THE RE-*ENERGIZE* STUDY

*A **R**andomiz**E**d Trial of **EN**t**ER**al **G**lutamine to minim**IZE** Thermal Injury*

Pharmacy Manual

Intended Audience: Pharmacists, Pharmacy Technicians

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

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THE RE-ENERGIZE STUDY

Critical Care Nutrition

Clinical Evaluation Research Unit

Document History

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Version 3: 23-Apr-2019	02-Sep-2016

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All questions related to the investigational product, storage, shipping, or resupply should be directed to the Central Pharmacy Depot Manager.

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

PLEASE NOTE: the Project Lead and Project Assistant are blinded to treatment allocations. Please take care not to unblind the PL or 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).

Glossary

ACU	Acute Care Unit (ICU or Burn Unit)
BMI	Body Mass Index
CERU	Clinical Evaluation Research Unit at Kingston General Hospital (Methods Centre)
CRS	Central Randomization System
DAL	Delegation of Authority Log
DNR	Do not resuscitate order
EN	Enteral Nutrition
FDA	Food and Drug Administration (USA)
GCP	Good Clinical Practice
HC	Health Canada
IP	Investigational Product
NPO	Nothing by mouth
PA	Project Assistant
PL	Project Lead or delegate
RC	Research Coordinator
SI	Site Investigator
TBSA	Total Body Surface Area
PO	Orally, by mouth

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 aged 18 – 39 years we require a TBSA (Total Burn Surface Area) burn ≥ 20%, or in the presence of an inhalation injury, a minimum of ≥ 15 % TBSA burn is acceptable. For patients aged 40 – 59 years we require a TBSA burn ≥ 15%. For patients aged 60 years or older we require a TBSA burn ≥ 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

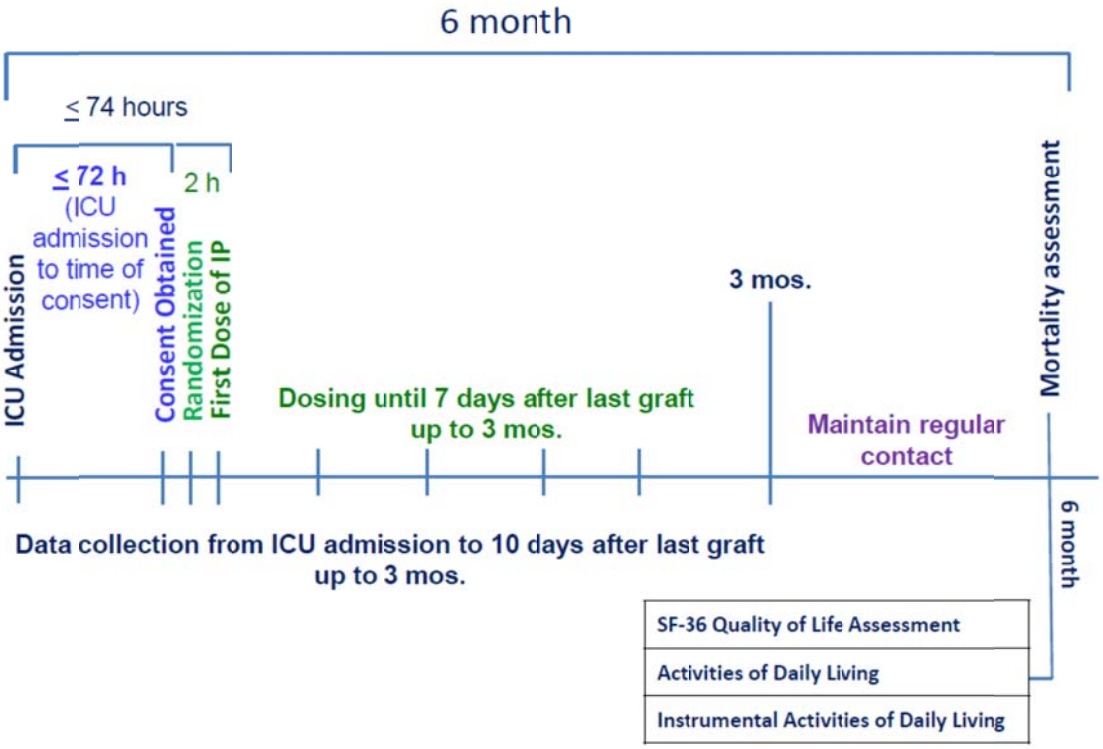
Trial Duration

Study Recruitment Period

4 years - based on approximately 1 patient per site per month, as demonstrated in the pilot study.

Diagram of Study Overview

Below is a diagrammatic representation of the RE-ENERGIZE Study. Refer to appropriate sections of the Study Procedures Manual for comprehensive instructions for study activities.



