN. This refers to the date EN was permanently discontinued, not stopped for temporary interruptions.

If EN is continued beyond ACU discharge, record ACU discharge date and time as the date and time that EN was stopped. If the patient is still receiving EN in the ACU at 3 months, place a check in the box titled “Still on EN at 3 months in ACU”.

**Parenteral Nutrition**
Was PN received during this ACU admission?
Indicate if the patient received PN during this ACU admission or not, Yes or No.

**Date/Time**
If the patient received PN, record the following:
- the start date and time of PN.
- the stop date and time of PN. This refers to the date PN was permanently discontinued, not stopped for temporary interruptions.

If PN is continued beyond ACU discharge, record ACU discharge date and time as the date and time that PN was stopped. If the patient is still receiving PN in the ACU at 3 months, place a check in the box titled “Still on PN at 3 months in ACU”.

**Daily Nutrition form**
The number of calories and protein received by the patient, the route by which they were administered, and the source will be recorded daily and entered into REDCap™. These data should be obtained from the Dietitian.
Duration of Data Collection
These data are to be collected daily from Study Day 1 (ACU admission) until 10 days post last successful grafting or ACU discharge or 3 months from ACU admission, whichever comes first.

Enteral Nutrition
Was Enteral Nutrition (EN) given?
For each day, indicate whether the patient received EN, Yes or No.

If ‘No’ to EN, using the list below, indicate ALL the reason(s) the patient did not receive EN on the specified Study day by placing a check in the box(es) provided:
- NPO for endotracheal extubation or intubation or other bedside procedure. If “Other” is indicated, please also check the “Other” box and specify the reason.
- NPO for operating procedure
- NPO for radiology procedure
- High NG drainage
- Increased abdominal girth, abdominal distension or pt. discomfort
- Vomiting or emesis
- Diarrhea
- No enteral access available / enteral access lost, displaced or malfunctioning
- Inotropes, vasopressor requirement
- Patient deemed too sick for enteral feeding
- On oral feeds
- Reason not known
- Other, please specify___________________

EN Formula
If ‘Yes’ to EN, using the EN Formula List (Appendix K), choose the number that corresponds to the type of enteral formula received. You may record up to 3 different formulas used in a day. Record the first formula received in the spaces provided for “Formula 1” and so on. If the formula given is not in the EN Formula List, select #82. Other Nutritional Formula and enter the name of the formula in the space provided. In the event that the patient receives more than 3 formulas in one day, select the 3 formulas that provide the largest volumes.

Total kilocalorie and protein received from EN
- Record the total calories (kilocalories) and protein from all the enteral nutrition formulas received in the study day. Do not include the calories from IV solutions (e.g. Dextrose).
- Do not record the calories from Propofol (volume to be entered separately).
- Do not include protein supplements as a part of this total (data collected separately).

Protein Supplements
Was a protein supplement given?
Record whether a protein supplement was received, “Yes” or “No”.

Protein supplement name
If protein supplement was received, record the number or name from the Protein Supplement List (Appendix L).
Add another protein supplement?
If there is more than one protein supplement, record the name of each supplement by ticking “Yes”.

Total kilocalorie and protein received from protein supplements
Record the total calories and protein received from protein supplements.

Parenteral Nutrition
Was Parenteral Nutrition (PN) given?
For each day, indicate whether the patient received PN, Yes or No.

Total kilocalories and protein received from PN
If yes, record the total calories (kilocalories) and grams of protein received from PN for that study day.
- Do not include the calories from IV solutions, e.g. Dextrose (data collected separately).
- Do not record the calories from Propofol (volume to be entered separately).

IV Fluids containing Glucose
Was IV fluid containing glucose given?
Indicate whether the patient received IV fluids containing glucose that day, Yes or No.

Total kilocalories received from IV fluids
If yes, record the total calories (kilocalories) received from IV fluids containing glucose for that study day.

Oral Nutrition
Was Oral Nutrition given?
Indicate whether the patient received any oral intake today, Yes or No

Propofol
Was Propofol received for ≥ 6 hours?
Indicate whether the patient received a continuous infusion of Propofol for ≥ 6hrs, Yes or No.

Total volume of Propofol received
If yes, record the total volume in mL of Propofol received for that day.

This is to be completed for each day regardless of whether the patient received enteral nutrition, parenteral nutrition or neither.

Burn Related Operative Procedures
All burn related operative procedures, type of procedure, and whether it was planned or unplanned will be recorded in REDCap™. Record the procedure in REDCap on the date the procedure occurred.

Duration of Data Collection
This data should be collected from admission to the ACU until 10 Days post last successful grafting operation, or discharge from the ACU, or 3 months after admission to the ACU, whichever comes first.
Note: This data only needs to be collected on days a burn related operative procedure is performed.

**Burn related operative procedure today?**
Indicate if there was a burn related operative procedure today, Yes or No.

**Was the Operative procedure planned or unplanned?**
Indicate if the patient had a planned or unplanned operative procedure.

**Type of operative procedure**
Indicate from the taxonomy the type(s) of operation procedure(s) performed on the day indicated. Select all that apply.
- Surgical excision (tangential or fascial)
- Excision and temporary covering (xenograft, allograft and artificial skin)
- Excision and autograft
- Delayed autograft
- Excision and primary closure/composite tissue transfer
- Other specify—example amputation

**Concomitant Medications**

**Duration of Data Collection**
Administration of the following concomitant medications will be recorded in REDCap™ from admission to the ACU until 10 Days after the last grafting operation, or discharge from the ACU, or 3 months after admission to the ACU, whichever comes first:

**Were concomitant medications received today?**
Indicate if concomitant medications were received today, Yes, No or Not Available.

**Concomitant Medications**
Indicate “yes” or “no” regarding administration of each of the following medications. If the information is not available, indicate by selecting the corresponding box:
- **Insulin**
  If insulin was given, record the total units received in the 24 hour period from all insulin IV, SC (subcutaneous) and bolus.
- **Opiates**
- **Motility agents** (metoclopramide, erythromycin, domperidone, other)
  Do NOT record stool softeners here.
- **Oxandrolone**
- **Propanolol**

**Microbiology**
Record only the following microbiology data in REDCap™. Only record venous or arterial blood cultures that test positive for **Gram negative bacteria** that occurred >72 hours after ACU admission until 10 days post last successful grafting or ACU discharge or 3 months from ACU admission, whichever comes first. See Appendix M for a list of
**Gram negative bacteria to be recorded** and **Gram positive bacteria** that are **not be recorded**. Do not include blood from a catheter line tip.

**Date**
Complete the date the sample was collected (i.e. not when the results were reported) in the date format of yyyy-mm-dd.

**Time**
Complete the time the sample was collected (i.e. not when the results were reported) in the format of hh:mm. If there are multiple cultures on the same study day, record all reports of Gram negative bacteremia.

**Gram Negative Culture #**
Record the number on the taxonomy corresponding to the name of the Gram negative bacteria reported. If the Gram negative bacteria does not appear on the list, select #44 Other and specify the bacteria name in the space provided.

**Protocol Violations**
A Protocol Violation is defined as non-compliance with the study protocol and/or procedures that may impact study participant safety, the integrity of study data and/or study participant willingness to participate in the study.

Compliance with the study procedures will be monitored by the central study team. Any deviation or failure to conduct procedures and assessments required in the protocol should be documented and reported to the central study team via REDCap™ by completing the Protocol Violation form within 24h of becoming aware of the violation. You do not need to print and fax the form to the project leader. An automated email notification will be generated and sent to the project leader within 24 hours of the data being entered into REDCap™.

Each site is responsible for determining if and when a protocol violation should be reported to the local REB.

Some examples of reportable protocol violations include, but are not limited to:
- Randomization of an ineligible patient.
- Investigational Product (IP) Daily dose delivered is < 80% prescribed over a 3 day average.
  
  **Example:**
  Prescribed dose: 35g/day  (80% = 28g)
  
  Dose received:  
  Day 7: 20g
  Day 8: 30g
  Day 9: 30g
  Total: 80g/3 days = 26.67g/day average (<28g)

A protocol violation should be reported on Day 7 as the dose received on that day and over the 3 day average are both less than 80% (28g) prescribed.

**When to report**
Protocol violations are to be reported from randomization until end of the study duration (10 days post last successful grafting or ACU discharge or 3 months from ACU admission, whichever comes first).

Protocol Violations that relate to the <80% dosing delivered do NOT have to be reported on the following days:
1) Day of randomization
2) Day of discharge or end of study treatment (7 days post last successful grafting)
3) Day of death

Are you reporting a Protocol Violation today?
Indicate if a protocol violation occurred today, Yes or No.
Note: This question only needs to be answered on days a protocol violation occurred.

Date Violation Occurred
Enter the protocol violation into REDCap based on the date the violation occurred.

Date Violation Discovered
Enter the date when the violation was identified by site research staff.

Is the local site investigator aware of the violation?
Indicate whether the local qualified investigator has been made aware of this violation, Yes or No.

Type of violation
Using the options provided, check the box for the type of violation:
- Dose delivered is <80% prescribed over a 3 day average
- Dispensing/dosing error (an incorrect dose/product was given to patient)
- Accidental unblinding (the integrity of the study blind has been compromised)
- Enrollment of a patient that does not fulfill inclusion/exclusion criteria
- Unapproved procedures performed (failure to obtain consent)
- Other, please specify (briefly describe the type of protocol violation)

Reason for the Violation
Check the appropriate box and briefly describe the reason for the violation on the lines provided.
Describe the circumstances surrounding these violations. Check all that apply
- High gastric residual volumes
- Bowel perforation/obstruction
- Held for procedure/OR
- Other, specify details or attach Note to File: ____________________

Are there supporting files to be emailed (preferred) or faxed?
Indicate if other supporting files are being sent.

