

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](https://clinicaltrials.gov).
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**Critical Care
Nutrition**



**Clinical Evaluation
Research Unit**

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

PLEASE NOTE: the Project Lead and Project Assistant (PA) are blinded. Please take care not to unblind the PL/PA in your communications, written or verbal.

In the event you are unable to reach the PL or PA, please contact the Principal Investigator (PI).

Please direct all questions related to the Investigational Product (IP), storage, shipping, or resupply to the Central Pharmacy Depot 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
CTSI	Clinical Trial Site Information (Canada)
CV	Curriculum Vitae
DOA	Delegation of Authority
EDCS	Electronic Data Capture System
EN	Enteral Nutrition
FDA	Food and Drug Administration (USA)
GCP	Good Clinical Practice
HC	Health Canada
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
PA	Project Assistant
PL	Project Lead
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
Sub-I	Sub-Investigator
TBSA	Total Body Surface Area

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 reduce acute care unit and hospital length of stay, decrease 6 month mortality, decrease hospital-acquired blood stream infections from Gram negative organisms, and improve the physical function of surviving burn injured patients.

Study Design

A large, multicenter, double-blind, pragmatic, randomized controlled trial of 1200 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, Europe, Latin America, and Asia.

Study Population

1200 adult patients with deep 2nd and/or 3rd degree burns requiring skin grafting. For patients age 18 – 39 years we require a TBSA (Total Body Surface Area) $\geq 20\%$, or in the presence of an inhalation injury, a minimum of $\geq 15\%$ TBSA is acceptable. For patients aged 40 – 59 years we require a TBSA burn $\geq 15\%$. 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 ≥ 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: Time to discharge alive

Secondary outcome: 6-month mortality

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

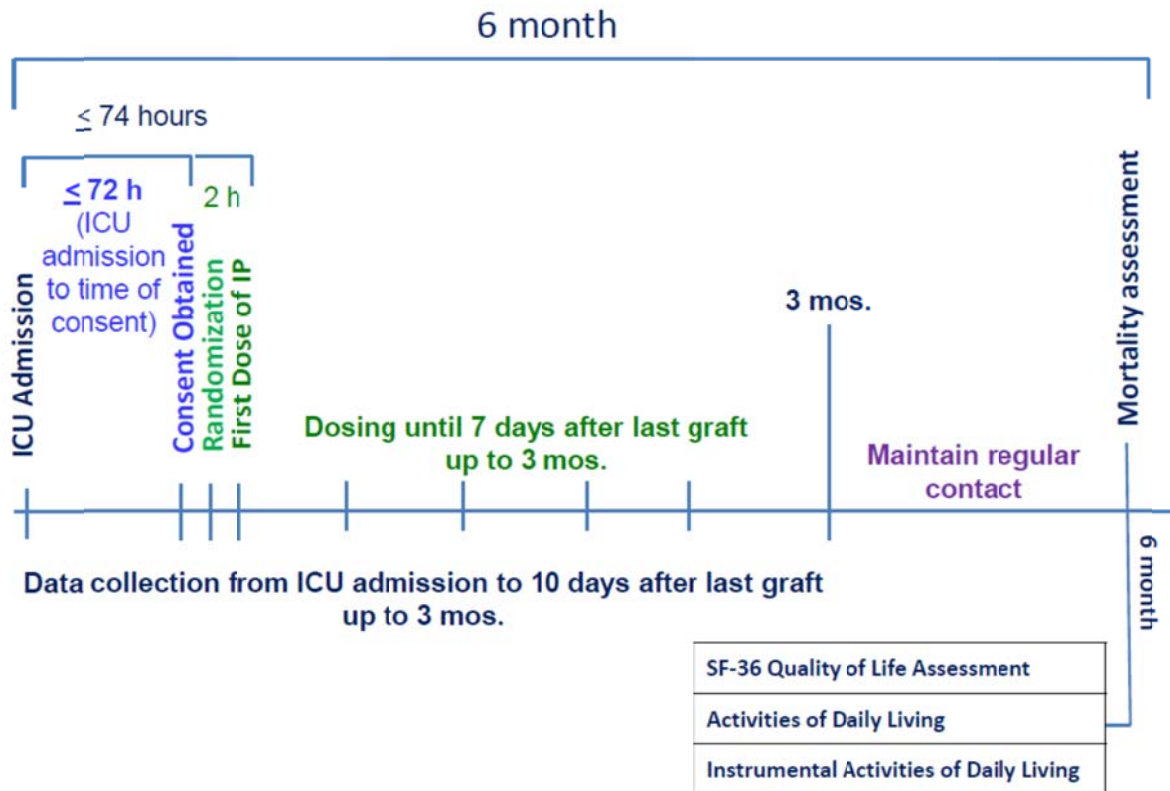
We anticipate the total study duration to be 5 years, broken down as follows: 6 month Start-up period, 4-year recruitment period, and a 6-month follow-up period

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 (SI), sub-Investigator (sub-I), Research Coordinator (RC), 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-I, 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 (DOA) 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 SI and sub-Is
- 7) Signed DOA 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 SI 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 SI and study team member (i.e. sub-I, RC, Dietitian, Pharmacist) must have documented training on the RE-ENERGIZE[®] study prior to initiation of any study procedure. New staff joining the study mid-stream must have documented training on the RE-ENERGIZE[®] study 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 conduct internal team training related to the study, training will be documented in accordance with 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 or delegate will request access to the study electronic data capture systems (EDCSs) (i.e. CRS and REDCap[™]) for all appropriate site research staff (e.g. RCs, pharmacists, SIs, sub-Is). At this point the site is considered activated and may initiate recruitment activities.

Investigator Responsibilities

Per ICH GCP section 4, the SI 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 SI'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 is identified for any planned absences (holiday, attending a conference, etc.)
- Confirmation of Participant Eligibility
- SAE Identification and Assessment
 - The SI 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 patient 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 and documented as percentage of Total Body Surface Area (%TBSA) to confirm eligibility. This assessment must be confirmed by the SI or sub-I. To aid in this assessment, we have attached the Lund and Browder chart as Appendix B.

The SI 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 (active)

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).

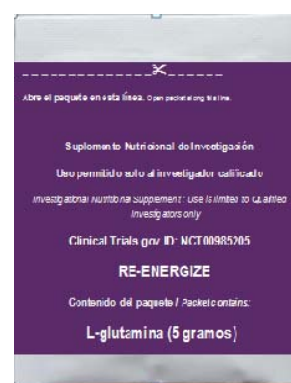
This product is pre-packaged in 5g individual packets.



(North America)



(Europe)



(Latin America & Spain)

The packets 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).

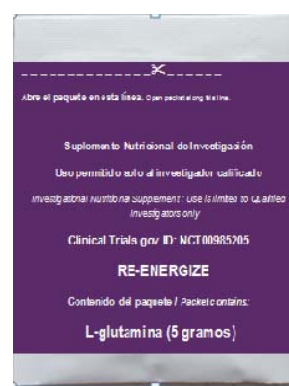
This product is pre-packaged in 5g individual packets.



(North America)



(Europe)



(Latin America & Spain)

The packets 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.

IP Handling and Administration

Duration of study treatment

Patients will receive the IP from randomization through ≥ 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, the decision has not yet been made about whether the patient will need another graft, the 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 7 days after the last successful grafting operation, the IP stops at discharge. Call the Project Lead 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 in keeping with the treatment duration defined above, do not restart the IP.

Determination of Dose

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

- Patients with a BMI <35 kg/m² will receive 0.5 g/kg/day of IP based on pre-burn dry weight (actual or estimated).
- Patients with a BMI ≥ 35 kg/m² will receive 0.5 g/kg/day of IP based on the adjusted body weight, as per the 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 IP dose calculation is based on the patient's pre-burn dry weight. All patients will remain on the initially calculated dosage of IP 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™**:

- Date and Time IP dose changed
- New dosing weight
- New IP prescription in # grams per day

Please NOTE:

- The new dosing weight will not be entered into the CRS.
- You will need to notify pharmacy of the new dosing weight.
- Pharmacy will need to calculate and document the new study IP prescription based on the new dosing weight.

If the IP prescription changes again, repeat the steps above. You may record a maximum of 5 IP prescriptions per patient in REDCap™.

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. RC must notify the pharmacy as soon as a patient is randomized to ensure IP is started within the 2h window.

The initiation of IP 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 IP will be reconstituted by the nurse or RC at the patient's bedside just prior to administration.

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

Administer the IP immediately after reconstituting with water. The IP will become thick and may be difficult to flush down the tube if it is not administered in a timely manner. If the IP is reconstituted and not administered right away, add more water and mix well just prior to administration.

Administering IP via feeding tube

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. Be sure to flush the tube with water after administering the IP. If a feeding tube is inserted, boluses are to be given via the feeding tube.

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 patient no longer needs a feeding tube

When the patient is tolerating oral feeds, the IP 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
- Chocolate Milk
- Applesauce or Apple Juice
- Cereal
- Mashed Potatoes (not too hot and do not reheat after mixing in the IP)

To ensure the patient receives the entire dose administered, mix the IP in the smallest amount of food or beverage required. For example, mix 10g of IP in only 100mL (~3.5 oz) of chocolate milk. If you mix the IP in 250mL (~8 oz.) and the patient does not finish it, only a partial dose of IP will be received.

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.

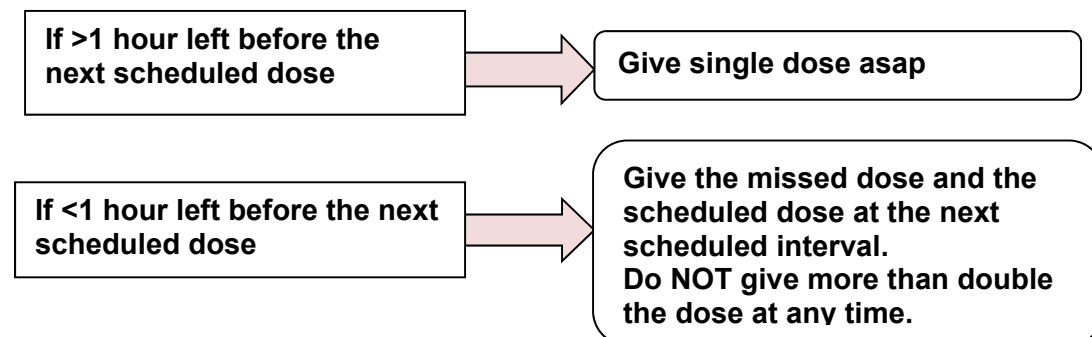
NOTE: There should be no difference in the taste of the glutamine and the maltodextrin.

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 IP for procedures or surgery. If possible, the IP 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 or next calendar 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



The purpose of restricting administration as indicated above is to optimize absorption. Administering the IP more frequently or in larger quantities does not pose a danger to the patient.

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 IP should continue despite high gastric residual volumes, **unless** there is an absolute need to stop the IP i.e. severe vomiting, perforation or leak, bowel obstruction, or a decision to stop the IP has been made by the SI/sub-I (i.e. Serious Adverse Event that is felt to be related to the IP).

To avoid interruptions in the delivery of the IP 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 patients 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 high urea levels 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 >30 mmol/L or >85 mg/dL

At the discretion of the clinical team, the IP 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 IP should not be discontinued or held.

Study Treatment Allocation

Blinding

All site personnel (i.e. SI, sub-Is, RCs, nurses, dietitians) as well as the central study team are blinded to patient 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 IP 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 either of these units as an Acute Care Unit (ACU). Screen patients admitted to the ACU daily for study eligibility. All of the patients who are screened and meet the Inclusion criteria must be entered into 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 EDCS section later in this manual.

Patient eligibility and suitability must be confirmed by the SI/sub-I. Though any attending physician or surgeon may also be involved in confirming suitability of a patient for the study, it is the SI or sub-I, as designated on the DOA log, who must confirm in writing that the patient is suitable. Documentation of eligibility must be signed by the SI/sub-I and include the date and time.

Inclusion Criteria

Patients must meet both inclusion criteria to be eligible for the study.

1) Deep 2nd and/or deep 3rd degree burns requiring grafting

SI/sub-I must confirm the presence of deep 2nd degree and/or 3rd degree burns requiring grafting as assessed by the responsible surgeon/physician.

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

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

2) Patient meets one of the following 4 criteria:

- a. Patients 18 –39 years of age with TBSA burn \geq 20%**
- b. Patients 18 –39 years of age with TBSA burn \geq 15% WITH inhalation injury**
(see table below for diagnosis of inhalation injury)
- c. Patients 40 – 59 years of age with TBSA burn \geq 15%**
- d. Patients \geq 60 years of age with TBSA burn \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"> • carbonaceous material • edema or ulceration
<i>NOTE: 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.</i>

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.

1) 72 hours from admission to Acute Care Unit (ACU) to time of consent

This refers to admission to your ACU. If a patient is transferred from another facility, the clock starts from the time of admission to your unit. For patients who are delayed in their presentation and transfer, please do not enroll if the arrival to your ACU is greater than 24 hrs after the burn injury.

The 72 hour window is determined from the time of ACU admission to time informed consent is obtained. While you have 72 hrs to enroll the patients, where possible, we would like to encourage you to enroll and randomize the patient as soon as possible as the beneficial effect of glutamine may be greater if started earlier.

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

2) Patients younger than 18 years of age

There is no upper age limit for patients enrolled in the study.

3) Patients with renal dysfunction will be excluded. Renal Dysfunction – defined as:

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

NOTE: Pre-resuscitation, some patients will present with compromised kidney function. During the resuscitative period, monitor the patient's kidney function for improvement. If kidney function improves with resuscitation, prior to exhausting the 72 hour post admission window for obtaining consent, please approach for consent and include this type of patient.