Roles & Responsibilities

CERU is responsible for the following:

- Providing procedures and tools for implementation of Pharmacy procedures
- Providing training on procedures and tools
- Supplying a username and password for access to the Central Randomization System (CRS)
- Ensuring that study procedures are followed and the trial is conducted according to Good Clinical Practices.

The local site Research Pharmacy is responsible for the following:

- Providing a computer with internet access for the CRS
- Notifying CERU of any technical difficulties or malfunctions related to the CRS
- Allowing only authorized study personnel access to the CRS.
- Preparation of Investigational Product in accordance with the randomized treatment and study procedures
- Maintenance of Dispensing, Accountability and Destruction records.
- Oversight of local investigational product inventory, including the initiation of resupply orders before inventory falls to critical levels.
- Reporting protocol deviations and violations related to pharmacy procedures in a timely manner.

Study Preparation

Delegation of Authority Log

Each site should have a senior pharmacy team member who will ensure that all pharmacy staff (i.e Pharmacists and/or pharmacy technicians) who will have a material effect on The RE-ENERGIZE Study have documentation of both duties and tasks delegated to them and completion of associated training.

A Pharmacy Delegation & Training Log (**See Appendix A**), or similar log, is to be kept by the Pharmacy team and sent to CERU upon request.

Training

Each member of the site research team should be qualified by education, training and experience to assume responsibility for the proper conduct of the trial. The Site Investigator is responsible for ensuring that s/he and the local staff are adequately trained in GCP (GCP 4.1.1). Each pharmacy team member (i.e. Pharmacist or pharmacy technician**)** must have documented training on the RE-ENERGIZE study prior to site activation, or in the case of new staff joining the study mid-stream, before they initiate any study related duties and/or tasks.
Study specific training will be provided by CERU Staff and conducted either in person or via webinar, a corresponding training record will be provided. In instances where members of the local pharmacy team conducts internal team training related to the study, they should document the training in accordance with their local SOPs (e.g. training record, attendance sheet, etc).

Central Randomization System (CRS) Access

The Central Randomization System (CRS) is a web-based system that will be used to both screen and randomize eligible patients into the RE-ENERGIZE Study. After each patient is randomized, the site pharmacy team member will access the patient treatment allocations through the Central Randomization System.

- Pharmacy team member(s) must complete the Pharmacy tab of the CRS Access Excel workbook, sent to the site electronically, and return it to the CERU Project Lead before CRS access will be granted.
- Once the completed Excel sheet is received, login information will be sent to the email address(es) provided.
- The Pharmacy is responsible for notifying the CERU Project Lead with any changes in personnel.

Access to the Central Randomization System (CRS) will be granted by CERU following the completion of required study training.

The Project Lead will notify the site Investigator, coordinators and pharmacists when their site is activated and they may begin patient recruitment.

Patient Population

Inclusion Criteria

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

2) **Patient meets one of the following 3 criteria:**
   a. Patients 18 – 39 years of age with TBSA burn ≥ 20%
   b. Patients 18 – 39 years of age with TBSA burn ≧ 15% WITH inhalation injury
   c. Patients 40 - 59 years of age with TBSA burn ≧ 15%
   d. Patients ≥ 60 years of age with TBSA burn ≧ 10%

Exclusion Criteria

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. An exception would be a patient who has been at another facility an extended period of time post burn prior to admission to your unit.

2) Patients younger than 18 years of age

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

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

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

4) Liver cirrhosis Child-Pugh class C liver disease

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) Contra-indication for EN: intestinal occlusion or perforation, intra-abdominal injury. (Being NPO is not considered a contraindication for Enteral Nutrition).

7) Patients with injuries from high voltage electrical contact.

8) Patients who are moribund (not expected to survive the next 72 hours in the judgement of the Site Investigator or delegated doctor in charge).
   Note that an isolated DNR does not fulfil this criteria.

9) Patients with extreme body sizes: BMI < 18 or > 50 kg/m^2
Ideally BMI should be calculated using the patient's pre-burn dry weight. Given that there may be some subjectivity involved in the determination of BMI, err on the side of including the patient.

10) Enrollment in another industry sponsored ICU intervention study *(co-enrollment in all non-randomized academic studies will be approved. For academic RCTs, forward a synopsis or abstract of the study to the Project Lead to obtain pre-approval of the study to which you would like to co-enroll.*

11) Received glutamine supplement for > 24 hours prior to randomization.
This refers to consistent administration of glutamine over the 24 hr period prior to randomization. If the patient received random or intermittent doses of open label glutamine, discontinue the glutamine prior to randomization.