Action taken by Research Coordinator/Responsible Delegate
Describe the action taken by the Research Coordinator/responsible delegate to prevent violation/problem from recurring.

Another Protocol Violation to add?
Indicate if more than one protocol violation occurred on the same day, Yes or No. Report all Protocol Violations that occurred on that day by selecting “Yes” and entering the PV data.

**Hospital Overview**
Record data related to grafting status, acute care unit and hospital discharge, and mortality in REDCap™.

**Date of Last Successful Graft**
Enter the date of the last successful grafting procedure in the format yyyy-mm-dd.

**Last successful graft never achieved?**
If the last successful graft was never achieved, indicate by placing a check in the “Yes” box and

**Reason never achieved**
If the last successful graft was never achieved, select the reason:
- Death, record the date/time
- Discharged from the ACU without requiring grafting procedure (healed without graft)
- Withdrew consent.
- Withdrew Life Sustaining Therapies
- Still receiving grafts at 3 months
- Other (Please Specify):

**ACU Discharge**
**Did the patient die in ACU?**
If the patient died in ACU, place a check in the “Yes” box and record the date and time of death.

*Note: Record the death date and time documented on the death certificate. If this information is not available, record the date and time from the physician note. If the latter is not provided, record the date and time documented in the nurses charting.*

If the patient was discharged from ACU, place a check in the “No, patient discharged” box and enter the date and time the patient was actually discharged from the ACU. Proceed to the Hospital discharge row.

If the patient is still in the ACU at 3 months from ACU admission, place a check in the “No, patient still in ACU at 3 months” box. Proceed to Follow-Up (6 Months) form.

**Hospital Discharge**
**Did the patient die in Hospital?**
If the patient died prior to hospital discharge, place a check in the “Yes” box and record the date and time of death.

If the patient was discharged from the hospital, place a check in the “No, patient discharged” box and enter the date and time the patient was actually discharged from the hospital. Proceed to ‘Discharged to’ row.
If the patient is still in the hospital at 3 months from ACU admission, place a check in the “No, patient still in hospital at 3 months” box. Proceed to Follow-Up form.

Discharged to
If patient was discharged, place a check in the box that applies to the location of the patient at hospital discharge.

- Ward in another hospital
- ACU in another hospital
- Long term care facility
- Rehabilitation unit
- Home
- Other (Please Specify):

Cause of Death
If patient died, document the cause of death from a post mortem report. If this is not available, record cause of death from the death certificate.

Follow-up (6 months)

Survival
The primary outcome of this trial is 6-month mortality. Every resource must be used to determine the status of each patient at 6 months (+/- 14 days) after admission to the ACU. The site must establish a system that ensures the ability to connect with the patient, SDM, family, or friend 6 months after ACU admission.

Was the survival status obtained?
Indicate if survival status was obtained, Yes or No.
NOTE: In order to select “No” you must complete and document all contact attempts as outlined in the Survival Status NOT Obtained section below.

Survival Status Obtained Date
Record the date of the contact or information retrieval.

Source of information
In the following section we use the word ‘alternative contact person’ to refer to anyone, other than the patient, who is able to provide the requested information. This may be a family member, friend, neighbor, or caregiver to name a few. This does not need to be a legal representative (SDM) of the patient.

Record the source of the survival status information.
- Patient
- Alternative Contact Person (record the relationship between the alternative contact person and the patient)
- Family Physician
- Medical Records
- Obituaries
- Internet
• Other (Please specify)

Survival Status
Indicate if the patient is Alive or Deceased.

Date of death known?
Indicate if date of death is known, yes or No.
-If deceased and the date of death is known, record the date of death.
-If deceased and the date of death is unknown, record the last date the patient was
known to be alive

Survival Status NOT Obtained
Confirm which of the following were completed
Confirm that all the listed avenues to access the patient survival status were completed. Record
all attempts* to contact the patient and/or on the “Month 6 Follow-up Assessments: Contact
Log”
• 3 attempts to contact the patient were made (mandatory)
• 3 attempts to contact the alternative contact person(s) were made (mandatory if
applicable)
• Family doctor contacted (mandatory if available)
• No medical records on the patient available at month 6 (mandatory)
• Internet searches for the patient name did not reveal survival status (mandatory)

Last date known to be alive
Record the last date the patient was known to be alive.

Month 6 Follow-up Assessments: Contact Log
Record all contacts and attempted contacts with the patient and alternative contact person(s) for
the Month 6 follow-up assessments on this log. There must be at least 3 attempts made to
contact the patient and, if unsuccessful, 3 attempts made to contact the alternative contact
person(s) to conduct the follow-up assessments.

An “attempt” is defined as exhausting all available contacts for the patient and
alternative contact person(s) (if available) at a given time point. Calls to the patient’s home,
cell, and work numbers without reaching the patient do not constitute 3 attempts. These are all
part of a single attempt to contact the patient as part of the first attempt outlined in the example
below:

For example, the first attempt may include all of the following:
• Trying to call the patients
  o Cellular number
  o Home number
  o Work number
  o Other numbers/contacts
• If the patient cannot be reached then try to contact the alternative contact person(s) by
calling their:
  o Cellular number
  o Home number
  o Work number
If both the patient and the alternative contact person(s) cannot be reached, conduct another “attempt” at a different time of day and/or on a different day.

The primary goals of the month 6 assessments are to ascertain survival status and to obtain results from the patient to complete the questionnaires. If the patient is alive but unable to complete the questionnaires, then a “alternative contact person(s)” such as a family member can complete the questionnaire for the patient.

Duration of Data Collection

The SF-36, ADL, IADL and employment status assessments are to be conducted 6 months (± 14 days) after ACU admission.

Was the patient/alternative contact person(s) contacted in advance to book an appointment for the month 6 follow-up visit?
Contact the patient/alternative contact person(s) 2 weeks prior to book a time for the month 6 follow-up assessment and record the date of contact on the log.
Completion of all 4 questionnaires is estimated to take 45 minutes. Each questionnaire may be completed on different days or at different times if need be. It is strongly recommended to schedule time in advance with the patient/alternative contact person(s) to ensure her/his availability.

Date of attempt to contact patient/alternative contact person(s)
Record the date and time of contact. If you cannot reach the patient/alternative contact person(s) try a different time at each attempt.

If the patient was deceased as per the medical records or obituaries before contacts were made, record the date and time the survival status information was retrieved.

Patient Contact Method (Select all that apply)
Record all methods used to contact the patient.
- In person with patient
- Called patient (cell)
- Called patient (work)
- Called patient (home)
- Other contact (please specify)

If the patient was deceased as per the medical records or obituaries before any contact attempts were made, select “Other” and record that the patient was deceased and record your source.

Is there a alternative contact person(s) available?
Record if information for alternative contact person(s) are available. If the patient completed all the assessments or was deceased before any contact attempts were made, select “Not required”.

Alternative contact person(s) Contact Method (Select all that apply)
If information is available, record all methods used to contact the alternative person.
- In person with alternative contact person(s)
- Called alternative contact person(s) (cell)
- Called alternative contact person(s) (work)
- Called alternative contact person(s) (home)
- Other contact (please specify)

Alternative Contact Person(s) Relationship with the Patient
Record the relationship between the proxy and the patient.
- Spouse/Partner
- Parent
- Child
- Friend.
- Other relationship (please specify)

Follow-up Assessments Completed
Indicate which of the following assessments were completed during this attempt, Yes, or No.
Record whether the patient or the alternative contact person(s) completed the assessment. This may be different from form to form.
Note: It is always preferred to complete questionnaires with the patient when possible.
- Was the SF-36 completed?
- Was the Katz ADL completed?
- Was the Lawton IADL completed?
- Was the Employment Status questionnaire completed?

Was there a second contact attempt?
If all the follow-up assessments were not completed in the first attempt, indicate if there was a second attempt. If yes, record the information above.

Was there a third contact attempt?
If all the follow-up assessments were not completed in the first or second attempt, indicate if there was a third attempt. If yes, record the information above.

Reason Follow-up NOT completed
What was the reason all the follow-up assessment could not be completed?
If the follow-up assessments can not be completed, record the reason why.
- Deceased (Record date on the survival assessment)
- Patient refused
- Alternative contact person(s) refused (only if patient did not re-consent)
- Other (Please specify)

If the patient is deceased, record the date of death or date last known to be alive on the “Month 6 Survival Assessments”.
Refused is defined as the patient/alternative contact person(s) is unwilling to complete the follow-up questionnaires. This does not include reasons such as “not a good time” or “I am not
feeling well today” etc. In those cases, set up a new date and time to call the patient/alternative contact person(s).

**Health Related Quality of Life questionnaires**

6 months (+/- 14 days) after admission to the acute care unit, the patient or family member/friend of the patient will be contacted via telephone and the following questionnaires administered. All associated data will be recorded in REDCap™.

- SF-36 Health related Quality of Life questionnaire
- Activities of Daily Living (Katz Index)
- Instrumental Activities of Daily Living (Lawton Index)
- Employment Status

**Adverse Events**

Adverse events are any untoward medical occurrences in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. Given the high acuity of diseases and morbidity related to burns, adverse events are NOT to be reported to CERU, only SAEs.

**Serious Adverse Events**

The site investigator is responsible for identifying, reporting and documenting the onset of serious adverse events (SAEs) during the course of the trial. SAEs should be documented in the subject source documents. It is the responsibility of the investigator to review all documentation (e.g. hospital progress notes, laboratory results, diagnostic reports, etc...) regarding each event.

**Reporting Period**

Subjects should be monitored for SAEs from randomization until 10 days post last successful graft, or discharge from the acute care unit, or 3 months after admission to the acute care unit, whichever comes first. All SAEs should be documented and reported to the central study team via REDCap™ within 24h of becoming aware of the event. Any follow-up information should be sent as soon as it becomes available.