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

4) Liver cirrhosis Child-Pugh class C liver disease

The Child-Pugh 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 is an exclusion criteria for this study.

Class A: 5 – 6 points

Class B: 7 – 9 points

Class C: 10 – 15 points

Child-Pugh class C scoring table

Criteria	Points assigned		
	1	2	3
Total Bilirubin SI units	< 2mg/dL or < 34 µmol/L	2 - 3 mg/dL or 34 – 51 µmol/L	> 3 mg/dL or > 51 µmol/L
Serum Albumin 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
Prothrombin time or INR	< 4 seconds < 1.7	4 – 6 seconds 1.7 – 2.3	> 6 seconds > 2.3
Ascites*	Absent	Slight	Moderate
Encephalopathy	None	Moderate	Severe
* Refer to ultrasound results. If ascites has been drained in the past, it should be considered Moderate.			

- 5) **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)
- 6) **Contraindication for EN** (intestinal occlusion or perforation, intra-abdominal injury). *This refers to an absolute contraindication for EN due to a medical/surgical condition. Being NPO for another reason, such a presumed intolerance to EN, is not considered a contraindication for Enteral Nutrition.*
- 7) **Patients with injuries from high voltage electrical contact.** *There has been extensive discussion by the steering committee regarding the inclusion or exclusion of patients with this type of injury. The determination has been made that burns from high voltage electrical contact are very different from thermal injuries and these patients must be excluded. Patients with external burns from an electrical ‘slap’ or ‘arc’ may be included as long as the external burn injury meets the inclusion criteria.*
- 8) **Patients who are moribund** (not expected to survive the next 72 hours). *This judgement must be made by the SI or delegated doctor in charge. NOTE: An isolated DNR does not fulfil this criteria.*
- 9) **Patients with extreme body sizes: BMI < 18 or > 50 kg/m²** *When calculating BMI, the patient’s pre-burn dry weight should be used or estimated. Given that there may be some subjectivity involved in the determination of BMI, err on*

the side of including the patient. For example, if you estimate the weight and the BMI turns out to be 17 or 51, re-set the weight for the patient to be included.

10) Enrollment in another industry sponsored ICU intervention study

Co-enrollment in all non-randomized (observational) academic studies will be approved. For academic randomized controlled trials, forward a synopsis or abstract of the study to the Project Lead to obtain pre-approval of co-enrollment. Co-enrollment in any industry sponsored trials of novel therapeutics or biologics, is not allowed. Co-enrollment into such trials is typically not permitted by industry either.

11) Received glutamine supplement for > 24 hours prior to randomization.

This refers to consistent administration of glutamine over the 24 hr period prior to randomization. If the patient received random or intermittent doses of open label glutamine, discontinue the glutamine prior to randomization. If they received glutamine for more than 24 hrs, they should be excluded.

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

Informed Consent

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

-ICH definition of informed consent

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

Following the confirmation of patient eligibility, the site should seek consent. The nature of the RE-ENERGIZE[®] study population is such that patients 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 SI/RC 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 her or him 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 patients must be consented to the study within 72 hours of Acute Care Unit admission.

Before you approach for consent:

- Familiarize yourself with the patient's history.
- Approach bedside nursing staff/medical staff for an update on the family's involvement and their degree of knowledge of the patient's condition.
- Confirm patient eligibility and appropriateness of enrollment with the SI or sub-I.

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 to the SDM.
- 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 must be qualified to do so, and knowledgeable of 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 ample time for the SDM to read it and ask questions.
- Ask the patient's SDM questions to assess their comprehension of the material reviewed. Ensure he/she fully understands the information.

- Ascertain the patient's or SDM's willingness to participate. Document the decision in the patient's medical chart of any patient or 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 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 6 months after admission to assess survival and conduct quality of life questionnaires. Refer to Appendix H for a patient/alternate contact person(s) information sheet.

Remember to:

- Communicate any important new information that becomes available, and that may be relevant to the patient/SDMs continuing consent
- Assess the patient 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:
 - SDM/patient's comprehension of the material reviewed
 - SDM/patient given ample opportunity to review the ICF and decide whether or not to participate in the research
 - All questions answered to the satisfaction of the SDM/patient
 - Informed consent obtained prior to initiating any study related procedures

Medical Chart Entry

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

<p>This patient is enrolled in <u>IRB study ID#</u>. '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. _____.</p> <p>Consent obtained from _____ (<i>relationship to patient</i>) on <u>dd/mm/yyyy</u> at <u>time</u> hrs. All questions & concerns addressed with patient/SDM at this time. Copy of consent was given to patient/SDM.</p> <p>Date/time of entry: _____</p> <p>Signature of Research Coordinator: _____</p>

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 IP 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 EDCs 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 EDCs for RE-ENERGIZE[®]:

1



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 RC/delegate and other study team members upon documentation of training on study procedures and receipt of Ethics Approval documentation and other essential documents.
- Study team members who are granted access to the CRS and/or REDCap[™] must appear on the DOA 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 IP as soon as possible.

Patient eligibility and suitability must be determined by the SI 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
✓	x	✓	✓	Randomized
✓	x	x	✓	Eligible but Not Randomized
✓	✓	Exclusion criteria met - Do not approach for consent	✓	Not Eligible
x	x	Inclusion criteria Not met - Do not approach for consent	x	Do Not Enter into CRS



<p>Each patient entered into the CRS, will receive a screening number. 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 not randomized</p> <p style="text-align: center;">↓</p> <p style="text-align: center; color: blue;">1002 - Q005</p> <p style="text-align: center;"> ⏟ ⏟ Site # Patient # </p>	<p>If the patient is subsequently randomized, they will also be issued a randomization number. The randomization IDs are assigned sequentially in an 8-character format:</p> <p style="text-align: center;">“R” indicates the patient has been randomized</p> <p style="text-align: center;">↓</p> <p style="text-align: center; color: blue;">1002 - R003</p> <p style="text-align: center;"> ⏟ ⏟ Site # Patient # </p>
---	---

Screening and randomization numbers advance independently of one another. The last 3 digits of the assigned randomization number will not always match the last 3 digits of the screening number.

Accessing & Entering a Patient in the CRS

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

Central Randomization System

User name:

Password:

Login

[Forgot Password?](#)

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.

Home

User profile

Contact us

Logout

Study Name

IMPACT

NEXIS

PROPEL

REENERGIZE - Definitive

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.

Home

User profile

Contact us

Logout

Site List

Add patient

Site Status Page

Find #: Find

(enter Patient #)

Screening ID	Randomization ID	Status
1002Q003	1002R003	Randomized
1002Q002	1002R002	Randomized
1002Q001	1002R001	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, (*complete the exclusion data*).
- 3) **Eligible:** Inclusion and Exclusion data have been entered, but Pre-Randomization form is not completed (*complete the pre-randomization data*).
- 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 #: Find

(enter Patient #)

Screening ID <input type="radio"/>	Randomization ID <input checked="" type="radio"/>	Status
1002Q001	1002R001	Randomized
1002Q005		Eligible but Not Randomized
1002Q004		Not Eligible
1002Q003		In Progress
1002Q002		Eligible

Inclusion Criteria form

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
- Logout
-
- Add patient
- Patient List

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 4 criteria	<input type="radio"/> Yes <input type="radio"/> No
a. Patients 18 - 39 years of age with TBSA \geq 20%	<input type="radio"/> a.
b. Patients 18 - 39 years of age with TBSA \geq 15% WITH inhalation injury	<input type="radio"/> b.
c. Patients 40 - 59 years of age with TBSA \geq 15%	<input type="radio"/> c.
d. Patients \geq 60 years of age with TBSA \geq 10%	<input type="radio"/> d.

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

Exclusion Criteria form

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.

<ul style="list-style-type: none"> Home User profile Contact us Logout Add patient Patient List Patient Status 	<p>A subject will not be eligible for this study if any of the following criteria apply:</p>	
	1. > 72 hrs from admission to Acute Care Unit to time of consent.	<input type="radio"/> Yes <input type="radio"/> No
	2. Patients younger than 18 years of age.	<input type="radio"/> Yes <input type="radio"/> No
	3. 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)	<input type="radio"/> Yes <input type="radio"/> No
	In patients with acute or chronic renal failure (pre-dialysis), an absolute increase of > 80 µmol/L or > 0.9 mg/dL from baseline or pre-admission creatinine or a urine output of < 500 mL/last 24 hours (or 80 mL/last 4 hours) will be required.	
	Patients with chronic renal failure on dialysis will be excluded.	
	4. Liver cirrhosis - Child's class C liver disease	<input type="radio"/> Yes <input 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 type="radio"/> No
	6. Contraindication for EN (intestinal occlusion or perforation, intra-abdominal injury).	<input type="radio"/> Yes <input type="radio"/> No
	7. Patients with injuries from high voltage electrical contact.	<input type="radio"/> Yes <input type="radio"/> No
	8. Patients who are moribund (not expected to survive the next 72 hours).	<input type="radio"/> Yes <input type="radio"/> No
	9. Patients with extreme body sizes: BMI < 18 or > 50 kg/m ² .	<input type="radio"/> Yes <input 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 type="radio"/> No	
11. Received glutamine supplement for > 24 hrs prior to randomization	<input type="radio"/> Yes <input type="radio"/> No	
12. Known allergy to maltodextrin, corn starch, corn, corn products or glutamine.	<input type="radio"/> Yes <input type="radio"/> No	
<input type="button" value="Save"/>		

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 is 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 Lead as soon as you become aware for direction on how to proceed.

Pre-Randomization form

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 SI or sub-I.

Enter the name of the physician who confirmed patient eligibility. This individual should be listed on the Site DOA 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 SDM 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 RC 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 IP.
Other (Please specify)	Specify the reason(s) for not approaching for consent that is not listed above.

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

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

- i. Too Overwhelmed
- ii. Not interested
- iii. Did not respond (timed out)
- iv. Other, please specify

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

<ul style="list-style-type: none"> Home User profile Contact us Logout Add patient Patient List Patient Status 	<p>Did you confirm eligibility of the subject with the site investigator, or sub-investigator?</p> <p><input checked="" type="radio"/> Yes <input type="radio"/> No</p>	<p>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.</p> <p>All times should be recorded using the 24 hour clock. Times must include 4 digits separated by a colon. 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.</p>
	<p>Please indicate the name of the physician who confirmed subject eligibility</p> <p>Dr. Jane Doe</p>	
	<p>Was SDM/subject approached for consent?</p> <p><input checked="" type="radio"/> Yes <input type="radio"/> No</p>	
	<p>Was consent obtained from the SDM/subject?</p> <p><input checked="" type="radio"/> Yes <input type="radio"/> No</p>	
	<p>Consent Date</p> <p>2019-02-01 (YYYY-MM-DD)</p>	
	<p>Consent Time</p> <p>15:32 (HH:MM 24hr)</p>	
	<p>Height</p> <p>172 <input checked="" type="radio"/> cm <input type="radio"/> inches</p>	
	<p>How was height obtained?</p> <p>Measured ▾</p>	
	<p>Weight</p> <p>185 <input type="radio"/> kg <input checked="" type="radio"/> lbs</p>	
	<p>How was weight obtained?</p> <p>Estimated ▾</p>	
<p>Save</p>		

- 1) Record the consent date/time
- 2) Record the patient's weight and height (to the nearest two decimal points).
- 3) Enter the patient's pre-burn dry weight. .
- 4) 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)
- 5) Select the unit of measure used for both weight and height by clicking on the appropriate radio button:
 - a. Weight - either kg or pounds


b. Height - either cm or inches

Once you click on the “**Save**” button, the patient will be randomized to the RE-ENERGIZE[®] Study.

Randomization Confirmation



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



Central Randomization System

- 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

Randomization #:	1001R012
Randomization Date:	2016-02-11 14:32 EST
Height:	150.00 cm
Weight:	45.00 kg
BMI:	20
Dosing Weight:	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.

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 Lead or delegate 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**.

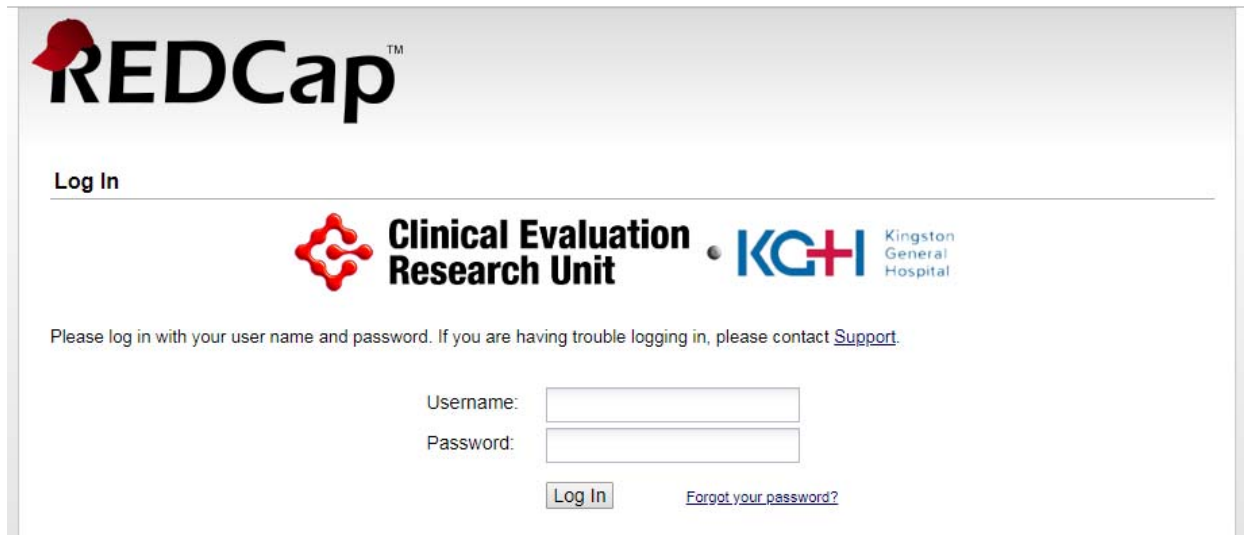
You will then be brought to the Patient Status screen.

