

A RandomizEd Trial of ENtERal Glutamine to  
minimIZE Thermal Injury

# Study Procedures Manual

Intended Audience: Site study staff who are responsible for the day to day operation of the study and collection and entry of study data into the electronic data capture systems, i.e. Research Coordinators, Site Investigators, sub-Investigators, Data Entry staff

This study is registered at [Clinicaltrials.gov](http://Clinicaltrials.gov).  
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**Critical Care  
Nutrition**



**Clinical Evaluation  
Research Unit**

## **Document History**

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## Study Contacts

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All questions related to study procedures should be directed to the Project Leaders (PL). North American sites should direct question to the Global Project Leader. European sites should direct questions to the European Project Leader.

PLEASE NOTE: the Project Leaders are blinded. Please take care not to unblind the PLs in your communications, written or verbal.

In the event you are unable to reach the respective Project Leader, please contact the Principal Investigator (PI) or European Partner.

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

## Glossary

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

## **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 2<sup>nd</sup> and/or 3<sup>rd</sup> degree burns requiring skin grafting. For patients age 18 – 59 years we require a TBSA (Total Body Surface Area)  $\geq 20\%$ , 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  $\geq 10\%$ .

### **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  $\geq 7$  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

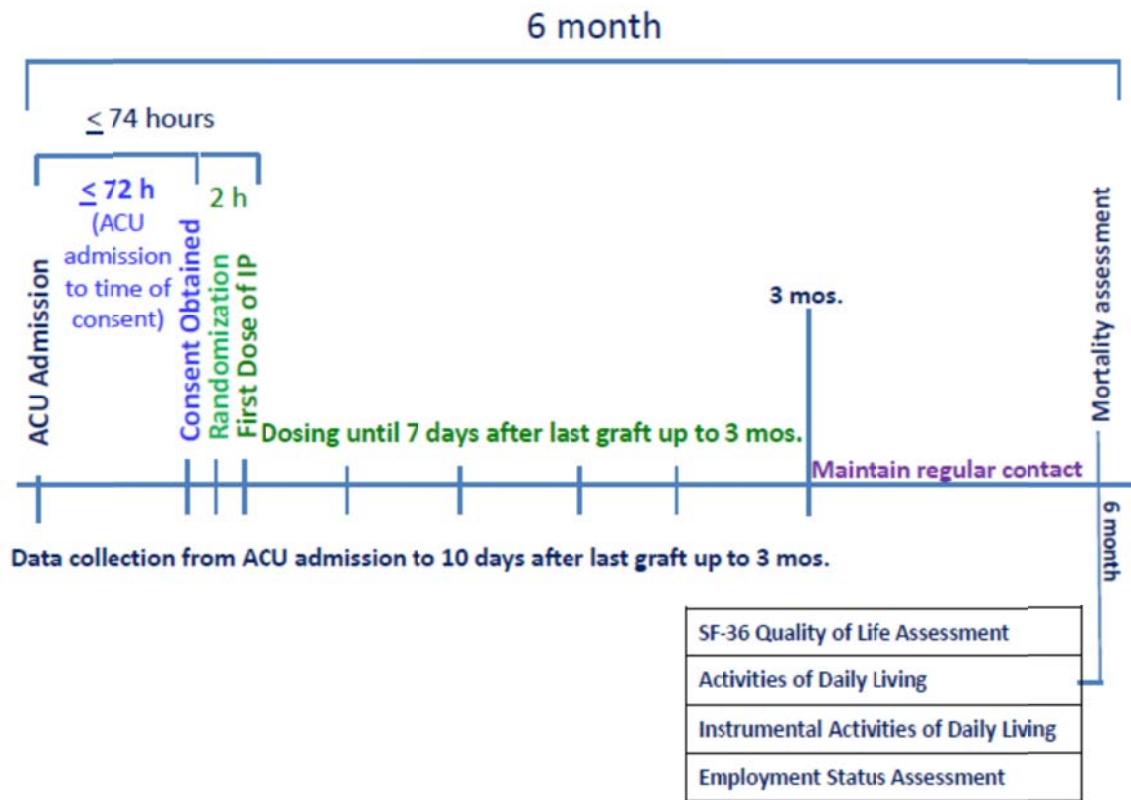


## Data processing and Statistical analysis

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.



## Site Study Staff

Throughout this document we refer to different roles associated with the completion of each task, i.e. Site Investigator, sub-Investigator, Research Coordinator, Dietitian, and Pharmacist. We acknowledge that one person may fulfill more than one role.

Example:

Dietitian refers to the team member responsible for assessing and monitoring the patients' nutritional needs during the course of the study. This staff member does not have to be a registered dietitian. At many sites, this will be the Investigator, sub-Investigator, or another staff member.

If you are the person fulfilling the duties associated with a particular role, the instructions in this manual attributed to that role apply to you.

Please ensure the Delegation of Authority log accurately reflects the tasks for which each team member is responsible.

## 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:

- 1) Signed Protocol Signature Page
- 2) Fully-executed Site Agreement
- 3) Ethics Board (REB/IRB) approval
- 4) Ethics approval of Informed Consent Forms (ICFs)
  - a. Country specific regulatory forms
  - b. Canada: REBA, CTSI, and QIUF
- 5) Regionally: Local requirements
- 6) CVs & medical licenses for the Site Investigator and sub-Investigators
- 7) Signed Delegation of Authority Log ( Appendix A)
- 8) Documentation of study specific training
- 9) Local laboratory reference ranges
- 10) Local laboratory accreditation

### **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. sub-Investigator, 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).

## Site Activation

Once the requisite regulatory documents 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, pharmacists, site investigators, sub-Investigators). At this point the site is considered activated and may initiate recruitment activities.

## 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
  - 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.
- Investigator oversight and review of all study specific assessments and investigations.
- Allow monitoring, auditing & regulatory inspections
- Perform Severity of Burn and Grafting Assessments
  - 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 B) and documented as percentage of Total Body Surface Area (%TBSA) to confirm eligibility. This assessment must be confirmed by the SI or sub-I.
  - Initial Grafting Assessment  
After written consent has been obtained, the responsible surgeon/physician must assess the deep 2<sup>nd</sup> and/or 3<sup>rd</sup> degree burn using the Lund and Browder chart (see Appendix B) to determine the %TBSA expected to require grafting. This assessment must be confirmed by the SI or sub-I.
- Final Grafting Assessment  
At the end of the study period, defined as  $\geq 10$  days post last successful graft, using the Lund and Browder chart (see Appendix B) the surgeon/physician must

assess the %TBSA that actually required grafting. This assessment must be confirmed by the SI or sub-I.

The Site Investigator and any applicable delegates at the research site are also responsible for:

- Supplying a computer and internet access to logon to the CRS and REDCap™
- Maintenance of local computer equipment
- Notifying CERU of any technical difficulties or malfunctions related to the CRS or REDCap™
- Screening & enrolling eligible patients
- Informed Consent of potential research participants/substitute decision makers
- Data collection and entry into the edcs REDCAP™
- Data query resolution

The Clinical Evaluation Research Unit (CERU) will provide training, procedures and tools for study implementation, access to the CRS and REDCap™, and ongoing support of research activities at the site.

## **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.



(North America)



(Europe)

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.



(North America)



(Europe)

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.

## **Investigational Product Handling and Administration**

### **Duration of study treatment**

Patients will receive the study intervention from randomization through  $\geq 7$  days post last successful graft, or ACU discharge (discharged to a location in the hospital where they will not continue to receive the same level of care), or 3 months from ACU admission, whichever comes first. If at 7 days post graft, there is question whether the patient will require additional grafting, IP will continue to be administered until the determination is made that no additional grafting is required. 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:

- Patients with a BMI  $<35$  will receive 0.5 g/kg/day of IP based on pre-burn dry weight (actual or estimated).
- Patients with a BMI  $\geq 35$  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 dose is the change, by the clinical team, in the weight used to dose clinical treatments. Below are examples of events that may trigger a change in IP dose:

- Amputation
- Greater than 10% weight loss.

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 E.

## 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 F (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.

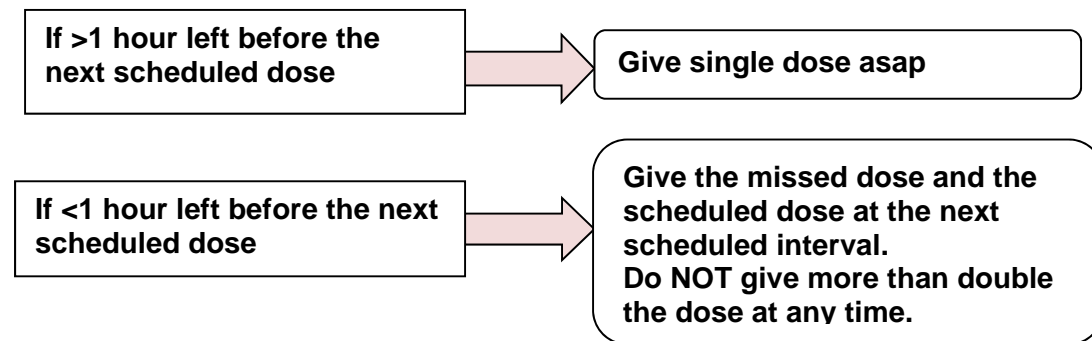
NOTE: There should be no difference in the taste of the glutamine and the maltodextrin.

**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 G) 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.

## Implementation and Recruitment

### **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, as designated on the Delegation of Authority log, who 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 2<sup>nd</sup> and/or deep 3<sup>rd</sup> 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 and confirmed by the SI/sub-I.

<b>The following injuries fulfill this criteria</b>	<b>Do NOT include the following burns</b>
<b>Thermal burn injuries:</b> <ul style="list-style-type: none"> <li>• Scald</li> <li>• Fire (includes both Flame and Flash)</li> <li>• Radiation</li> <li>• Chemical</li> <li>• Unknown</li> <li>• Other, specify _____</li> </ul>	<b>Do Not include burn injuries from:</b> <ul style="list-style-type: none"> <li>• High voltage electrical contact (see exclusion #7.)</li> <li>• Frostbite</li> <li>• Stevens-Johnson Syndrome (SJS)</li> <li>• Toxic Epidermal Necrolysis (TEN)</li> </ul>

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  $\geq$  20%
- b. Patients 18 – 59 years of age with TBSA  $\geq$  15% WITH inhalation injury (see table below for diagnosis of inhalation injury)
- c. Patients  $\geq$  60 years of age with TBSA  $\geq$  10%

Diagnosis of inhalation injury requires both of the following 2 criteria:

1) History of exposure to products of combustion;	2) Bronchoscopy confirming one of the following: <ul style="list-style-type: none"> <li>• carbonaceous material</li> <li>• edema or ulceration</li> </ul>
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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.

Note: please do not enroll patients who will not be reachable 6 months after admission to the ACU, i.e. homeless, or illegal aliens. 6 Month mortality is the primary outcome of this study.

- **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 ACU is greater than 24 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.*

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

- **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

Criteria	Points assigned		
	1	2	3
<b>Total Bilirubin</b> SI units	< 2mg/dL or < 34 µmol/L	2 - 3 mg/dL or 34 – 51 µmol/L	> 3 mg/dL or > 51 µmol/L

<b>Serum Albumin</b> SI units	> 3.5 g/dL or > 35 g/L	2.8—3.5 g/dL 28 – 35 g/L	< 2.8 g/dL or < 28 g/L
<b>Prothrombin time or INR</b>	< 4 seconds < 1.7	4 – 6 seconds 1.7 – 2.3	> 6 seconds > 2.3
<b>Ascites*</b>	Absent	Slight	Moderate
<b>Encephalopathy</b>	None	Moderate	Severe
* Refer to ultrasound results. If ascites has been drained in the past, it should be considered Moderate.			

- **Pregnant or lactating females (urine/blood tests for pregnancy will be done on all women of childbearing age by each site as part of standard of ACU practice)**

- **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.*

- **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 from high voltage electrical contact are very different from thermal injuries and these patients must be excluded.*

- **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.*

- **Patients with extreme body sizes: BMI < 18 or > 50 kg/m<sup>2</sup>**

*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.*

- **Enrollment in another industry sponsored ICU intervention study**

*(Co-enrollment in all non-randomized (observational) 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. We can not allow co-enrollment in any industry sponsored trials of novel therapeutics or biologics, normally these kind of trials do not permit co-enrollment either).*

- **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.*

- **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:

- a) A guardian appointed by the court if the court order authorizes the guardian to make health care decisions
- b) A person with a "power of attorney for personal care" authorizing him or her to make health care decisions
- c) A representative appointed by the Consent and Capacity Board (any person may apply to the board to be appointed as the substitute decision maker)
- d) A spouse or partner
- e) A child or parent (custodial parent if the patient is a minor)
- f) A brother or sister
- g) 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:**

- Familiarize yourself with the subject's history.
- Approach bedside nursing staff/medical staff for an update on the family's involvement and their degree of knowledge of the subject's condition.
- 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:

- 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.
- 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.
- The study team member obtaining consent is qualified to do so, and is knowledgeable in the study procedures.
- Review the study details with the SDM in a quiet, private location.
- Do not coerce or unduly influence the SDM for the patient to participate, or continue to participate in the study.
- 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.
- Provide a copy of the consent form to the patient's SDM and allow for ample time to read it and ask questions.
- Ask the patient's SDM questions to assess their comprehension of the material reviewed. Ensure she/he fully understands the information.
- Ascertain the patient's SDMs willingness to participate. Document the decision of any patient's LAR/SDM who declines to participate.
- Sign and record the date and time written informed consent was obtained:
  - From the patient's SDM
  - By the person conducting the informed consent discussions
- Document the consent process in the patient's medical chart.
- Provide the patient's SDM with a copy of the signed document.
- 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 H for a patient/alternate 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

## **Randomization**

### **Timing of Randomization**

All patients should be randomized as soon as possible following receipt of written informed consent. Treatment allocation will be assigned through the Central Randomization System (CRS). Study procedures should be initiated as soon as the patient is randomized. The study intervention should be started within 2 hours after randomization.

### **Randomizing a patient in the CRS**


All patients will be randomized to the study using the CRS. Refer to the Electronic Data Capture Systems in the following section for detailed instructions on navigating the CRS.

### **Medical/Physician Orders**


Following randomization and pharmacy notification, study specific Medical/Physician Orders should be prepared and filed in the medical chart (see example in Appendix I).

## 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/> or via: <http://www.criticalcarenutrition.com>



2 **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/> or via: <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 training on 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.

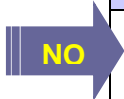
Patient eligibility and suitability must be determined by the Site Investigator or sub-I. Sites are encouraged to use the **Inclusion/Exclusion criteria eCRF worksheets** to document screening and confirmation of eligibility by the SI/sub-I.

**Types of Patients to be entered into the CRS**

- **All patients who meet the inclusion criteria** must be entered into the CRS, including:
  1. patients that do not meet any exclusion criteria and consent is obtained (Randomized patients)
  2. patients that do not meet any exclusion criteria and consent is **not** obtained (Eligible but Not Randomized patients)
  3. patients that meet an exclusion criteria (Not Eligible patients)

The table below provides several examples of the types of patients who should be entered into the CRS.


Inclusion Criteria Present	Exclusion Criteria Present	Informed Consent Obtained	Enter into CRS	Comments
✓	✗	✓	✓	Randomized
✓	✗	✗	✓	Eligible but Not Randomized
✓	✓	<b>Exclusion criteria met - Do not approach for consent</b>	✓	Not Eligible
✗	✗	<b>Inclusion criteria Not met - Do not approach for consent</b>	✗	<b>Do Not Enter into CRS</b>



<p>Each patient entered into the CRS, will receive a <b>screening number</b>. The screening numbers are assigned sequentially in an 8-character format:</p> <p style="text-align: center;">“Q” indicates the patient is being screened but <b>not randomized</b></p> <p style="text-align: center;">↓</p> <p style="text-align: center;">1002 - Q005</p> <p style="text-align: center;"> <span style="margin-right: 40px;">{ Site #</span> <span>{ Patient #</span> </p>	<p>If the patient is subsequently <b>randomized</b>, they will also be issued a <b>randomization number</b>. The randomization IDs are assigned sequentially in an 8-character format:</p> <p style="text-align: center;">“R” indicates the patient has been <b>randomized</b></p> <p style="text-align: center;">↓</p> <p style="text-align: center;">1002 - R005</p> <p style="text-align: center;"> <span style="margin-right: 40px;">{ Site #</span> <span>{ Patient #</span> </p>
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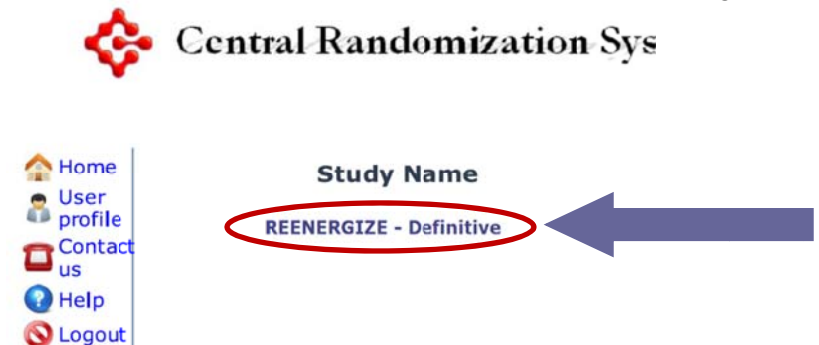
## Accessing & Entering a Patient in the CRS

URL: <https://ceru.hpcvl.queensu.ca/CRS/>



To access the CRS enter your assigned User name and Password. Click **LOGIN**.