**Regulatory Reporting**

The central study team will be responsible for reporting any events that meet the criteria for expedited reporting. Cooperation from the site is required to ensure any regulatory timelines are adhered to in the reporting of SAE reports.

As with any study there may be other risks or side effects that we do not know about with administration of these study supplements. The Site Investigator must adhere closely to the ICH-GCP Guidelines, however when in doubt he/she can contact the Project Leader for the study.
Patient Confidentiality
By definition, and in the context of a clinical trial, confidentiality refers to prevention of disclosure, to other than authorized individuals, of a Patient’s identity and of records that could identify a Patient. Care and diligence in protecting confidential Patient information must be exercised throughout the duration of the RE-ENERGIZE Study.

With this in mind, prior to forwarding any documentation (i.e. as attachments to a Serious Adverse Event [SAE] report) to CERU, all patient identifiers other than the Patient’s Initials should be masked.

Reportable SAEs
All Serious Adverse Events that are unexpected or related must be reported to CERU within 24 hrs of becoming aware of the event by filling out the Serious Adverse Events Initial Report in REDCAP™. (see Appendix N for worksheet ).

Initial SAE Report
This form must be completed by the Site Investigator or sub-I in consultation with the Research Coordinator and requires the signature of the Site Investigator/sub-I.

All known data elements on the form must be completed within 24 hrs of discovery of the event. It may be that certain aspects of the form may change (for example, the date of resolution may not be known at the time of reporting) and this should be made clear in the narrative form that will follow at a later date.

The following fields of the Initial form must be completed:
- Patient identification
  - Your RE-ENERGIZE ® site number
  - RE-ENERGIZE ® enrollment number
  - Age
  - Gender, select male or female
  - Height
  - Weight
- Name of Site Investigator
- Name of person reporting the SAE
- SAE #: Record the sequential SAE # for the patient; i.e. for the first SAE for the patient, enter 01. For the second SAE for the patient, enter 02.
- Serious Adverse Event Reported (only one per form):
  Record the event that you are reporting (must be serious and unexpected).

Do NOT record death (outcome) as a SAE but the underlying cause of death.
Do not record respiratory failure as a SAE but what was felt to cause the respiratory failure i.e. sepsis.

- Date SAE reported
- Date became aware of SAE
- Seriousness of the SAE: (select all that apply):
  - patient died (if so, record this date in the Outcomes section)
  - life threatening
- requires or prolongs hospitalization
- results in persistent or significant disability/incapacity
- may require medical or surgical intervention to prevent one of the other outcomes.
- congenital anomaly/birth defect
- other serious medical event

- **Outcomes:** Select the most appropriate at the time of the initial report:
  - complete recovery/return to baseline (include date of recovery)
  - alive with sequelae
  - death (include date of death)
  - SAE persisting
  - unknown/lost to follow up

- **Record the date (dd/mmm/yyyy format) and time (hh:mm) for the following:**
  - Onset of SAE
  - ICU admission
  - Start of study supplement
  - Stop of study supplement (if available at the time of this report)

- **Action taken:** Select all that apply from the following
  - none
  - uncertain
  - procedure or physical therapy
  - blood or blood products
  - prescription drug therapy
  - non-prescription drug therapy
  - hospitalization
  - IV fluids
  - Other

- **Action taken with Study Supplements:** Select only one of the following:
  - none (including not on study supplements)
  - dose reduced, interrupted or therapy delayed (include date/time)
  - study supplements stopped permanently due to SAE (include date/time).

- **Relationship of SAE to the study supplements:** The determination of the relationship of the event to the supplements is to be done by the Site Investigator/delegate in collaboration with the Research Coordinator. To assist the Investigator in making this assessment, the following definitions have been provided (select only one):
  - **Not related:** A serious adverse event that is clearly due to extraneous causes (disease, environment, etc.) and does not meet the criteria for drug relationship listed under “Possibly” or “Probably”.
  - **Unlikely related:** A serious adverse event that is more likely due to other causes than the study supplements
- **Possibly related**: Suggests that the association of this SAE with the study supplements is unknown and the event is not reasonably supported by other conditions.

- **Probably related**: Suggests that a reasonable temporal sequence of this SAE with study supplement administration exists and the association of the event with the study supplement seems likely.

Once the SAE form is completed, save by clicking “PDF with saved data”, print and file in the patient study folder. Scan and email any accompanying documents, such as labs, x-rays, CT scans to the Project Leader at: danserem@kgh.kari.net. Remember to de-identify any patient records before sending them.

For SAE Initial Report Worksheet, see Appendix N.

### Follow-up/Final SAE Report

For every SAE that was reported, a **Serious Adverse Events Follow-up/Final Report** must be completed in REDCAP™

In the event that the event has not resolved, been explained or stabilized, the Project Leader will collaborate with the Research Coordinator for additional details and further follow-up reporting.

This form must be completed by the Site Investigator/designate by reviewing the Serious Adverse Events Report (Initial) and the patient’s medical chart. To make this process easier, it is strongly recommended that this be done as close to the event as possible.

Since the information in the Follow-up/Final Report will be reviewed by the Data Monitoring Committee, it must include details on the patients admitting diagnosis, co-morbidities, a chronological complete narration of the events leading to the SAE, the nature of the SAE, action taken with the study supplements, the outcome and the relationship of the event to the study supplements.

The following additional documentation is required and is to be attached to the follow-up/final report:

- Medication the patient received in the 48 hours before the onset of the SAE
- Laboratory results related to the SAE must also be provided.
Examples: if the event is cardiac arrest, provide cardiac enzymes; if the event is cholestasis/pancreatitis, provide liver function tests & amylases. For further clarification about which lab tests are relevant, the Research Coordinator is encouraged to ask the Site Investigator.

All data fields in the Follow-up/Final form must be completed:

- **Patient identification**: Site #, enrollment # and SAE # can be copied from the initial reporting form.
- Patient medical history, co-morbid illness and reason for admission to hospital: provide a detailed narrative of this information.
- Admitting diagnosis to ICU and chronological events leading to the SAE: provide a detailed narrative of this information.
- **Chronological events proceeding the SAE until time of report**: provide a detailed narrative of this information and attach other reports/details as needed.
- **Concomitant Medications**: list all medications given within 48 hrs before the onset of the SAE.
- **Laboratory Results and Investigations**: record all lab results and investigations done that are pertinent to the SAE. For example, cardiac enzymes, ECG results in the event of a cardiac arrest.
- **Confirmation of Unexpected nature of the SAE**: record the pertinent clinical features that, in the opinion of the Site Investigator, made him/her think that the event was unexpected vs. due to the progression of underlying disease.
- **Relationship of SAE to the Study supplements**: The determination of the relationship of the event to the supplements is to be done by the Site Investigator/delegate in collaboration with the Research Coordinator. To assist the Investigator in making this assessment see earlier in this section for definitions.

- **Rationale for relationship of the SAE to the study supplements vs. progression of underlying disease**: If the event is considered to be related to the study supplement, record the pertinent clinical features that, in the opinion of the Site Investigator, made him/her think that the event was related to the study supplements vs. the progression of underlying disease. Refer to the definitions of degree of relationship to the study supplements (not related, unlikely related, possibly related, probably related).

- **Outcomes**: Select the most appropriate at the time of the FOLLOW-UP report
  - complete recovery/return to baseline (include date of recovery)
  - alive with sequelae
  - death (include date of death)
  - SAE persisting
  - unknown/lost to followup

- **Action taken**: Select all actions taken from the onset of SAE, including those that occurred between the initial report and the follow-up report:
  - none
  - uncertain
  - procedure or physical therapy
  - blood or blood products
  - prescription drug therapy
  - non-prescription drug therapy
- hospitalization
- IV fluids
- Other

- **Action taken with Study Supplements:**
  - none (including not on study supplements)
  - dose reduced, interrupted or therapy delayed (include date/time)
  - study supplements stopped permanently due to SAE (include date/time).

- **Event reported to IRB (Institutional Review Board) / REB (Research Ethics Board):**
  indicate whether this event was reported to your IRB/REB.

- **Further Details:** add any further details concerning the SAE.

The completed Follow-up/Final Report must be signed by the Site Investigator and filed in the patient study folder. Scan and email relevant medication and lab documentation to the Project Leader at: danserem@kgu.kari.net, remember to de-identify any patient records before sending them.

For SAE Follow-up/Final Report worksheet, see Appendix O.

## SAE Completion

Any subject who experiences a serious adverse event during the study period, should be followed by the Research Coordinator until the event:

- resolves
- an outcome is reached, or
- the event is otherwise explained or stabilized.

The Project Leader will follow up with the Research Coordinator at the site to obtain documentation regarding the status of the subject. This information will be forwarded to the Data Monitoring Committee.

If follow-up information reveals that the event no longer meets the serious, unexpected, or drug related criteria, this information will be provided to Health Canada, the Medical Monitor, the US Department of Defense, the Data Monitoring Committee, Steering Committee & the manufacturer of the investigational products

### SAEs on REDCAP™

SAE forms must be completed in REDCAP™. REDCAP™ may be accessed via [http://www.criticalcarenutrition.com](http://www.criticalcarenutrition.com) or directly at: [https://ceru.hpcvl.queensu.ca/EDC/redcap/](https://ceru.hpcvl.queensu.ca/EDC/redcap/)

The SAE forms are listed at the bottom of the Event Grid.
Refer to the worksheets provided for the data elements required. All SAEs must be entered into REDCAP™ in real time.

Upon completing the form, save the form.

After saving the form, save as a PDF using the button shown below onto your desktop. Print the PDF copy.

The Site Investigator must sign the hard copy of the form. File the form in the patient study folder. If there are accompanying documents, scan and email them to the project leader at: danserem@kgh.kari.net. Remember to de-identify any patient records before sending them.