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

REDCap™ Data Entry

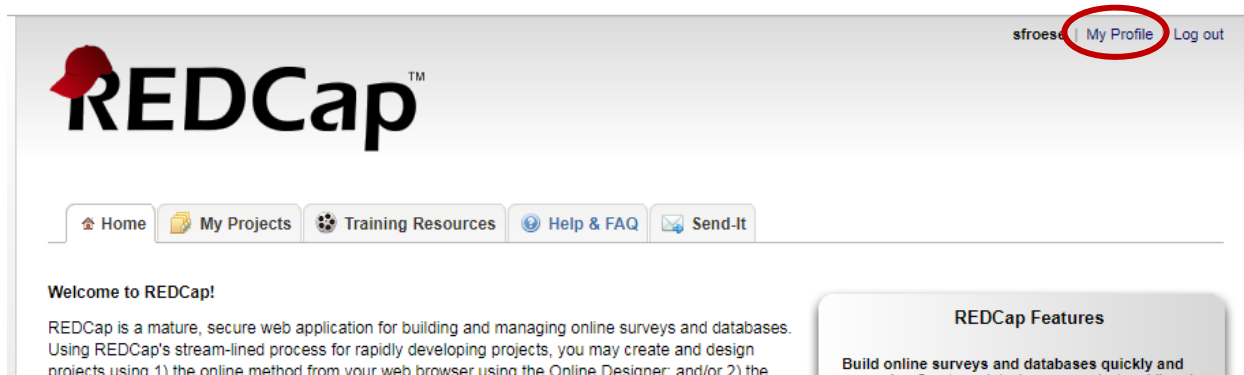
The REDCap™ (**R**esearch **E**lectronic **D**ata **C**apture) is a web-based system used for the RE-ENERGIZE® Study.

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



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

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



Navigating REDCap™

My Databases

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

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 just to the right of ‘Choose an existing Patient ID’.

REENERGIZE - Definitive TEST

[Query Module](#) New: 35 Outstanding: 0 D/M Responded: 0 User Responded: 0 F.A.R.: 5 IT 33

[View / Edit Records](#)

You may view an existing record/response by selecting it from the drop-down lists below. To create a new record/response, type new value in the text box below and hit Tab or Enter. To quickly find a record without using the drop-downs, the text box will auto populate with existing record names as you begin to type in it, allowing you to select it.

Arm 1: Patient
Arm 2: Laboratory Units

Then select your site number from the ‘—select record —’ dropdown list.

Total records: 91

Choose an existing Patient ID Arm 2: Laboratory Units ▾

-- select record -- ▾

-- select record --

--No Group--

10011001 - Query Stage

Harborview Medical Center

1097

Hospital I

1008

Joseph M Still Research Fo

1032

Kingston General Hospital

Data Search

Choose a field to search
(excludes multiple choice fields)

-- select search field --

Search query

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




Logged in as dansereauma | Log out

-  My Projects
-  Project Home
-  Project Setup

Project status: **Development**

Data Collection

 **View / Edit Records**
- View or edit existing records

 **Patient ID 1002** [Select other record](#)

Applications

-  Data Exports, Reports, and Stats
-  File Repository
-  E-signature and Locking Mgmt



Clinical Evaluation Research Unit

REENERGIZE - Definitive TE

 **Event Grid**

The grid below displays the form-by-form procedure into the project for one particular Patient ID. You may click on the colored buttons to access the forms you wish, you may modify the events below. [Define My Events](#) page.

Patient ID 1002
(Arm 2: Laboratory Units)

Day 1 to Day 1

Data Collection Instrument	Day 1
Laboratory Units	●

The laboratory units form will open.

This form is only completed once.

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

Laboratory Units

Re-assign this record to another Data Access Group?

Editing existing Patient ID 1002

Event Name: **Day 1 (Arm 2: Laboratory Units)**

Patient ID	1002
T-bilirubin	<input checked="" type="radio"/> mg/dL <input type="radio"/> µmol/L
Serum Creatinine	<input type="radio"/> mg/dL <input type="radio"/> µmol/L
Glucose	<input type="radio"/> mg/dL <input type="radio"/> mmol/L
Urea	<input type="radio"/> mg/dL <input type="radio"/> mmol/L
Form Status	
Complete?	<input type="radio"/> <input checked="" type="radio"/> Incomplete ▼

The left side of the screen is the main navigation panel. Select 'View / Edit Records' to return to 'Choose an existing Patient ID'. Select a randomized patient from the dropdown list to open the grid and begin entering data for the selected patient.

REDCap
 Logged in as dansereaua | Log out
 My Projects
 Project Home
 Project Setup
 Project status: Development

Data Collection

- View / Edit Records** - View or edit existing records

Applications

- Data Exports, Reports, and Stats
- File Repository
- E-signature and Locking Mgmt
- Data Quality and Resolve Issues

Resources

- Apache II Calculator
- MAP Calculator
- Admin Functions

Reports [Edit reports](#)

1) test [Help & Information](#)

Clinical Evaluation Research Unit **KG+H** Kingston General Hospital

REENERGIZE - Definitive TEST

Query Module New: 35 Outstanding: 0 D/M Responded: 0 User Responded: 33

View / Edit Records

You may view an existing record/response by selecting it from the drop-down lists below. To create a new value in the text box below and hit Tab or Enter. To quickly find a record without using the drop-down populate with existing record names as you begin to type in it, allowing you to select it.

Total records: 91

Choose an existing Patient ID -- select record

Data Search

Choose a field to search (excludes multiple choice fields)

Search query

Begin typing to search the project data, then click an item in the list to navigate to that record.

-- select record
 --No Group--
 10011001 - 1
 Columbia - St
 1055R001 -
 Harborview M
 1097R001
 1097R002
 1097R003
 1097R004
 1097R005
 ...

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 view 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 (SD) 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 SD 4.

	Day 1 to Day 30	Day 31 to Day 60	Day 61 to 6 Month Follow-Up						
Data Collection Instrument	Day 1 Jul 24	Day 2 Jul 25	Day 3 Jul 26	Day 4 Jul 27	Day 5 Jul 28	Day 6 Jul 29	Day 7 Jul 30	Day 8 Jul 31	Day 9 Aug 01
Baseline									
Organ Dysfunction									
Ventilation/RRT									
Study Intervention									
Daily Monitoring									
Laboratory									
Nutrition Assessment/Timing									
Daily Nutrition									
Burn Related Operative Procedures									
Concomitant Medications									
Microbiology									
Protocol Violation									
Hospital Overview									
Survival Assessment									

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

Each grid contains 30 SDs. The buttons at the top of the grid represent each 30 day segment. Navigate to a specific set of SDs/dates, by clicking on the corresponding button at the top of the grid.

Hospital Overview, Survival Assessment and Month 6 Questionnaires all appear after SD 90, on the far right of the 'Day 61 to 6 Month Follow-Up' set of SDs on the data entry grid.

Data Collection Instrument	74 05	Day 75 Oct 06	Day 76 Oct 07	Day 77 Oct 08	Day 78 Oct 09	Day 79 Oct 10	Day 80 Oct 11	Day 81 Oct 12	Day 82 Oct 13	Day 83 Oct 14	Day 84 Oct 15	Day 85 Oct 16	Day 86 Oct 17	Day 87 Oct 18	Day 88 Oct 19	Day 89 Oct 20	Day 90 Oct 21	Outcomes	6 Month Follo
Baseline																			
Organ Dysfunction																			
Ventilation/RRT																			
Study Intervention																			
Daily Monitoring	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●		
Laboratory			●								●								
Nutrition Assessment/Timing																			
Daily Nutrition																			
Burn Related Operative Procedures	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●		
Concomitant Medications	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●		
Microbiology	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●		
Protocol Violation	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●		
Hospital Overview																		●	
Survival Assessment																			●
Contact Log																			●
SF-36																			●
ADL																			●
IADL																			●

Slide the navigation scroll bar at the bottom of the table to reveal the right side of the Event Grid.

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

Events for Arm 1: Arm 1

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	Day 14 Jan 23	Day 15 Jan 24	Day 16 Jan 25	Day 17 Jan 26	Day 18 Jan 27	Day 19 Jan 28	Day 20 Jan 29	Day 21 Jan 30	Day 22 Jan 31	Day 23 Feb 01	Day 24 Feb 02	Day 25 Feb 03	
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																										
ADL																										
IADL																										
Employment Status																										
SF-36																										
Serious Adverse Event Initial 1	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Serious Adverse Event Fup Final 1	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Serious Adverse Event Admin 1	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Serious Adverse Event Initial 2	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Serious Adverse Event Fup Final 2	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Serious Adverse Event Admin 2	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

Form Links

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

The screenshot shows the 'Daily Monitoring' form interface. On the left, a navigation menu titled 'Data Entry Forms' lists various forms, with 'Daily Monitoring' circled in red. The main form area is titled 'Daily Monitoring' and shows 'Editing existing Patient ID "1001R001"'. It includes a dropdown for 'Assign this record to a Data Access Group?' and a table for recording data. The table has two rows, each with a 'Number of packets given' field (set to 3) and a 'Route' field (with radio buttons for PO, EN, and Not Given/Not Applicable).

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:

Legend for status icons:

- Incomplete
- Unverified
- Complete
- Incomplete (no data saved) ?

Incomplete (grey dot)	The form has not been opened and no data has been entered on a form. Blank forms will automatically be set to incomplete.
Incomplete (red dot)	The form has been opened and data has been entered on the form. . The data entered in this form is not complete.
Unverified (yellow dot)	Data entry is at least partially complete on the form. The RC wants to double check data already entered on a form or return to complete data entry.
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.

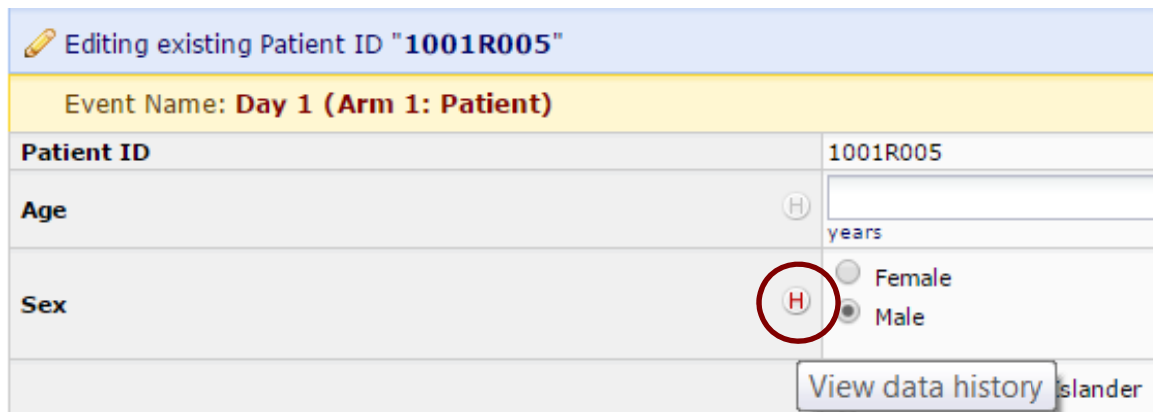
Save and go to Grid	This option will save your progress and return you to the Event Grid.
Save and Stay	This option will save your progress and allow you to continue working on that form.
Save and go to Next Form	This option will save your progress and bring you to the next form on the same SD. <i>For 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>
Save and go to Next Event	This option will save your progress and bring you to the same form on the next SD.
Cancel	This option will take you to the Event Grid screen. All newly entered data will be lost. Only the last saved version will remain

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

Data Conventions in REDCap™

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

- Midnight should be entered as 00:00
- To access individual forms, single click the corresponding 'dot' on the event grid.
- To enter data directly into 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 SD.
 - 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  just left of the field, which turns red when you hover over it with the mouse .



Editing existing Patient ID "1001R005"

Event Name: Day 1 (Arm 1: Patient)

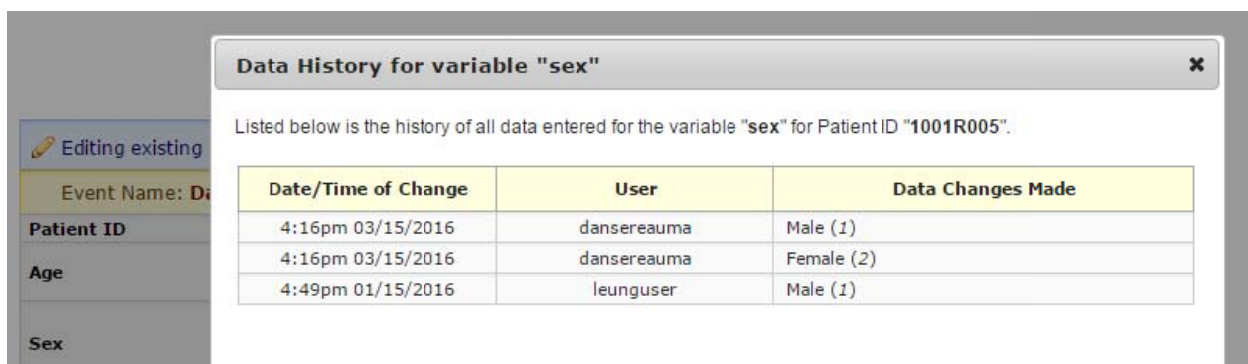
Patient ID: 1001R005

Age: years

Sex: Female Male

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.