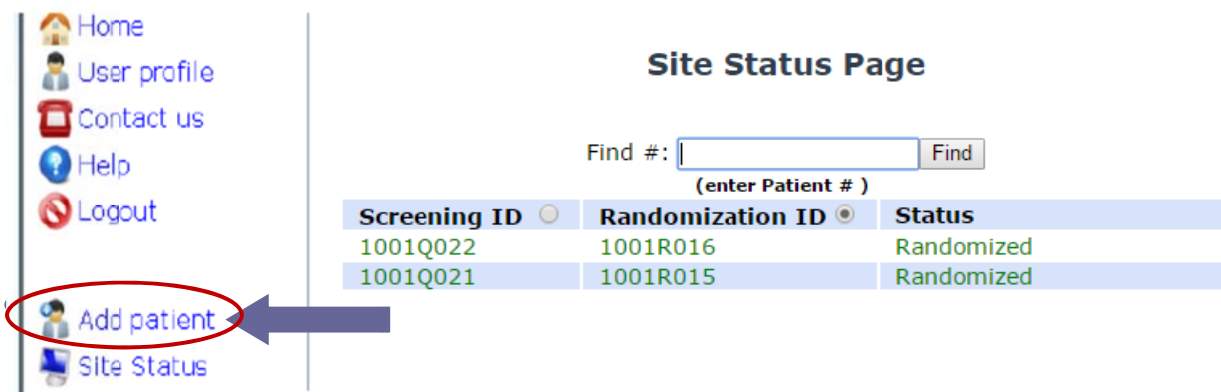
Once you have logged in successfully, you will be brought to the **Home** screen.



The **Home** screen lists all clinical trials your site is participating in with CERU that are using the CRS. Click on **RE-ENERGIZE - Definitive**.

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

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



Screening ID	Randomization ID	Status
1001Q022	1001R016	Randomized
1001Q021	1001R015	Randomized

Each patient entered in the CRS will have a status associated with it. There are 5 possible designations:

- 1) **Randomized:** The patient was eligible, consent was obtained and the patient was enrolled into the study.
- 2) **In Progress:** Inclusion data only have been entered.
- 3) **Eligible:** Inclusion and Exclusion data have been entered, but Pre-Randomization form is not completed.
- 4) **Not Eligible:** Inclusion and Exclusion data have been entered and patient meets an Exclusion criteria.
- 5) **Eligible but Not Randomized:** This patient was eligible but consent was not obtained.

## Site Status Page

Find #:

(enter Patient # )

Screening ID	Randomization ID	Status
1002Q001	1002R001	Randomized
1002Q005		Eligible but Not Randomized
1002Q004		Not Eligible
1002Q003		In Progress
1002Q002		Eligible

## Inclusion Criteria

After selecting 'Add patient', you will be brought to the **Inclusion Criteria form**. Complete the fields by clicking on the appropriate radio buttons. Then click 'Save'.

- Home
- User profile
- Contact us
- Help
- Logout
- Add patient
- Patient List

### Inclusion Form

A subject will be eligible for inclusion in this study only if all of the following criteria apply:

1. Deep 2nd and/or 3rd degree burns requiring skin grafting	<input type="radio"/> Yes <input type="radio"/> No
2. Patient meets one of the following criteria	<input type="radio"/> Yes <input type="radio"/> No
a. Patients 18 - 59 years of age with TBSA ≥ 20%	<input type="radio"/> a.
b. Patients 18 - 59 years of age with TBSA ≥ 15% WITH inhalation injury	<input type="radio"/> b.
c. Patients ≥ 60 years of age with TBSA ≥ 10%	<input type="radio"/> c.

- 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.

Exclusion Form	
A subject will not be eligible for this study if any of the following criteria apply:	
1. > 72 hrs from admission to Acute Care Unit to time of consent.	<input type="radio"/> Yes <input checked="" type="radio"/> No
2. Patients younger than 18 years of age.	<input type="radio"/> Yes <input checked="" type="radio"/> No
3. In patients without known renal disease, renal dysfunction defined as a serum creatinine >171 mmol/L 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 mmol/L 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.	<input type="radio"/> Yes <input checked="" type="radio"/> No
4. Liver cirrhosis - Child's class C liver disease	<input type="radio"/> Yes <input checked="" type="radio"/> No
5. Pregnancy (urine/blood tests for pregnancy will be done on all women of childbearing age by each site as part of standard ICU practice).	<input type="radio"/> Yes <input checked="" type="radio"/> No
6. Contraindication for EN (intestinal occlusion or perforation, intra-abdominal injury).	<input type="radio"/> Yes <input checked="" type="radio"/> No
7. Patients with injuries from high voltage electrical contact.	<input type="radio"/> Yes <input checked="" type="radio"/> No
8. Patients who are moribund (not expected to survive the next 72 hours).	<input type="radio"/> Yes <input checked="" type="radio"/> No
9. Patients with extreme body sizes: BMI < 18 or > 50 kg/m <sup>2</sup> .	<input type="radio"/> Yes <input checked="" type="radio"/> No
10. Enrolment in another industry sponsored ICU intervention study (co-enrollment in academic studies will be considered on a case by case basis)	<input type="radio"/> Yes <input checked="" type="radio"/> No
11. Received glutamine supplement for > 24 hrs prior to randomization	<input type="radio"/> Yes <input checked="" type="radio"/> No
12. Known allergy to maltodextrin, corn starch, corn, corn products or glutamine.	<input type="radio"/> Yes <input checked="" type="radio"/> No

Click on the radio buttons to select 'Yes; or ;No; for each exclusion criterion.

If you click “Yes” to any one criteria, this patient is not eligible for the study. Click **SAVE**. No more data entry required for this patient.

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, will NOT be included.***

***For such patients, please enter them in the CRS and select ‘Yes’ for exclusion #11.***

If a patient is found to meet an exclusion criteria after the patient is randomized, 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 approaching for consent:

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

If the SDM/patient was approached for consent, was consent obtained?

If 'No', record the primary reason consent was not obtained:

- Too Overwhelmed
- Not interested
- Did not respond (timed out)



iv. Other, please specify

If consent IS obtained, complete all fields on the Pre-Randomization form.

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

Dates are to be entered in the format YYYY-MM-DD, or click in the box to activate the date picker feature and select the date from the calendar.

All times should be recorded using the 24 hour clock. Times must include 4 digits. Enter leading zero(s) for times prior to 10 AM.  
Example: 12:23 AM is entered as 00:23 and 7:15 AM entered as 07:15.  
Click **SAVE**.

- 2) Record the consent date/time
- 3) Record the patient's weight and height (to the nearest two decimal points).
- 4) Enter the patient's pre-burn dry weight. .
- 5) Using the dropdown menu, indicate how each the weight and height were obtained:
  - a. Measured
  - b. Estimated (obtained verbally from a healthcare professional or family)
  - c. Unknown (there is no record of how the weight or height was obtained)
- 6) Select the unit of measure used for both weight and height by clicking on the appropriate radio button:
  - a. Weight - either kg or pounds

Height - either cm or inches

Once you click on the "**Save**" 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 (IP should start within 2 hrs after randomization)***



- Home
- User profile
- Contact us
- Help
- Logout

- Add patient
- Patient List
- Patient Status

This is a test site

## Randomization Confirmation

You have **successfully** RANDOMIZED this subject to the REENERGIZE trial

<b>Randomization #:</b>	1001R012
<b>Randomization Date:</b>	2016-02-11 14:32 EST
<b>Height:</b>	150.00 cm
<b>Weight:</b>	45.00 kg
<b>BMI:</b>	20
<b>Dosing Weight:</b>	45 kg

[Print page for your records](#)

**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. Select 'Print page for your records'.

From the Randomization Confirmation form you can add a new patient, return to the Patient Status Page, or view all patients entered in the CRS by clicking on the corresponding menu option on the left hand side.

The Patient Status Page will show you which forms have been completed for that patient and their status.



- Home
- User profile
- Contact us
- Help
- Logout

- Add patient
- Patient List

This is a test site

## Patient Status Page

- Inclusion Form
- Exclusion Form
- Pre-Randomization Form
- Randomization Confirmation

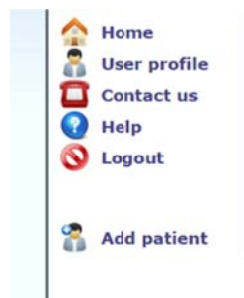
You can open a specific form by clicking on it.

Each form has a status assigned:

Status	Symbol	Description
Completed	✓	All data has been completed and saved.
Not Completed	✗	Data has not yet been entered on the form.
Locked	🔒	The patient has been randomized and the form is locked. (Data is no longer able to be edited by the site user.)

If you have made an error and the form is locked please notify the Project Leader to have the data corrected.

"The Patient List allows you to view all patients entered in the CRS and their status. To view a patient, click their Screening ID or their Status.



**Site Status Page**

Find #:  Find

(enter Patient # )

Screening ID	Randomization ID	Status
1001Q004	1001R002	Randomized
1001Q001	1001R001	Randomized
1001Q005		Eligible but Not Randomized
1001Q003		Eligible but Not Randomized
1001Q002		Not Eligible

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

You will then be brought to the Patient Status screen.

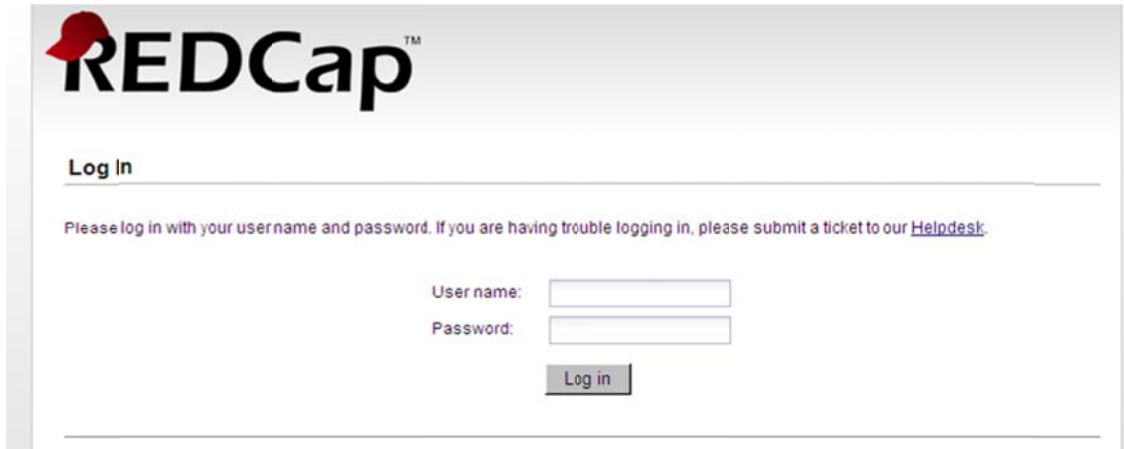
All patient data collected following randomization must be entered on to the eCRF (REDCAP™).

## REDCap™ Data Entry

The REDCap™ (**R**esearch **E**lectronic **D**ata **C**apture) is a web-based system used for the RE-ENERGIZE Study.

REDCap™ can be accessed at the REDCap™ login link

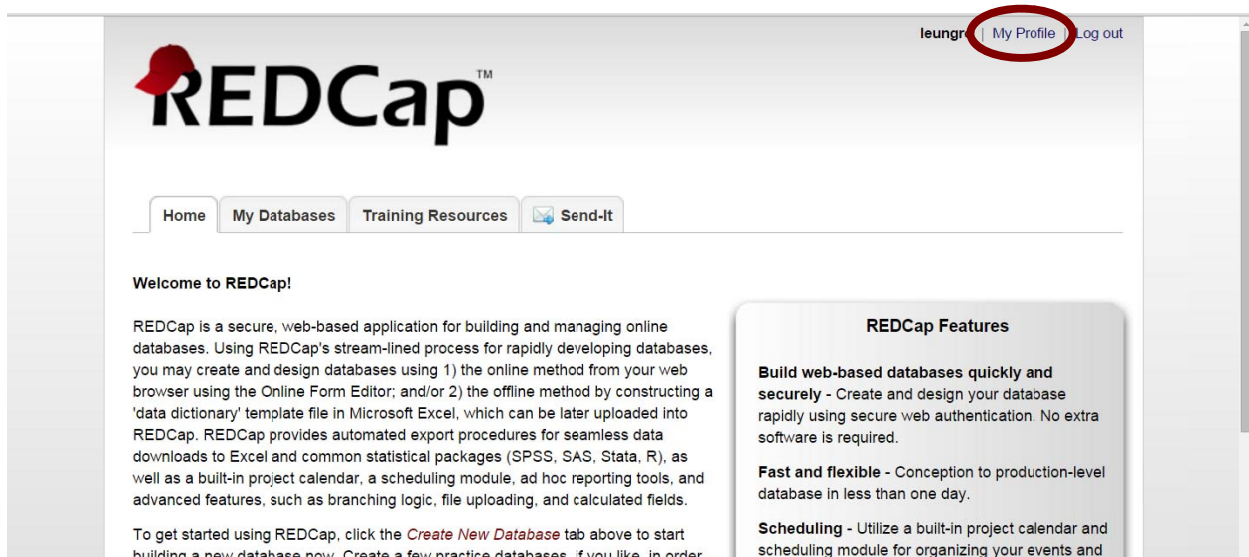
<https://ceru.hpcvl.queensu.ca/EDC/redcap/>.



The screenshot shows the REDCap login interface. At the top left is the REDCap logo. Below it is a 'Log In' heading. A message reads: 'Please log in with your username and password. If you are having trouble logging in, please submit a ticket to our [Helpdesk](#).' Below this are two input fields: 'User name:' and 'Password:'. A 'Log in' button is positioned below the password field.

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™.



The screenshot shows the REDCap user dashboard. At the top right, the user's name 'leungr' is visible, along with a 'My Profile' link circled in red and a 'Log out' link. The REDCap logo is prominently displayed on the left. Below the logo is a navigation bar with buttons for 'Home', 'My Databases', 'Training Resources', and 'Send-It'. The main content area features a 'Welcome to REDCap!' message, a detailed description of the system's capabilities, and a 'REDCap Features' section. The features listed are: 'Build web-based databases quickly and securely', 'Fast and flexible', and 'Scheduling'.

## 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.

Select “RE-ENERGIZE - Definitive”



My Databases	Records	Fields
CANTREAT	32	609
REENERGIZE_1	15	682
REENERGIZE - Definitive	51	609

### Data Entry Field

You will be brought to the ‘Data Entry’ page. Once your first patient is randomized, select ‘Arm 2: Laboratory Units’ from the dropdown box on the right following the word ‘from’.

REENERGIZE - Definitive

Query Module New: 0 Outstanding: 0 D/M Responded: 0 User Responded: 0 F.A.R.

Data Entry

Please choose a record below or enter a new one, after which you will be taken to the Event Grid so that you may enter forms for which you wish to enter data.

Choose an existing Patient ID  from Arm 1: Patient  
Arm 1: Patient  
Arm 2: Laboratory Units

Then select your site number from the dropdown box beside ‘Choose an existing Patient ID’.

Next you will see a grid with only one form, the Laboratory Units form. Click on the green dot to open the form

**My Databases**  
Database Information

---

**Data Entry Forms**

**Data Entry**  
- Add or modify a database record

---

**Applications**

---

**Resources**

Investigator Confirmation  
Apache II Calculator  
MAP Calculator  
Admin Functions

---

**Queries for Patient #1002**

New	0
Outstanding	0
D/M Responded	0
User Responded	0
F.A.R.	0
IT Staff	0
Resolved	0
Removed/Ignored	0

---

**Help & Information**

Helpdesk

### Data Entry: Event Grid

The grid below displays the form-by-form progress of data entered into the data events. You may click on the colored buttons to access that form for that event navigating to the [Define My Events](#) page.