09 February 2016
Appendices
A. Lund and Browder chart
B. Delegation of Authority Log
C. NutreStore™ (L-Glutamine) monograph
D. Maltrin M-100 maltodextrin monograph
E. Contact Information sheet
F. Nursing Procedures
G. Dosing Weight Chart
H. Enteral Feeding Protocol
I. Medical/Physician Orders
J. Comorbidities list
K. EN Formula List
L. Protein Supplement List
M. Gram Negative Bacteria List (sub-List of Gram Positive bacteria)
N. SAE Initial Report worksheet
O. SAE Follow-up/Final Report worksheet
<table>
<thead>
<tr>
<th>Region</th>
<th>Percent Thickness (%)[URL]</th>
<th>Percent Thickness (%) [URL]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td></td>
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<tr>
<td>Neck</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdomen</td>
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<tr>
<td>Arms (left)</td>
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<td></td>
</tr>
<tr>
<td>Arms (right)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legs (left)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legs (right)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*NB: Do not include erythema*
This log is used by the Qualified Investigator (i.e. Site Investigator) to indicate the Site Staff that have a material effect on the conduct of the Study and to whom the Investigator has delegated significant Study related duties/tasks. The signatures and details on this log will also facilitate tracking of edits/changes of the Site records. This log is to be kept by the Qualified Investigator and the Sponsor.

**Name of Qualified Investigator:** ______________________________ **Signature of Qualified Investigator:** ______________________________

<table>
<thead>
<tr>
<th>Print Name</th>
<th>Signature</th>
<th>Initials</th>
<th>Study Role (Qualified Investigator*, sub-QI*, Research Coordinator (RC), Pharmacist, Technician, Dietitian)</th>
<th>Key Delegated Tasks Reference numbers (see next page)</th>
<th>Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

*Qualified Investigator: the Site Investigator responsible for the conduct of the RE-ENERGIZE study at your site.
*Sub QI: Investigator other than the Qualified Investigator that is responsible for tasks related to the RE-ENERGIZE study at your site.
Delegation of Authority Log

<table>
<thead>
<tr>
<th>Print Name</th>
<th>Signature</th>
<th>Initials</th>
<th>Study Role (Qualified Investigator, sub-QI*, Research Coordinator (RC), Pharmacist, Technician, Dietitian)</th>
<th>Key Delegated Tasks (see next page)</th>
<th>Dates</th>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Reference: ICH GCP 4.1.5 and 8.3.24
# Delegation of Authority Log

## Key Delegated Tasks

<table>
<thead>
<tr>
<th>Reference Number</th>
<th>Key Delegated Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Screening subjects for eligibility</td>
</tr>
<tr>
<td>2</td>
<td>Conducting informed consent discussions for eligible patients</td>
</tr>
<tr>
<td>3</td>
<td>Obtaining written informed consent</td>
</tr>
<tr>
<td>4</td>
<td>Patient enrolment/randomization and follow-up</td>
</tr>
<tr>
<td>5</td>
<td>Checking eligibility criteria</td>
</tr>
<tr>
<td>6</td>
<td>Daily monitoring of patient health, safety and study compliance</td>
</tr>
<tr>
<td>7</td>
<td>Data collection, includes:</td>
</tr>
<tr>
<td></td>
<td>- Case Report Form entries</td>
</tr>
<tr>
<td></td>
<td>- Case Report Form corrections</td>
</tr>
<tr>
<td></td>
<td>- Data query resolution</td>
</tr>
<tr>
<td>8</td>
<td>Source documentation maintenance, includes:</td>
</tr>
<tr>
<td></td>
<td>- Study worksheets, checklists, monitoring sheets</td>
</tr>
<tr>
<td></td>
<td>- Data from electronic &amp; hard copy medical chart</td>
</tr>
<tr>
<td>9</td>
<td>Reporting of Protocol Violations/Unanticipated Problems involving risk</td>
</tr>
<tr>
<td>10</td>
<td>Identification of Serious Adverse Events and documentation</td>
</tr>
<tr>
<td>11</td>
<td>Maintenance of Regulatory Documents</td>
</tr>
<tr>
<td>12</td>
<td>REB submissions and communications</td>
</tr>
<tr>
<td>13</td>
<td>Perform study specific training</td>
</tr>
<tr>
<td>14</td>
<td>Performing clinical assessments including burn outcomes, SAEs and ICU infection adjudication</td>
</tr>
<tr>
<td>15</td>
<td>Confirmation of completeness and accuracy of data collected</td>
</tr>
<tr>
<td>16</td>
<td>Maintenance of Product inventory</td>
</tr>
<tr>
<td>17</td>
<td>Checking of treatment assignment online</td>
</tr>
<tr>
<td>18</td>
<td>Study treatment dispensing &amp; accountability, including maintenance of logs</td>
</tr>
<tr>
<td>19</td>
<td>Optimizing delivery of enteral nutrition and compliance with Guidelines for Nutrition</td>
</tr>
<tr>
<td>20</td>
<td>Drawing of blood samples</td>
</tr>
<tr>
<td>21</td>
<td>Processing and Storage of blood supplies</td>
</tr>
<tr>
<td>22</td>
<td>Batch shipping of frozen samples</td>
</tr>
</tbody>
</table>

Reference: ICH GCP 4.1.5 and 8.3.24
NutreStore™ (L-glutamine powder for oral solution) for oral administration is formulated as a white crystalline powder in a paper-foil-plastic laminate packet. Each packet of NutreStore™ contains 5 g of L-glutamine. The amino acid glutamine is also known as (S)-2-aminoglutaric acid, L-glutamic acid 5-amido (S), 2,5-diamino-5-sorbutonenic acid, or L-glutamine. The molecular formula of glutamine is C5H12N2O6, and the molecular weight is 146.15. Glutamine has the following structural formula:

**CLINICAL PHARMACOLOGY**

L-glutamine has important functions in regulation of gastrointestinal cell growth, function, and regeneration. Under normal conditions, glutamine concentration is maintained in the body by dietary intake and synthesis from endogenous glutamine. Data from clinical studies indicate that the role of and nutritional requirements for glutamine during catabolic illness, trauma, and infection may differ significantly from the role of and nutritional requirements for glutamine in healthy individuals. Glutamine concentrations decrease and tissue glutamine metabolism increases during many catabolic disease states, and thus glutamine is often considered a "conditionally essential" amino acid.

When glutamine was administered in combination with recombinant human growth hormone (rh-GH) to rats, whole body, hyperinsulin-like growth factor I, and body weight were significantly higher than in animals either glutamine or rh-GH was administered alone.

**Pharmacokinetics**

The pharmacokinetics of L-glutamine as described below are based on literature data in human subjects. The pharmacokinetics in patients with short bowel syndrome have not been determined. The plasma glutamine concentrations in these patients following oral administration are expected to be highly variable depending on the length, segment, and presence/absence of ileal-cecal valve for the remnant bowel.

**Absorption**

Following single dose oral administration of glutamine at 0.1 g/kg to six subjects, mean peak blood glutamine concentration was 1028 μM (± 50 μM/L) occurring approximately 30 minutes after administration. The pharmacokinetics following multiple oral doses have not been adequately characterized.

**Distribution**

After an intravenous (IV) bolus dose in three subjects, the volume of distribution was estimated to be approximately 200 mL/kg.

**Metabolism**

Endogenous glutamine participates in various metabolic activities, including the formation of glutamate, and the synthesis of proteins, nucleotides, and amino sugars. Exogenous glutamine is anticipated to undergo similar metabolism.

**Elimination**

Elimination is the major route of elimination for glutamine. Although glutamine is eliminated by glomerular filtration, it is almost completely reabsorbed by the renal tubules. After an IV bolus dose in three subjects, the terminal half-life of glutamine was approximately 1 hour.

**Effect of Race, Age, and Gender**

There are no studies to determine the effect of race, age, or gender.
Table 3—Controlled Trial Adverse Events—Initial 4 Week Treatment Period

<table>
<thead>
<tr>
<th>Group</th>
<th>nGh-Scd</th>
<th>nGh-Scd+Gltn</th>
<th>Scd+Gltn</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>16 (100)</td>
<td>15 (100)</td>
<td>16 (100)</td>
</tr>
<tr>
<td>B</td>
<td>13 (81)</td>
<td>13 (81)</td>
<td>12 (75)</td>
</tr>
<tr>
<td>C</td>
<td>11 (69)</td>
<td>11 (69)</td>
<td>12 (75)</td>
</tr>
</tbody>
</table>

Total Number of Subjects with at Least One AE: 46

Table 4—Controlled Trial Adverse Events—Weeks 5 to 18

<table>
<thead>
<tr>
<th>Group</th>
<th>nGh-Scd</th>
<th>nGh-Scd+Gltn</th>
<th>Scd+Gltn</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10 (100)</td>
<td>10 (100)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>B</td>
<td>10 (100)</td>
<td>10 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>C</td>
<td>10 (100)</td>
<td>10 (100)</td>
<td>10 (100)</td>
</tr>
</tbody>
</table>

Table 4—Controlled Trial Adverse Events—Weeks 8 to 18

<table>
<thead>
<tr>
<th>Group</th>
<th>nGh-Scd</th>
<th>nGh-Scd+Gltn</th>
<th>Scd+Gltn</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>12 (80)</td>
<td>12 (80)</td>
<td>13 (80)</td>
</tr>
<tr>
<td>B</td>
<td>13 (80)</td>
<td>13 (80)</td>
<td>13 (80)</td>
</tr>
<tr>
<td>C</td>
<td>14 (80)</td>
<td>14 (80)</td>
<td>14 (80)</td>
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</table>

Table 4—Controlled Trial Adverse Events—Weeks 9 to 18

<table>
<thead>
<tr>
<th>Group</th>
<th>nGh-Scd</th>
<th>nGh-Scd+Gltn</th>
<th>Scd+Gltn</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>12 (80)</td>
<td>12 (80)</td>
<td>13 (80)</td>
</tr>
<tr>
<td>B</td>
<td>13 (80)</td>
<td>13 (80)</td>
<td>13 (80)</td>
</tr>
<tr>
<td>C</td>
<td>14 (80)</td>
<td>14 (80)</td>
<td>14 (80)</td>
</tr>
</tbody>
</table>

The safety profile in patients receiving oral glatiramer acetate with growth hormone was similar to the safety profile in patients receiving glatiramer acetate without glatiramer. During the initial 4 week treatment period, 100% of patients receiving growth hormone with and without glatiramer acetate required at least one adverse event (AE), whereas 89% of patients receiving growth hormoneplacebo with glatiramer reported at least one AE. During weeks 5 to 18, 81% of patients receiving growth hormone with glatiramer, 80% of patients receiving growth hormone without glatiramer and 75% of patients receiving growth hormone placebo with glatiramer experienced at least one AE. There were no deaths in this study.