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

Investigational Product

Patients randomized to the RE-ENERGIZE Study will receive one of the following:

Name of Group	Intervention
Active	Glutamine
Control	Maltodextrin (placebo)

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

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

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

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

*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.

The Central Randomization System is programmed to calculate the patient's BMI based on the height and weight entered on the pre-Randomization form, and then calculate the patient's dosing weight based on the BMI. IP dosing is then calculated and displayed in accordance with the patient's Dosing Weight.

Duration of Study Intervention

Patients will receive the IP from randomization through 7 days post last successful graft, or ACU discharge, or 3 months from ACU admission, whichever comes first.

Changes in IP Dosing

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. Pharmacy will be notified by the site investigator/delegate if there is a change in dosing weight.

Clinical Supplies

The active and control products will both be supplied in pre-packaged 5g packets. The active and control have the same visual appearance and taste.

Glutamine

Glutamine is the 'active' arm of treatment for the study.

Nutrestore™ (L Glutamine)

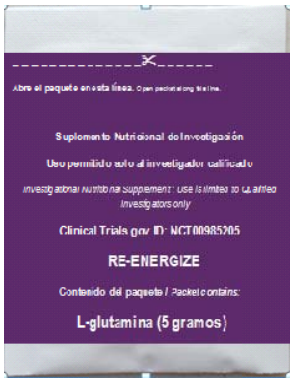
Nutrestore is an amino acid (L Glutamine) powder that is approved for oral use in short bowel syndrome by the FDA. L Glutamine is produced normally by the body and has important functions in regulation of gastrointestinal cell growth, function, and regeneration. Under normal conditions, glutamine concentration 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 glutamine is often considered a "conditionally essential" amino acid.

Glutamine will be supplied to all sites in pre-blinded packets. Labelling on the packets varies slightly by region. The lot # on the back of each packet will be exposed and must be covered prior to being dispensed for patient administration.	**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 (**See Appendix B**). This product is pre-packaged in 5g individual packets.  North America  Europe  Latin America & Spain 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]

Each packet is 10.2 cm (4 inches) high X 7.6 cm (3 inches) wide X less than 0.3 cm ($^1/_8$ inch) thick.

Maltodextrin (placebo)
Maltodextrin is the 'control' arm of the treatment for the study.

Maltrin® M100 Maltodextrin (control)
The MALTRIN® M100 maltodextrin is produced by Grain Processing Corporation (GPC) and then packaged by Anderson Packaging for the trial. 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. Patients will receive an iso-calorically delivered amount of maltodextrin (control) mixed with water or other liquids. 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.

Maltodextrin will be supplied to all sites in pre-blinded packets. Labelling on the packets varies slightly by region. The lot # on the back of each packet will be exposed and will need to be covered prior to being dispensed for patient administration.	**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 (**See Appendix C**). This product is pre-packaged in 5g individual packets.    North America Europe Latin America & Spain STORAGE: Store under ambient conditions; protect from excessive heat and excessive humidity for extended periods of time.

Documentation of storage temperature must be provided upon request. If temperature is monitored and records are maintained and available for the storage area, a separate, study specific temperature log is not required. If the temperature of the storage area is not monitored, please maintain a study specific temperature log. Refer to **Appendix D** for a Temperature Log template.

IP Dispensing

The RE-ENERGIZE Study is being conducted globally. To maintain dosing consistency across all study patients, please dispense the IP in 5 gram increments.

1 dose = 5 grams

Daily study dose is calculated and displayed in the Central Randomization System (CRS) using the following formula:

Dosing Weight in kg X 0.5 = g/day (rounded to the nearest 5g)

Example:

Wt. 75 kg X 0.5 = 37.5g/day rounded to the nearest 5g = 40g/day
Wt. 74 kg X 0.5 = 37g per day rounded to the nearest 5g = 35g/day

The Dosing Weight Chart below displays g/day based on Dosing Weight and provides a dosing regimen based on q4h administration.

Dosing Weight Chart below:

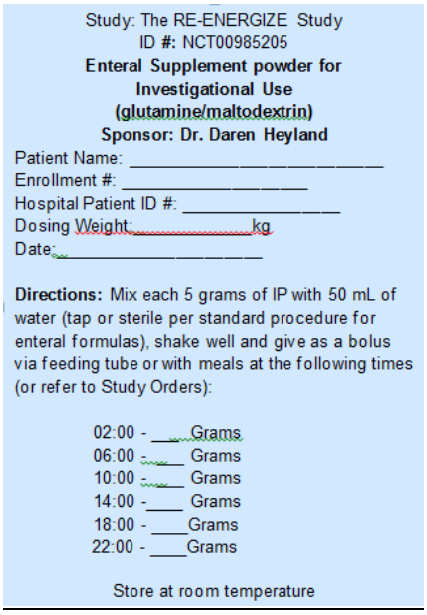
Dose #	1	2	3	4	5	6	q4h	
Dosing weight (kg)	Number of 5g doses						Total	
							doses	g/day
35-44	1	0	1	0	1	1	4	20
45-54	1	1	1	0	1	1	5	25
55-64	1	1	1	1	1	1	6	30
65-74	2	1	1	1	1	1	7	35
75-84	2	1	1	2	1	1	8	40
85-94	2	1	1	2	1	2	9	45
95-104	2	1	2	2	1	2	10	50
105-114	2	2	2	2	1	2	11	55
115-124	2	2	2	2	2	2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