**Patient ID "1002"**

Data Entry Form	Events for Arm 2: Laboratory Units
	Day 1
Baseline	
Organ Dysfunction	
Ventilation/RRT	
Burn Grafting Assessment	
Study Intervention	
Daily Monitoring	
Laboratory Units	<span style="color: green;">●</span>
Laboratory	

The laboratory units form will open.

Event Name: Day 1 (Arm 2: Laboratory Units)	
<b>Patient ID</b>	1002
<b>T-bilirubin</b>	<input type="radio"/> mg/dL <input type="radio"/> μmol/L
<b>Ammonia</b>	<input type="radio"/> μg/dL <input checked="" type="radio"/> μmol/L
<b>Serum Creatinine</b>	<input type="radio"/> mg/dL <input type="radio"/> μmol/L
<b>Glucose</b>	<input type="radio"/> mg/dL <input checked="" type="radio"/> mmol/L
<b>Urea</b>	<input type="radio"/> mg/dL <input type="radio"/> mmol/L
<b>Albumin</b>	<input type="radio"/> g/dL <input checked="" type="radio"/> g/L
<b>Lactate</b>	<input type="radio"/> mg/dL <input checked="" type="radio"/> mmol/L <input type="radio"/> mEq/L
<b>Platelets</b>	<input type="radio"/> 10 <sup>3</sup> /μL <input checked="" type="radio"/> 10 <sup>9</sup> /L
<b>WBC</b>	<input checked="" type="radio"/> 10 <sup>3</sup> /μL <input type="radio"/> 10 <sup>9</sup> /L

For each laboratory test listed, select the units the assay is reported in at your site.

This form is only completed once.

The left side of the screen is the main navigation panel. Select 'Data Entry' and click in the 'Choose an existing Patient ID' box to choose from a list of patients randomized at your site and ready for data entry.

**My Databases**  
Database Information

**Data Entry Forms**  
Data Entry  
- Add or modify a database record

**Applications**

**Resources**  
Apache II Calculator  
MAP Calculator  
Admin Functions

**Help & Information**  
Helpdesk  
General Help  
Video Tutorials  
If you are experiencing problems, please contact your database administrator.

**Query Module** New: 0 Outstanding: 0 D/M Responded: 0 User Responded: 0 F.A.R.

**Data Entry**

Please choose a record below or enter a new one, after which you will be taken to the Event Grid so that you may enter data for the selected entry forms for which you wish to enter data.

Choose an existing Patient ID [dropdown] from [Arm 1: Patient]

**NOTICE:**  
This database is currently a PRODUCTION database. Any data entered into the database. Any data entered into the database is pushed into production mode.

Kingston General Hospital  
1001R001 - Finalized  
1001R002 - Finalized  
1001R003 - Follow-Up Stage  
1001R004 - Follow-Up Stage  
1001R005 - Query Stage  
1001R006 - Query Stage  
1001R007  
1001R008  
1001R009  
1001R010  
1001R011  
1001R012  
1001R013  
1001R014  
1001R015

Click on the drop-down list to select a randomized patient.

### Event Grid Field

After you have selected a patient, you will be brought to the Event Grid. The Event Grid gives the user a snap shot 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.

Patient ID "1001R001"

< Previous Jan 10-Feb 08 Feb 09-Mar 09 Mar 10-Apr 08 Next >

Data Entry Form	Day 1 Jan 10	Day 2 Jan 11	Day 3 Jan 12	Day 4 Jan 13	Day 5 Jan 14	Day 6 Jan 15	Day 7 Jan 16	Day 8 Jan 17	Day 9 Jan 18	Day 10 Jan 19	Day 11 Jan 20	Day 12 Jan 21	Day 13 Jan 22
Baseline	●												
Organ Dysfunction	●												
Severity Of Burn Assessment	●												
Study Intervention	●												
Laboratory Units	●												
Nutrition Assessment/Timing	●												
Daily Monitoring	●	●	●	●	●	●	●	●	●	●	●	●	●
Daily Laboratory	●	●	●	●	●	●	●	●	●	●	●	●	●
Daily Nutrition Data	●	●	●	●	●	●	●	●	●	●	●	●	●
Study Blood Work				●			●						●
Burn Related Operative Procedures	●	●	●	●	●	●	●	●	●	●	●	●	●
Concomitant Medications	●	●	●	●	●	●	●	●	●	●	●	●	●
Microbiology				●	●	●	●	●	●	●	●	●	●
Ventilation/RRT	●												
Hospital Overview													
Protocol Violation	●	●	●	●	●	●	●	●	●	●	●	●	●
Survival Assessment													
Contact Log													

Use the buttons across the top of the grid to navigate between 30 study day segments







## Form Links

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

The screenshot shows the 'Data Entry Forms' navigation menu on the left, with 'Daily Monitoring' highlighted in red. The main form area displays the 'Daily Monitoring' form for Patient ID 1001R001. The form includes fields for 'Number of packets given' (value 3) and 'Route' (radio buttons for PO, EN, Not Given/Not Applicable). A 'reset value' link is visible next to the route options.

## Form Status

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 incomplete, unverified or complete. The status is indicated on the Event Grid Field using the following convention:

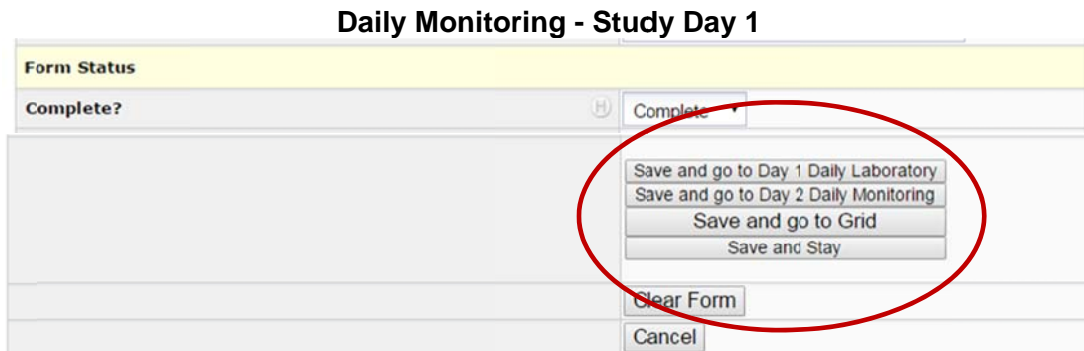
Form Status Legend	
	Incomplete
	Unverified
	Complete
	Locked




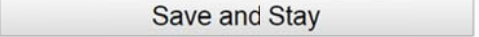
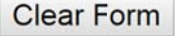
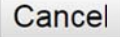
Incomplete (red dot)	No data has been entered on a form. Blanks forms will automatically be set to incomplete.
Unverified (yellow dot)	Data entry is partially completed on a form. The RC wants to double check data already entered on a form. Partially completed forms will automatically be set to unverified.
Complete (green dot)	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.
Locked (lock symbol)	Locked status will appear on all forms after all finalization checks are completed. Data on locked forms cannot be changed.

### Form Saving

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**



	This option will save your progress and bring you to the next form on the same study day. <i>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.</i>
	This option will save your progress and bring you to the same form on the next study day.
	This option will save your progress and return you to the Event Grid.
	This option will save your progress and allow you to continue working on that form.
	This option will allow you to clear the entire form in case the entire form was completed in error.
	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 any text field, **single click** anywhere in the box and type the 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 Available**' option. This includes:
  - Data that is unavailable because 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** just left of the field.

Editing existing Patient ID "1001R005"

Event Name: Day 1 (Arm 1: Patient)

Patient ID: 1001R005

Age:  years

Sex:  Male  Female

View data history

A window will pop up listing the data entry history for that field showing the date and time the data was entered, the user who entered the data, and the data entered at that time.

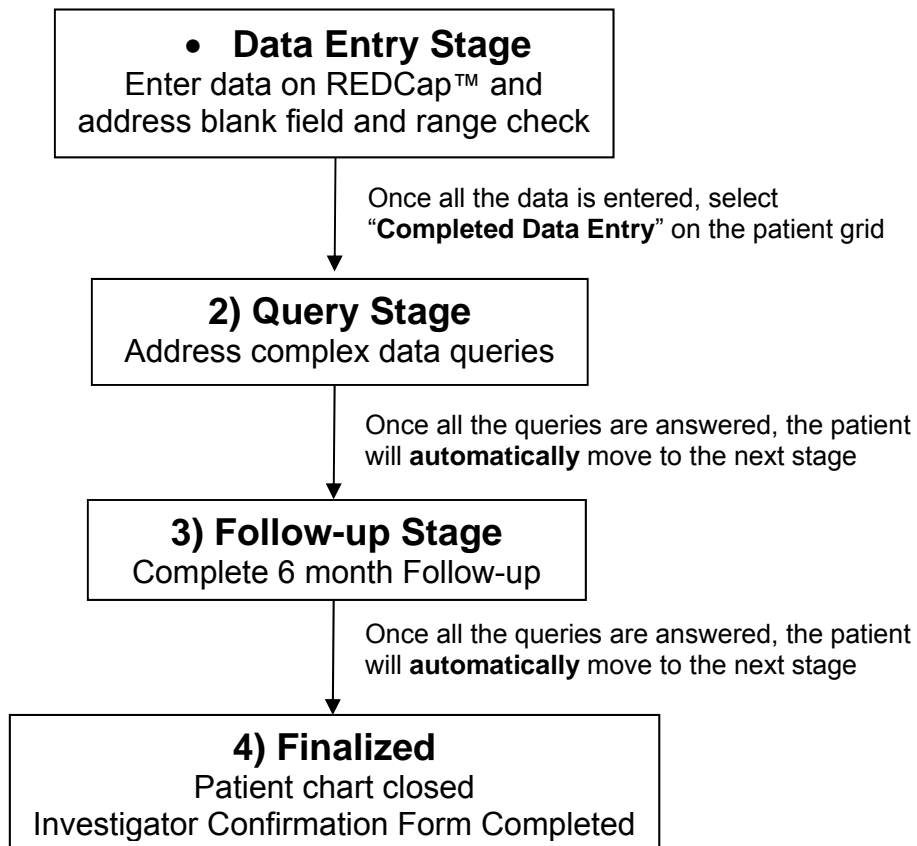
Data History for variable "sex"

Listed below is the history of all data entered for the variable "sex" for Patient ID "1001R005".

Date/Time of Change	User	Data Changes Made
4:16pm 03/15/2016	dansereauma	Male (1)
4:16pm 03/15/2016	dansereauma	Female (2)
4:49pm 01/15/2016	leunguser	Male (1)

## 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.



Once all data has been completed up to and including hospital overview (Month 6 follow-up excepted), and all simple queries such as missing fields and ranges have been resolved, the user can proceed to the 'Query Stage'. If all simple queries have been resolved the numbers in the query menu on the left hand side will all be '0'. To move to the 'Query Stage' click on the 'Completed Data Entry' button at the bottom of the Grid.

The screenshot shows the REDCap interface. On the left is a sidebar with 'Data Entry Forms', 'Applications', and 'Resources'. Under 'Resources', there is a section 'Queries for Patient #1001R001' with a list of query types and their counts (all 0). Below this is a 'Completed Data Entry' button circled in red. The main area shows a 'Contact Log' grid with rows for various forms and columns for dates. Red dots in the grid indicate incomplete data. A 'Form Status Legend' is located at the bottom right of the grid area, showing icons for Incomplete (red dot), Unverified (yellow dot), Complete (green dot), and Locked (lock icon).

Once the 'Completed Data Entry' button has been selected, REDCap™ will run checks to ensure certain data has been entered. 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 move to the "Query Stage".

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

The screenshot shows a warning message for Patient 10011004. The message reads: "Warning - There is 1 error preventing this patient's status from reaching Queries". Below this, it says "You must address each of these errors before the patient's status will reach Queries." A table lists the error: "Hospitalization Overview" form with the message "The Hospitalization Overview form must be completed." and a "Link to form" button labeled "Go to event".

Once all errors have been addressed the patient will enter the 'Query Stage' where complex data queries will fire. Once all queries have been resolved the patient will automatically move to the 'Follow-up Stage' and all forms excluding the Month 6 follow-up forms will be locked.

Data Entry Form	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
	Jun 17	Jun 18	Jun 19	Jun 20	Jun 21	Jun 22	Jun 23	Jun 24	Jun 25
Baseline	●🔒								
Severity Of Burn Assessment	●🔒								
Nutrition Assessment/Timing	●🔒								
Laboratory Units	●🔒								
Daily Monitoring	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒
Daily Organ Dysfunction	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒
Daily Laboratory	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒
Daily Nutrition Data	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒
Study Blood Work				●🔒			●🔒		
Burn Related Operative Procedures	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒
Blood Products	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒
Concomitant Medications	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒	●🔒

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 and we will unlock the form.

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.



**REDCap**  
 Logged in as leunguser | Log out  
 My Databases  
 Database Information

**Data Entry Forms**  
 Data Entry  
 - Add or modify a database record

**Applications**

**Resources**  
 Investigator Confirmation  
 Apache II Calculator

**Queries for Patient #1001R001**

New  
 Outstanding

**Clinical Evaluation Research Unit** • **KGH** Kingston General Hospital

**REENERGIZE - Definitive TEST**

**Data Entry: Event Grid**

The grid below displays the form-by-form progress of data entered into the database for one participant events. You may click on the colored buttons to access that form for that event. If you wish, you may navigate to the [Define My Events](#) page.

**Patient ID "1001R001"**

< Previous **Jan 10-Feb 08** Feb 09-Mar 09 Mar 10-Apr 08 Next >

Data Entry Form	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
	Jan 10	Jan 11	Jan 12	Jan 13	Jan 14	Jan 15	Jan 16

## Investigator Confirmation

**REENERGIZE** Randomization Number

**Investigator Confirmation Form**  
 (Go to REDCAP for e-version)

The data collected in the RE-ENERGIZE Case Report Forms were collected in accordance with the study protocol and established procedures. The data was collected under my supervision.

The data and statement are complete and accurate to the best of my knowledge.

Full Name of Investigator \_\_\_\_\_

Signature of the Investigator \_\_\_\_\_ Date (yyyy-mm-dd) \_\_\_\_\_

55

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 of the signed Investigator Confirmation form. File the original in your study files.

## **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

### **Duration of Data Collection**

Some data is collected from ACU admission through  $\geq 7$  days after the last graft, while other data is collected from ACU admission through  $\geq 10$  days after the last graft (stop of study intervention plus 3 days). See below for further clarification:

Until  $\geq 7$  days post last successful graft.

Data collected for  $\geq 7$  days post last successful graft must be collected until the study intervention has been stopped or 7 days after the last grafting operation, whichever is longer.

Until  $\geq 10$  days post last successful graft.

Data collected for  $\geq 10$  days post last successful graft must be collected until the study intervention is stopped plus 3 additional days or 10 days after the last graft, whichever is longer.

### **Patient/Alternate 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/alternate contact person(s) information sheet (Appendix H). It is ideal to obtain a alternate contact person(s) that lives with the patient and at least 2 alternate 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  $\geq 18$  years of age to be eligible to participate in The RE-ENERGIZE Study).

### Sex

Check the appropriate box (male or female).

### Ethnicity

Choose the appropriate patient ethnicity from the following list:

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

### APACHE II

Go to the following website <http://www.sfar.org/scores2/apache22.php> to calculate the APACHE II score. Record the calculated score. Reminder: 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.

### 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.

### 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.

### 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.



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).

Burn Injury Date and Time

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)

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%.

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:

- History of exposure to products of combustion
- Bronchoscopy revealing one of the following below the glottis
- Evidence of carbonaceous material
- Signs of edema or ulceration

High Dose Vitamin C Resuscitation

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.

**Organ Dysfunction form**

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

Vasopressors

Indicate whether or not the patient received vasopressors.

If 'Yes', select the highest dose received from the 3 groupings below:

- Dopamine  $\leq 5$   $\mu\text{g}/\text{kg}/\text{min}$  or  
Dobutamine (any dose)
- Dopamine 6 - 15  $\mu\text{g}/\text{kg}/\text{min}$  or  
Epinephrine  $\leq 0.1$   $\mu\text{g}/\text{kg}/\text{min}$  or  
Norepinephrine  $\leq 0.1$   $\mu\text{g}/\text{kg}/\text{min}$
- Dopamine  $> 15$   $\mu\text{g}/\text{kg}/\text{min}$  or  
Epinephrine  $> 0.1$   $\mu\text{g}/\text{kg}/\text{min}$  or  
Norepinephrine  $> 0.1$   $\mu\text{g}/\text{kg}/\text{min}$

If 'No', enter MAP (mean-arterial pressure), see below.