OVERDOSAGE

Single oral doses of glatiramer acetate at about 20-22 kg/m², 8-11 kg/m², and 19 kg/m² were lethal in mice, rats, and rabbits, respectively.

DOSAGE AND ADMINISTRATION

NuteStore™ should be administered as a cotherapy with recombinant human growth hormone [see the package insert for somatropin (rDNA origin) for injection for full prescribing information] followed by continued Nutrastore™ for up to 16 weeks.

The recommended dosage of Nutrastore™ is 30 g daily in divided doses (5 g taken 6 times each day orally) for up to 16 weeks. Each dose of Nutrastore™ (3 g) should be reconstituted in 8 oz (250 mL) of water prior to consumption.

Nutrastore™ should be taken with meals or snacks at 2- to 3-hour intervals while awake. The volume of water may be varied according to the patient’s preference. In the event of a patient’s transient intolerance to intake, a dose may be delayed for up to 2 hours. The safety and efficacy of Nutrastore™ have not been studied beyond 16 weeks of treatment.

HOW SUPPLIED

Nutrastore™ is supplied in preprinted paper-foldable plastic laminate pouches containing 5 g of L-glutamine powder.

84 packets (3 g each) - NDC 42457-001-84

STORAGE

Nutrastore™ (L-glutamine powder for oral solution) should be stored at 25°C (77°F) with excursions allowed to 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature].

For additional information concerning Nutrastore™, contact:

Emmus Medical, Inc.
20725 S. Western Ave., Suite 136
Torrance, CA 90601-3814
Tel: 1-877-420-6493
www.nutrastore.com

Manufactured by:
Anderson Packaging, Inc.
4525 Assembly Drive
Rockford, IL 61109
Rx only

Revised October 2008

Nutrastore™ is a trademark of Emmus Medical, Inc. under license from Cato Holding Company.

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SMM-007-02 0810
# MATERIAL SAFETY DATA SHEET

## L-GLUTAMINE

### SECTION I

<table>
<thead>
<tr>
<th>MANUFACTURER'S NAME</th>
<th>EMERGENCY TELEPHONE NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kyowa Hakko Kogyo Co., Ltd.</td>
<td>1-212-319-5353 (N.Y. Office)</td>
</tr>
<tr>
<td></td>
<td>1-949-425-0707 (West Coast Office)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADDRESS (Number, Street, City, State, and ZIP Code)</th>
<th>TELEPHONE NUMBER FOR INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-6-1, Ohtemachi Chiyoda-ku, Tokyo, Japan, 100-8185</td>
<td>1-212-319-5353 (N.Y. Office)</td>
</tr>
<tr>
<td></td>
<td>1-949-425-0707 (West Coast Office)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DATE PREPARED</th>
<th>PREPARER</th>
</tr>
</thead>
<tbody>
<tr>
<td>August 1, 2003</td>
<td>Quality Assurance Department</td>
</tr>
<tr>
<td></td>
<td>Bio-Chemicals Company</td>
</tr>
</tbody>
</table>

### SECTION II - HAZARDOUS INGREDIENTS / IDENTITY INFORMATION

<table>
<thead>
<tr>
<th>CHEMICAL NAME AND SYNONYMS</th>
<th>CHEMICAL FAMILY</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-Glutamine</td>
<td>Amino Acid</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FORMULA</th>
<th>CAS NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_5H_9N_2O_3 (146.15)</td>
<td>56-85-9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INGREDIENT</th>
<th>PERCENT</th>
<th>HAZARDOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-Glutamine</td>
<td>Pure material</td>
<td>No</td>
</tr>
</tbody>
</table>

HAZARDOUS MIXTURES OF OTHER LIQUIDS, SOLIDS, OR GASES: None

### SECTION III - PHYSICAL DATA

<table>
<thead>
<tr>
<th>BOILING POINT</th>
<th>SPECIFIC GRAVITY (H_2O = 1)</th>
<th>MELTING POINT</th>
<th>EVAPORATION RATE (Butyl Acetate = 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>Unknown</td>
<td>Not Applicable</td>
<td>Not Applicable (solid)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VAPOR PRESSURE (mmHg)</th>
<th>SOLUBILITY IN WATER</th>
<th>APPEARANCE AND ODOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>Soluble</td>
<td>White crystals or crystalline powder, odorless</td>
</tr>
</tbody>
</table>

### SECTION IV - FIRE AND EXPLOSION HAZARD DATA

<table>
<thead>
<tr>
<th>FLASH POINT (Method used)</th>
<th>FLAMMABLE LIMITS</th>
<th>EXTINGUISHING MEDIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>None</td>
<td>Water, Foam, CO_2, Dry chemical</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SPECIAL FIRE FIGHTING PROCEDURES</th>
<th>UNUSUAL FIRE AND EXPLOSION HAZARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>As with most organic solids, dust from this material may pose an explosion of fire hazard, if suspended in air and there is a source of ignition.</td>
</tr>
</tbody>
</table>

OSHA 174, Sept., 1985
### SECTION V - REACTIVITY DATA

<table>
<thead>
<tr>
<th>STABILITY</th>
<th>UNSTABLE</th>
<th>CONDITIONS TO AVOID</th>
</tr>
</thead>
<tbody>
<tr>
<td>STABLE</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

**Incompatibility (Materials to Avoid):** Oxidizer

**Hazardous Decomposition or Byproducts:** None

**Hazardous Polymerization:**
- **May Occur:** Conditions to Avoid
- **Will Not Occur:** X

### SECTION VI - HEALTH HAZARD DATA

<table>
<thead>
<tr>
<th>Route(s) of Entry:</th>
<th>Inhalation?</th>
<th>Skin?</th>
<th>Ingestion?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not determined</td>
<td>Not determined</td>
<td>Not determined</td>
</tr>
</tbody>
</table>

**Health Hazards (Acute and Chronic):**
This material is considered to be non-toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

**Carcinogenicity:**
- **NTP:** No
- **IARC Monographs:** No
- **OSHA Regulated:** No

**Signs and Symptoms of Exposure:**
May cause irritation of skin or eyes. Wash thoroughly with water.

**Medical Conditions Generally Aggravated by Exposure:**
Not expected

**Emergency and First Aid Procedures:**
Wash thoroughly with water. If irritation occurs, consult a physician.

### SECTION VII - PRECAUTIONS FOR SAFE HANDLING AND USE

**Steps to be Taken in Case Material is Released or Spilled:**
Material is solid. Use solid waste clean-up procedures.

**Waste Disposal Method:**
With chemical wastes

**Precautions to be Taken in Handling and Storing:**
Controlled room temperature in tight container.

**Other Precautions:**

### SECTION VIII - CONTROL MEASURES

**Respiratory Protection (Specify Type):**
Gauze mask (recommended)

**Ventilation:**
- **Local Exhaust:** Special
- **Mechanical (General):** Other

**Protective Gloves:**
- Recommended

**Other Protective Equipment:**
- **Eye Protection:** Recommended

**Work / Hygienic Practices:**

OSHA 174, Sept., 1985
DESCRIPTION
MALTRIN® maltodextrins are bland, minimally sweet white carbohydrate powders produced from corn of U.S. origin. They are products with varying length polymer profiles that provide a wide range of viscosity and solubility characteristics.

REGULATORY
MALTRIN® maltodextrins are generally recognized as safe (GRAS) as direct food ingredients at levels consistent with good manufacturing practices (21 CFR 184.1444). The correct labeling is “maltodextrin”, but all label declarations should be reviewed with appropriate legal counsel.

PACKAGING, STORAGE AND SHELF LIFE
• Packaged in: 50-pound net, multiwall paper bags that are individually shrink wrapped; 2,000-pound tote bags; 25-kilogram bags.
• Store under ambient conditions; protect from excessive heat and excessive humidity for extended periods of time.
• Under good storage conditions the shelf life should be a minimum of two years.
• MALTRIN® maltodextrins will remain stable, but may pick up moisture if stored in excessive humidity, so reevaluation for moisture is recommended after one year to confirm the product still meets desired specifications.