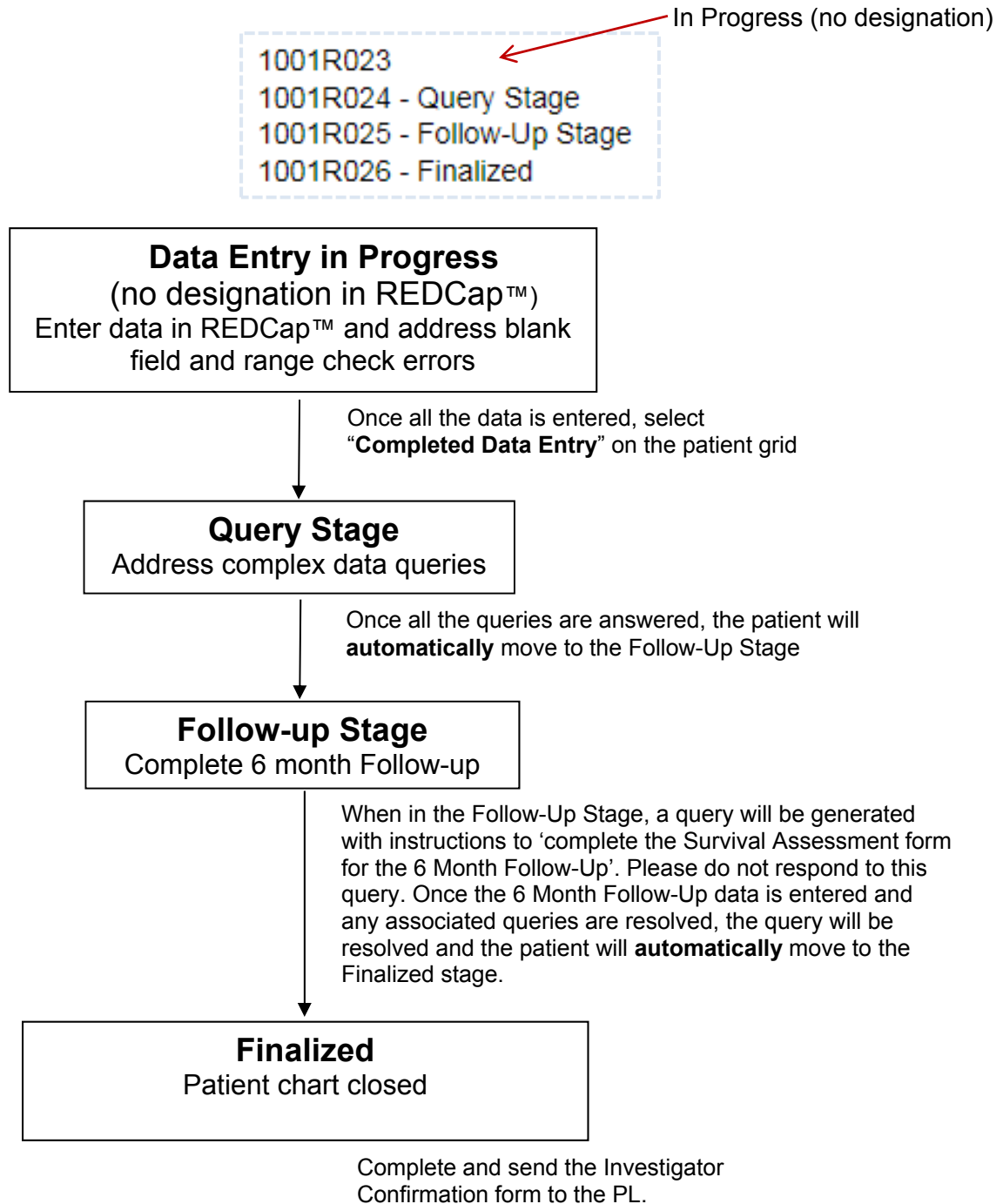
Data History for variable "sex"

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, the 'Data Entry Forms' sidebar is visible, with a 'Queries for Patient #1001R001' menu containing items like 'New', 'Outstanding', 'D/M Responded', 'User Responded', 'F.A.R.', and 'IT Staff', all with a count of 0. Below this menu is a 'Completed Data Entry' button, which is circled in red. The main area displays a 'Contact Log' grid with columns for dates and rows for various forms. Red dots in the grid indicate that these forms are incomplete. A 'Form Status Legend' is located at the bottom right of the grid, showing symbols 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 an error message for Patient 10011004. The message reads: "Warning - There is 1 error preventing this patient's status from reaching Queries. You must address each of these errors before the patient's status will reach Queries." Below the message is a table with three columns: 'Form', 'Error Message', and 'Link to form'. The table contains one entry: 'Hospitalization Overview' with the error message 'The Hospitalization Overview form must be completed.' and a link '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 Lead if modifications to the data are required and we will unlock the form.

After the completion of all data entry (i.e. patient status is 'Finalized'), the Investigator Confirmation form must be completed and forwarded to the Project Lead.

Use the Investigator Confirmation form found on the next to the last page of the eCRF worksheets. The form is not available in REDCap™.

Investigator Confirmation

The form is titled "Investigator Confirmation Form" and is for the "RE-ENERGIZE STUDY". It contains the following text:

RE-ENERGIZE STUDY

Patient ID _____

Investigator Confirmation Form

The data collected in the RE-ENERGIZE Case Report Forms was 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)

Enter the 8 character patient randomization number above the line labelled 'Patient ID' at the top right of the form. 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 her/his supervision and in accordance with study procedures.
- The data and statement are complete and accurate to the best of her/his knowledge.

Forward a scan of the signed Investigator Confirmation form to the PL. 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 EDCS 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 (SDs)

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

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

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

The SDs would be:

SD 1 = 2015-09-08 from 16:00 to 2015-09-08 at 23:59

SD 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 ≥ 7 days after the last graft, while other data is collected from ACU admission through ≥ 10 days after the last graft (stop of IP plus 3 days). See below for further clarification:

Until > 7 days post last successful graft.

Data collected for ≥ 7 days post last successful graft must be collected until the IP has been stopped or 7 days after the last grafting operation, whichever is longer.

Until > 10 days post last successful graft.

Data collected for ≥ 10 days post last successful graft must be collected until the IP 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 an 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 ≥ 18 years of age to be eligible to participate in The RE-ENERGIZE[®] Study).

Sex

Check the appropriate box (female or male).

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. There is a hyperlink to the website in REDCap[™] in the Resources section on the left side menu. 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. If testing was not order for all variables, enter all of the data available and report the partial APACHE II score.

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). Select 'Yes' or 'No' to comorbidities. If the patient has comorbidities not listed in the taxonomy, select 'No' to comorbidities. If the patient has comorbidities listed in the taxonomy, select 'Yes' and then select all comorbidities the patient has from the list of 37 provided.

○ 37. Alcohol Abuse

We would like to monitor the number of patients 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 patient 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 Admission

IMPORTANT: ensure the date entered is correct. All dates on the REDCap™ grid are generated from this date.

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 occurred. If the time of the burn is not available check the 'Not 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 does NOT meet the inclusion criteria for enrollment into this study.

- Scald
- Fire (Includes both flame and flash burns)
- Chemical
- Radiation
- Unknown
- Other (please specify) _____

Do NOT Include

- Electrical Burns (this refers to through and through electrical burns wherein much of the trauma is internal).
 - Thermal burns as a result of an electrical 'arc' or 'slap' are allowed
- Frost Bite
- Steven-Johnson Syndrome (SJS)
- Toxic Epidermal Necrolysis (TEN)

Contact the Project Lead with any questions related to qualifying burn types.

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%.

High Dose Vitamin C Resuscitation

Indicate whether the patient received high dose Vitamin C as part of her/his resuscitation protocol by selecting 'Yes' or 'No'.

- As a guide, high dose Vitamin C resuscitation is commonly considered approximately 66mg/kg/hr administered intravenously for the first 24 - 48 hours after ACU admission.

Organ Dysfunction form

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

PaO₂/FiO₂ (PF ratio)

Record the lowest PaO₂ / FiO₂ (PF ratio) observed in the first 24 hours after admission by selecting from the options below. The PaO₂ and FiO₂ values should come from the same blood gas measurement. **If no PF ratio, record N/A** by selecting the first option.

- ≥ 400 mmHg **or N/A**
- 300 – 399 mmHg
- 200 – 299 mmHg
- 100 – 199 mmHg with respiratory support
- < 100 mmHg with respiratory support

Platelets (lowest)

Record the lowest serum platelets observed in the first 24 hours after admission by selecting from options below. If no Platelet data, record N/A by selecting the first option.

- $> 150 \times 10^9/L$ ($10^3/\mu L$) **or N/A**
- $100 - 149 \times 10^9/L$ ($10^3/\mu L$)
- $50 - 99 \times 10^9/L$ ($10^3/\mu L$)
- $20 - 49 \times 10^9/L$ ($10^3/\mu L$)
- $< 20 \times 10^9/L$ ($10^3/\mu L$)

Vasopressors

Indicate whether or not the patient received vasopressors.

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

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

If 'No', enter Mean Arterial Pressure (MAP) (), see below.

MAP (lowest)

Indicate the lowest MAP observed in the first 24 hours after admission by selecting one of the options below:

- < 70 mmHg
- ≥ 70 mmHg

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

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

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)

Indicate the volume range of urine output in the first 24 hours after admission by selecting from the list below:

- < 200 mL/day
- 200 - 499 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.

Record the first episode of mechanical ventilation, even if it is less than 48 hours in duration (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.

After the patient has been successfully **breathing without mechanical ventilation** for \geq 48 hours, record the date and time mechanical ventilation was discontinued.

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 5cmH₂O without pressure support or intermittent mandatory ventilation assistance.

If the 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, select 'Same as death date & time'.

If the patient is still mechanically ventilated 3 months after ACU admission, select 'Still vented 3 months post ACU admission'.

Was mechanical ventilation re-instituted \geq 48 hours after the previous mechanical ventilation stop date/time?

If the patient never restarted invasive mechanical ventilation, then select 'No' and proceed to the Renal Replacement Therapy (Dialysis) section.

In the event that the patient is restarted on invasive mechanical ventilation after being extubated successfully for 48 hrs, select 'Yes' to open the next event on the form.

Ventilation Event 2

Invasive Mechanical Ventilation #2 Start

Do **not** record episodes of temporary ventilation (defined as <48 hrs).

Record the date and time invasive mechanical ventilation was restarted.

If the patient never restarted invasive mechanical ventilation, then select '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 start and stop dates 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 by selecting 'Yes' or 'No'.

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) Start

Record the start date of RRT.

RRT stop date

Record one of the following:

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

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

Study Intervention form

The IP 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 in REDCap™.

Study Intervention

Start Date and Time

Enter the date and time the first dose of IP was administered in the format YYYY-MM-DD and HH:MM (24 hr clock).

Was Study Intervention started > 2 hours after Randomization?

If the IP was started greater than 2 hours after randomization, indicate 'Yes' by placing a check in the corresponding box.

Reason Study Intervention was started > 2 hours after randomization

When 'Yes' is selected in REDCap™, a field opens to enter the reason. Choose the reason from the list provided (see below):

- Pharmacy delay
- Patient NPO for surgery
- Awaiting tube placement and/or verification
- Patient not available (procedure)
- Nurse not available
- Other (specify): _____

If 'Other' is selected, an explanation must be entered in the space provided.

Stop Date and Time

Enter the date and time the last dose of IP 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. ≥ 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 IP prescription in grams/day.

Each packet contains 5 grams of IP. If 10 packets per day are to be given, select 50 from the drop down list provided.

Did the study intervention prescription change?

If the IP prescription changes, select 'Yes' by placing a check in the corresponding box. When 'Yes' is selected in REDCap™, a field opens to enter the date/time the change occurred, the new dosing weight, and the new prescription in grams/day, .

Changes to the IP prescription are documented in REDCap™. The change in prescription will NOT be reflected in the CRS.

If the IP prescription changes again, repeat the steps above. You may record a maximum of 5 IP prescriptions per patient in REDCap™.

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 a lower extremity 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 IP and to identify any dose related Protocol Violations.

IP 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:

- IP administration: from randomization to ≥ 7 days after the 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 IP administration.

NOTE: Duration of IP is from randomization to ≥ 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 IP should continue until the determination is made that no additional grafting will occur, or until ACU discharge, or until 3 months after ACU admission .

Prescribed # grams per day

To assist in determining the daily percentage of IP received, there is a place at the top of each worksheet to record the number of grams per day of IP the patient is to receive. This data is not entered in REDCap™.

Date

Enter the date corresponding to the calendar day for the data being collected. Select the SD 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 IP was given on each SD.

Grams given

Select the # grams given, (5 to 30) from the drop down list, at each administration as documented in the medical chart.