MAP (lowest)

Indicate the lowest MAP observed during the study day by selecting one of the options below:

- $< 70$  mmHg
- $\geq 70$  mmHg

If the MAP is not available you can calculate it using the formula:

$$\text{MAP} = 1/3 \text{ lowest systolic BP} + 2/3 \text{ corresponding diastolic BP}$$

*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
- $< 500$  mL/day
- $\geq 500$  mL/day
- Not Available

## **Ventilation/RRT form**

### **Invasive Mechanical Ventilation**

Duration of Data Collection

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

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

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)  $\leq 5\text{cmH}_2\text{O}$  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, 4, 5

#### Invasive Mechanical Ventilation #3, 4, 5

Follow the instructions as listed for Mechanical Ventilation start # 2 and stop # 2 for the third, fourth, and fifth episodes of mechanical ventilation, if applicable.

## **Renal Replacement Therapy**

### Duration of Data Collection

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

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

### 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 start date of RRT.

RRT stop date

Record one of the following:

1. Same as death date & time
2. At 3 months, still on renal replacement therapy (dialysis) in hospital
3. Continued past hospital discharge
4. Actual stop date →

If selecting 'Actual stop date', record the date RRT was permanently discontinued.

## **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 2<sup>nd</sup> and/or 3<sup>rd</sup> degree burn using the Lund and Browder chart (see Appendix B) 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 2<sup>nd</sup> and/or 3<sup>rd</sup> degree burn requiring grafting is an inclusion criteria. This should not be zero.*

#### Last Successful Graft

Indicate whether or not the last successful grafting was achieved

If 'Yes', enter the date in the format *yyyy-mm-dd*.

If the last successful graft was never achieved, select the reason:

- Death
- Withdrew Consent (including consent for data collection)
- Withdrew Life Sustaining Therapies
- Discharged without receiving a graft
- Receiving grafts after ACU discharge (< 3 mo.)
- Still receiving grafts in ACU at 3 months
  - Other, specify: \_\_\_\_\_

If 'death' or 'withdrew consent' is indicated, do not record the Final Assessment.

#### 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.

Exception: Do not record final assessment if 'Death' or 'Withdrew Consent' was indicated in the 'Last Successful Graft' section above.

#### 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  $\geq 10$  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 total at the time of assessment, %TBSA that required grafting as determined by the surgeon/physician on the date of the final/last assessment. This may be more, less or equal to the initial area expected to require grafting.

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?

If study intervention was started, indicate 'Yes' or 'No' by placing a check in the corresponding box.

If the study intervention is started more than 2 hrs after randomization, select 'Yes' and choose the reason from the list provided (below):

5. Pharmacy delay
6. Patient NPO for surgery
7. Awaiting tube placement and/or verification
8. Patient not available (procedure)
9. Nurse not available
10. Other (specify): \_\_\_\_\_

If you select 'Other', 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 the last dose of study supplement was administered in the format yyyy-mm-dd and hh:mm

The stop date should be at the end of the study period i.e.  $\geq 7$  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, dosing weight, and date/time the change occurred.

NOTE: IP prescription should not change.

Exception: if the patient has a change in body weight sufficient for the clinical team to alter dosage of clinical treatments (such as an amputation), 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 effect 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  $\geq 7$  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  $\geq 7$  days post last successful graft, or until ACU discharge, or until 3 months from ACU admission, whichever comes first. If at 7 days post graft there is question whether another grafting procedure may be required, the study intervention should continue until the determination is made that no additional grafting will occur.

### 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. This data is not collected on the Daily Monitoring form in record.

### Date

Enter the date corresponding to the calendar day for the data being collected. Select the study day in REDCap™ on which the recorded date appears to enter the data associated with this date.

### # Times the IP was given

Select the number of times, (0 to 10) from the dropdown list the, the study intervention was given on each study day.

### # Grams given

Select the # grams given, (5 to 30) from the drop down list, 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 select the # of grams administered.

### Route

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

- PO
- EN

### Percentage of study intervention received

Divide the total number of grams actually given on each study day 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 form**

If blood chemistry and/or hematology testing are conducted per standard of care. enter the indicated results 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  $\geq 10$  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 defined as +/- 24 hours from study day 21, 28, 35, 42, 49, 56, 63, 70, 77, 84 and 90.
  - 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.

#### Laboratory Values

Record the highest or lowest for the day as indicated below. Exception: record glucose taken closest to 8:00 AM:

- Creatinine (highest)
- Bilirubin, total (highest)
- Urea (highest)
- PaO<sub>2</sub>/FiO<sub>2</sub> (lowest)
- Glucose (8:00 AM)
- Ammonia (highest)
- Albumin (highest)
- Lactate (highest)
- Platelets (lowest)
- WBC (highest)
- WBC (lowest)

A. The PaO<sub>2</sub> and FiO<sub>2</sub> values should come from the same blood gas measurement.



- B. If there is only one WBC value recorded for the 24 hr period, record the one value as both the highest and lowest.

If a laboratory value is not available, select 'Not Available'.

NOTE: There are no protocolized laboratory tests for this study.

### **Nutrition Assessment/Timing form**

In the following section, the word dietitian refers to the team member responsible for assessing and monitoring the patients' nutritional needs during the course of the study.

### **Nutrition Assessment**

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

#### Duration of Data Collection

The nutrition prescription for calories and protein will need to be calculated by the dietitian at baseline (ACU admission or at the first dietitian assessment) and as needed thereafter.

#### Baseline Assessment

Record the date the baseline prescription was calculated. 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.

The dietitian is to use the patient's pre-burn dry weight when calculating the nutrition prescription. 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:

$$\text{Adjusted Body Weight (ABW)} = \text{Ideal Body Weight (IBW) based on a BMI of 25} \\ + [(\text{pre-burn dry weight} - \text{IBW}) \times 0.25]$$

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  $\geq 50\%$  burns, use 1.5g/kg/day to 2.5g/kg/day
- If  $< 50\%$  burns, use 1.2 g/kg/day to 2g/kg/day

#### Prescription changes

If the prescription changes from baseline during the study, indicate 'Yes' to the question '*Was another prescription made?*' and record the date, total calories prescribed (kcal), and total protein prescribed (grams) in the corresponding rows. Up to 6 prescriptions may be entered for each patient.

Note: Energy and protein requirements are independent of the enteral formula prescribed. Do NOT change prescription to accommodate an enteral 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  $\geq 10$  days post last successful grafting or ACU discharge or 3 months from ACU admission, whichever comes first.

This data is to be collected daily whether the patient is receiving enteral nutrition, parenteral nutrition or neither.

### 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:

- 1) NPO for endotracheal extubation or intubation or other bedside procedure. If 'Other' is indicated, please also check the 'Other' box and specify the reason.
- 2) NPO for operating procedure
- 3) NPO for radiology procedure
- 4) High NG drainage
- 5) Increased abdominal girth, abdominal distension or pt. discomfort
- 6) Vomiting or emesis
- 7) Diarrhea
- 8) No enteral access available / enteral access lost, displaced or malfunctioning
- 9) Inotropes, vasopressor requirement
- 10) Patient deemed too sick for enteral feeding
- 11) On oral feeds
- 12) Reason not known
- 13) Other , please specify\_\_\_\_\_

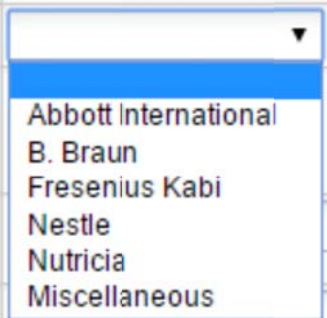
#### EN Formula

If 'Yes' to EN, enter the 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. In the event that the patient receives more than 3 formulas in one day, select the 3 formulas that provide the largest volumes.

In REDCap, there are more than 400 formulas in the dropdown lists.

First, select the company from the dropdown list. If the company is not in the list, select 'Miscellaneous'.

<b>Was Enteral Nutrition (EN) given?</b>	(H)	<input checked="" type="radio"/> Yes <input type="radio"/> No
<b>Formula 1 - Company</b>	(H)	<input type="text"/>
-Was a second EN formula given?	(H)	
<b>Total kilocalorie received from EN</b>	(H)	
<b>Total protein received from EN</b>	(H)	



Then select the formula from the list under the specified company. If the formula given is not in the EN Formula List, select 'Other (specify)' at the bottom of the list and enter the name of the formula in the space provided.

#### Total kilocalorie and protein received from EN

Record the total calories (kilocalories) and protein from all of the enteral nutrition formulas received in the study day.

- Do not include the calories from IV solutions, e.g. Dextrose (collected separately).
- Do not record the calories from Propofol (volume entered separately).
- Do not include protein supplements as part of this total (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, enter the name of the Protein Supplement. There is an extensive list in REDCap. If the Protein Supplement given is not in the list, select 'Other: please specify company and product name' and enter the information in the space provided..

##### 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.

NOTE: If protein supplements are given orally, record the calories and protein as part of oral nutrition adequacy. Please do NOT enter Protein Supplements received orally in the Protein Supplements received box. .

#### 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 record the calories from Propofol (volume entered separately).
- Do not include calories from IV fluids containing glucose

#### Oral Nutrition

##### Was Oral Nutrition given?

Indicate whether the patient received any oral intake today, Yes or No

If yes, indicate the adequacy of intake that was received via the oral route:

- A. 1- 24% of prescribed intake
- B. 25 - 49% of prescribed intake
- C. 50 - 74% of prescribed intake
- D. > 75% of prescribed intake
- E. Unknown

Oral intake and the percent adequacy received from oral intake should be recorded every study day the patient receives oral nutrition, even if they are also receiving EN and/or PN.

Propofol

Was Propofol received for  $\geq 6$  hours?

Indicate whether the patient received a continuous infusion of Propofol for  $\geq 6$ hrs, Yes or No.

Total volume of Propofol received

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

**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  $\geq 10$  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 by selecting 'Yes'.

Was the Operative procedure planned or unplanned?

Indicate if the operative procedure was planned or unplanned..

Type of operative procedure

Select the type(s) of operative procedure(s) performed on each study day from the taxonomy provided, see below 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

If you select 'Other', you must specify the procedure in the space provided.

**Concomitant Medications and Heart Rate**

The following information is recorded on the Concomitant medications form in REDCap™

### Heart Rate

Record both the highest and lowest heart rate observed on each study day.

### Duration of Data Collection

Administration of the following concomitant medications will be recorded in REDCap™ from admission to the ACU until  $\geq 10$  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

Record only the concomitant medications or medication types indicated below.

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** (morphine, fentanyl, hydromorphone, other narcotic)
- **Motility agents** (metoclopramide, erythromycin, domperidone, other)  
Do NOT record stool softeners here.
- **Oxandrolone**
- **Beta Blockers**

If 'yes' to Beta blockers, select received on each study day the from the list below:

- A. Esmolol
- B. Labetolol
- C. Metoprolol
- D. Propranolol
- E. Other (specify)

If 'Other' is selected, enter the name of the Beta Blocker in the text box.

Enter the dose, units, and route of administration for each beta blocker received.

### **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  $\geq 10$  days post last successful grafting or ACU discharge or 3 months from ACU admission, whichever comes first. 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.

#### Multiple samples on the same day

If multiple cultures are taken on the same study day, record all different Gram negative bacteremia reported. Do not record the same bacteria more than once on each study day, even if reported from specimen collected at different times on that day.

#### Gram Negative Culture #

Record the name, or the corresponding number on the taxonomy, of the Gram negative bacteria reported, refer to Appendix K for a list of **Gram negative bacteria to be recorded** and **Gram positive bacteria that are not be recorded**. If there is a Gram negative bacteria reported that 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 6: 30g Day 7: 20g <u>Day 8: 30g</u>	
3 Day Average	Total:	80g/3 days = 26.67g/day average (<28g)

A protocol violation should be reported on Day 7:

- A. dose received is less than 80% (28g) prescribed AND
- B. 3 day average is less than 80% (28g) prescribed

Do not report Day 6 or Day 8 in the example above:

- Dose received on those study days is NOT less than 80%

#### When to report

Protocol violations are to be reported from randomization until end of the study

duration ( $\geq$  10 days post last successful grafting or ACU discharge or 3 months from ACU admission, whichever comes first).

Do NOT report dose related Protocol Violations ( $<80\%$  over a 3 day average) on the following days:

- Day of randomization
- Day of discharge or end of study treatment (7 days post last successful grafting)
- Day of death

Are you reporting a Protocol Violation today?

Indicate if a protocol violation occurred today by selecting 'Yes'.

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
- Open label glutamine given
- Unapproved EN formula given
- Other, (specify)

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 acute care unit and hospital discharge, and mortality in REDCap™.

### ACU Discharge and readmission

This data is being collected until 3 months after ACU admission, to a maximum of 5 ACU admissions.

### Consent withdrawn/denied during this ACU stay?

Indicate if consent was withdrawn or denied during this ACU stay. If 'Yes', enter the date and time consent was withdrawn/denied and the type of withdrawal/denial from the list below:

- A. Stop intervention, continue data collection
- B. Stop intervention, stop data collection (keep previous data)
- C. Stop intervention, stop data collection (discard previous data)

### Did the patient die during this ACU stay?

If the patient died in ACU, select 'Yes' and enter 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 neither the death certificate nor the physician note is available, record the date and time of death charted in the nursing notes.*

Proceed to the Hospital discharge row.

If the patient was discharged from ACU, select 'No, patient discharged' and enter the date and time the patient was actually discharged from the ACU.

### Was the patient re-admitted to the ACU?

Select 'Yes' or 'No' to indicate whether the patient was readmitted to the ACU up to and including 3 months after ACU admission. If 'Yes', enter the date and time the patient was readmitted.

Continue to enter ACU discharge and readmission data until 3 months after the first ACU admission to a maximum of 5 admissions.

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 Month 6 Follow-Up Assessments form.

### Hospital Discharge

#### Did the patient die in Hospital?

If the patient died prior to hospital discharge, select 'Yes' and record the date and time of death.

If the patient was discharged from the hospital, select 'No, patient discharged' 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, select 'No, patient still in hospital at 3 months'. Proceed to Month 6 Follow-Up Assessments form.

### Discharged to

If patient was discharged, select the location the patient was discharged to from the list below:

- 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 a post mortem report is not available, record the cause of death from the death certificate.

## **Month 6 Follow-up Assessments**

### **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 'alternate 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
- Alternate Contact Person (record the relationship between the alternate 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 alternate 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 contact attempts, of the patient and alternate 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 alternate contact person(s) to conduct the follow-up assessments.

**An 'attempt' is defined as exhausting all available contacts for the patient or alternate 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
  - Cellular number
  - Home number
  - Work number
  - Other numbers/contacts
  -
- If the patient cannot be reached, conduct another 'attempt' at a different time of day and/or on a different day.
  
- If the patient cannot be reached after 3 separate attempts, try to contact the alternate contact person(s) by calling their:
  - Cellular number
  - Home number
  - Work number
  - Other numbers/contacts

If the alternate 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 an 'alternate contact person(s)' such as a family member can complete the questionnaire for the patient.

Duration and Timing of Month 6 Follow-up Data Collection

Month 6 Follow-up Assessments are completed once.

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

NOTE: Late data is preferred to missing data. If you are not able to reach the patient or alternate contact person within the expected assessment period (+/- 14 days from 6 months after admission to your ACU), please continue to attempt to contact the patient to perform the assessments.

Was the patient/alternate contact person(s) contacted in advance to book an appointment for the month 6 follow-up visit?

Contact the patient/alternate 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/alternate contact person(s) to ensure her/his availability.

Who did you contact or attempt to contact for this follow-up?

Select the appropriate response:

- A. Patient
- B. Alternate contact person(s)
- C. Both Patient and Alternate
- D. No attempts were made

If you select 'No attempts were made, please indicate the reason:

- A. Missed (Explain why the follow-up was missed)
- A. No RC (study team member) at site
- B. Other (specify)

If you select either 'Missed' or 'Other', please explain further in the space provided.

Date of attempt to contact patient/alternate contact person(s)

Record the date and time of contact. If you cannot reach the patient/alternate 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 an alternate contact person(s) available?

Record if information for alternate contact person(s) are available. If the patient completed all the assessments or was deceased before any contact attempts were made, select 'Not required'.

Alternate contact person(s) Contact Method (Select all that apply)

If information is available, record all methods used to contact the alternate person.