1) Determine the number of doses to be given per administration based on the number of administrations per day. If the patient's treatment dosage is 40g/day and the patient is receiving the IP q4 hours, the patient would receive 2 doses of 5g each at 2 administration intervals and 1 dose of 5g each at 4 administration intervals for a total of 8 doses/day (refer to chart above).

2) Obtain the appropriate product according to the treatment assignment, glutamine or maltodextrin.

3) Prepare and affix one label to each dose of the IP to be dispensed. Ensure each one dose packet is blinded by covering the Lot # on the back of the packet.

Sample Label template


Study: The RE-ENERGIZE Study
ID #: NCT00985205
Enteral Supplement powder for Investigational Use (glutamine/maltodextrin)
Sponsor: Dr. Daren Heyland
Patient Name: _____
Enrollment #: _____
Hospital Patient ID #: _____
Dosing Weight: _____kg
Date: _____

Directions: Mix each 5 grams of IP with 50 mL of water (tap or sterile per standard procedure for enteral formulas), shake well and give as a bolus via feeding tube or with meals at the following times (or refer to Study Orders):

02:00 - ___Grams
06:00 - ___ Grams
10:00 - ___ Grams
14:00 - ___ Grams
18:00 - ___Grams
22:00 - ___Grams

Store at room temperature

Recommended:

Prepare and dispense enough IP doses to last one week for each patient that is randomized.

4) Send blinded IP to the ACU. IP dispensed to the ACU is to be stored at room temperature in a secure location.

5) Complete the patient specific Investigational Product Dispensing Log (patient's name, date, which product was dispensed, expiry date, lot #, etc) and the Investigational Product Accountability Logs (amount received, destroyed, batch #, etc) (**see Appendices E, F & G**) and keep these with the Pharmacy study files.

6) Repeat steps 2 - 5 weekly for the duration of study intervention which is ≥ 7 days after the last successful grafting procedure (anticipated to be an average of 28 days), or discharge from the ACU, or death, whichever occurs first.

7) Destroy all expired products as per local procedures and record the destruction of product on the corresponding Investigational Product Accountability Log (**Appendices F & G**).

8) Pharmacy team member will be asked to provide the following, upon request:

- Documentation that product is maintained at the required temperature.

Minor changes to these procedures to meet local pharmacy practices may be permissible upon approval by the Project Lead

Central Randomization System (CRS) Procedures

Only the Pharmacy team is unblinded!

Dispensing is to be done within 2 hrs of randomization

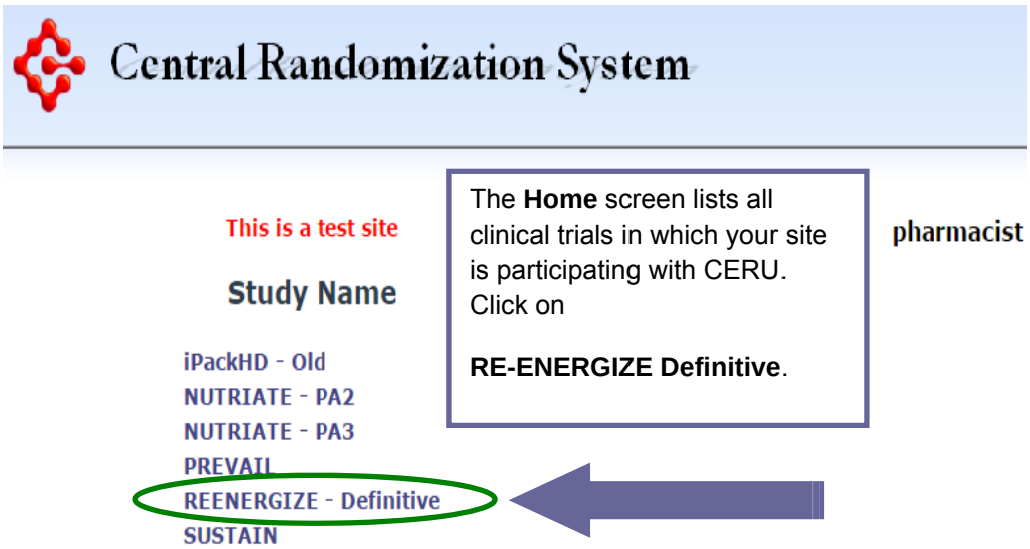
1) After the Research Coordinator has confirmed eligibility and randomized the patient using the Central Randomization System (CRS), the research coordinator will immediately notify the pharmacy and provide:
   a. the 8 digit randomization number (automatically generated online)
   b. the patient's pre-burn dry weight
   c. any other details required by the pharmacist to correctly confirm the subject (e.g. medical record number, name, age)