- Each packet of IP 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 IP was administered at each interval:

- PO (oral intake with beverage or food)
- EN (administered via tube)

Percentage of study intervention received today

Divide the total number of grams actually given on each SD by the number of grams prescribed per day to determine the percentage of IP 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 IP 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 testing is 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 SD 14

- Weekly: From day 15 to ≥ 10 days post last successful graft, d/c from the ACU, or 3 mos. after admission, whichever comes first.
 - Collect weekly lab data from a single day during that study week defined as +/- 24 hours from SD 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 for the day as indicated below. Exception: record glucose taken closest to 8:00 AM:

- Creatinine (highest)
- *Bilirubin, total (highest)*
- *Urea (highest)*
- *Glucose (closest to 8:00 AM)*

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

NOTE: There are no protocolized laboratory tests for this study. Enter the data for tests ordered as standard of care.

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 for the first 12 days of admission. If the prescription changes on SD 12 or after, do not record the change in REDCap™.

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 lead to a prescription of 25 - 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. Only record prescriptions from ACU admission through SD 12.

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 from admission to the ACU through 12 days after admission.

Enteral Nutrition

Was EN received during this ACU admission?

Indicate if the patient received EN during this ACU admission or not, by selecting one of the following options:

- Yes, started during the first 12 days of ACU admission
- Yes, started after first 12 days of ACU admission
- No

Date/Time

If the patient received EN during the first 12 days of this admission, record the the start date and time EN was initiated. Record the stop date and time EN was permanently discontinued by selecting one of the following options:

- Same as death date & time
- Still receiving EN after Day 12 post ACU admission
- Actual EN Stop date & time

If the patient dies during the first 12 days after admission and is receiving EN at the time of death, select 'Same as death date & time'. Remember to complete the death date & time on the Hospital Overview form.

If EN is continued beyond 12 days after admission, select 'Still receiving EN after Day 12 post ACU admission..

If EN is permanently discontinued on or before day 12 post admission, enter the actual date and time EN was discontinued.

Parenteral Nutrition

Was PN received during this ACU admission?

Indicate if the patient received PN during the first 12 days of this ACU admission or not, by selecting one of the following options:

- Yes, started during the first 12 days of ACU admission
- Yes, started after first 12 days of ACU admission
- No

Date/Time

If the patient received PN, during the first 12 days of this admission record the start date and time PN was initiated. Record the stop date and time PN was permanently discontinued by selecting one of the following options:

- Same as death date & time
- Still receiving PN after Day 12 post ACU admission
- Actual PN Stop date & time

If the patient dies during the first 12 days after admission and is receiving EN at the time of death, select 'Same as death date & time'. Remember to complete the death date & time on the Hospital Overview form.

If PN is continued beyond 12 days after admission, select 'Still receiving PN after Day 12 post ACU admission..

If PN is permanently discontinued on or before day 12 post admission, enter the actual date and time PN was discontinued.

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, for the first 12 days of admission, and entered into REDCap™. These data should be obtained from the dietitian or team member responsible for assessing and monitoring the patients' nutritional needs.

Additionally, several medications which may have a material effect on nutrition are captured on this form:

- Propofol
- Insulin
- Opiates
- Motility agents

Duration of Data Collection

These data are to be collected daily from SD 1 (ACU admission) through SD 12, or ACU discharge, whichever comes first.

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

Enteral Nutrition (EN)

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 SD 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'.

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

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 SD.

- Do not include the calories from IV solutions (PN data will be collected separately).

- Do not record the calories from Propofol (volume will be entered separately).
- Do not include protein supplements in this total (protein supplements will be collected separately).

Protein Supplements

Was a protein supplement given?

Record whether a protein supplement was given enterally via tube feed, 'Yes' or 'No'.

Protein supplement name

If a 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 dropdown list, select '*Other: please specify company and product name*', then enter the information in the space provided.

Add another protein supplement?

If a second protein supplement was given on the same SD, select 'Yes' and select the name of the supplement given from the dropdown list. If the Protein Supplement given is not in the dropdown list, select '*Other: please specify company and product name*', then enter the information in the space provided.

You may enter up to 2 different protein supplements each day. If more than 2 protein supplements were given, record the 2 that provided the largest volume.

Total kilocalorie and protein received from protein supplements

Record the total calories and protein received from protein supplements.

NOTE: Please do NOT enter Protein Supplements received orally in REDCap™.

Parenteral Nutrition (PN) Was Parenteral Nutrition (PN) given?

For each day, from admission to ACU through SD12, indicate whether the patient received PN, 'Yes' or 'No'.

PN: Provision of carbohydrates plus protein and/or lipid, with or without micronutrients, electrolytes or other additives, delivered directly into a vein.

Infusion of dextrose alone does **not** constitute parenteral nutrition (ie. If a participant only received dextrose in the absence of amino acids and lipids you should answer 'No' for whether or not the participant received parenteral nutrition).

Total kilocalories and protein received from PN

If yes, record the total calories (kilocalories) and grams of protein received from PN for that SD.

- Do not record the calories from Propofol (volume will be entered separately).
- Do not include calories from IV dextrose alone, this does not constitute PN.

Oral Nutrition

Was Oral Nutrition given?

Indicate whether the patient received any oral nutrition on each SD from admission through SD 12, Yes or No.

Record 'Yes' to oral intake every SD the patient receives oral nutrition, from admission through SD 12, even if they also received EN and/or PN.

Propofol

Was Propofol received for ≥ 6 hours?

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

Total volume of Propofol received

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

Insulin

Was Insulin received today?

Indicate whether the patient received insulin on each SD, 'Yes', 'No', or 'Not Available'.

If 'Yes' insulin was given, record the total units received in the 24 hour period from all insulin IV, SC (subcutaneous) and bolus.

Opiates

Were Opiates received today?

Indicate if the patient received any opiates (eg. morphine, fentanyl, hydromorphone, other narcotic) on each SD, 'Yes', 'No', or 'Not Available'.

Motility Agents

Were Motility Agents received today?

Indicate if the patient received any motility agents (eg. metoclopramide, erythromycin, domperidone, fentanyl, other) on each SD, 'Yes', 'No', or 'Not Available'.

- Do NOT record stool softeners as motility agents.
- Do not include erythromycin prescribed as an antibiotic.

Burn Related Operative Procedures

All burn related operative procedures, type of procedure, and whether it was planned or unplanned will be recorded in REDCap™. Enter data related to the procedure in REDCap™ on the date the procedure occurred.

Duration of Data Collection

This data is collected from admission to the ACU until ≥ 10 Days post last successful grafting operation (stop of IP plus 3 days), 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 SD from the taxonomy provided 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

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



Examples of 'Other' burn related operative procedures to enter into REDCap™:

- Amputation
- Escharotomy



Examples of procedures NOT to be entered:

- tracheotomies
- dressing changes, even if conducted in the operating room (OR)

Concomitant Medications and Heart Rate

Specific medications or medication types and Heart Rate are recorded on the Concomitant Medications form in REDCap™

Duration of Data Collection

This data is recorded from admission to the ACU until \geq 10 Days after the last grafting operation (stop of IP plus 3 days), or discharge from the ACU, or 3 months after admission to the ACU, whichever comes first:

Heart Rate

Record both the Highest and Lowest heart rate documented on each calendar day. If only one heart rate is recorded, enter it as both the highest and the lowest for that day.

If there is no documentation of heart rate on a SD, do not enter zero, leave the fields blank. A query will be generated for the missing data. Respond to the query by providing the reason the heart rate was not entered on the specified date.

Concomitant Medications

For the purposes of this study, we are only collecting data on the following concomitant medications or medication types:

- Oxandrolone, Nandrolone, Testosterone (anabolic steroids)
- Beta Blockers (any)

Were concomitant medications received today?

Indicate if *specific* concomitant medications (*oxandrolone, nandrolone, testosterone, or any Beta Blockers*) were received today, 'Yes', 'No' or 'Not Available'.

If neither beta blockers nor the specific anabolic steroids listed above were given, answer 'No'.

If 'Yes', *the specific* concomitant medications were received, indicate which medications by selecting the appropriate response(s) from the lists.

Oxandrolone/Nandrolone

Was Oxandrolone, Nandrolone, or Testosterone received today?

Indicate if the patient received any of the anabolic steroids listed by selecting the appropriate response from the list below:

- Yes, Oxandrolone
- Yes, Nandrolone
- Yes, Testosterone
- No
- Not Available

Beta-Blockers

Were Beta-Blockers received today?

Indicate if the patient received any Beta-Blockers by selecting the appropriate response from the list below:

- Yes
- No
- Not Available

If the data is missing (eg. missing flowsheet) for a given day and there is no way to confirm what the patient did or did not receive, select 'Not Available'.

Microbiology

Record only the following microbiology data in REDCap™.

Only record venous or arterial blood cultures that test positive for **Gram negative bacteria** that occurred >72 hours after ACU admission until ≥ 10 days post last successful grafting (stop of IP plus 3 days), or ACU discharge, or 3 months from ACU admission, whichever comes first.

NOTE: Do not include blood from a catheter line tip.

Any Gram Negative Bacteremia to report?

Record this data in REDCap™ on the microbiology form that coincides with the date the sample was taken. Select 'Yes' to open the form and enter the microbiology data.

Gram Negative Bacteremia 1

Date sample collected

Record the date the sample was taken (i.e.: not when the results were reported) in the format YYYY-MM-DD or select the date from the date picker.

Time sample collected

Record the time the sample was taken (i.e.: not when the results were reported) in the format HH:MM.

Gram Negative Culture Species

Record the name of the Gram negative bacteria reported from the taxonomy, 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.

Was there another Gram negative culture today?

If there was a second blood culture collected on the same date that grew a different Gram negative bacteria, select 'Yes' to open the form and enter the microbiology data.

Repeat the steps above to record up to 5 different Gram negative bacteria reported from blood cultures taken on the same date.

Do not record the same bacteria more than once on each SD, even if it was reported from specimens collected at different times on that date. Record all different Gram negative bacteremia reported from specimens taken on the same date.. Record the bacteremia on every day a blood culture was taken and Gram negative bacteria grew.

Protocol Violations

A Protocol Violation (PV) 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 central study team at CERU. An automated email notification will be generated and sent to the Project Lead within 24 hours of the data being entered into REDCap™.

Duration of Data Collection

Protocol violations are to be reported from randomization until end of the study duration defined as ≥ 10 days post last successful grafting operation (stop of IP plus 3 days), or ACU discharge, or 3 months from ACU admission whichever comes first).

Each site is responsible for determining if and when a protocol violation should be reported to the local ethics board (REB/IRB).

Some examples of reportable protocol violations include, but are not limited to:

- Randomization of an ineligible patient.
- IP Daily dose delivered is $< 80\%$ prescribed over a 3 day average.

Example:

Prescribed dose:	35g/day	(80% = 28g)
Dose received:	Day 6: 30g	(85.7%)
	Day 7: 20g	(57.1%)
	<u>Day 8: 30g</u>	<u>(85.7%)</u>
3 Day Average	Total:	80g/3 days = 26.67g/day (76.2%) 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 SDs is NOT less than 80%

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

- Day of Randomization
- Day of Discharge
- Last Day IP was administered
- Day of Death

Are you reporting a Protocol Violation today?

Record a protocol violation on the PV form that coincides with the date the PV occurred, not the date it was discovered. If a protocol violation occurred today, select 'Yes' to open the PV form and enter the data.

Date Violation Discovered

Enter the date the violation was identified by site research staff. This may be different than the date the PV occurred.

Is the local SI aware of the violation?

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

NOTE: The Site Qualified Investigator needs to be made aware of all protocol violations.

Violation

Using the options provided, check the box for the type of violation being reported:

- Dose delivered over a 3 day average is <80% prescribed
- 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
- Vomiting/emesis
- Bowel perforation/obstruction
- Held for procedure
- Patient declined/refused study supplement
- Other, specify details _____

Are there supporting files to be emailed (preferred) or faxed?

Indicate if other supporting files are being sent to the central study team via email or fax:

- Yes, by email (preferred)
- Yes, by fax
- No

Action taken by RC/Responsible Delegate

Describe the action taken by the RC/responsible delegate to prevent violation/problem from recurring.

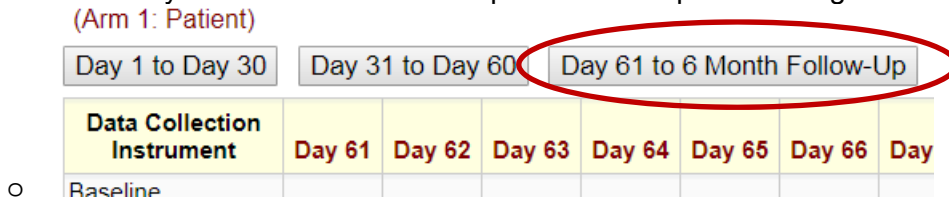
Another Protocol Violation to add?

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.

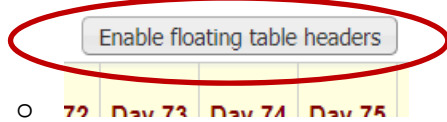
Hospital Overview

Record data related to last graft, acute care unit discharge, hospital discharge, and mortality on the Hospital Overview form in REDCap™. The Hospital Overview form in REDCap™ may be located as follows:

- 1) Select a patient
- 2) Click on the 'Day 61 to 6 Month Follow-Up' tab at the top left of the grid:



- 3) Click the 'Enable floating table headers' tab at the top right of the grid:



- 4) Scroll right until you see the 'Outcomes' column after 'Day 90':



- 5) Scroll down until you see the gray dot at the intersection of the 'Outcomes' column and the 'Hospital Overview' row:

If 'Not Available – Consent withdrawn for data collection', proceed to the ACU Stay #1 and select 'Yes' to the question 'Consent withdrawn/denied during this ACU stay?'.

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. This includes withdrawal of consent to take the IP and/or withdrawal of continued data collection and/or complete withdrawal from the study. If 'Yes', enter the date and time consent was withdrawn/denied and the type of withdrawal/denial from the list below:

- Stop intervention, continue data collection
(If a patient withdraws consent, this is always the preferred type of withdrawal. If the patient does not want to take the study supplements anymore, please request he/she allow you to contact her/him and/or check medical records to find out how he/she is doing.)
- Stop intervention, stop data collection (keep previous data)
- Stop intervention, stop data collection (discard previous data)

If the patient withdraws consent for data collection, after entering the date and time consent was withdrawn and selecting the type of withdrawal, save the data in the form and do not enter any more data.

If consent was not withdrawn, or consent was not withdrawn for data collection, proceed to the next question on the form.

Did the patient die during this ACU stay?

Select the response from the options provided:

- Yes
- No, Patient Discharged
- No, Patient Still In ACU At 3 months

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.

Cause of Death

If the patient died, enter the cause of death in the open text field. Document the cause of death from a post mortem report. If a post mortem report is not available, document the cause of death from the death certificate.

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?

These data are collected to capture readmissions to your ACU from within your hospital up to 3 months after the patient was first admitted for this burn injury. Do not record readmissions once the patient has been discharged from your hospital and do not record readmissions that occur greater than 3 months after the initial admission.

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 from within your hospital.

If 'No, proceed to the 'Hospital Stay' section of the form.

Continue to enter ACU discharge and readmission data from within your hospital until 3 months after the first ACU admission to a maximum of 5 admissions. Do not enter readmissions that occur more than 3 months after admission. Do not enter readmissions that occur after the patient is discharged from your hospital.

If the patient is still in the ACU at 3 months after ACU admission, select 'No, Patient Still In ACU At 3 months'. and mark your calendar to contact the patient at 6 months after ACU admission to complete the Survival Assessment form and 6 Month Follow-Up questionnaires.

Hospital Discharge

Consent withdrawn/denied during this Hospital stay?

If the patient withdraws consent for data collection after ACU discharge and prior to Hospital discharge, select 'Yes' and indicate the type of withdrawal.

NOTE: There is no option to select 'stop intervention' after the patient is discharged from the ACU. Do not select 'Yes' if the patient withdrew consent during her/his ACU stay. The data regarding consent withdrawal during the ACU admission are captured in the ACU Stay #1 fields:

Consent withdrawn/denied during this Hospital stay?

- Stop data collection (keep previous data)
- Stop data collection (discard previous data)

If the patient withdraws consent while in your hospital after ACU discharge, enter the date and time consent was withdrawn, select the type of withdrawal, and save the data in the form. Do not enter any more data.

Did the patient die in Hospital?

Record whether the patient died in your hospital after ACU discharge by selecting from the options provided:

- Yes
- No, Patient Discharged
- No, Patient Still In ACU At 3 months

, If 'Yes', record the date and time the patient died.

Cause of Death

If the patient died, enter the cause of death in the open text field. Document the cause of death from a post mortem report. If a post mortem report is not available, document the cause of death from the death certificate.

If 'No, Patient Discharged', enter the date and time the patient was actually discharged from the hospital. If the hospital discharge time is not available, select 'Yes' to the question 'Time not available?' Proceed to the 'Discharged to' row.

If 'No, Patient Still In Hospital At 3 months', mark your calendar to contact the patient at 6 months after admission to complete the Survival Assessment form and 6 Month Follow-Up questionnaires.

Discharged to

If the patient was discharged from your hospital, select the location to which the patient was discharged from the options provided:

- Ward in another hospital
- ACU in another hospital
- Long term care facility
- Rehabilitation unit
- Home
- Other (specify)
 - If you select 'Other (specify)', in the open text field please enter the location to which the patient was discharged.

Month 6 Follow-up Assessments

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 may complete the questionnaires for the patient.

At 6 months after the patient was **admitted** to your ACU, contact the patient or alternate to complete the 6 Month Follow-Up forms. The Survival Assessment form and 6 Month Follow-Up questionnaires in REDCap™ may be located as follows:

- 1) Select a patient
- 2) Click on the 'Day 61 to 6 Month Follow-Up' tab at the top left of the grid:

(Arm 1: Patient)

Day 1 to Day 30	Day 31 to Day 60	Day 61 to 6 Month Follow-Up					
Data Collection Instrument	Day 61	Day 62	Day 63	Day 64	Day 65	Day 66	Day
Baseline							

- 3) Click the 'Enable floating table headers' tab at the top right of the grid:

Enable floating table headers

- 4) Scroll right until you see the '6 Month Follow-Up' column in the grid after the 'Day 90' and 'Outcomes' columns:

Indicate if survival status was obtained, 'Yes' or 'No'.

Survival Status Obtained Date

If 'Yes', record the date the information was obtained.

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, caregiver, or other individual. The alternate contact does not need to be a legal representative (SDM) of the patient.

Record the source of the survival status information.

- Patient
- Alternate Contact Person(s) (Specify relationship
 - Specify the alternative contact's relationship with the patient (Record the relationship between the alternate contact person and the patient in the open text field. Do not include information that could potentially identify the patient, such as proper names, in this field.)
- Family Physician
- Medical Records
- Obituaries
- Internet
- Other (Please specify)

Survival Status

Indicate if the patient is Alive or Deceased.

If 'Alive', save the form and proceed to the 6 Month Follow-Up questionnaires.

If 'Deceased', continue completing the survival assessment form.

Date of death known?

Indicate if the date the patient expired is known, 'Yes' or 'No'.

If 'Yes', enter the date of death.

If 'No', enter the last date the patient was known to be alive

Was the survival status obtained?

If 'No', 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. 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 survival assessment. Record all attempts* to contact the patient and/or the alternate by selecting from the list below (Choose ALL that were completed):

- 3 attempts to contact the patient were made (**mandatory**)
- 3 attempts to contact the alternative contact person(s) were made (**mandatory if applicable**)
- Family doctor contacted (**mandatory if available**)
- No medical records on the patient available at month 6 (**mandatory**)
- Internet searches for the patient name did not reveal survival status (**mandatory**)

Last date known to be alive

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

Attempt to Contact

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 patient's
 - 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(s)
 - Home number(s)
 - Work number(s)
 - 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.

Duration and Timing of 6 Month Follow-up Questionnaires

Month 6 Follow-up Questionnaires are completed once. The SF-36, ADL, and IADL 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 defined period (\pm 14 days from 6 months after admission to your ACU), please continue to attempt to contact the patient to perform the assessments.

SF-36

Was the SF-36 completed?

If 'Yes', enter the SF-36 data in REDCap™.

Reason not done

If 'No', select the reason the SF-36 was not completed from the list provided:

- Deceased (*Record death date on the Survival Assessment form.*)
- Patient Refused
- Alternate Refused
- Both Patient and Alternate Refused
- Not able to reach patient and/or alternate
- Withdrew
- Missed
- Other (specify)

If the patient is deceased, record the date of death on the 'Survival Assessment' form. If the death date is not known, enter the date the patient was last known to be alive.

Refused

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

Month 6 Follow-up Questionnaires are completed once. The SF-36, ADL, and IADL assessments are to be conducted 6 months (+/- 14 days) after admission to the acute care unit. Contact the patient or family member/friend of the patient via telephone and administer the following questionnaires. 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)

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.

Was the questionnaire (SF-36 or ADL or IADL) completed?

At the top of each questionnaire, indicate whether or not the respective questionnaire was completed by selecting 'Yes' or 'No'.

If 'Yes', enter the date the questionnaire was completed and the patient's/alternate's responses in REDCap™.

If 'No', select the reason the SF-36 was not completed from the list provided:

Reason not done

- Deceased (*Record death date on the Survival Assessment form.*)
- Patient Refused
- Alternate Refused
- Both Patient and Alternate Refused
- Not able to reach patient and/or alternate
- Withdrew
- Missed
- Other (specify)

If the patient is deceased, record the date of death on the 'Survival Assessment' form. If the death date is not known, enter the date the patient was last known to be alive.

Refused

Refused is defined as the patient/alternate 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 to complete the questionnaires.

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 beginning 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. The completed worksheet is your source document for the completed questionnaire. Record the data in REDCap™.

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 at the beginning of the Katz ADL questionnaire. 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. Record the patient's response for each activity on the questionnaire worksheet.

Maintain the completed worksheet with the patient study files. The completed worksheet is your source document for the completed questionnaire. Record the data in REDCap™.

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, record the corresponding response on the questionnaire worksheet.

Maintain the completed worksheet with the patient study files. The completed worksheet is your source document for the completed questionnaire. Record the data in REDCap™.

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 next 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, enter the data obtained and complete the 'Reason not done' at the top of the questionnaires that were not started per instructions above under 'Was the questionnaire completed?'

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, see example below:

The screenshot shows a web interface with a sidebar on the left containing 'Help & Information' links like 'Helpdesk', 'General Help', and 'Video Tutorials'. The main area is a grid of data entry forms. The forms listed are: Microbiology, Protocol Violation, Hospital Overview, Survival Assessment, Contact Log, SF-36, ADL, IADL, and Employment Status. The 'Employment Status' form is expanded, showing a 'Serious Adverse Event Report' dropdown menu with options 1, 2, and 3. Below the dropdown is a 'Completed Data Entry' button and 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

Patients should be monitored for SAEs from randomization until ≥ 10 days post last successful graft (at a minimum for 3 days after the IP is 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 24 hours of becoming aware of the event. Any follow-up information should be entered 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 SI must adhere closely to the ICH-GCP Guidelines. Questions may be directed to the Project Lead or Principal Investigator.

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.

Prior to forwarding any documentation (i.e. as attachments to a Serious Adverse Event [SAE] report) to CERU, all patient identifiers must be masked. This includes the following:

- Name
- Initials
- Medical record Number
- Date of Birth
- Other unique hospital identifiers, such as a lab accession number for example.

Reportable SAEs

All **Serious** Adverse Events that are **unexpected or related** must be reported to CERU **within 24 hours** of becoming aware of the event by filling out the **Serious Adverse Events Initial Report** in REDCAP™ (see Appendix O 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:

- Cardiac arrest in a patient without a history of cardiac disease.
- New seizure in the absence of a previous seizure disorder.
- Worsening encephalopathy in the absence of liver disease.
- **Related SAE:** An event that is serious (see definition above) and is considered by the SI to be possibly or probably related to the IP. 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 of the SAE. Record the condition that led to death as the SAE, for example: sepsis

Respiratory Failure

Do not record respiratory failure as a 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. On the left, there are two labels: "Date of Report:" and "Report type:". To the right of "Date of Report:" is a date input field with a calendar icon and the placeholder text "YYYY-MM-DD". To the right of "Report type:" are three radio button options: "Initial", "Follow-up", and "Final".

Initial SAE Report

The RC must complete the SAE form in consultation with the SI or sub-I and requires the signature of the SI/sub-I.

All known data elements on the form must be completed within 24 hrs of discovery of the event. Certain aspects of the form may change (for example, the outcome of the event may not be known at the time of reporting). Additional data may be entered on the Follow-up and/or Final reports.

Responsible Investigator/Site Information

- **Name of Responsible Investigator**
- **Institution** (name of your hospital or facility)
- **Report completed by** (name of person completing the SAE report)
- **Date of Report** (this is the date you are entering the data into REDCap™)
- **Report type:**
 - Initial
 - Follow-up
 - Final

Patient Information

- **RZ#** (the patient Randomization Number)
- **Age**
- **Sex** (select male or female)
- **Date patient started study intervention**

Event Information (only enter one SAE per form)

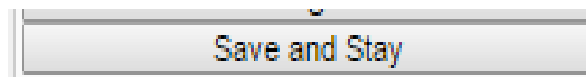
- **Event Onset Date**
- **Event Onset Time**
 - If the event onset time is not available, select the 'Not Available' option.
- **Name of Event**
- **Date Became Aware of Event**
- **Description of Event**
- **Seriousness Criteria** (select all that apply):
 - Death (if so, record this date in the 'Outcome' 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 or birth defect
- Other serious medical event
- **Outcome:** Select the most appropriate at the time of the initial report:
 - SAE persisting at time of report
 - Complete recovery/return to baseline
 - Resolved (no sequelae)
 - Resolved with sequelae, specify
 - Death, specify date/time
 - Unknown/Lost to follow up
- **Is the event unexpected?** (If the event is not unexpected, do not enter it as an SAE for this study)
- **PI rationale for unexpected nature of event** (provide pertinent clinical information that, in the opinion of the SI, caused her/him to think the event was unexpected vs. due to the progression of underlying condition or disease.)
- **Relationship of Study Intervention to event** (The determination of the relationship of the SAE to the supplements must be made by the SI/sub-I and recorded by the RC. To assist the Investigator in making this assessment, the following definitions have been provided (select **only** one):
 - **Not related:** A serious adverse event that is clearly due to extraneous causes (disease, environment, etc.) and does not meet the criteria for drug relationship listed under 'Possibly' or 'Probably'.
 - **Unlikely related:** A serious adverse event that is more likely due to other causes than the study supplements
 - **Possibly related:** Suggests that the association of this SAE with the study supplements is unknown and the event is not reasonably supported by other conditions.
 - **Probably related:** Suggests that a reasonable temporal sequence of this SAE with study supplement administration exists and the association of the event with the study supplement seems likely.
- If the SAE is considered to be related to the study supplement, record the pertinent clinical features that, in the opinion of the SI, made her/him think that the event was related to the study supplements vs. the progression of underlying disease. **Action taken with Study Intervention** (Select **only** one)
 - Study Intervention completed at time of event onset
 - Study Intervention ongoing
 - Study Intervention interrupted (temporarily), specify date
 - Study Intervention permanently stopped, specify date
- **Action Taken to Treat the Event** (Select **all** that apply)
 - None
 - Uncertain
 - Surgery
 - Other procedure (non-surgical)
 - Blood or blood products
 - Drug therapy
 - Other
- **Treatment Details** (provide additional information in the open text field if necessary) Other Report Information (Attach documents or complete the relevant CRF related to the information requested.)
- **Past medical history/comorbidities** (complete the Baseline CRF or attach a separate document)

- **Laboratory tests and investigations related to event** (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. If labs and/or other investigations pertinent to the SAE were not ordered, select 'None' in the 'Laboratory tests and investigations related to event:' field.)
- **Other Relevant Information** (If additional documentation is not being provided, select 'None'.)
- **Other event information the investigator wishes to report** (In the open text field, enter any additional information, not captured on the report or supporting documents, the responsible investigator would like to add.)