- In person with alternate contact person(s)
- Called alternate contact person(s) (cell)
- Called alternate contact person(s) (work)
- Called alternate contact person(s) (home)
- Other contact (please specify)

Alternate Contact Person(s) Relationship with the Patient

Record the relationship between the alternate 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 alternate 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

- Alternate 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/alternate 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/alternate 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 (Appendix L)
- Activities of Daily Living-Katz Index (Appendix M)
- Instrumental Activities of Daily Living-Lawton Index (Appendix N)
- Employment Status (Appendix O)

### **SF-36**

The SF-36 Quality of Life survey is to be completed at 6 months (+/- 14 days) after ACU admission. Read the explanation at the top of the survey to the patient. Ensure the patient understands the responses should reflect her/his views about her/his own health. Remember not to interpret the questions for the patient. Each question means what he/she thinks it means, there is no right or wrong answer. Read each question to the patient followed by the response options. Record the patient's response on the questionnaire worksheet. Maintain the completed worksheet with the patient study files, this is your source document for the completed questionnaire. Record the data in REDCap™.

Every attempt should be made to obtain this information from the patient directly however, if the patient is not available, able, or willing to answer the questions, the assessment may be completed by an alternate contact person.

### **Katz ADL Index**

The Katz Index of Independence in Activities of Daily Living is to be completed at 6 months (+/- 14 days) after ACU admission to assess the level of patient independence related to self-care. The patient's responses should reflect what he/she is actually able to do, not what they think they might be able to do under ideal circumstances. Read the definitions of 'Independence' and 'Dependence' to the patient as stated on the top of the Katz ADL form. Read each of the 6 activities to the patient followed by the independent and dependent descriptions. Allow the patient to make her/his own determination. Based on the patient's response, record either 1 or 0 in the space provided for each activity. Maintain the completed worksheet with the patient study files, this is your source document for the completed questionnaire. Record the data in REDCap™.

Every attempt should be made to obtain this information from the patient directly however, if the patient is not available, able, or willing to answer the questions, the assessment may be

completed by an alternate contact person.

### **Lawton IADL Index**

The Lawton Instrumental Activities of Daily Living is to be completed at 6 months (+/- 14 days) after ACU admission to assess the level of patient functional ability related to domestic and community activities. The patient's responses should reflect her/his highest functional level, not the activities they actual do. For example, if a patient is not the person in the household that does the laundry, but the patient is capable of doing her/his own laundry independently select '*Does personal laundry completely*'. Read each of the 8 activities to the patient followed by the response options. Remind the patient to indicate her/his highest functional ability. Allow the patient to make her/his own determination. Based on the patient's response for each activity, circle the corresponding number on the form. Maintain the completed worksheet with the patient study files, this is your source document for the completed questionnaire. Record the data in REDCap™.

Every attempt should be made to obtain this information from the patient directly however, if the patient is not available, able, or willing to answer the questions, the assessment may be completed by an alternate contact person.

### **Employment Status**

The Employment Status questionnaire is to be completed at 6 months (+/- 14 days) after ACU admission to assess the effect of the burn injury on the patient's employment status. Read each question to the patient and record her/his response. Where applicable, read the response options to the patient. Allow the patient to make her/his own determination. Read each question sequentially. Follow the instructions on the form regarding skipping questions associated with responses to questions 1, 5, and 6. Indicate the patient's response to each question by marking the corresponding box. Maintain the completed worksheet with the patient study files, this is your source document for the completed questionnaire. Record the data in REDCap™.

Every attempt should be made to obtain this information from the patient directly however, if the patient is not available, able, or willing to answer the questions, the assessment may be completed by an alternate contact person.

### **It is encouraged to schedule reminders in your calendar for the month 6 follow up interviews.**

If you are unable to complete all questionnaires during a single telephone call, make every effort to complete the questionnaire you are working on. Ask if you may call them back to finish the remaining questionnaires. The following day is ideal, however anytime during the assessment window is acceptable. Schedule a time that is convenient for the patient.

If they do not wish to finish the remaining questionnaires, even at a later date, complete the Month 6 Follow-up Assessments: Contact Log as per instructions above.

### **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**

SAE forms must be completed in REDCAP™ in real time.

REDCAP™ may be accessed via <http://www.criticalcarenutrition.com> or directly at: <https://ceru.hpcvl.queensu.ca/EDC/redcap/>

The SAE forms are listed at the bottom of the Event Grid. You may enter up to 3 adverse events each day. Use the drop down box in the SAE row each day to access the form, example below:

The screenshot shows a portion of the REDCAP interface. On the left is a sidebar with 'Help & Information' and links to 'Helpdesk', 'General Help', and 'Video Tutorials'. The main area is a grid with rows for 'Microbiology', 'Protocol Violation', 'Hospital Overview', 'Survival Assessment', 'Contact Log', 'SF-36', 'ADL', and 'IADL'. The 'Serious Adverse Event Report' row is highlighted with a red box, and a dropdown menu is open showing options 1, 2, and 3. Below the dropdown is a 'Form Status Legend'.

A **Serious Adverse Event (SAE)** is defined as any untoward medical occurrence that at any dose:

- Results in death.
- Is life-threatening (refers to an event in which the study participant was, in the opinion of the qualified investigator (QI), at risk of death from the event if medical intervention had not occurred. NOTE: This does not include an event that hypothetically had it occurred in a more serious form, might have caused death).
- Requires in patient hospitalization or prolongation of existing hospitalization.
- Results in persistent or significant disability/incapacity (i.e. a substantial disruption in an individual's ability to conduct normal life functions).
- Is a congenital anomaly or birth defect.
- Other medically important condition (Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious events when, based on medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed above).

## **Reporting Period**

Subjects should be monitored for SAEs from randomization until  $\geq 10$  days post last successful graft (at a minimum for 3 days after study intervention was stopped), 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 P for worksheet).

- **Unexpected SAE:** An event that is serious (see definition above) and is **not** expected due to the progression of the underlying disease or co-morbid illnesses.

Examples of **serious and unexpected** SAEs and hence **MUST** be reported to CERU within 24 hrs of becoming aware of the event:

- a) Cardiac arrest in a patient without a history of cardiac disease.
- b) New seizure in the absence of a previous seizure disorder.
- c) Worsening encephalopathy in the absence of liver disease.

- **Related SAE:** An event that is serious (see definition above) and is considered by the site investigator to be possibly or probably related to the study intervention. Refer to the definitions of relatedness provided in the following section under the heading 'Relationship of SAE to study supplements'.

### **Death (outcome)**

Do not record death as an SAE.

If a reportable SAE results in death, record death as the outcome. Record the condition that lead to death as the SAE, for example: sepsis

### **Respiratory Failure**

Do not record respiratory failure as an SAE.

Record the condition that caused respiratory failure as the SAE, for example: sepsis.

## SAE Report Types

Initial, Follow-up, and Final SAE reports are completed on the same SAE form. When completing the SAE form, indicate the Report type by selecting the corresponding button, see below:

The screenshot shows a portion of a web form. The top section is labeled 'Date of Report:' and contains a text input field with a calendar icon to its right. Below this, the 'Report type:' section features three radio button options: 'Initial', 'Follow-up', and 'Final'. The 'Initial' option is selected.

## Initial SAE Report

The Research Coordinator must complete the SAE form in consultation with the Site Investigator or sub-I 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). This may be clarified in the narrative on the Final report.

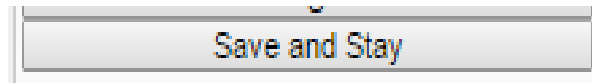
The following fields of the Initial form must be completed:

- Patient identification
  - Your RE-ENERGIZE<sup>®</sup> **site number**
  - RE-ENERGIZE<sup>®</sup> **enrollment number**
  - **Age**
  - Sex, select **male** or **female**
  - **Height**
  - **Weight**
- **Name of Site Investigator**
- **Name of person reporting the SAE**
- **Date of Report**
- **Report type: Initial, Follow-up, or Final**
- **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).
- 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
- A. **Action taken with Study Supplements:** Select **only one** of the following:
- a. none (including not on study supplements)
  - b. dose reduced, interrupted or therapy delayed (include date/time)
  - c. study supplements stopped permanently due to SAE (include date/time).
- B. **Relationship of SAE to the study supplements:** The determination of the relationship of the event to the supplements is to be made by the Site Investigator/sub-I and recorded by the Research Coordinator. To assist the Investigator in making this assessment, the following definitions have been provided (select **only one**):
- C. **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'.
  - D. **Unlikely related:** A serious adverse event that is more likely due to other causes than the study supplements
  - E. **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.
  - F. **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.

Upon completing the form, select 'Save and Stay'.

The screenshot shows a data entry form with a sidebar on the left containing a list of applications. The main form area includes fields for Signature, Date of Signature, and Comments. Below these is a 'Form Status' section with a 'Complete?' dropdown menu set to 'Incomplete'. At the bottom of this section, there are four buttons: 'Save and go to Day 1 Serious Adverse Event Fup Final 1', 'Save and go to Day 2 Serious Adverse Event Initial 1', 'Save and go to Grid', and 'Save and Stay'. The 'Save and Stay' button is highlighted with a red rectangular box.



After saving the form, select the 'PDF with saved data' button on the top right of the form, see example below, and save the form to your desktop.

The screenshot shows the 'REENERGIZE\_Test' form interface. The top header includes the 'Clinical Evaluation Research Unit' logo and 'KG+ Kingston General Hospital'. The form title is 'REENERGIZE\_Test' and the event is 'Day 1'. The main content area shows 'Editing existing Patient ID "10021014"' and 'Event Name: Day 1 - 2011-06-21'. Below this is a table with patient information: Patient ID (10021014), Site number (1002-1014), and Enrolment # (1014). On the right side of the form, there are two buttons: 'Download page as PDF' and 'PDF with saved data'. The 'PDF with saved data' button is highlighted with a red rectangular box.



Print and file the completed SAE form 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](mailto:danserem@kgh.kari.net) . Remember to de-identify any patient records before sending them.

For SAE Report Worksheet, see Appendix P.

### 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.
  
- **Patient medical history**, co-morbid illness and reason for admission to hospital: provide a detailed narrative of this information.
- **Admitting diagnosis** to ACU and chronological events leading to the SAE: provide a detailed narrative of this information
- **Chronological events preceding 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@kgh.kari.net](mailto:danserem@kgh.kari.net) .

**IMPORTANT:** Remember to de-identify any patient records before sending them to the Project Leader.

For SAE Report worksheet, see Appendix P.

Any patient 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

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 Data Monitoring Committee, Steering Committee & the manufacturer of the investigational products.

## **Appendices**

- A. Delegation of Authority Log**
- B. Lund and Browder chart**
- C. NutreStore™ (L-Glutamine) monograph**
- D. Maltrin M-100 maltodextrin monograph**
- E. Nursing Procedures**
- F. Dosing Weight Chart**
- G. Enteral Feeding Protocol**
- H. Contact Information sheet**
- I. Medical/Physician Orders**
- J. Comorbidities list**
- K. Gram Negative Bacteria List (sub-List of Gram Positive bacteria)**
- L. SF-36 Health related Quality of Life questionnaire**
- M. Activities of Daily Living (Katz Index)**
- N. Instrumental Activities of Daily Living (Lawton Index)**
- O. Employment Status**
- P. SAE Report worksheet**







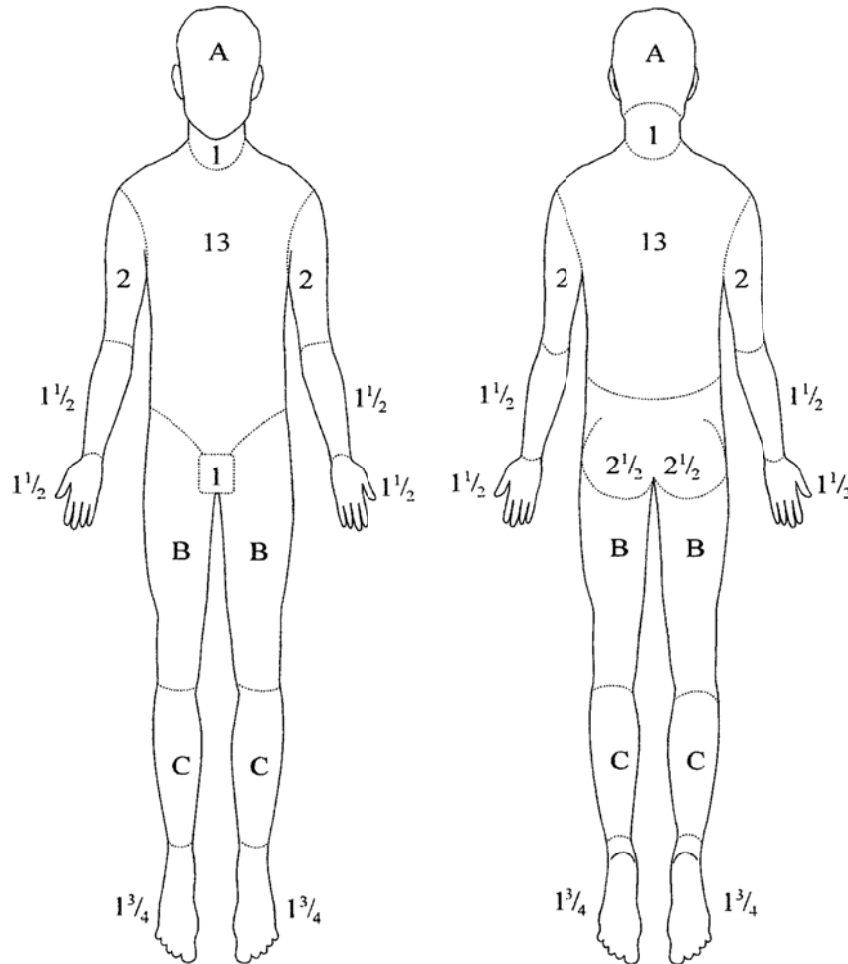
# Delegation of Authority Log

## Key Delegated Tasks

Reference Number	Key Delegated Tasks
1	Screening subjects for eligibility
2	Conducting informed consent discussions for eligible patients
3	Obtaining written informed consent
4	Patient enrollment/randomization and follow-up
5	Checking eligibility criteria
6	Daily monitoring of patient health, safety and study compliance
7	Data collection, includes: <ul style="list-style-type: none"> <li>❖ Case Report Form entries</li> <li>❖ Case Report Form corrections</li> <li>❖ Data query resolution</li> </ul>
8	Source documentation maintenance, includes: <ul style="list-style-type: none"> <li>❖ Study worksheets, checklists, monitoring sheets</li> <li>❖ Data from electronic &amp; hard copy medical chart</li> </ul>
9	Reporting of Protocol Violations/Unanticipated Problems involving risk
10	Serious Adverse Events identification, documentation, and reporting
11	Maintenance of Regulatory Documents
12	REB submissions and communications
13	Perform study specific training
14	Performing clinical assessments including burn outcomes, SAEs and ICU infection adjudication
15	Confirmation of completeness and accuracy of data collected
16	Maintenance of Product inventory
17	Checking of treatment assignment online
18	Study treatment dispensing & accountability, including maintenance of logs
19	Optimizing delivery of enteral nutrition and compliance with Guidelines for Nutrition

# Therapeutic Guidelines

## Lund and Browder chart for calculating the percentage of total body surface area burnt (Fig 14.19)



Region	Partial thickness (%) [NB1]	Full thickness (%)
head		
neck		
anterior trunk		
posterior trunk		
right arm		
left arm		
buttocks		
genitalia		
right leg		
left leg		
<b>Total burn</b>		

NB1: Do not include erythema

Area	Age 0	1	5	10	15	Adult
A = half of head	9½	8½	6½	5½	4½	3½
B = half of one thigh	2¾	3¼	4	4½	4½	4¼
C = half of one lower leg	2½	2½	2¾	3	3¼	3½

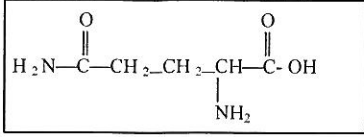
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**(NOO-tre-stor) - Full Prescribing Information**

**DESCRIPTION**

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-amide, (S)-2,5-diamino-5-oxopentanoic acid, or L-glutamine. The molecular formula of glutamine is C<sub>5</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub>, and the molecular weight is 146.15 d. 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 glutamate. 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, villous height, bowel growth, plasma insulin-like growth factor I, and body weight were significantly higher than in animals when either glutamine or rh-GH was administered alone.

**Pharmacokinetics**

The pharmacokinetics of L-glutamine as described below are based on literature data in healthy 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 (or 150 μg/mL) 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 synthesis of proteins, nucleotides, and amino sugars. Exogenous glutamine is anticipated to undergo similar metabolism.

**Elimination**

Metabolism 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.

**Drug-Drug Interactions**

No drug-drug interaction studies have been conducted. Because metabolism of glutamine is mediated via non-CYP enzymes, glutamine pharmacokinetics are unlikely to be affected by other agents through CYP enzyme inhibition or induction.