2) The pharmacy team member will access the RE-ENERGIZE CRS Login Page at: https://ceru.hpcvl.queensu.ca/CRS/

To access the CRS with Pharmacy user access, enter your assigned User name and Password. Click **LOGIN**.

NOTE: Access to the web-based CRS will be assigned by The Clinical Evaluation Research Unit (CERU) upon receipt of the CRS Access Log completed by the site pharmacy team.

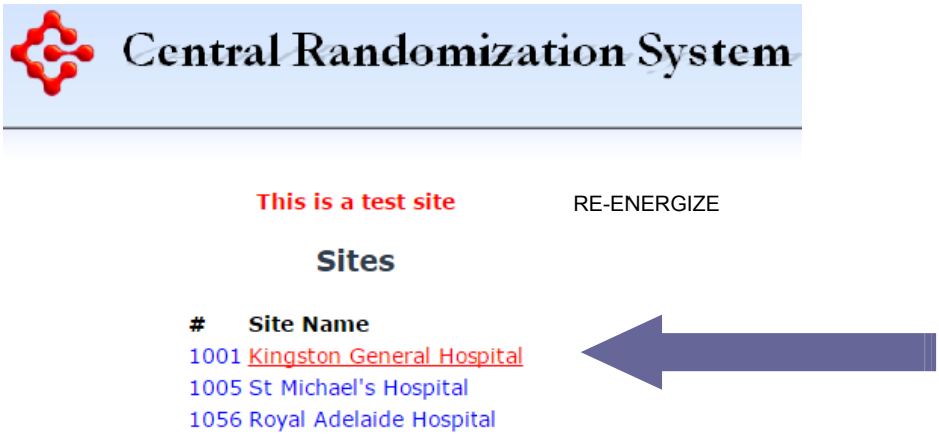
3) After you Login, you will be taken to the Home Screen, see below:



The **Home** screen lists all clinical trials in which your site is participating with CERU. Click on

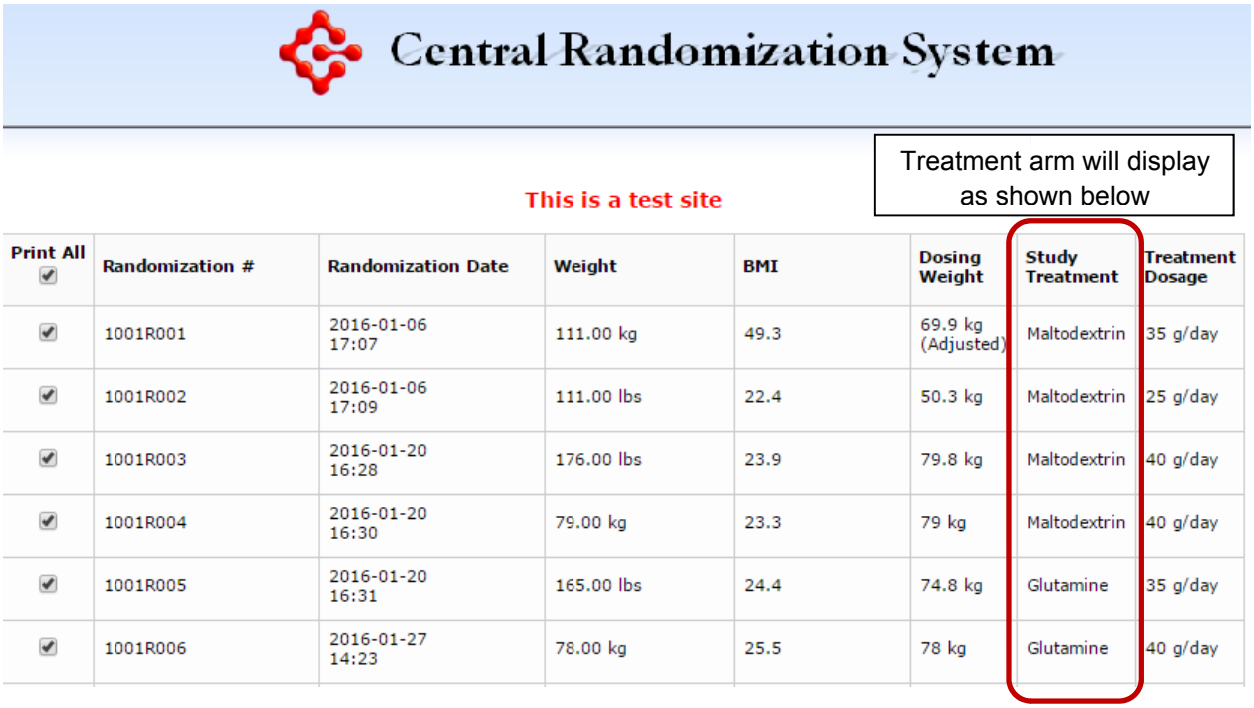
RE-ENERGIZE Definitive.

4) If you provide pharmacy services to more than one site participating in The RE-ENERGIZE Study, you will be taken to a screen that lists those sites, see example below:



Select the site at which the patient was randomized.

5) If you provide pharmacy services to only one site participating in The RE-ENERGIZE Study, you will be taken directly to the pharmacy treatment allocation and dosage table, see below:



Print All	Randomization #	Randomization Date	Weight	BMI	Dosing Weight	Study Treatment	Treatment Dosage
☑	1001R001	2016-01-06 17:07	111.00 kg	49.3	69.9 kg (Adjusted)	Maltodextrin	35 g/day
☑	1001R002	2016-01-06 17:09	111.00 lbs	22.4	50.3 kg	Maltodextrin	25 g/day
☑	1001R003	2016-01-20 16:28	176.00 lbs	23.9	79.8 kg	Maltodextrin	40 g/day
☑	1001R004	2016-01-20 16:30	79.00 kg	23.3	79 kg	Maltodextrin	40 g/day
☑	1001R005	2016-01-20 16:31	165.00 lbs	24.4	74.8 kg	Glutamine	35 g/day
☑	1001R006	2016-01-27 14:23	78.00 kg	25.5	78 kg	Glutamine	40 g/day

The treatment allocation is concealed, therefore you will only see the treatment displayed as each new patient is randomized.

6) Check the treatment assignment on the CRS (see table above) which will be one of the following two:

Name of Group	Intervention
Active	Glutamine
Control	Maltodextrin (placebo)

7) The 8 character randomization number, including the 4 digit Site ID, and 4 character (one alpha and 3 numeric) enrollment (randomization) number will display in the column on the left (see table above). The pharmacy team member will use the 8 character randomization number provided by the Research Coordinator to confirm the treatment allocation for the correct patient.

8 character randomization #

1012 - R 001

Site # **Enrollment #**

8) The CRS will display the patient weight as entered by the research coordinator and the calculated BMI in accordance with the accompanying height entered by the research coordinator on the pre-randomization page.

9) The CRS is programmed to calculate the patient's dosing weight, and indicate if the weight has been adjusted due to a BMI of 35 or above.

10) The CRS will also calculate the daily treatment dosage and round to the nearest 5g. The daily Treatment Dosage will display in the right hand column as # g/day.

11) Print off the treatment assignment for the patient by clicking on the box in the left hand column next to the patient randomization #. This treatment assignment page must be signed by 2 pharmacy team members and filed in the patient Pharmacy Study files.

12) Click the "Logout" button to end the session.

Administration of IP

The IP will be reconstituted by the nurse or RC at the patient's bedside just prior to administration. IP will be mixed with sterile or tap water, per local standard for enteral feeds, in a clean specimen container.

Doses of 1 or more packets, 5 grams each, may be administered every 4 hours until the calculated dose has been administered. Each 5g packet of IP is to be mixed in 50 mL of water and given as a bolus via the enteral route. The intervention will begin as soon as possible, independent of initiation of enteral nutrition. The boluses are to be given via either a small bore feeding tube or a larger bore gastric/Levine tube. The boluses are to be given via a feeding tube once the latter has been inserted.

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 (except alcohol) or non-heated food such as:

- Yogurt
- Applesauce
- Cereal
- Pudding

Mixing the IP with soda or highly acidic juices (such as grapefruit juice, orange juice, or lemonade) is not recommended as the IP degrades or becomes unstable in an acidic medium.

Interrupted or missed doses
Interruptions or missed doses of the intervention should not occur. In the event that an interruption or a missed dose does happen, the missed doses should be made up the same day by giving additional doses or doubling the scheduled dose, according to the following:

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

Administration of IP will be recorded on the Medication Administration Record.

Ordering of Investigational Product

1. Site pharmacists or pharmacy technicians are responsible for maintaining sufficient levels of Investigational Product (IP) to allow for uninterrupted dosing of active study subjects.
2. Resupply of IP will be shipped to sites on Monday's, Tuesday's, and Wednesday's (subject t to change for statutory holidays) however orders may be placed Monday through Friday.
3. Please allow 7 days for your IP delivery to arrive at your site.
4. Minimum quantities of both components should be calculated based on the following

    A. *If the average subject receives 8 packets per day, 15 days X 8 packets = 120 packets*
    B. *For example if the Glutamine Bulk inventory equals (250 packs) and you enroll a subject who will receive (8 packs daily) then you have 31 day's supply. In ten days' time, you need to think about placing an order. By the time you receive your reorder your inventory will have dropped to 90 packs.*
    C. *IMPORTANT REMINDER: In the event you have more than 1 participant on either the Active or Placebo arms, order extra accordingly.*

5. Orders should be placed by emailing **securedata@epipharm.com**
6. The body of the Email should contain the following:

    Site ID: 1012
    Glutamine: 150
    Placebo: None
    Ordered By: John Doe

7. The Central Pharmacy Depot will process the order on the next business day for shipping on Monday, Tuesday, or Wednesday.
8. Document the receipt of your shipment on the applicable IP Accountability Log.
9. Acknowledge receipt of your order and place the completed waybill in your study binder
10. Contact the Central Pharmacy Depot at 613.549.6666 ext. 3339 or email securedata@epipharm.com if you encounter problems with your order.

APPENDICES

Appendix A: Pharmacy Delegation and Training Log

Appendix B: NutreStore™ (L-glutamine) monograph

Appendix C: Maltrin M-100® maltodextrin monograph

Appendix D: Temperature Log

Appendix E: IP Dispensing Log

Appendix F: IP Accountability Log - Glutamine

Appendix G: IP Accountability Log - Maltodextrin

Pharmacy Delegation & Training Log

THE RE–ENERGIZE STUDY

The participating site pharmacy at _____ has established a Standard Operating Procedure for the RE-ENERGIZE Study.

This log (or a similar log) is used by the Pharmacist at each site to:	Key Delegated Tasks
1) Indicate the pharmacy staff that have been delegated duties/tasks related to The RE-ENERGIZE Study and 2) Ensure that all pharmacy staff that have a material effect on The RE-ENERGIZE Study have been trained on the study procedures. This log (or similar log) is to be kept by the Pharmacy and sent to the Sponsor upon request.	1. Checking the treatment assignment on the Central Randomization System 2. Preparation and checking of Investigational Product 3. Labeling of Investigational Product 4. Maintaining Dispensing Logs 5. Maintaining Investigational Product Accountability & Destruction Records 6. Maintaining and managing inventory 7. Requesting resupply of inventory 8. Other (specify): _____

(site name)

Pharmacy personnel listed in this log have been trained according to the Standard Operating Procedures.

Name of Pharmacy contact*: _____ Signature of Pharmacy Contact: _____

*Pharmacy contact: is the main pharmacist/pharmacy technician that has been trained by the Methods Centre to carry out all pharmacy tasks related to the RE-ENERGIZE Study at the site.

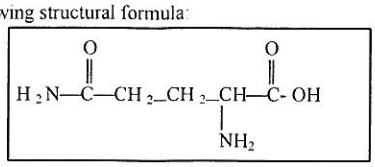
Print Name	Signature	Initials	Study Role (Pharmacist, Technician, etc)	Key Delegated Tasks (see above)	Training	
					Date of training	Trained by: Trainer, Webinar, Self-Study, other - specify (if Trainer - provide name)

NutreStore™
[L-glutamine powder for oral solution]

(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-aminoglutaramic acid, L-glutamic acid 5-amide, (S)-2,5-diamino-5-oxopentanoic acid, or L-glutamine. The molecular formula of glutamine is $C_5H_{10}N_2O_3$, 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

[1]SOD[GLN] = Specialized Oral Diet supplemented with Glutamine; rhGH + SOD = Human Growth Hormone plus Specialized Oral Diet; rhGH + SOD[GLN] = Human Growth Hormone plus Specialized Oral Diet supplemented with Glutamine
*** p = 0.023, treatment comparison between rhGH + SOD[GLN] versus rhGH+SOD**

GROUP A: rh-GH + SOD for 4 weeks followed by SOD for 12 weeks
GROUP B: rh-GH + SOD [GLN] for 4 weeks followed by SOD[GLN] for 12 weeks.
GROUP C: rh-GH placebo + SOD [GLN] for 4 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 rhGH+SOD[1] N=16 n(%)	Group B rhGH+SOD[GLN][1] N=16 n (%)	Group C 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	**15 (94)**	**15 (94)**	**4 (44)**
Edema, Peripheral	11 (69)	13(81)	1 (11)
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)**
Ear or Hearing Symptoms	0 (0)	2 (13)	0 (0)