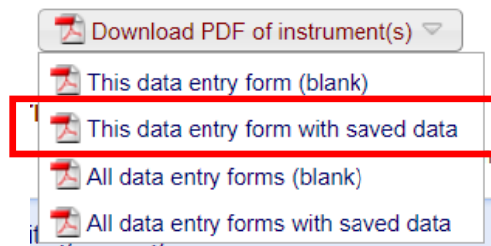
Upon completing the form, select 'Save and Stay'.

The screenshot shows a form with several sections: 'Signature', 'Date of Signature', 'Comments', and 'Form Status'. The 'Form Status' section has a dropdown menu for 'Complete?' currently set to 'Incomplete'. Below this, there are several 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, go to the 'Download PDF of instrument(s)' dropdown list at the top left of the form. Select 'This data entry form with saved data', see example below. Save the Initial report to your computer.

The screenshot shows the 'Actions' dropdown menu. The menu is open, showing several options: 'Download PDF of instrument(s)', 'This data entry form (blank)', 'This data entry form with saved data', 'All data entry forms (blank)', and 'All data entry forms with saved data'. The option 'This data entry form with saved data' is highlighted with a red rectangular box. Below the menu, the form content is partially visible, showing 'Event Name: Day 1 - Form #1', 'Patient ID', 'Responsible Investigator/Site Information', and 'Name of Responsible Investigator:'.



File the completed SAE form with the patient study documents. Email any accompanying documents, such as labs, x-rays, CT scans to the Project Lead. Remember to de-identify any patient records before sending them.

For SAE Report Worksheet, see Appendix O.

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 SAE has not resolved, been explained or stabilized, the Project Lead will collaborate with the RC for additional details and further follow-up reporting.

This form **must be completed by the SI/designate** by reviewing the Serious Adverse Events (Initial) Report 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.

The information in the Follow-up/Final Report will be reviewed by the Data Monitoring Committee and must be complete..

The following documentation must be included with the Follow-up/Final report:

- **Chronological events preceding the SAE until time of report:** provide a detailed narrative of this information in the open text field 'Description of Event' and attach additional reports/details if needed.
- **Concomitant Medications:** list all medications given within 48 hrs before the onset of the SAE.

The completed-Follow-up/Final Report must be signed by the SI and filed in the patient study folder.

IMPORTANT: Remember to de-identify any patient records before sending them to the Project Lead and/or delegate.

For SAE Report worksheet, see Appendix O.

Any patient who experiences a serious adverse event during the study period, should be followed by the RC 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 IPs.

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. SAE Report worksheet**



Delegation of Authority Log

This log is used by the Qualified Investigator (i.e. Site Investigator) to indicate the Site Staff that have a material effect on the conduct of the Study and to whom the Investigator has delegated significant Study related duties/tasks. The signatures and details on this log will also facilitate tracking of edits/changes of the Site records. This log is to be kept by the Qualified Investigator and the Sponsor.

Name of Qualified Investigator: _____

Signature of Qualified Investigator: _____

Print Name	Signature	Initials	Study Role (Qualified Investigator*, sub-QI*, Research Coordinator (RC), Pharmacist, Technician, Dietitian)	Key Delegated Tasks Reference numbers (see next page)	Dates	
					Start	End

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



Delegation of Authority Log

Print Name	Signature	Initials	Study Role (Qualified Investigator, sub- QI*, Research Coordinator (RC), Pharmacist, Technician, Dietitian)	Key Delegated Tasks (see next page)	Dates	
					Start	End

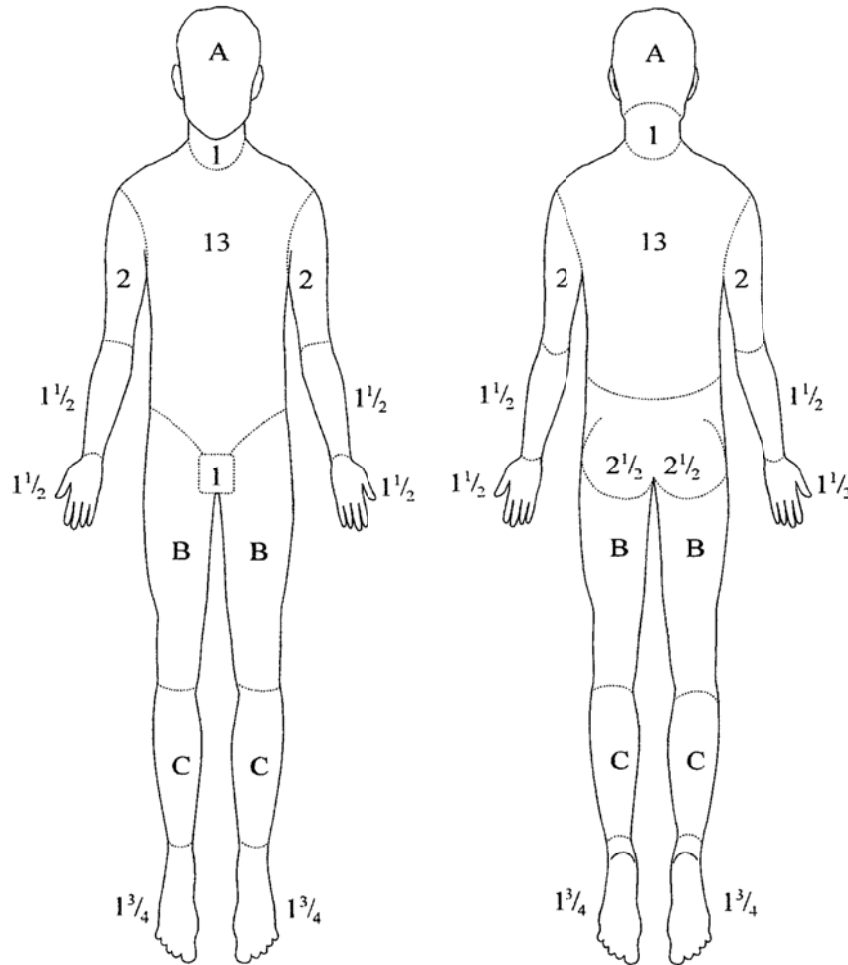
Delegation of Authority Log

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"> ❖ Case Report Form entries ❖ Case Report Form corrections ❖ Data query resolution
8	Source documentation maintenance, includes: <ul style="list-style-type: none"> ❖ Study worksheets, checklists, monitoring sheets ❖ Data from electronic & hard copy medical chart
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		
Total burn		

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	4¾
C = half of one lower leg	2½	2½	2¾	3	3¼	3½

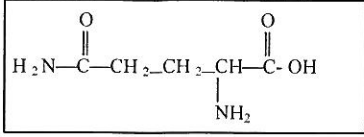
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(NOO-tre-stor) - Full Prescribing Information

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 C₅H₁₀N₂O₃, 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 ¹	Group B rhGH + SOD GLN ¹	Group C SOD GLN ¹
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

¹SOD|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 week 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 ¹ N=16 n(%)	rhGH+SOD[GLN] ¹ N=16 n(%)	SOD [GLN] ¹ N=9 n(%)
Total Number of Subjects with At Least One AE	16 (100)	16 (100)	8 (89)
Body as a Whole: General Disorders			
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)
Gastrointestinal System Disorders	12 (75)	12 (75)	6 (67)
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)
Musculoskeletal System Disorders	7 (44)	7 (44)	1 (11)
Arthralgia	7 (44)	5 (31)	0 (0)
Myalgia	2 (13)	0 (0)	1 (11)
Resistance Mechanism Disorders	6 (38)	3 (19)	4 (44)
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)
Application Site Disorders	5 (31)	4 (25)	1 (11)
Injection Site Reaction	3 (19)	4 (25)	1 (11)
Injection Site Pain	5 (31)	0 (0)	0 (0)
Central and Peripheral Nervous System Disorders	4 (25)	4 (25)	2 (22)
Dizziness	1 (6)	2 (13)	0 (0)
Headache	1 (6)	1 (6)	1 (11)
Hypoesthesia	1 (6)	1 (6)	1 (11)
Skin and Appendages Disorders	4 (25)	4 (25)	2 (22)
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)
Respiratory System Disorders	1 (6)	5 (31)	1 (11)
Rhinitis	0 (0)	3 (19)	1 (11)
Metabolic and Nutritional Disorders	3 (19)	1 (6)	1 (11)
Dehydration	3 (19)	0 (0)	1 (11)
Thirst	0 (0)	0 (0)	1 (11)
Urinary System Disorders	2 (13)	1 (6)	1 (11)
Pyelonephritis	0 (0)	0 (0)	1 (11)
Psychiatric Disorders	1 (6)	0 (0)	2 (22)
Depression	0 (0)	0 (0)	2 (22)
Reproductive Disorders, Female	2 (13)	0 (0)	1 (11)
Breast Pain, Female	1 (6)	0 (0)	1 (11)
Hearing and Vestibular Disorders	0 (0)	2 (13)	0 (0)
Far or Hearing Symptoms	0 (0)	2 (13)	0 (0)

¹SOD[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 ¹ N=15 n(%)	rhGH+SOD [GLN] ¹ N=16 n(%)	SOD[GLN] ¹ N=9 n(%)
Total Number of Subjects with At Least One AE	12 (80)	13 (81)	7 (78)
Gastrointestinal System Disorders	7 (47)	7 (44)	3 (33)
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)
Resistance Mechanism Disorders	6 (40)	5 (31)	5 (56)
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)
Body as a Whole: General Disorders	4 (27)	2 (13)	1 (11)
Fever	2 (13)	1 (6)	1 (11)
Fatigue	2 (13)	0 (0)	0 (0)
Respiratory System Disorders	2 (13)	4 (25)	1 (11)
Rhinitis	1 (7)	3 (19)	0 (0)
Laryngitis	0 (0)	0 (0)	1 (11)
Pharyngitis	0 (0)	0 (0)	1 (11)
Reproductive Disorders, Female	0 (0)	4 (25)	1 (11)
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)
Musculoskeletal System Disorders	2 (13)	2 (13)	0 (0)
Arthralgia	2 (13)	2 (13)	0 (0)
Psychiatric Disorders	0 (0)	1 (6)	1 (11)
Depression	0 (0)	0 (0)	1 (11)
Insomnia	0 (0)	0 (0)	1 (11)
Urinary System Disorders	0 (0)	0 (0)	2 (22)
Pyelonephritis	0 (0)	0 (0)	1 (11)
Renal Calculus	0 (0)	0 (0)	1 (11)
Application Site Disorders	0 (0)	0 (0)	1 (11)
Injection Site Reaction	0 (0)	0 (0)	1 (11)
Liver and Biliary System Disorders	0 (0)	0 (0)	1 (11)
Hepatic Function Abnormal	0 (0)	0 (0)	1 (11)
Vascular Extracardiac Disorders	0 (0)	0 (0)	1 (11)
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

¹SOD[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

NutreStore™ is a trademark of Emmaus Medical, Inc. under license from Cato Holding Company.

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SMM-007-02 0810

MATERIAL SAFETY DATA SHEET

IDENTITY(As Used on Label and List)
L-GLUTAMINE

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 ₂ , 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 Recommended	EYE PROTECTION	Recommended
OTHER PROTECTIVE EQUIPMENT		
WORK / HYGIENIC PRACTICES		



MALTRIN[®] M100

Maltodextrin

DESCRIPTION

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

REGULATORY

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

PACKAGING, STORAGE AND SHELF LIFE

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

PRODUCT ATTRIBUTES

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

APPLICATIONS

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

LOT CODES

Lot codes can be interpreted as follows: The first alpha character represents the product, followed by the last two numbers of the year and then the Julian date. Numbers following the Julian date represent the product line and the lot of the day.

Example: M1310801: M = MALTRIN[®]; 13 = 2013; 108 = Apr. 18; 01 = first lot

Technical Information

MALTRIN® M100

Maltodextrin

TYPICAL NUTRITIONAL INFORMATION

Values per 100 grams of product

Calories	378
Calories from Fat	0 g
Total Fat	0 g
Saturated Fat	0 g
Trans Fat	0 g
Monounsaturated Fat	0 g
Polyunsaturated Fat	0 g
Protein	0 g
Total Carbohydrate	94.5 g
Sugars	4 g
Dietary Fiber	0 g
Soluble Fiber	0 g
Insoluble Fiber	0 g
Sugar Alcohols	0 g
Other Carbohydrates	90.5 g
Calcium	16 mg
Iron	0 mg
Sodium	90 mg
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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The information presented in this document is believed to be correct. Any recommendations or suggestions are made without guarantee or representation as to results for any particular usage. You are responsible for determining that the use of any GPC product, as well as your product and its use, and any claims made about your product, all comply with applicable laws and regulations for your particular jurisdiction. The information contained in this document is offered solely for your independent investigation, verification and consideration.