**CLINICAL TRIALS**

A randomized, controlled, 3-arm, double-blind, parallel-group clinical study evaluated the efficacy and safety of oral glutamine as a cotherapy with recombinant human growth hormone (rh-GH) in subjects with short bowel syndrome (SBS) who were dependent on intravenous parenteral nutrition (IPN) for nutritional support. The primary endpoint was the change in weekly total IPN volume defined as the sum of the volumes of IPN, supplemental lipid emulsion (SLE), and intravenous hydration fluid. The secondary endpoints were the change in weekly IPN caloric content and the change in the frequency of IPN administration per week.

All subjects received a specialized oral diet (SOD) for the duration of the study. Following a two-week equilibration period, treatment was administered in a double blind manner. Group A (N=16) received rh-GH for four weeks plus oral glutamine placebo for 16 weeks, Group B (N=16) received rh-GH for four weeks plus oral glutamine for 16 weeks, and Group C (N=9), received rh-GH placebo for four weeks plus oral glutamine for 16 weeks. The efficacy of glutamine was assessed by comparing the cotherapy (rh-GH and oral glutamine) to rh-GH alone.

After 4 weeks of treatment with subcutaneous rh-GH (0.1 mg/kg/d) and oral glutamine (30 g/d) (Group B), subjects with SBS reduced their requirement for IPN volume (-7.7 L/wk), IPN caloric content (-5751 kcal/wk), and weekly frequency of IPN administration (-4.2 d/wk).

**Table 1: Results for Endpoints after 4 weeks of Treatment**

	Group A rhGH + SOD <sup>1</sup>	Group B rhGH + SOD GLN <sup>1</sup>	Group C SOD GLN <sup>1</sup>
Total IPN volume (L/wk)			
Mean at Baseline	10.3	10.5	13.5
Mean Change	-5.9	-7.7*	-3.8
Total IPN Calories (kcal/wk)			
Mean at Baseline	7634.7	7895.0	8570.4
Mean Change	-4338.3	-5751.2	-2633.3
Frequency of IPN or SLE (days/wk)			
Mean at Baseline	5.1	5.4	5.9
Mean Change	-3.0	-4.2	-2.0

<sup>1</sup>SOD|GLN = Specialized Oral Diet supplemented with Glutamine; rhGH + SOD = Human Growth Hormone plus Specialized Oral Diet; rhGH + SOD|GLN = Human Growth Hormone plus Specialized Oral Diet supplemented with Glutamine. \*p = 0.023, treatment comparison between rhGH + SOD|GLN versus rhGH+SOD

GROUP A: rh-GH + SOD for 4 weeks followed by SOD for 12 weeks.  
GROUP B: rh-GH + SOD |GLN for 4 weeks followed by SOD|GLN for 12 weeks.  
GROUP C: rh-GH placebo + SOD |GLN for 4 weeks followed by SOD |GLN for 12 weeks.

IPN volume requirements were significantly reduced in subjects receiving subcutaneous rh-GH and oral glutamine (Group B) when compared with IPN volume requirements in subjects receiving either treatment alone.

**Table 2 - Persistence of Treatment Effect**

Change in IPN* Volume, Calories, and Frequency Week 2 to Week 18 ITT Population			
Endpoint	Group A [n=16]	Group B [n=16]	Group C [n=9]
Change in weekly IPN Volume (L/wk)	-5.9	-7.2	-4.7
Change in weekly IPN Calories (kcal/wk)	-3522.2	-5347.3	-2254.0
Change in weekly IPN frequency (days/wk)	-2.9	-3.9	-1.9

\*IPN is Total IPN excluding supplemental lipid emulsion (SLE) and hydration fluid.  
Group A: rh-GH + SOD for 4 weeks followed by SOD for 12 weeks.  
Group B: rh-GH + SOD |GLN for 4 weeks followed by SOD |GLN for 12 weeks.  
Group C: rh-GH placebo + SOD |GLN for 4 weeks followed by SOD |GLN for 12 weeks.

The change in weekly IPN volume, calories and frequency was assessed from Week 2 to Week 18. The data support that the treatment effect is maintained for 16 weeks. The efficacy of oral glutamine beyond 16 weeks of treatment has not been adequately studied.

**CONTRAINDICATIONS**

None known.

**INDICATION AND USAGE**

**Treatment of Short Bowel Syndrome**

NutreStore™ (L-glutamine powder for oral solution) is indicated for the treatment of Short Bowel Syndrome (SBS) in patients receiving specialized nutritional support when used in conjunction with a recombinant human growth hormone that is approved for this indication. (See Dosage and Administration). Glutamine and recombinant human growth hormone therapy should be used in conjunction with optimal management of Short Bowel Syndrome. Optimal management of Short Bowel Syndrome may include a specialized oral diet, enteral feedings, parenteral nutrition, fluid and micronutrient supplements. A specialized oral diet may consist of a high carbohydrate, low-fat diet, adjusted for individual patient requirements and preferences.

**PRECAUTIONS**

**General**

In patients with SBS, NutreStore™ should only be taken under the direction of a physician, registered dietician, or nutritionist. NutreStore™ is not for parenteral use.

**Laboratory Tests**

Routine monitoring of renal and hepatic function is recommended in patients receiving IPN, particularly in those with renal or hepatic impairment. Glutamine is metabolized to glutamate and ammonia which may increase in patients with hepatic dysfunction.

**Drug Interactions**

Formal drug interaction studies have not been conducted.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Long-term studies in animals have not been performed to evaluate carcinogenic potential of L-glutamine. Studies to evaluate its potential for impairment of fertility or its mutagenic potential have not been conducted.

**Pregnancy: Teratogenic Effects: Pregnancy Category C:**

Animal reproduction studies have not been conducted with glutamine. It is also not known whether glutamine can cause fetal harm when administered to a pregnant woman or whether it can affect reproduction capacity. Glutamine should be given to a pregnant woman only if clearly needed.

**Labor and Delivery**

The effect of L-glutamine on labor and delivery is unknown.

**Nursing Mothers**

It is not known whether L-glutamine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when L-glutamine is administered to a nursing woman.

**Pediatric Use**

The safety and effectiveness of L-glutamine in pediatric patients has not been established.

**Geriatric Use**

The clinical trial enrolled SBS patients between the ages of 20 and 75 years. Only 8 of the 41 subjects evaluated were ≥ 65 years of age. The clinical trial of oral glutamine did not include sufficient numbers of subjects aged 65 years and over to determine if they respond differently than younger subjects. In general, dose selection for an elderly patient should be individualized, because of the greater frequency of decreased hepatic, renal, or cardiac function, as well as concomitant disease in this population.

**ADVERSE REACTIONS**

Table 3 provides the number of subjects by system-organ class experiencing at least one adverse event during the 4-week treatment period of the SBS study. To be listed in

Table 3, an adverse event must have occurred in more than 10% of subjects in any treatment group.

**Table 3 - Controlled Trial Adverse Events—Initial 4 Week Treatment Period**

Adverse Experiences	Group A	Group B	Group C
	rhGH+SOD <sup>1</sup> N=16 n(%)	rhGH+SOD[GLN] <sup>1</sup> N=16 n(%)	SOD [GLN] <sup>1</sup> N=9 n(%)
<b>Total Number of Subjects with At Least One AE</b>	<b>16 (100)</b>	<b>16 (100)</b>	<b>8 (89)</b>
<b>Body as a Whole: General Disorders</b>			
Edema, Peripheral	15 (94)	15 (94)	4 (44)
Edema, Facial	8 (50)	7 (44)	0 (0)
Pain	3 (19)	1 (6)	1 (11)
Chest Pain	3 (19)	0 (0)	0 (0)
Fever	0 (0)	1 (6)	2 (22)
Back Pain	1 (6)	0 (0)	1 (11)
Flu-like Disorder	0 (0)	1 (6)	1 (11)
Malaise	2 (13)	0 (0)	0 (0)
Edema, Generalized	2 (13)	0 (0)	0 (0)
Abdomen, Enlarged	0 (0)	0 (0)	1 (11)
Allergic Reaction	0 (0)	0 (0)	1 (11)
Rigors (Chills)	0 (0)	0 (0)	1 (11)
<b>Gastrointestinal System Disorders</b>	<b>12 (75)</b>	<b>12 (75)</b>	<b>6 (67)</b>
Flatulence	4 (25)	4 (25)	2 (22)
Abdominal Pain	4 (25)	2 (13)	1 (11)
Nausea	2 (13)	5 (31)	0 (0)
Tenesmus	1 (6)	3 (19)	3 (33)
Vomiting	3 (19)	3 (19)	1 (11)
Hemorrhoids	1 (6)	0 (0)	1 (11)
Mouth Dry	1 (6)	0 (0)	1 (11)
<b>Musculoskeletal System Disorders</b>	<b>7 (44)</b>	<b>7 (44)</b>	<b>1 (11)</b>
Arthralgia	7 (44)	5 (31)	0 (0)
Myalgia	2 (13)	0 (0)	1 (11)
<b>Resistance Mechanism Disorders</b>	<b>6 (38)</b>	<b>3 (19)</b>	<b>4 (44)</b>
Infection	0 (0)	1 (6)	3 (33)
Infection Bacterial	3 (19)	0 (0)	1 (11)
Infection Viral	1 (6)	2 (13)	0 (0)
Moniliasis	2 (13)	0 (0)	0 (0)
<b>Application Site Disorders</b>	<b>5 (31)</b>	<b>4 (25)</b>	<b>1 (11)</b>
Injection Site Reaction	3 (19)	4 (25)	1 (11)
Injection Site Pain	5 (31)	0 (0)	0 (0)
<b>Central and Peripheral Nervous System Disorders</b>	<b>4 (25)</b>	<b>4 (25)</b>	<b>2 (22)</b>
Dizziness	1 (6)	2 (13)	0 (0)
Headache	1 (6)	1 (6)	1 (11)
Hypoesthesia	1 (6)	1 (6)	1 (11)
<b>Skin and Appendages Disorders</b>	<b>4 (25)</b>	<b>4 (25)</b>	<b>2 (22)</b>
Rash	1 (6)	2 (13)	0 (0)
Pruritis	0 (0)	1 (6)	1 (11)
Sweating Increased	2 (13)	0 (0)	0 (0)
Nail Disorder	0 (0)	0 (0)	1 (11)
<b>Respiratory System Disorders</b>	<b>1 (6)</b>	<b>5 (31)</b>	<b>1 (11)</b>
Rhinitis	0 (0)	3 (19)	1 (11)
<b>Metabolic and Nutritional Disorders</b>	<b>3 (19)</b>	<b>1 (6)</b>	<b>1 (11)</b>
Dehydration	3 (19)	0 (0)	1 (11)
Thirst	0 (0)	0 (0)	1 (11)
<b>Urinary System Disorders</b>	<b>2 (13)</b>	<b>1 (6)</b>	<b>1 (11)</b>
Pyelonephritis	0 (0)	0 (0)	1 (11)
<b>Psychiatric Disorders</b>	<b>1 (6)</b>	<b>0 (0)</b>	<b>2 (22)</b>
Depression	0 (0)	0 (0)	2 (22)
<b>Reproductive Disorders, Female</b>	<b>2 (13)</b>	<b>0 (0)</b>	<b>1 (11)</b>
Breast Pain, Female	1 (6)	0 (0)	1 (11)
<b>Hearing and Vestibular Disorders</b>	<b>0 (0)</b>	<b>2 (13)</b>	<b>0 (0)</b>
Far or Hearing Symptoms	0 (0)	2 (13)	0 (0)

<sup>1</sup>SOD[GLN] = Specialized Oral Diet supplemented with Glutamine; rhGH+SOD = Human Growth Hormone plus Specialized Oral Diet; rhGH + SOD [GLN] = Human Growth Hormone plus Specialized Oral Diet supplemented with Glutamine  
Group A: rh-GH + SOD for 4 weeks followed by SOD for 12 weeks  
Group B: rh-GH + SOD [GLN] for 4 weeks followed by SOD [GLN] for 12 weeks

weeks.  
Group C: rh-GH placebo + SOD [GLN] for 4 weeks followed by SOD [GLN] for 12 weeks

Table 4 summarizes the number of subjects by system-organ class who experienced an adverse event during weeks 5 to 18 of the randomized, controlled SBS study. To be listed in Table 4, an adverse event must have occurred in more than 10% of subjects in any treatment group.

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

Adverse Experiences	Group A	Group B	Group C
	rhGH+SOD <sup>1</sup> N=15 n(%)	rhGH+SOD [GLN] <sup>1</sup> N=16 n(%)	SOD[GLN] <sup>1</sup> N=9 n(%)
<b>Total Number of Subjects with At Least One AE</b>	<b>12 (80)</b>	<b>13 (81)</b>	<b>7 (78)</b>
<b>Gastrointestinal System Disorders</b>	<b>7 (47)</b>	<b>7 (44)</b>	<b>3 (33)</b>
Nausea	3 (20)	0 (0)	2 (22)
Vomiting	2 (13)	3 (19)	0 (0)
Abdominal Pain	3 (20)	1 (6)	0 (0)
Tenesmus	0 (0)	3 (19)	1 (11)
Pancreatitis	0 (0)	1 (6)	1 (11)
Constipation	0 (0)	0 (0)	1 (11)
Crohn's Disease Aggravated	0 (0)	0 (0)	1 (11)
Gastric Ulcer	0 (0)	0 (0)	1 (11)
Gastrointestinal Fistula	0 (0)	0 (0)	1 (11)
<b>Resistance Mechanism Disorders</b>	<b>6 (40)</b>	<b>5 (31)</b>	<b>5 (56)</b>
Infection Bacterial	0 (0)	2 (13)	3 (33)
Infection Viral	3 (20)	1 (6)	1 (11)
Infection	1 (7)	2 (13)	1 (11)
Sepsis	3 (20)	1 (6)	0 (0)
<b>Body as a Whole: General Disorders</b>	<b>4 (27)</b>	<b>2 (13)</b>	<b>1 (11)</b>
Fever	2 (13)	1 (6)	1 (11)
Fatigue	2 (13)	0 (0)	0 (0)
<b>Respiratory System Disorders</b>	<b>2 (13)</b>	<b>4 (25)</b>	<b>1 (11)</b>
Rhinitis	1 (7)	3 (19)	0 (0)
Laryngitis	0 (0)	0 (0)	1 (11)
Pharyngitis	0 (0)	0 (0)	1 (11)
<b>Reproductive Disorders, Female</b>	<b>0 (0)</b>	<b>4 (25)</b>	<b>1 (11)</b>
Vaginal Fungal Infection	0 (0)	0 (0)	1 (11)
Skin and Appendages Disorders	2 (13)	2 (13)	1 (11)
Rash	1 (7)	0 (0)	1 (11)
<b>Musculoskeletal System Disorders</b>	<b>2 (13)</b>	<b>2 (13)</b>	<b>0 (0)</b>
Arthralgia	2 (13)	2 (13)	0 (0)
<b>Psychiatric Disorders</b>	<b>0 (0)</b>	<b>1 (6)</b>	<b>1 (11)</b>
Depression	0 (0)	0 (0)	1 (11)
Insomnia	0 (0)	0 (0)	1 (11)
<b>Urinary System Disorders</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>2 (22)</b>
Pyelonephritis	0 (0)	0 (0)	1 (11)
Renal Calculus	0 (0)	0 (0)	1 (11)
<b>Application Site Disorders</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>1 (11)</b>
Injection Site Reaction	0 (0)	0 (0)	1 (11)
<b>Liver and Biliary System Disorders</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>1 (11)</b>
Hepatic Function Abnormal	0 (0)	0 (0)	1 (11)
<b>Vascular Extracardiac Disorders</b>	<b>0 (0)</b>	<b>0 (0)</b>	<b>1 (11)</b>
Vascular Disorder	0 (0)	0 (0)	1 (11)

Group A: rh-GH + SOD for 4 weeks followed by SOD for 12 weeks  
Group B: rh-GH + SOD [GLN] for 4 weeks followed by SOD [GLN] for 12 weeks  
Group C: rh-GH placebo + SOD [GLN] for 4 weeks followed by SOD [GLN] for 12 weeks

<sup>1</sup>SOD[GLN] = Specialized Oral Diet supplemented with Glutamine; rhGH+SOD = Human Growth Hormone plus Specialized Oral Diet; rhGH + SOD [GLN] = Human Growth Hormone plus Specialized Oral Diet supplemented with Glutamine

The safety profile in patients receiving oral glutamine with growth hormone was similar to the safety profile in patients receiving growth hormone without glutamine. During the initial 4 week treatment period, 100% of patients receiving growth hormone with and without glutamine reported at least one adverse event (AE), whereas 89% of patients receiving growth hormone placebo with glutamine reported at least one AE. During weeks 5 to 18, 81% of patients receiving growth hormone with glutamine, 80% of patients receiving growth hormone without glutamine and 78% of patients receiving growth hormone placebo with glutamine experienced at least one AE. There were no deaths in this study.