[1]**SOD[GLN] = Specialized Oral Diet supplemented with Glutamine; rhGH+SOD = Human Growth Hormone plus Specialized Oral Diet; rhGH + SOD [GLN] = Human Growth Hormone plus Specialized Oral Diet supplemented with Glutamine**

Group A: rh-GH + SOD for 4 weeks followed by SOD for 12 weeks

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

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 rhGH+SOD[1] N=15 n (%)	Group B rhGH+SOD [GLN][1] N=16 n (%)	Group C 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 Fistual	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

[1]**SOD[GLN] = Specialized Oral Diet supplemented with Glutamine; rhGH+SOD = Human Growth Hormone plus Specialized Oral Diet; rhGH + SOD [GLN] = Human Growth Hormone plus Specialized Oral Diet supplemented with Glutamine**

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

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

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

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

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

HOW SUPPLIED

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

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

STORAGE

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

For additional information concerning NutreStore™, contact:

Emmaus MEDICAL, INC.

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

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

Rx only

Revised October 2008

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SMM-007-02 0810

MATERIAL SAFETY DATA SHEET

IDENTITY(As Used on Label and List)

L-GLUTAMINE

SECTION I

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

SECTION II - HAZARDOUS INGREDIENTS / IDENTITY INFORMATION

CHEMICAL NAME AND SYNONYMS	CHEMICAL FAMILY
L-Glutamine	Amino Acid
FORMULA	CAS NUMBER
$C_5H_{10}N_2O_3$ (146.15)	56-85-9

INGREDIENT	PERCENT	HAZARDOUS
L-Glutamine	Pure material	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)	FLAMMABLE LIMITS	LEL	UEL
None	None		

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	EYE PROTECTION
Recommended	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.
• E. coli	Negative/10 g
• Salmonella	Negative/25 g

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

CARBOHYDRATE LABELING INFORMATION**

• DP1 (glucose) grams per 100 grams	1
• DP2 (maltose) grams per 100 grams	3

** Carbohydrate information reported “as is”.

DEGREE OF POLYMERIZATION (DP PROFILE)***

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

*** DP profile data reported “as is”.

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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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THE RE–*ENERGIZE* STUDY

Investigational Product Temperature Log

Site Name _____ **Site #** _____

Investigational Product is to be **stored** in a cool dry area **15°- 30° Celsius / 59°- 86° Fahrenheit**.

Record the temperature daily. Provide comment for days temperature is not recorded.
Keep log with study IP documents. To be provided to CERU Central Pharmacy Manager/Unblinded Monitor upon request.

Month _____ **Year** _____

Temperature recorded in (circle one) Celsius Fahrenheit							
Date	**Temperature**	**Initials**	**Comments**		**Date**	**Temperature**	**Initials**	**Comments**
1					**16**			
2					**17**			
3					**18**			
4					**19**			
5					**20**			
6					**21**			
7					**22**			
8					**23**			
9					**24**			
10					**25**			
11					**26**			
12					**27**			
13					**28**			
14					**29**			
15					**30**			
					31			

Investigational Product Dispensing Log - Patient

THE RE-*ENERGIZE* STUDY

Treatment Allocation:

☐ Glutamine
☐ Maltodextrin (placebo)

Site: _____ Page _____ of _____

Patient ID#:_____ Patient Initials:_____Randomization #:_____

1. Prescription date: _____ Dosing Weight: _____ Total Daily Dose: _____ grams

2. Prescription date: _____ Dosing Weight: _____ Total Daily Dose: _____ grams

3. Prescription date: _____ Dosing Weight: _____ Total Daily Dose: _____ grams

Did the prescription change ?

☐ Yes ☐ No

Date	Glutamine			Maltodextrin			Initials	
	Total Daily Dose (g)	Quantity Dispensed (# 5g packets)	Lot & Expiry	Total Daily Dose (g)	Quantity Dispensed (# 5g packets)	Lot & Expiry	Prepared By	Checked By

Investigational Product Accountability Log
Glutamine

THE RE–ENERGIZE STUDY

Site: _____ Page ____ of ____

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

Date	Quantity		Lot #	Expiry Date	Quantity Dispensed	Patient Randomization #	Balance of Product	Signature
	Received	Destroyed						

Investigational Product Accountability Log
Maltodextrin

THE RE–ENERGIZE STUDY

Site: _____ Page ____ of ____

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

Date	Quantity		Lot #	Expiry Date	Quantity Dispensed	Patient Randomization #	Balance of Product	Signature
	Received	Destroyed						