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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

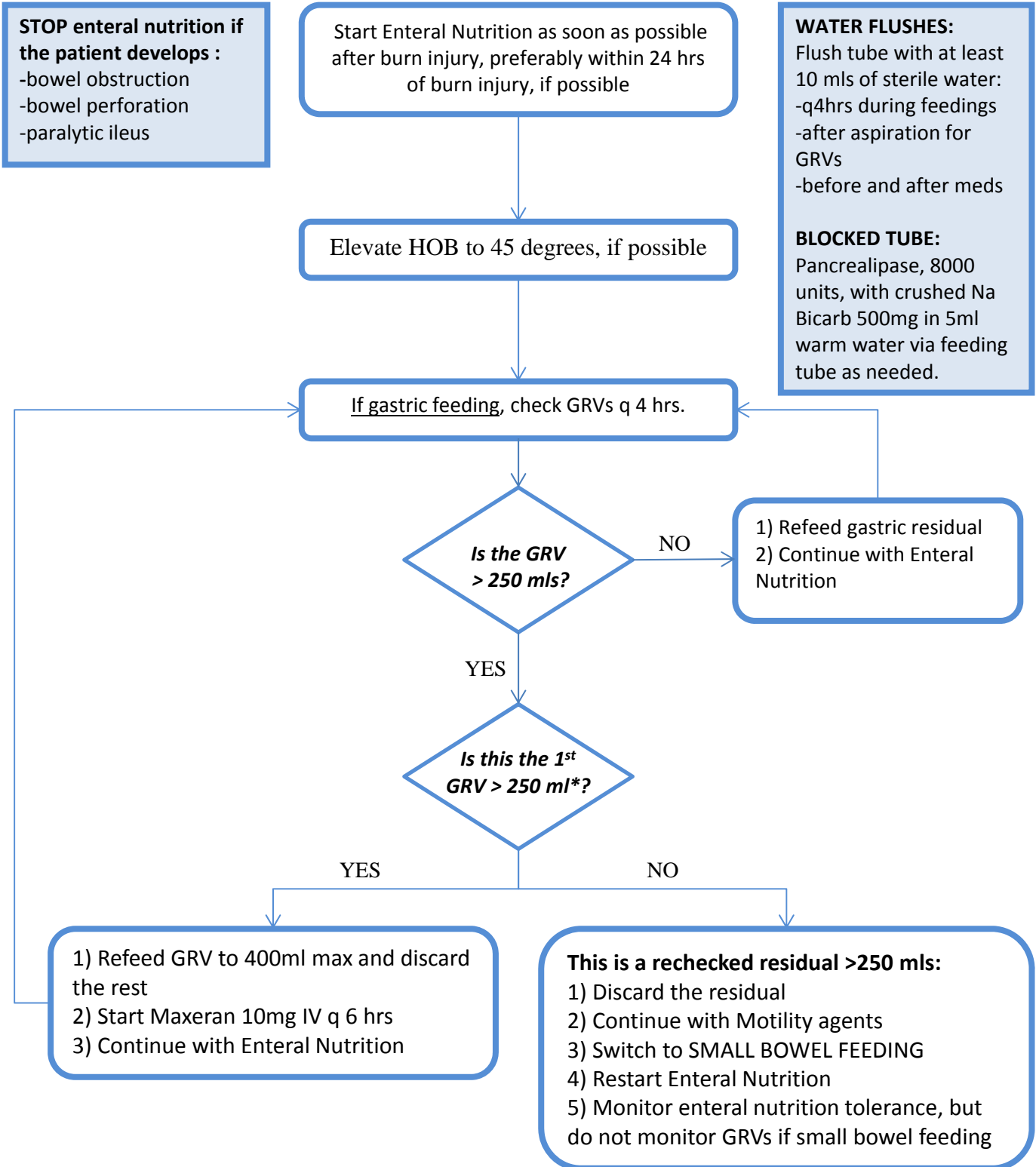
IP Investigational Product

ACU Acute Care Unit (burn unit or ICU)

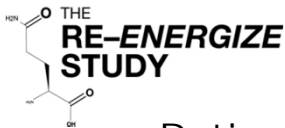
Dosing Weight Chart

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



* 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: _____
Last Name, First Name Middle Name

alternate name (i.e. nicknames/alias): None #1 _____ #2 _____

Home Phone: (____) _____ - _____ Not Available Cell Phone: (____) _____ - _____ Not Available

Alternate: (____) _____ - _____ Not Available Alternate: (____) _____ - _____ Not Available

Email Address: _____

Work Phone: (____) _____ - _____ Not Available Alternate: (____) _____ - _____ Not Available

Someone who lives with participant:

Name: _____
Last Name, First Name Middle Name

Home Phone: (____) _____ - _____ Not Available Cell Phone: (____) _____ - _____ Not Available

Work Phone: (____) _____ - _____ Not Available Alternate: (____) _____ - _____ 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: _____
Last Name, First Name Middle Name

Home Phone: (____) _____ - _____ Not Available Cell Phone: (____) _____ - _____ Not Available

Work Phone: (____) _____ - _____ Not Available Alternate: (____) _____ - _____ Not Available

Relationship to Patient (e.g., father, sister, friend): _____

Name: _____
Last Name, First Name Middle Name

Home Phone: (____) _____ - _____ Not Available Cell Phone: (____) _____ - _____ Not Available

Work Phone: (____) _____ - _____ Not Available Alternate: (____) _____ - _____ Not Available

Relationship to Patient (e.g., father, sister, friend): _____

Name: _____
Last Name, First Name Middle Name

Home Phone: (____) _____ - _____ Not Available Cell Phone: (____) _____ - _____ Not Available

Work Phone: (____) _____ - _____ Not Available Alternate: (____) _____ - _____ 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.

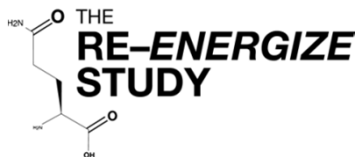
- Administer study supplement at the following times (*enter # grams*):

<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*)



Randomization Number

Comorbidities

Check all the comorbidities that apply.

If the patient has no comorbidities, check 'No Comorbidities'.

No Comorbidities

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

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

Pulmonary
9. Chronic obstructive pulmonary disease (COPD, emphysema)
10. Asthma

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

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

Renal
17. Moderate or severe renal disease

Gastrointestinal
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)

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

Psychological
29. Anxiety or Panic Disorders
30. Depression

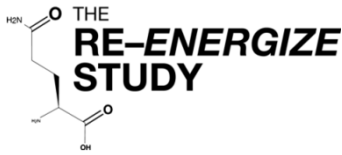
Muskoskeletal
31. Arthritis (Rheumatoid or Osteoarthritis)
32. Degenerative Disc disease (back disease, spinal stenosis or severe chronic back pain)
33. Osteoporosis
34. Connective Tissue disease

Miscellaneous
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)

Gram Negative Bacteria			
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

Gram Positive Bacteria (Do NOT include)
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.



Patient ID _____

SF-36 (1/5)

Was the SF-36 completed?	<input type="checkbox"/> Yes <input type="checkbox"/> No
If completed: Date SF-36 completed	(YYYY-MM-DD)
Completed by	<input type="checkbox"/> Patient <input type="checkbox"/> Alternate
If Not completed: Reason not done	<input type="checkbox"/> Deceased <input type="checkbox"/> Patient Refused <input type="checkbox"/> Alternate Refused <input type="checkbox"/> Both Patient and Alternate Refused <input type="checkbox"/> Not able to reach patient and/or alternate <input type="checkbox"/> Withdrew <input type="checkbox"/> Missed <input type="checkbox"/> Other (specify) _____

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 **x** in the one box that best describes your answer.

1. In general, would you say your health is					
Excellent <input type="checkbox"/>	Very Good <input type="checkbox"/>	Good <input type="checkbox"/>	Fair <input type="checkbox"/>	Poor <input type="checkbox"/>	Not Done <input type="checkbox"/>
2. <u>Compared to one year ago</u> , how would you rate your health in general <u>now</u> ?					
Much better now than one year ago <input type="checkbox"/>	Somewhat better now than one year ago <input type="checkbox"/>	About the same as one year ago <input type="checkbox"/>	Somewhat worse now than one year ago <input type="checkbox"/>	Much worse now than one year ago <input type="checkbox"/>	Not Done <input type="checkbox"/>

SF-36 (2/5)

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	Not Done
a) <u>Vigorous activities</u> , such as running lifting heavy objects, participating in strenuous sports	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) <u>Moderate activities</u> , such as moving a table, pushing a vacuum cleaner, bowling or playing golf	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Lifting or carrying groceries	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) Climbing <u>several</u> flights of stairs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e) Climbing <u>one</u> flight of stairs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f) Bending, kneeling or stooping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g) Walking <u>more than a kilometer</u>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h) Walking <u>several hundred meters</u>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i) Walking <u>one hundred meters</u>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j) Bathing or dressing yourself	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Patient ID

SF-36 (5/5)

10. During the <u>past 4 weeks</u> , how much of the time has your <u>physical health or emotional problems</u> 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	Not Done
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

11. How TRUE or FALSE is <u>each</u> of the following statements is for you?						
	Definitely true	Mostly true	Don't know	Mostly false	Definitely false	Not Done
a) I seems to get sick a little easier than other people	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) I am as healthy as anyone I know	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) I expect my health to get worse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) My health is excellent	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Thank you for completing these questions!



Patient ID _____

Katz Index of Independence in Activities of Daily Living

Was the ADL completed?	<input type="checkbox"/> Yes <input type="checkbox"/> No
If completed: Date ADL completed	(YYYY-MM-DD)
Completed by	<input type="checkbox"/> Patient <input type="checkbox"/> Alternate
If Not completed: Reason not done	<input type="checkbox"/> Deceased <input type="checkbox"/> Patient Refused <input type="checkbox"/> Alternate Refused <input type="checkbox"/> Both Patient and Alternate Refused <input type="checkbox"/> Not able to reach patient and/or alternate <input type="checkbox"/> Withdrew <input type="checkbox"/> Missed <input type="checkbox"/> Other (specify) _____

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

Lawton Instrumental Activities of Daily Living (IADLs) (1/2)

Was the IADL completed?	<input type="checkbox"/> Yes <input type="checkbox"/> No
If completed: Date IADL completed	(YYYY-MM-DD)
Completed by	<input type="checkbox"/> Patient <input type="checkbox"/> Alternate
If Not completed: Reason not done	<input type="checkbox"/> Deceased <input type="checkbox"/> Patient Refused <input type="checkbox"/> Alternate Refused <input type="checkbox"/> Both Patient and Alternate Refused <input type="checkbox"/> Not able to reach patient and/or alternate <input type="checkbox"/> Withdrew <input type="checkbox"/> Missed <input type="checkbox"/> Other (specify) _____

A. Ability to Use Telephone	<input type="checkbox"/> Operates telephone on own initiative; looks up and dials numbers <input type="checkbox"/> Dials a few well-known numbers <input type="checkbox"/> Answers telephone, but does not dial <input type="checkbox"/> Does not use telephone at all
B. Shopping	<input type="checkbox"/> Takes care of all shopping needs independently <input type="checkbox"/> Shops independently for small purchases <input type="checkbox"/> Needs to be accompanied on any shopping trip <input type="checkbox"/> Completely unable to shop
C. Food Preparation	<input type="checkbox"/> Plans, prepares, and serves adequate meals independently <input type="checkbox"/> Prepares adequate meals if supplied with ingredients <input type="checkbox"/> Heats and serves prepared meals or prepares meals but does not maintain adequate diet <input type="checkbox"/> Needs to have meals prepared and served
D. Housekeeping	<input type="checkbox"/> Maintains house alone with occasion assistance (heavy work) <input type="checkbox"/> Performs light daily tasks such as dishwashing, bed making <input type="checkbox"/> Performs light daily tasks, but cannot maintain acceptable level of cleanliness <input type="checkbox"/> Needs help with all home maintenance tasks <input type="checkbox"/> Does not participate in any housekeeping tasks
E. Laundry	<input type="checkbox"/> Does personal laundry completely <input type="checkbox"/> Launders small items, rinses socks, stockings, etc <input type="checkbox"/> All laundry must be done by others

Lawton IADLs (2/2)

<p>F. Mode of transportation</p>	<ul style="list-style-type: none"> <input type="checkbox"/> Travels independently on public transportation or drives own car <input type="checkbox"/> Arranges own travel via taxi, but does not otherwise use public transportation <input type="checkbox"/> Travels on public transportation when assisted or accompanied by another <input type="checkbox"/> Travel limited to taxi or automobile with assistance of another <input type="checkbox"/> Does not travel at all
<p>G. Responsibility for Own Medications</p>	<ul style="list-style-type: none"> <input type="checkbox"/> Is responsible for taking medication in correct dosages at correct time <input type="checkbox"/> Takes responsibility if medication is prepared in advance in separate dosages <input type="checkbox"/> Is not capable of dispensing own medication
<p>H. Ability to Handle Finances</p>	<ul style="list-style-type: none"> <input type="checkbox"/> Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track of income <input type="checkbox"/> Manages day-to-day purchases, but needs help with banking, major purchases, etc <input type="checkbox"/> Incapable of handling money



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:
---------------	------	--	--

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 #:

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

OTHER REPORT INFORMATION

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

SIGNATURES

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