#### OVERDOSAGE

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

#### DOSAGE AND ADMINISTRATION

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

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

NutreStore™ 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 oral intake, a dose may be delayed for up to 2 hours. The safety and efficacy of NutreStore™ have not been studied beyond 16 weeks of treatment.

#### HOW SUPPLIED

NutreStore™ is supplied in preprinted paper-foil-plastic laminate packets containing 5 g of L-glutamine powder.

84 packets (5gm each) - NDC 42457-001-84

#### 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].

For additional information concerning NutreStore™, contact:



Emmaus Medical, Inc.  
20725 S. Western Ave., Suite 136  
Torrance, CA 90501-1884  
Tel: 1-877-420-6493  
www.nutrestore.com

Manufactured by:  
Anderson Packaging, Inc.  
4545 Assembly Drive  
Rockford, IL 61109

Rx only

Revised October 2008

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SMM-007-02 0810

**MATERIAL SAFETY DATA SHEET**

IDENTITY(As Used on Label and List)
<b>L-GLUTAMINE</b>

SECTION I	
MANUFACTURER'S NAME  Kyowa Hakko Kogyo Co., Ltd.	EMERGENCY TELEPHONE NUMBER  1-212-319-5353 (N.Y. Office) 1-949-425-0707 (West Coast Office)
ADDRESS (Number, Street, City, State, and ZIP Code)  1-6-1, Ohtemachi Chiyoda-ku, Tokyo, Japan, 100-8185	TELEPHONE NUMBER FOR INFORMATION  1-212-319-5353 (N.Y. Office) 1-949-425-0707 (West Coast Office)
	DATE PREPARED  August 1, 2003
	PREPARER  Quality Assurance Department Bio-Chemicals Company

SECTION II - HAZARDOUS INGREDIENTS / IDENTITY INFORMATION		
CHEMICAL NAME AND SYNONYMS  L-Glutamine	CHEMICAL FAMILY  Amino Acid	
FORMULA  $C_5H_{10}N_2O_3$ (146.15)	CAS NUMBER  56-85-9	
INGREDIENT  L-Glutamine	PERCENT  Pure material	HAZARDOUS  No
HAZARDOUS MIXTURES OF OTHER LIQUIDS, SOLIDS, OR GASES  None		

SECTION III - PHYSICAL DATA			
BOILING POINT	Unknown	SPECIFIC GRAVITY ( $H_2O = 1$ )	Unknown
VAPOR PRESSURE(mmHg.)	Unknown	MELTING POINT	Not Applicable
VAPOR DENSITY(AIR= 1)	Not Applicable(solid)	EVAPORATION RATE ( Butyl Acetate = 1)	Not Applicable (solid)
SOLUBILITY IN WATER	Soluble		
APPEARANCE AND ODOR  White crystals or crystalline powder, odorless			

SECTION IV - FIRE AND EXPLOSION HAZARD DATA			
FLASH POINT (Method used)  None	FLAMMABLE LIMITS  None	LEL	UEL
EXTINGUISHING MEDIA  Water, Foam, CO <sub>2</sub> , Dry chemical			
SPECIAL FIRE FIGHTING PROCEDURES  None			
UNUSUAL FIRE AND EXPLOSION HAZARD 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.			

SECTION V - REACTIVITY DATA			
STABILITY	UNSTABLE		CONDITIONS TO AVOID
	STABLE	X	
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			
ROUTE(S) OF ENTRY:	INHALATION?	SKIN?	INGESTION?
	Not determined	Not determined	Not determined
HEALTH HAZARDS(ACUTE AND CRONIC)			
This material is considered to be non-toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.			
CARCINOGENICITY	NTP?	IARC MONOGRAPHS?	OSHA REGULATED?
	No	No	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	EYE PROTECTION	
Recommended	Recommended	
OTHER PROTECTIVE EQUIPMENT		
WORK / HYGIENIC PRACTICES		





# MALTRIN<sup>®</sup> M100

## Maltodextrin

### DESCRIPTION

MALTRIN<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup>; 13 = 2013; 108 = Apr. 18; 01 = first lot

*Technical Information*



# MALTRIN® M100

## Maltodextrin

### TYPICAL NUTRITIONAL INFORMATION

Values per 100 grams of product

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

#### 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, Panthothenic Acid, Biotin, or minerals Chromium, Copper, Iodine, Manganese, Molybdenum, Selenium, Zinc.

### 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.
• <u>E. coli</u>	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".

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M100 TI 011314



RandomizEd Trial of ENtERal Glutamine to minimIZE Thermal Injury

## Nursing Procedures

### Investigational Product Administration

1. Determine the number of grams of investigational product to be given to the patient and the dosing times according to the pharmacy orders.
2. At each dosing time, pour the correct dose of the investigational product (IP) needed into a clean specimen cup.
3. Per each 5g of IP add 50 mL of sterile or tap water (per your standard practice for enteral nutrition formulas) to the cup and mix well.
4. Transfer the mixture into a syringe.
5. Administer through the feeding tube as a bolus. Give via Nasogastric/Levine tube if the feeding tube is not in place. Flush with water.
6. The bolus must be administered as soon after mixing as possible. If there is a delay in the administration, the bolus will need to be shaken to re-suspend the powder. Additional water may be added if necessary.
7. 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 or RN discretion **as long as the patient receives the daily prescribed dose in grams.**
  - a. Mix the IP with any non-heated beverage or food (alcohol excepted), such as:
    - Yogurt
    - Applesauce or apple juice
    - Cereal
    - Mashed potatoes
  - b. Avoid mixing the IP in water for oral administration. Patients have reported disliking the taste.

**Do NOT mix the IP with soda or highly acidic juices such as grapefruit juice, orange juice or lemonade as it degrades or becomes unstable in an acidic medium.**

8. Record the number of grams given on the Medication Administration Record as "RE-ENERGIZE supplement" at each scheduled interval.
9. Do NOT stop the study intervention for procedures or surgery. If any missed doses occur, they should be made up on the same calendar day, per the following:
  - a. There must be at least one hour between doses
  - b. Do not give more than double the prescribed dose at one time
10. Keep all the **unused** packages with the patient's ID on it and give to Research Coordinator.
11. Inform the Research Coordinator of any interruptions in administration of the IP.
12. Continue administering the investigational product until you are informed by the Site Investigator or Research Coordinator the patient is no longer on the study.



RandomizEd Trial of ENtERal Glutamine to minimIZE Thermal Injury

## Glossary

IP      Investigational Product

ACU    Acute Care Unit (burn unit or ICU)

## Dosing Weight Chart

Dose #	1	2	3	4	5	6	q4h	
Dosing weight (kg)	Number of 5g doses						Total	
							doses	g/day
35-44	1	0	1	0	1	1	4	20
45-54	1	1	1	0	1	1	5	25
55-64	1	1	1	1	1	1	6	30
65-74	2	1	1	1	1	1	7	35
75-84	2	1	1	2	1	1	8	40
85-94	2	1	1	2	1	2	9	45
95-104	2	1	2	2	1	2	10	50
105-114	2	2	2	2	1	2	11	55
115-124	2	2	2	2	2	2	12	60
125-134	3	2	2	2	2	2	13	65
135-144	3	2	3	2	2	2	14	70

## 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

**WATER FLUSHES:**

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

Elevate HOB to 45 degrees, if possible

**BLOCKED TUBE:**

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

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 1<sup>st</sup> GRV > 250 ml\*?

YES

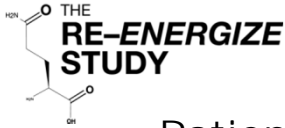
- 1) Refeed GRV to 400ml max and discard the rest
- 2) Start Maxeran 10mg IV q 6 hrs
- 3) Continue with Enteral Nutrition

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

\* 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.



Randomization Number \_\_\_\_\_

## Patient/Alternate Contact Person(s) Information Form

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

Name: _____		
<i>Last Name,</i>	<i>First Name</i>	<i>Middle Name</i>
alternate name (i.e. nicknames/alias): <input type="checkbox"/> None #1 _____ #2 _____		
Home Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Cell Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	
Alternate: (____) _____ - _____ <input type="checkbox"/> Not Available	Alternate: (____) _____ - _____ <input type="checkbox"/> Not Available	
Email Address: _____		
Work Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Alternate: (____) _____ - _____ <input type="checkbox"/> Not Available	

### Someone who lives with participant:

Name: _____		
<i>Last Name,</i>	<i>First Name</i>	<i>Middle Name</i>
Home Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Cell Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	
Work Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Alternate: (____) _____ - _____ <input type="checkbox"/> Not Available	
Relationship to Patient (e.g., father, sister, friend): _____		

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

Name: _____		
<i>Last Name,</i>	<i>First Name</i>	<i>Middle Name</i>
Home Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Cell Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	
Work Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Alternate: (____) _____ - _____ <input type="checkbox"/> Not Available	
Relationship to Patient (e.g., father, sister, friend): _____		

Name: _____		
<i>Last Name,</i>	<i>First Name</i>	<i>Middle Name</i>
Home Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Cell Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	
Work Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Alternate: (____) _____ - _____ <input type="checkbox"/> Not Available	
Relationship to Patient (e.g., father, sister, friend): _____		

Name: _____		
<i>Last Name,</i>	<i>First Name</i>	<i>Middle Name</i>
Home Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Cell Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	
Work Phone: (____) _____ - _____ <input type="checkbox"/> Not Available	Alternate: (____) _____ - _____ <input type="checkbox"/> Not Available	
Relationship to Patient (e.g., father, sister, friend): _____		



# Medical Chart Order

(sample)

- 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.

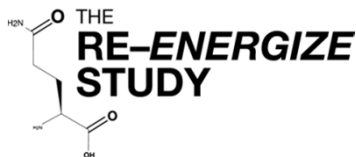
- Administer study supplement at the following times (*enter # grams*):

<u>OG/NG/Feeding Tube</u>	OR	<u>PO</u>
02:00 - _____ grams		08:00 - _____ grams
06:00 - _____ grams		12:00 - _____ grams
10:00 - _____ grams		16:00 - _____ grams
14:00 - _____ grams		20:00 - _____ grams
18:00 - _____ grams		
22:00 - _____ grams		

- A missed dose should be given as soon as possible as follows:
  - If more than one hour until the next scheduled dose, give missed dose immediately.
  - 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:

- Never give doses less than one hour apart
- 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'.

<b>No Comorbidities</b>
-------------------------

<b>Myocardial</b>
1. Angina
2. Arrhythmia
3. Valvular
4. Myocardial infarction
5. Congestive heart failure (or heart disease)

<b>Vascular</b>
6. Hypertension
7. Peripheral vascular disease or claudication
8. Cerebrovascular disease (Stroke or TIA)

<b>Pulmonary</b>
9. Chronic obstructive pulmonary disease (COPD, emphysema)
10. Asthma

<b>Neurologic</b>
11. Dementia
12. Hemiplegia (paraplegia)
13. Neurologic illnesses (such as Multiple sclerosis or Parkinsons)

<b>Endocrine</b>
14. Diabetes Type I or II
15. Diabetes with end organ damage
16. Obesity and/or BMI > 30 (weight in kg/(ht in meters) <sup>2</sup> )

<b>Renal</b>
17. Moderate or severe renal disease

<b>Gastrointestinal</b>
18. Mild liver disease
19. Moderate or severe liver disease
20. GI Bleeding
21. Inflammatory bowel
22. Peptic ulcer disease
23. Gastrointestinal Disease (hernia, reflux)

<b>Cancer/immune</b>
24. Any Tumor
25. Lymphoma
26. Leukemia
27. AIDS
28. Metastatic solid tumor

<b>Psychological</b>
29. Anxiety or Panic Disorders
30. Depression

<b>Muskoskeletal</b>
31. Arthritis (Rheumatoid or Osteoarthritis)
32. Degenerative Disc disease (back disease, spinal stenosis or severe chronic back pain)
33. Osteoporosis
34. Connective Tissue disease

<b>Miscellaneous</b>
35. Visual Impairment (cataracts, glaucoma, macular degeneration)
36. Hearing Impairment (very hard of hearing even with hearing aids)
37. Alcohol Abuse



**Gram Negative Bacteria**  
(sub-List: Gram Positive Bacteria)

<b>Gram Negative Bacteria</b>			
1	Acinetobacter sp.	23	Legionella sp.
2	Aeromonas sp.	24	Moraxella sp.
3	Alcaligenes sp.	25	Morganella sp.
4	Bacteroides sp.	26	Mycoplasma sp.
5	Bartonella sp.	27	Neisseria sp.
6	Bortetella sp.	28	Pasteurella sp.
7	Burkholderia sp.	29	Porphyromonas sp.
8	Campylobacter sp.	30	Prevotella sp.
9	Capnocytophaga sp.	31	Proteus sp.
10	Chlamydia sp.	32	Providencia sp.
11	Citrobacter sp.	33	Pseudomonas sp.
12	Coxiella sp.	34	Ralstonia sp.
13	Ehrlichia sp.	35	Rickettsia sp.
14	Eikenella sp.	36	Salmonella sp.
15	Enterobacter sp.	37	Salmonella sp.
16	Escherichia sp.	38	Serratia sp.
17	Francisella sp.	39	Shigella sp.
18	Fusobacterium sp.	40	Stenotrophomonas sp.
19	Hafnia sp.	41	Streptobacillus sp.
20	Helicobacter sp.	42	Vibrio sp.
21	Haemophilus sp.	43	Yersinia sp.
22	Klebsiella sp.	44	Other, please specify

<b>Gram Positive Bacteria</b> <b>(Do NOT include)</b>
Actinomyces sp.
Aerococcus sp.
Bacillus sp.
Clostridium sp.
Corynebacterium sp.
Diphtheroids sp.
Enterococcus sp.
Erysipelothrix sp.
Lactobacillus sp.
Listeria sp.
Nocardia sp.
Peptostreptococcus/ Peptococcus sp.
Propionibacterium sp.
Rhodococcus sp.
Staphylococcus sp.
Streptococcus sp.

SF-36

## Your Health and Well-Being

**This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Thank you for completing this survey!**

**For each of the following questions, please mark an  in the one box that best describes your answer.**

**1. In general, would you say your health is:**

Excellent	Very good	Good	Fair	Poor
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**2. Compared to one year ago, how would you rate your health in general now?**

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?**

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a <u>Vigorous activities</u> , such as running, lifting heavy objects, participating in strenuous sports.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
b <u>Moderate activities</u> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
c Lifting or carrying groceries .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
d Climbing <u>several</u> flights of stairs.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
e Climbing <u>one</u> flight of stairs.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
f Bending, kneeling, or stooping.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
g Walking <u>more than a kilometre</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
h Walking <u>several hundred metres</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
i Walking <u>one hundred metres</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
j Bathing or dressing yourself.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3

**4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the <u>amount of time</u> you spent on work or other activities .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b <u>Accomplished less</u> than you would like.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c Were limited in the <u>kind</u> of work or other activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
d Had <u>difficulty</u> performing the work or other activities (for example, it took extra effort).....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the <u>amount of time</u> you spent on work or other activities .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b. <u>Accomplished less</u> than you would like .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c. Did work or other activities <u>less carefully than usual</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?**

Not at all	Slightly	Moderately	Quite a bit	Extremely
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**7. How much bodily pain have you had during the past 4 weeks?**

None	Very mild	Mild	Moderate	Severe	Very severe
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6

**8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?**

Not at all	A little bit	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

**9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
▼	▼	▼	▼	▼

- a Did you feel full of life? .....  1 .....  2 .....  3 .....  4 .....  5
- b Have you been very nervous? .....  1 .....  2 .....  3 .....  4 .....  5
- c Have you felt so down in the dumps that nothing could cheer you up? .....  1 .....  2 .....  3 .....  4 .....  5
- d Have you felt calm and peaceful? .....  1 .....  2 .....  3 .....  4 .....  5
- e Did you have a lot of energy? .....  1 .....  2 .....  3 .....  4 .....  5
- f Have you felt downhearted and depressed? .....  1 .....  2 .....  3 .....  4 .....  5
- g Did you feel worn out? .....  1 .....  2 .....  3 .....  4 .....  5
- h Have you been happy? .....  1 .....  2 .....  3 .....  4 .....  5
- i Did you feel tired? .....  1 .....  2 .....  3 .....  4 .....  5



10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
▼	▼	▼	▼	▼
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

11. How TRUE or FALSE is each of the following statements for you?

Definitely true	Mostly true	Don't know	Mostly false	Definitely false
▼	▼	▼	▼	▼

- a I seem to get sick a little easier than other people..... 1..... 2..... 3..... 4..... 5
- b I am as healthy as anybody I know..... 1..... 2..... 3..... 4..... 5
- c I expect my health to get worse..... 1..... 2..... 3..... 4..... 5
- d My health is excellent..... 1..... 2..... 3..... 4..... 5