PRODUCT ATTRIBUTES
• Heated solutions at 30% solids remain clear
• Minimal contribution to viscosity at solids below 30%
• Very low hygroscopicity
• Low sweetness

APPLICATIONS
• Source of energy for nutritional products
• Aids in spray drying flavors or other ingredients
• Carrier and dispersant for dry-blend mixes and seasonings
• Prevents sugar crystallization in confections, frostings and glazes
• Contributes to total solids in frozen desserts

LOT CODES
Lot codes can be interpreted as follows: The first alpha character represents the product, followed by the last two numbers of the year and then the Julian date. Numbers following the Julian date represent the product line and the lot of the day.
Example: M1310801: M = MALTRIN®; 13 = 2013; 108 = Apr. 18; 01 = first lot
MALTRIN® M100
Maltodextrin

TYPICAL NUTRITIONAL INFORMATION
Values per 100 grams of product

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>378</td>
</tr>
<tr>
<td>Calories from Fat</td>
<td>0 g</td>
</tr>
<tr>
<td>Total Fat</td>
<td>0 g</td>
</tr>
<tr>
<td>Saturated Fat</td>
<td>0 g</td>
</tr>
<tr>
<td>Trans Fat</td>
<td>0 g</td>
</tr>
<tr>
<td>Monounsaturated Fat</td>
<td>0 g</td>
</tr>
<tr>
<td>Polyunsaturated Fat</td>
<td>0 g</td>
</tr>
<tr>
<td>Protein</td>
<td>0 g</td>
</tr>
<tr>
<td>Total Carbohydrate</td>
<td>94.5 g</td>
</tr>
<tr>
<td>Sugars</td>
<td>4 g</td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>0 g</td>
</tr>
<tr>
<td>Soluble Fiber</td>
<td>0 g</td>
</tr>
<tr>
<td>Insoluble Fiber</td>
<td>0 g</td>
</tr>
<tr>
<td>Sugar Alcohols</td>
<td>0 g</td>
</tr>
<tr>
<td>Other Carbohydrates</td>
<td>90.5 g</td>
</tr>
<tr>
<td>Calcium</td>
<td>16 mg</td>
</tr>
<tr>
<td>Iron</td>
<td>0 mg</td>
</tr>
<tr>
<td>Sodium</td>
<td>90 mg</td>
</tr>
<tr>
<td>Magnesium</td>
<td>6 mg</td>
</tr>
<tr>
<td>Potassium</td>
<td>5 mg</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>8 mg</td>
</tr>
</tbody>
</table>

STANDARD SPECIFICATIONS*

- Dextrose Equivalent: 9.0-12.0
- Moisture, %: 6.0 max.
- Ash (sulfated), %: 0.5 max.
- pH (20% solution): 4.0-4.7
- Bulk Density (packed), lb/cu ft: 30.0-39.0
- Aerobic Plate Count, CFU/g: 100 max.
- Yeast/Mold, CFU/g: 100 max.
- E. coli: Negative/10 g
- Salmonella: Negative/25 g

* Any specification different from or not listed above must be agreed upon between the customer and Grain Processing during specification approval.

CARBOHYDRATE LABELING INFORMATION**

- DP1 (glucose) grams per 100 grams: 1
- DP2 (maltose) grams per 100 grams: 3

** Carbohydrate information reported “as is”.

DEGREE OF POLYMERIZATION (DP PROFILE)***

- DP1-7, %: 30
- DP8-25, %: 35
- DP26-40, %: 1
- Greater than DP40, %: 34

*** DP profile data reported “as is”.

Mandatory Nutrition Facts listed in bold

The above information is considered to be typical and not part of the product specification. Each value represents the average analyses performed using samples from several product lots. All nutrient data is reported for 100 grams of “as is” product, assuming 5 percent moisture and 94.5 grams of carbohydrate.

NOT a significant source of Vitamin A, Vitamin C, Vitamin D, Vitamin E, Vitamin K, Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Panthoenic Acid, Biotin, or minerals Chromium, Copper, Iodine, Magnesium, Molybdenum, Selenium, Zinc.

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The information presented in this document is believed to be correct. Any recommendations or suggestions are made without guarantee or representation as to results for any particular usage. You are responsible for determining that the use of any GPC product, as well as your product and its use, and any claims made about your product, all comply with applicable laws and regulations for your particular jurisdiction. The information contained in this document is offered solely for your independent investigation, verification and consideration.
## Patient/Alternate Contact Person(s) Information Form

**Participant contact information:** (verify contact information with medical record or alternative)

<table>
<thead>
<tr>
<th>Name: ____________________________</th>
<th>Last Name, First Name Middle Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternative name (i.e. nicknames/alias):</td>
<td>□ None #1 __________ #2 __________</td>
</tr>
<tr>
<td>Home Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Alternate: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Cell Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Alternate: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Email Address: ____________________________</td>
<td></td>
</tr>
<tr>
<td>Work Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Alternate: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
</tbody>
</table>

### Someone who lives with participant:

<table>
<thead>
<tr>
<th>Name: ____________________________</th>
<th>Last Name, First Name Middle Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Work Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Relationship to Patient (e.g., father, sister, friend):</td>
<td>____________________________</td>
</tr>
</tbody>
</table>

### Someone with different address from participant: (obtain complete information for at least 2 people)

<table>
<thead>
<tr>
<th>Name: ____________________________</th>
<th>Last Name, First Name Middle Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Work Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Relationship to Patient (e.g., father, sister, friend):</td>
<td>____________________________</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name: ____________________________</th>
<th>Last Name, First Name Middle Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Work Phone: (_____) _____ - _______</td>
<td>□ Not Available</td>
</tr>
<tr>
<td>Relationship to Patient (e.g., father, sister, friend):</td>
<td>____________________________</td>
</tr>
</tbody>
</table>

11
Nursing Procedures
Investigational Product Administration

1. Determine the number of grams of the investigational product to be given to the patient and the dosing time according to the pharmacy orders and confirm per the Dosing Weight Chart, attached.

2. At each dose time, pour the correct dose of the investigational product (IP) needed into a clean specimen cup.

3. Per each 5 g of IP add 50 mL of sterile water/tap water (per your standard practice for enteral nutrition formulas) to the cup and mix well.

4. Transfer the mixture into a syringe.

5. Infuse the prescribed amount (for the dose time) through the feeding tube as boluses every 4 hours. Give via Nasogastric/Levine tube if the feeding tube is not in place. Flush with water.

6. When the patient is tolerating oral feeds, mix the study intervention in appropriate liquid/food (apple juice, koolade or oatmeal) and give TID or QID with meals/snacks. There is flexibility with the timing of the boluses and they may be given according to the patient’s preference or RN discretion as long as:
   a. the patient receives the daily prescribed number of packets
   b. patient does not receive more than double the prescribed dose at any time

Do NOT mix the study intervention with orange juice, grapefruit juice or lemonade.

7. Record the number of grams given at each scheduled interval over the 24 hrs period (according to flow sheet) on the Medication Administration Record as “RE-ENERGIZE supplement”.

8. Do NOT stop the bolus infusion for procedures or surgery. In the event of a missed dose or interruption in the bolus, follow these steps:

9. The bolus infusion is to be administered as close as possible to the scheduled time. In the event that there is a delay in the administration, the bolus will need to be shaken to re-suspend the powder.

10. Keep all the unused packages in a bag with the patient’s ID on it and give to Research Coordinator.

11. Inform the Research Coordinator of any interruptions in the boluses.

12. Continue with administering boluses of the investigational product until 7 days after the last successful grafting procedure, or until ACU discharge or 3 months from ACU admission, whichever comes first (Research Coordinator to notify when this will be).

Glossary

IP        Investigational Product

ACU      Acute Care Unit (burn unit or ICU)
<table>
<thead>
<tr>
<th>Dose #</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>q4h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing weight (kg)</td>
<td>Number of 5g doses</td>
<td>Total doses</td>
<td>g/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>45-54</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>55-64</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>65-74</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>75-84</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>85-94</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>95-104</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>105-114</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>115-124</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>125-134</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>135-144</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>14</td>
</tr>
</tbody>
</table>
Enteral Feeding Protocol

STOP enteral nutrition if the patient develops:
- bowel obstruction
- bowel perforation
- paralytic ileus

Start Enteral Nutrition as soon as possible after burn injury, preferably within 24 hrs of burn injury, if possible

Elevate HOB to 45 degrees, if possible

If gastric feeding, check GRVs q 4 hrs.

Is the GRV > 250 mls?

NO

1) Refeed gastric residual
2) Continue with Enteral Nutrition

YES

Is this the 1st GRV > 250 ml*?

NO

This is a rechecked residual >250 mls:
1) Discard the residual
2) Continue with Motility agents
3) Switch to SMALL BOWEL FEEDING
4) Restart Enteral Nutrition
5) Monitor enteral nutrition tolerance, but do not monitor GRVs if small bowel feeding

YES

1) Refeed GRV to 250ml max and discard the rest
2) Start Maxeran 10mg IV q 6 hrs
3) Continue with Enteral Nutrition

WATER FLUSHES:
Flush tube with at least 10 mls of sterile water:
-q4hrs during feedings
-after aspiration for GRVs
-before and after meds

BLOCKED TUBE:
Pancrealipase, 8000 units, with crushed Na Bicarb 500mg in 5ml warm water via feeding tube as needed.

* Gastric residual volume (GRV) of 250 mls is the minimum threshold volume. Volumes higher than 250 mls are acceptable if allowed at the individual site.
• This patient is enrolled in _________________IRB study ID#, A Randomized Trial of Enteral Glutamine to Minimize Thermal Injury, The RE-ENERGIZE study.

• Administer _______ grams of study supplement per day. Divide into 6 doses and give q4h via:
  - OG/NG/FEEDING TUBE: dissolve each 5 g in 50 mL water by shaking well in a clean specimen container, give as a bolus and flush tube as usual
  OR
  - PO: dissolve each 5 g in 50 mL of juice, apple sauce, oatmeal or other potable substance and give with meals TID or QID.

• Administer study supplement at the following times (enter # grams):

<table>
<thead>
<tr>
<th>Times</th>
<th>OG/NG/Feeding Tube</th>
<th>OR</th>
<th>PO</th>
</tr>
</thead>
<tbody>
<tr>
<td>02:00</td>
<td>_____ grams</td>
<td>08:00</td>
<td>_____ grams</td>
</tr>
<tr>
<td>06:00</td>
<td>_____ grams</td>
<td>12:00</td>
<td>_____ grams</td>
</tr>
<tr>
<td>10:00</td>
<td>_____ grams</td>
<td>16:00</td>
<td>_____ grams</td>
</tr>
<tr>
<td>14:00</td>
<td>_____ grams</td>
<td>20:00</td>
<td>_____ grams</td>
</tr>
<tr>
<td>18:00</td>
<td>_____ grams</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22:00</td>
<td>_____ grams</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• A missed dose should be given as soon as possible as follows:
  o If more than one hour until the next scheduled dose, give missed dose immediately.
  o If less than one hour until the next scheduled dose, give the missed dose with the scheduled dose at the scheduled time.

To optimize absorption:
  o Never give doses less than one hour apart
  o Never give more than 2 scheduled doses at a time

• Please save all unused packages in a labelled bag for Research Coordinator to pick up.

• Call Research Coordinator ____________(name) with any questions or concerns at _________(pager or extension)
Comorbidities

Check all the comorbidities that apply. If the patient has no comorbidities, check “No Comorbidities.”

<table>
<thead>
<tr>
<th>No Comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastrointestinal</strong></td>
</tr>
<tr>
<td>1. Angina</td>
</tr>
<tr>
<td>2. Arrhythmia</td>
</tr>
<tr>
<td>3. Valvular</td>
</tr>
<tr>
<td>4. Myocardial infarction</td>
</tr>
<tr>
<td>5. Congestive heart failure (or heart disease)</td>
</tr>
<tr>
<td><strong>Vascular</strong></td>
</tr>
<tr>
<td>6. Hypertension</td>
</tr>
<tr>
<td>7. Peripheral vascular disease or claudication</td>
</tr>
<tr>
<td>8. Cerebrovascular disease (Stroke or TIA)</td>
</tr>
<tr>
<td><strong>Pulmonary</strong></td>
</tr>
<tr>
<td>9. Chronic obstructive pulmonary disease (COPD, emphysema)</td>
</tr>
<tr>
<td>10. Asthma</td>
</tr>
<tr>
<td><strong>Neurologic</strong></td>
</tr>
<tr>
<td>11. Dementia</td>
</tr>
<tr>
<td>12. Hemiplegia (paraplegia)</td>
</tr>
<tr>
<td>13. Neurologic illnesses (such as Multiple sclerosis or Parkinsons)</td>
</tr>
<tr>
<td><strong>Endocrine</strong></td>
</tr>
<tr>
<td>14. Diabetes Type I or II</td>
</tr>
<tr>
<td>15. Diabetes with end organ damage</td>
</tr>
<tr>
<td>16. Obesity and/or BMI &gt; 30 (weight in kg/(ht in meters)^2)</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
</tr>
<tr>
<td>17. Moderate or severe renal disease</td>
</tr>
<tr>
<td><strong>Cancer/immune</strong></td>
</tr>
<tr>
<td>24. Any Tumor</td>
</tr>
<tr>
<td>25. Lymphoma</td>
</tr>
<tr>
<td>26. Leukemia</td>
</tr>
<tr>
<td>27. AIDS</td>
</tr>
<tr>
<td>28. Metastatic solid tumor</td>
</tr>
<tr>
<td><strong>Psychological</strong></td>
</tr>
<tr>
<td>29. Anxiety or Panic Disorders</td>
</tr>
<tr>
<td>30. Depression</td>
</tr>
<tr>
<td><strong>Muskoskeletal</strong></td>
</tr>
<tr>
<td>31. Arthritis (Rheumatoid or Osteoarthritis)</td>
</tr>
<tr>
<td>32. Degenerative Disc disease (back disease, spinal stenosis or severe chronic back pain)</td>
</tr>
<tr>
<td>33. Osteoporosis</td>
</tr>
<tr>
<td>34. Connective Tissue disease</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
</tr>
<tr>
<td>35. Visual Impairment (cataracts, glaucoma, macular degeneration)</td>
</tr>
<tr>
<td>36. Hearing Impairment (very hard of hearing even with hearing aids)</td>
</tr>
<tr>
<td>37. Alcohol Abuse</td>
</tr>
</tbody>
</table>
## ENERAL NUTRITION FORMULAS

<table>
<thead>
<tr>
<th>Code</th>
<th>Formula Name</th>
<th>Code</th>
<th>Formula Name</th>
</tr>
</thead>
<tbody>
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<td>1</td>
<td>Ensure</td>
<td>42</td>
<td>Isosource VHN</td>
</tr>
<tr>
<td>2</td>
<td>Ensure Fibre</td>
<td>43</td>
<td>Isosource 1.5 Cal</td>
</tr>
<tr>
<td>3</td>
<td>Ensure HP</td>
<td>44</td>
<td>Novasource Renal</td>
</tr>
<tr>
<td>4</td>
<td>Ensure Plus</td>
<td>45</td>
<td>Novasource Pulmonary</td>
</tr>
<tr>
<td>5</td>
<td>Ensure Prebiotics</td>
<td>46</td>
<td>Nutren 1.0</td>
</tr>
<tr>
<td>6</td>
<td>Glucerna</td>
<td>47</td>
<td>Nutren 1.0 Fiber</td>
</tr>
<tr>
<td>7</td>
<td>Glucerna Select</td>
<td>48</td>
<td>Nutren 1.5</td>
</tr>
<tr>
<td>8</td>
<td>Jevity</td>
<td>49</td>
<td>Nutren 2.0</td>
</tr>
<tr>
<td>9</td>
<td>Jevity 1 Cal</td>
<td>50</td>
<td>Nutren Glytrol</td>
</tr>
<tr>
<td>10</td>
<td>Jevity 1.2 Cal or Jevity Plus</td>
<td>51</td>
<td>Nutren Renal</td>
</tr>
<tr>
<td>11</td>
<td>Jevity 1.5 Cal</td>
<td>52</td>
<td>Nutren Pulmonary</td>
</tr>
<tr>
<td>12</td>
<td>Nepro</td>
<td>53</td>
<td>Nutren Replete</td>
</tr>
<tr>
<td>13</td>
<td>Osmolite 1 Cal</td>
<td>54</td>
<td>Nutren Replete Fiber</td>
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<tr>
<td>14</td>
<td>Osmolite 1.2 Cal</td>
<td>55</td>
<td>Nutrihep</td>
</tr>
<tr>
<td>15</td>
<td>Osmolite 1.5 Cal</td>
<td>56</td>
<td>Peptamen</td>
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<tr>
<td>16</td>
<td>Osmolite with Fiber</td>
<td>57</td>
<td>Peptamen 1.5</td>
</tr>
<tr>
<td>17</td>
<td>Osmolite HN</td>
<td>58</td>
<td>Peptamen DT</td>
</tr>
<tr>
<td>18</td>
<td>Osmolite HN Plus</td>
<td>59</td>
<td>Peptinex 1.0</td>
</tr>
<tr>
<td>19</td>
<td>Osmolite High Protein</td>
<td>60</td>
<td>Peptinex 1.5</td>
</tr>
<tr>
<td>20</td>
<td>Oxepa</td>
<td>61</td>
<td>Peptamen with Prebio 1</td>
</tr>
<tr>
<td>21</td>
<td>Optimental</td>
<td>62</td>
<td>Peptamen AF 1.2</td>
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<td>22</td>
<td>Promote</td>
<td>63</td>
<td>Renecal</td>
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<tr>
<td>23</td>
<td>Promote with Fiber</td>
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<td>Resource 2.0</td>
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<td>24</td>
<td>Pulmocare</td>
<td>65</td>
<td>Resource Diabetic</td>
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<td>25</td>
<td>Suplena</td>
<td>66</td>
<td>Resource Standard</td>
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<tr>
<td>26</td>
<td>Two Cal HN</td>
<td>67</td>
<td>Supplements- Beneprotein Instant Protein Powder</td>
</tr>
<tr>
<td>27</td>
<td>Vital</td>
<td>68</td>
<td>Supplements – Microlipid</td>
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<tr>
<td>28</td>
<td>Vital HN</td>
<td>69</td>
<td>Supplements – Resource Benecalorie</td>
</tr>
<tr>
<td>29</td>
<td>Supplement: Polycose powder</td>
<td>70</td>
<td>Supplements - MCT Oil</td>
</tr>
<tr>
<td>30</td>
<td>Supplement: Polycose Liquid</td>
<td>71</td>
<td>Supplements- Resource Benefiber</td>
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<td>31</td>
<td>Supplement: Promod</td>
<td>72</td>
<td>Traumacal</td>
</tr>
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<td>32</td>
<td>Supplement: Prosure</td>
<td>73</td>
<td>Baxter: Restore-X</td>
</tr>
<tr>
<td>33</td>
<td>Boost 1.0 Standard</td>
<td>74</td>
<td>MEAD JOHNSON: Portagen</td>
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<tr>
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<td>Boost 1.5 Plus Calories</td>
<td>75</td>
<td>Hormel Health: Propass</td>
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<td>35</td>
<td>Compleat</td>
<td>76</td>
<td>National Nutrition: Prosource liquid</td>
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<tr>
<td>36</td>
<td>Diabetisource AC</td>
<td>77</td>
<td>National Nutrition: Prosource powder</td>
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<tr>
<td>37</td>
<td>Fibersource</td>
<td>78</td>
<td>Global Health: Procel</td>
</tr>
<tr>
<td>38</td>
<td>Fibersource HN</td>
<td>79</td>
<td>Medical Nutrition: Pro-stat</td>
</tr>
<tr>
<td>39</td>
<td>Isosource</td>
<td>80</td>
<td>Wyeth: Enercal</td>
</tr>
<tr>
<td>40</td>
<td>Isosource HN</td>
<td>81</td>
<td>Wyeth: Enercal Plus</td>
</tr>
<tr>
<td>41</td>
<td>Isosource HN with fibre</td>
<td>82</td>
<td>Other Nutritional Formula specify</td>
</tr>
</tbody>
</table>
## PROTEIN SUPPLEMENT FORMULAS

<table>
<thead>
<tr>
<th>Code</th>
<th>Formula Name</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Abbott: Promod</td>
</tr>
<tr>
<td>2</td>
<td>Global Health: Procel</td>
</tr>
<tr>
<td>3</td>
<td>Hormel Health: Propass</td>
</tr>
<tr>
<td>4</td>
<td>Kramer Novis: Pre Protein Powder</td>
</tr>
<tr>
<td>5</td>
<td>Llorens: Proteinex WC</td>
</tr>
<tr>
<td>6</td>
<td>Medical Nutrition: Pro-stat</td>
</tr>
<tr>
<td>7</td>
<td>Mirrus Advanced Nutrition: Impact Whey</td>
</tr>
<tr>
<td>8</td>
<td>National Nutrition: Prosource liquid</td>
</tr>
<tr>
<td>9</td>
<td>National Nutrition: Prosource powder</td>
</tr>
<tr>
<td>10</td>
<td>National Nutrition: Prosource no carb</td>
</tr>
<tr>
<td>11</td>
<td>Nestle: Beneprotein Instant Protein Powder</td>
</tr>
<tr>
<td>12</td>
<td>Nutricia: Casilan</td>
</tr>
<tr>
<td>13</td>
<td>Nutricia: Pro-stat</td>
</tr>
<tr>
<td>14</td>
<td>Nutricia: Protifar</td>
</tr>
<tr>
<td>15</td>
<td>Nutricia: Uti-stat</td>
</tr>
<tr>
<td>16</td>
<td>Panacea Biotec Ltd: Proseventy</td>
</tr>
<tr>
<td>17</td>
<td>Pharm D: Valens Myotein</td>
</tr>
<tr>
<td>18</td>
<td>Prosynthesis Laboratories: Unjury</td>
</tr>
<tr>
<td>19</td>
<td>Victus: Enterex Proteinex</td>
</tr>
<tr>
<td>20</td>
<td>Other protein supplement: Please specify</td>
</tr>
<tr>
<td>Gram Negative Bacteria</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>1 Acinetobacter sp.</td>
<td>23 Legionella sp.</td>
</tr>
<tr>
<td>2 Aeromonas sp.</td>
<td>24 Moraxella sp.</td>
</tr>
<tr>
<td>3 Alcaligenes sp.</td>
<td>25 Morganella sp.</td>
</tr>
<tr>
<td>4 Bacteroides sp.</td>
<td>26 Mycoplasma sp.</td>
</tr>
<tr>
<td>5 Bartonella sp.</td>
<td>27 Neisseria sp.</td>
</tr>
<tr>
<td>6 Bortetella sp.</td>
<td>28 Pasteurella sp.</td>
</tr>
<tr>
<td>7 Burkholderia sp.</td>
<td>29 Porphyromonas sp.</td>
</tr>
<tr>
<td>8 Campylobacter sp.</td>
<td>30 Prevotella sp.</td>
</tr>
<tr>
<td>9 Capnocytophaga sp.</td>
<td>31 Proteus sp.</td>
</tr>
<tr>
<td>10 Chlamydia sp.</td>
<td>32 Providencia sp.</td>
</tr>
<tr>
<td>11 Citrobacter sp.</td>
<td>33 Pseudomonas sp.</td>
</tr>
<tr>
<td>12 Coxiella sp.</td>
<td>34 Ralstonia sp.</td>
</tr>
<tr>
<td>13 Ehrlichia sp.</td>
<td>35 Rickettsia sp.</td>
</tr>
<tr>
<td>14 Eikenella sp.</td>
<td>36 Salmonella sp.</td>
</tr>
<tr>
<td>15 Enterobacter sp.</td>
<td>37 Salmonella sp.</td>
</tr>
<tr>
<td>16 Escherichia sp.</td>
<td>38 Serratia sp.</td>
</tr>
<tr>
<td>17 Francisella sp.</td>
<td>39 Shigella sp.</td>
</tr>
<tr>
<td>18 Fusobacterium sp.</td>
<td>40 Stenotrophomonas sp</td>
</tr>
<tr>
<td>19 Hafnia sp.</td>
<td>41 Streptobacillus sp.</td>
</tr>
<tr>
<td>20 Helicobacter sp.</td>
<td>42 Vibrio sp</td>
</tr>
<tr>
<td>21 Haemophilus sp.</td>
<td>43 Yersinia sp.</td>
</tr>
<tr>
<td>22 Klebsiella sp.</td>
<td>44 Other, please specify</td>
</tr>
<tr>
<td><strong>(Do NOT include)</strong></td>
<td></td>
</tr>
<tr>
<td>Actinomyces sp.</td>
<td></td>
</tr>
<tr>
<td>Aerococcus sp.</td>
<td></td>
</tr>
<tr>
<td>Bacillus sp.</td>
<td></td>
</tr>
<tr>
<td>Clostridium sp.</td>
<td></td>
</tr>
<tr>
<td>Corynobaacterium sp.</td>
<td></td>
</tr>
<tr>
<td>Diphteroids sp.</td>
<td></td>
</tr>
<tr>
<td>Enterococcus sp.</td>
<td></td>
</tr>
<tr>
<td>Erysipelothrix sp.</td>
<td></td>
</tr>
<tr>
<td>Lactobacillus sp.</td>
<td></td>
</tr>
<tr>
<td>Listeria sp.</td>
<td></td>
</tr>
<tr>
<td>Nocardia sp.</td>
<td></td>
</tr>
<tr>
<td>Peptostreptococcus/Peptococcus sp.</td>
<td></td>
</tr>
<tr>
<td>Propionibacterium sp.</td>
<td></td>
</tr>
<tr>
<td>Rhodococcus sp.</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus sp.</td>
<td></td>
</tr>
<tr>
<td>Streptococcus sp.</td>
<td></td>
</tr>
</tbody>
</table>
The RE-ENERGIZE® Study

Serious Adverse Events (SAE) - Initial Report Worksheet

Go to the REDCap SAE forms and complete the INITIAL SAE report. Save, print off and fax to CERU at 613 548 2428 attention: Project Leader within 24 hours of becoming aware of the event.

Complete one form for EVERY adverse event that is Serious and Unexpected or Related. Report only those SAEs that occur from the time of randomization to the end of the study period (10 days post last successful grafting or until ICU/burn unit discharge or 6 months from ICU admission, whatever comes first).

**Patient Information**

<table>
<thead>
<tr>
<th>Site number</th>
<th>Initials</th>
<th>Male</th>
<th>Height (cm)</th>
<th>Name of Site Investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolment #</td>
<td>DOB</td>
<td>Female</td>
<td>Weight (kg)</td>
<td>Person Reporting SAE</td>
</tr>
</tbody>
</table>

Date (yyyy/mm/dd)

**Description of Serious Adverse Event Reported**

(only one per form)

**Seriousness** (select all that apply)

- Patient died --> please document date in Outcomes
- Life threatening
- Requires or prolongs hospitalization
- Results in persistent or significant disability/incapacity
- May require medical or surgical intervention to prevent one of other outcomes.
- Congenital anomaly/birth defect
- Other serious medical event

**Outcomes** (at the time of initial report) - select only one

- Complete recovery/return to baseline - Date of recovery
- Alive with sequelae
- Death - death date
- SAE persisting
- Unknown/lost to follow-up

**Action taken with Study Supplement** (select only one)

- None (including not on study supplement)
- Dose reduced, interrupted or therapy delayed
- Study Supplement stopped permanently due to SAE

**Relationship of SAE to Study Supplement**

- Not related
- Possibly related
- Unlikely related
- Probably related

**Action taken** (select all that apply)

- Complete Follow up/Final report within required timelines

Print Form

Version: August 17, 2011
Go to the REDCap SAE forms and complete the Follow-up or Final SAE report. Save, print off and fax to CERU at 613 548 2428 attention: Project Leader within **10 days of becoming aware of SAE.** To be completed by the Site Investigator for **EVERY** initial SAE that was reported to CERU.

<table>
<thead>
<tr>
<th>Patient Identification</th>
<th>Site #</th>
<th>Enrol. #</th>
<th>Initials</th>
<th>SAE #</th>
</tr>
</thead>
</table>

Past medical history, allergies, co-morbid illness and reason for admission to hospital

Admitting diagnosis to ICU and chronological events leading to the SAE

Chronological events proceeding SAE until time of this report

- Further details attached

**Concomitant Medications** (List all concomitant medications given within 48 hours preceding the onset of the event)

**Laboratory Results and Investigations** (Related to the SAE)

- No relevant results to report
The RE-ENERGIZE\textsuperscript{©} Study

Serious Adverse Events (SAE) - Follow-up/Final Report Worksheet

Relationship of SAE to study supplement
- Not related
- Possibly related
- Unlikely related
- Probably related

Rationale for relationship of SAE to study supplements vs. progression of underlying illness (based on timing of supplement, SAE, etc...)

Action taken with Study supplement
- None (including not on study supplement)
- Dose reduced, interrupted or therapy delayed
- Study Supplement stopped permanently due to SAE

Action taken
- None
- Hospitalization
- Uncertain
- IV fluids
- Procedure or physical therapy
- Other, specify below

Outcomes (at time of this report)
- Complete recovery/return to baseline - Date or recovery yyyy-mm-dd
- Alive with sequelae yyyy-mm-dd
- Death - death date yyyy-mm-dd
- SAE persisting yyyy-mm-dd
- Unknown/lost to follow-up

Action taken
- Complete recovery/return to baseline
- Alive with sequelae
- Death
- SAE persisting
- Unknown/lost to follow-up

Event Reported to IRB
- Yes
- No
- N/A

For Medical Monitor
- Agree with Site Investigator report/assessment
- Disagree with Site Investigator report/assessment

Comments:

Further Details Concerning the SAE
- No further details to report