*Thank you for completing these questions!*

## Katz Index of Independence in Activities of Daily Living

ACTIVITIES POINTS (1 or 0)	INDEPENDENCE: (1 POINTS) <i>No</i> supervision, direction or personal assistance	DEPENDENCE: (0 POINTS) <i>With</i> supervision, direction, personal assistance or total care
<b>BATHING</b>  POINTS: _____	<b>(1 POINT)</b> Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area or disabled extremity	<b>(0 POINTS)</b> Needs help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing.
<b>DRESSING</b>  POINTS: _____	<b>(1 POINT)</b> Gets clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes	<b>(0 POINTS)</b> Needs help with dressing self or needs to be completely dressed
<b>TOILETING</b>  POINTS: _____	<b>(1 POINT)</b> Goes to toilet, gets on and off, arranges clothes, cleans genital area without help	<b>(0 POINTS)</b> Needs help transferring to the toilet, cleaning self or uses bedpan or commode
<b>TRANSFERRING</b>  POINTS: _____	<b>(1 POINT)</b> Moves in and out of bed or chair unassisted. Mechanical transferring aides are acceptable	<b>(0 POINTS)</b> Needs help in moving from bed to chair or requires a complete transfer
<b>CONTINENCE</b>  POINTS: _____	<b>(1 POINT)</b> Exercises complete self control over urination and defecation	<b>(0 POINTS)</b> Is partially or totally incontinent of bowel or bladder
<b>FEEDING</b>  POINTS: _____	<b>(1 POINT)</b> Gets food from plate into mouth without help. Preparation of food may be done by another person	<b>(0 POINTS)</b> Needs partial or total help with feeding or requires parenteral feeding
<b>TOTAL POINTS = _____</b> 6= High ( <i>patient independent</i> )    0= Low ( <i>patient very dependent</i> )		

## Lawton Instrumental Activities of Daily Living (IADLs)

<b>A. Ability to Use Telephone</b>	1. Operates telephone on own initiative; looks up and dials numbers	<b>1</b>
	2. Dials a few well-known numbers	<b>1</b>
	3. Answers telephone, but does not dial	<b>1</b>
	4. Does not use telephone at all	<b>0</b>
<b>B. Shopping</b>	1. Takes care of all shopping needs independently	<b>1</b>
	2. Shops independently for small purchases	<b>0</b>
	3. Needs to be accompanied on any shopping trip	<b>0</b>
	4. Completely unable to shop	<b>0</b>
<b>C. Food Preparation</b>	1. Plans, prepares, and serves adequate meals independently	<b>1</b>
	2. Prepares adequate meals if supplied with ingredients	<b>0</b>
	3. Heats and serves prepared meals or prepares meals but does not maintain adequate diet	<b>0</b>
	4. Needs to have meals prepared and served	<b>0</b>
<b>D. Housekeeping</b>	1. Maintains house alone with occasion assistance (heavy work)	<b>1</b>
	2. Performs light daily tasks such as dishwashing, bed making	<b>1</b>
	3. Performs light daily tasks, but cannot maintain acceptable level of cleanliness	<b>1</b>
	4. Needs help with all home maintenance tasks	<b>1</b>
	5. Does not participate in any housekeeping tasks	<b>0</b>
<b>E. Laundry</b>	1. Does personal laundry completely	<b>1</b>
	2. Launders small items, rinses socks, stockings, etc	<b>1</b>
	3. All laundry must be done by others	<b>0</b>
<b>F. Mode of transportation</b>	1. Travels independently on public transportation or drives own car	<b>1</b>
	2. Arranges own travel via taxi, but does not otherwise use public transportation	<b>1</b>
	3. Travels on public transportation when assisted or accompanied by another	<b>1</b>
	4. Travel limited to taxi or automobile with assistance of another	<b>0</b>
	5. Does not travel at all	<b>0</b>
<b>G. Responsibility for Own Medications</b>	1. Is responsible for taking medication in correct dosages at correct time	<b>1</b>
	2. Takes responsibility if medication is prepared in advance in separate dosages	<b>0</b>
	3. Is not capable of dispensing own medication	<b>0</b>
<b>H. Ability to Handle Finances</b>	1. Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track of income	<b>1</b>
	2. Manages day-to-day purchases, but needs help with banking, major purchases, etc	<b>1</b>
	3. Incapable of handling money	<b>0</b>

**TOTAL POINTS = \_\_\_\_\_**      *Scoring:* For each category, circle the item description that most closely resembles the client's highest functional level (either 0 or 1).



# Employment Status Questionnaire

Administered to:  Patient     Alternate Contact Person     Not Done

## Baseline Employment Status

1    **Have you ever been employed earning wages or salary, either full-time or part-time, including self-employment?**

Yes      
 No      
 No answer   

---

**Interviewer:** if "No" or "No Answer" skip to Current Employment Status (question 5)

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2    [If yes] **Which best describes your employment situation just prior to hospital admission? (Select ONE answer)**

- Working - Full Time (at least 32 hours per week)
- Working - Part Time
- On leave but still employed     (skip question 4)
- Temporarily laid off     (skip question 4)
- Unemployed and looking for work     (skip question 4)
- Wanting to work, but unemployed due to health related reason     (skip question 4)
- Going to school     (skip questions 3 and 4)
- Keeping house or being home maker     (skip questions 3 and 4)
- Retired     (skip question 4)
- Receiving/Awaiting approval for disability payments     (skip question 4)
- Other (specify): \_\_\_\_\_
- No Answer     (skip questions 3 and 4)
- Don't know     (skip questions 3 and 4)

3    **What is your occupation, or what kind of work did you do?**

**Interviewer:** Refer to Occupation List (page 6) to categorize response below

\_\_\_\_\_ No Answer     Don't know

4    **On average, how many hours per week did you work in the 6 months before being hospitalized?**

\_\_\_\_\_ No Answer     Don't know

## Current Employment Status

5 Which best describes your current employment situation? (Select ONE answer)

- Retired or disability (or awaiting disability) AND this is same status as at baseline  (*Questionnaire is complete*)
- Working - Full Time (at least 32 hours per week)  (*skip question 6*)
- Working - Part Time  (*skip question 6*)
- On sick leave but still employed  (*skip question 6*)
- Temporarily laid off
- Unemployed – presently in a health care facility
- Unemployed and Looking for Work
- Wanting to work, but unemployed due to health related reason
- Going to School (If a participant is both “going to school” and “working part time,” ask how many hours for each one and tick whichever option is greater)  (*skip question 6*)
- Keeping house or being home maker
- New Retirement (i.e. started after hospital d/c)
- Receiving New/Awaiting New Approval for Disability payments (i.e. started after hospital d/c)  (*skip question 6*)
- Other (specify): \_\_\_\_\_
- No Answer
- Don't know

6 [If not working/retired/disabled/in school] Are you planning to return to work or education?

☑ Yes  No  No Answer

[If Yes] Please tick the statement that best applies to you now:

- I intend to return to the same job or educational course that I was doing before my Burn Injury
- I intend to go back to different job or educational course than before my Burn Injury
- I am unemployed and actively looking for work
- I am actively looking for an educational course
- Other (please describe): \_\_\_\_\_
- \_\_\_\_\_
- \_\_\_\_\_

**7 Have you worked at all since you left the hospital?**

Yes (*Proceed to question 8*)

No → Why have you not worked? \_\_\_\_\_ (*Questionnaire is complete*)

[If No] **Interviewer:** Please categorize above text response (*see right for options*)

Health related reasons

Looking for work

On disability

Homemaker

Retired

No response

In school

Other

**8 How many weeks after hospital discharge did you return to work? (*record using weeks ONLY*)**

\_\_\_\_\_ No Answer  Don't know

**9 What is your occupation, or what kind of work do/did you do?**

**Interviewer:** Refer to Occupation List (page 6) to categorize response below

\_\_\_\_\_ No Answer  Don't know

**10 On average, how many hours per week do/did you work?**

\_\_\_\_\_ No Answer  Don't know

**11 During the past FOUR WEEKS, how many complete work days or shifts have you missed due to your Burn Injury?**

\_\_\_\_\_ No Answer  Don't know  N/A  (*Have not worked in the last 4 weeks*)

**12 During the past FOUR WEEKS, how many partial days or shifts have you missed due to your Burn Injury, including leaving work early or taking time for doctor's visits?**

\_\_\_\_\_ No Answer  Don't know  N/A  (*Have not worked in the last 4 weeks*)

**13 Thinking about your work experience since leaving hospital, have you ever had to make a significant change in your work duties because of your Burn Injury?**

(*IF REQUIRES PROMPT: Such changes can include a change in work processes, a change in your mix of responsibilities or other changes in job activities.*)

Yes  No  No Answer  Don't know

[If Yes] Please describe this change: \_\_\_\_\_

**Interviewer:** Please categorize above text response (*see right for options*)

Decreased hours

Stopped work/laid off

Limited physically

Change in job duties

Limited cognitively

No response

Other

**14 During the past FOUR WEEKS, how would you rate your EFFECTIVENESS on the job after your Burn Injury?**

100% means your Burn Injury did not affect your job effectiveness

0% means you were unable to work at all because of your Burn Injury.

**How would you rate your effectiveness as a percent?**

\_\_\_\_\_ %    No Answer     Don't know     N/A  (Have not worked in the last 4 weeks)

**15 Are you limited in the kind or amount of work you can do because of your Burn Injury?**

Yes     No     No Answer     Don't know

**16 Have you ever had to change your job or occupation because of your Burn Injury?**

Yes     No     No Answer     Don't know

**17 Has your employer or university/school made any of the following changes to help you with your job or coursework, following your Burn Injury?**

**Allowed you a phased return to work?** Yes     No

[If yes] How long did this phased return last? \_\_\_\_ months    \_\_\_\_ weeks

**Allowed you to take more breaks?** Yes     No

[If yes] Approximately how many extra breaks do you take daily? \_\_\_\_ breaks

[If yes] Approximately how long does each break last? \_\_\_\_ minutes

**Allowed you to permanently reduce your working hours/days?** Yes     No

**Reduced the quantity of work you have to do?** Yes     No

**Reduced your responsibilities?** Yes     No

**Provided more responsibilities?** Yes     No

**Provided more supervision or support at work?** Yes     No

**Allowed you to work from home?** Yes     No

**Used any help, such as Government program, occupational health, etc. To support you?** Yes     No

[If yes] Please describe who was involved: \_\_\_\_\_

---

**Interviewer:** If the Answer to Question 5 was **part-time**, ask the question below.  
Otherwise, the questionnaire is complete.

---

**18** [If working part time]

**Which best describes the reason you are working part time?** *(Select ONE answer)*

- Related to your Burn Injury
- Related to other illness
- Related to other reason
- Don't know
- No Answer

---

**Interviewer:** If the Answer to Question 5 was **New Retirement**, ask the question below.  
Otherwise, the questionnaire is complete.

---

**19** [If retired] **Which best describes the reason why you have retired?** *(Select ONE answer)*

- Related to your Burn Injury
- Reasons not related to your Burn Injury
- No Answer

---

**Interviewer:** If the Answer to Question 5 was **Going to school**, ask the question below.  
Otherwise, the questionnaire is complete.

---

**20** [If going to school] **Which best describes your educational situation?** *(Select ONE answer)*

- I am at same college/university, doing the same or a similar educational course as before
- I am at the same college/university, doing a different educational course as before
- I am at a different college/university, doing the same or a similar course as before
- I am at a different college/university, doing a different course as before
- If so, please state what it is: \_\_\_\_\_
- Other(please describe): \_\_\_\_\_
- No Answer

## Occupation List

Q3 & 10 Options (What is your occupation)

1	Management
2	Business and Financial Operations
3	Computer and Mathematical
4	Architecture and Engineering
5	Life, Physical, and Social Science
6	Community and Social Services
7	Legal
8	Education, Training, and Library
9	Arts, Design, Entertainment, Sports, and Media
10	Healthcare Practitioner and Technical
11	Healthcare Support
12	Protective Service
13	Food Preparation and Serving Related
14	Building and Grounds Cleaning and Maintenance
15	Personal Care and Service
16	Sales and Related
17	Office and Administrative Support
18	Farming, Fishing, and Forestry
19	Construction and Extraction
20	Installation, Maintenance, and Repair
21	Production
22	Transportation and Material Moving



**SERIOUS ADVERSE EVENT**  
 REFER TO **STUDY PROCEDURES MANUAL** FOR DETAILED INSTRUCTIONS.

PATIENT INITIALS:

ID:

MEDICAL CHART #:

NAME OF RESPONSIBLE INVESTIGATOR:	
INSTITUTION:	
REPORT COMPLETED BY:	
DATE OF REPORT:	TYPE OF REPORT: <input type="checkbox"/> INITIAL <input type="checkbox"/> FOLLOW-UP # ____ <input type="checkbox"/> FINAL

**PATIENT INFORMATION**

PATIENT RZ #:	AGE:	SEX: <input type="checkbox"/> MALE <input type="checkbox"/> FEMALE	DATE PATIENT STARTED STUDY INTERVENTION:
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**Event Information**

EVENT ONSET DATE/TIME:	NAME OF EVENT:
DATE BECAME AWARE OF EVENT:	
DESCRIPTION OF EVENT:	
SERIOUSNESS CRITERIA (CHECK ALL THAT APPLY): <input type="checkbox"/> DEATH <input type="checkbox"/> LIFE-THREATENING <input type="checkbox"/> REQUIRES OR PROLONGS HOSPITALIZATION <input type="checkbox"/> RESULTS IN PERSISTANT OR SIGNIFICANT DISABILITY/INCAPACITY <input type="checkbox"/> MAY REQUIRE MEDICAL OR SURGICAL INTERVENTION TO PREVENT ON OF THE OTHER OUTCOMES <input type="checkbox"/> CONGENITAL ANOMALY OR BIRTH DEFECT <input type="checkbox"/> OTHER SERIOUS MEDICAL EVENT	
OUTCOME: <input type="checkbox"/> SAE PERSISTING AT TIME OF REPORT <input type="checkbox"/> COMPLETE RECOVERY/RETURN TO BASELINE <input type="checkbox"/> RESOLVED (NO SEQUELAE) <input type="checkbox"/> RESOLVED WITH SEQUELAE, SPECIFY <input type="checkbox"/> DEATH, SPECIFY DATE/TIME <input type="checkbox"/> UNKNOWN/LOST TO FOLLOW-UP	
IS THE EVENT UNEXPECTED? <input type="checkbox"/> YES <input type="checkbox"/> NO	
RELATIONSHIP OF STUDY INTERVENTION TO EVENT: <input type="checkbox"/> NOT RELATED <input type="checkbox"/> UNLIKELY RELATED <input type="checkbox"/> POSSIBLY RELATED <input type="checkbox"/> PROBABLY RELATED	



**SERIOUS ADVERSE EVENT**  
 REFER TO ***STUDY PROCEDURES MANUAL*** FOR DETAILED INSTRUCTIONS.

PATIENT INITIALS:

ID:

MEDICAL CHART #:

ACTION TAKEN WITH STUDY INTERVENTION: <input type="checkbox"/> STUDY INTERVENTION COMPLETED AT TIME OF EVENT ONSET <input type="checkbox"/> STUDY INTERVENTION ONGOING <input type="checkbox"/> STUDY INTERVENTION INTERRUPTED (TEMPORARILY), SPECIFY DATE _____ <input type="checkbox"/> STUDY INTERVENTION PERMANENTLY STOPPED, SPECIFY DATE _____
ACTION TAKEN TO TREAT THE EVENT: <input type="checkbox"/> NONE <input type="checkbox"/> UNCERTAIN <input type="checkbox"/> SURGERY <input type="checkbox"/> OTHER PROCEDURES (NON-SURGICAL) <input type="checkbox"/> BLOOD OR BLOOD PRODUCTS <input type="checkbox"/> DRUG THERAPY <input type="checkbox"/> OTHER
TREATMENT DETAILS:

**OTHER REPORT INFORMATION**

PAST MEDICAL HISTORY/COMORBIDITIES:	<input type="checkbox"/> SEPARATE PAGE ATTACHED <input type="checkbox"/> DEMOGRAPHIC CRF COMPLETED
LABORATORY TESTS AND INVESTIGATIONS RELATED TO EVENT:	<input type="checkbox"/> SEPARATE PAGE ATTACHED <input type="checkbox"/> NONE
OTHER RELEVANT INFORMATION:	<input type="checkbox"/> SEPARATE PAGE ATTACHED <input type="checkbox"/> NONE
OTHER EVENT INFORMATION THE INVESTIGATOR WISHES TO REPORT:	

**SIGNATURES**

REPORT COMPLETED BY:	SIGNATURE:	DATE:
SITE INVESTIGATOR:	SIGNATURE:	DATE: