The *REDOXS*© Study
REducing Deaths due to OXidative Stress

A randomized trial of glutamine and antioxidant supplementation in critically ill patients

Implementation Manual

Completion of Electronic Case Report Forms

This study is registered at Clinicaltrials.gov.
Identification number NCT00133978

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Table of Contents

Introduction

The Implementation Manual functions as a resource for successful completion of electronic case report forms (eCRFs) for the REducing Deaths due to OXidative Stress Study (The REDOXS© Study)

The manual is formatted to provide written instruction for each electronic CRF. A webshot of the actual web page will follow written instructions.

ECRFs are the primary mode of data capture used in the REDOXS© Study. The Study Coordinator (SC) is expected to enter data online as soon as it becomes available. Paper CRFs and worksheet templates are available as tools to assist in capturing the required data elements prior to online data entry.

> *Please keep ALL worksheets/documents that you use as these will be referred to at the time of source verification.*

The following CRFs are the only forms that are not to be entered electronically. These must be completed on paper and faxed to the Clinical Evaluation Research Unit (CERU) within the specified timelines:

- **Protocol Violation** (within 24 hours of becoming aware of the violation for select sites*)
- **Serious Adverse Events** (within 24 hours of becoming aware of the event)

Taxonomies and other supporting material are found as appendices to the manual.

In the event that additional clarification is required; please contact the Project Leader (PL)

- The Project Leader will provide additional details at the time of training.

Study Contacts

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Acronyms

Bili	Bilirubin
BP	Blood Pressure
BS	Blood Sugar
CERU	Clinical Evaluation Research Unit
Cr	Creatinine
CRF	Case Report Form
DOB	Date of Birth
eCRF	Electronic Case Report Form
EN	Enteral Nutrition
GCS	Glasgow Coma Score
GRV	Gastric Residual Volume
HR	Heart Rate
ICU	Intensive Care Unit
MODS	Multi-Organ Dysfunction Syndrome
PL	Project Leader
PN	Parenteral Nutrition
RC	Research Coordinator
RR	Respiratory Rate
SC	Study Coordinator
SAE	Serious Adverse Event
SI	Site Investigator
SIRS	Systemic Inflammatory Response Syndrome
Temp	Temperature
U/O	Urine Output
WBC	White Blood Count

General Guidelines

Accessing the Website

- The Clinical Evaluation Research Unit (CERU) will provide a username and password **only** to authorized personnel who are participating in the REDOXS© Study.
- All authorized personnel accessing the web site must sign an electronic data capture signature sheet provided by CERU. This sheet will be provided at the study start-up session.
- The Study Coordinator (SC) and Study Pharmacist will be responsible for notifying the CERU Project Leader (PL) with any changes in study personnel accessing the web.
- The Web Based Data Capturing System for the REDOXS© Study can be accessed by following the **REDOXS login link** on the www.criticalcarenutrition.com website, or directly at https://ceru.hpcvl.queensu.ca/REDOXS_RCT
- All authorized study personnel must log onto the web site using their own username and password prior to data entry.
- Your user profile and password can be changed at any time by clicking the appropriate links on the REDOXS© home page.

Completion of Electronic Case Report Forms

- All screening, randomization, and data collection activities will be completed on the web. **Only** patients meeting **inclusion criteria** should be entered on the web.
- The site number will be programmed for each site by CERU.
- Dates are entered using DD/MMM/YYYY format i.e. 24/Jul/2004. Single "click" on day and choose appropriate day from the drop down box. Repeat again for month and year. By using the drop down boxes provided you are assured proper date format is obtained.
- Enter all times using the 24-hour period format i.e. 22:37. There is no need to enter a colon as the web application will format the time for you.
    - Midnight (24:00 hours) should be entered as 00:00
- To access eCRFs single click the appropriate link using the left side of your mouse.
- To expand a menu or taxonomy click on '+' next to the title of the menu/taxonomy. To collapse the menu or taxonomy click on '-'.
- To enter data directly into each field **single click** on the left side of the mouse pointer and type information or select from the available taxonomy.
- If no data has been entered and saved on a eCRF it will be marked with a red on the Patient Status Page.
- If there is still outstanding data on an eCRF it will be marked with an amber on the Patient Status Page.
- If all data fields have been completed on an eCRF it will be marked with a green on the Patient Status Page.
- The RESET form button will take you back to the last saved version.

Input Warnings

- The web based data entry system has been programmed with various range & logic checks to simplify the query process.
- You will not be able to proceed with locking or finalizing data entry until you have addressed these input warnings.

- In the event that the values that you have entered are beyond web ranges, you will receive an input warning. Please follow the instructions on the screen to either "view/edit" the data or to "accept" it. If you accept data that is beyond the web ranges, you will be prompted to add a comment in the text box on the screen.

Edit data entered on the web

To edit previously saved information, access the appropriate eCRF, change the appropriate field(s) and save the form. To ensure Good Clinical Practice is maintained, all changes will be tracked and logged by the computer program. You **cannot** delete patients. Please contact the PL if you have any queries regarding editing or deleting data.

Duration of Data Collection

Study Day 1 is from ICU admission to the end of your 24 hr ICU flow sheet. *Study Day 2 and subsequent days are the 24 hr period according to your ICU flow sheet.*

- All **data including daily data, daily nutrition data, vasopressors and concomitant medication** needs to be collected **from Study day 1 and each day following until the end of the flow sheet on day 30, unless ICU discharge (actual) or death occurs before day 30.**
    - EXCEPTIONS
        - Study Supplement Compliance: collect data for duration of the study supplements (which is a maximum of 28 days from randomization).
        - Microbiology: start 7 days before ICU admission until day 30, unless ICU discharge (actual) or death occurs before day 30.
        - Antibiotics: start 7 days before ICU admission and stop dates may extend beyond ICU discharge.
        - Patients with ICU stay < 5 days and transferred to ward: collect all daily data from Study Day 1 and continue for 5 days in total = 120 hrs.

Study Days follow your ICU flow sheet clock.

Example: 7-7 or 12-12

								ICU Discharge or Death or Study Day 30		
	Day -7	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	→	**Day 28**	**Day 29**	**Day 30**
ICU Admission		x								
Daily Data Daily Nutrition Data Vasopressors Concomitant Medications		x	x	x	x	x	x	x	x	x
Study Supplement Compliance		x	x	x	x	x	x	x		
Microbiology	x	x	x	x	x	x	x	x	x	x
Antibiotics	x	x	x	x	x	x	x	x	x	x

Readmission to ICU

If a patient is re-admitted to your ICU ***within*** 48 hrs of discharge, consider this to be a continuation of the previous stay. Restart the study supplements and continue to collect data. (Consider whether the reason for re-admission to ICU should be reported as a Serious Adverse Event (SAE). Refer to the SAE manual for definitions.) If a patient is re-admitted to your ICU ***after*** 48 hours of discharge, this is *not* considered to be a continuation of previous stay and patient cannot be randomized to the study again.

Time frames for completion of data entry

- The screening and randomization must be entered on the web immediately to ensure that the study supplements are started as soon as possible after ICU admission.
- The remaining web pages can be completed retrospectively but it is encouraged that a daily paper worksheet be kept to make the data collection easier.
- Deadline for completion of data entry:
    - Within 2 months from ICU admission except for 3, 6 month follow up and SF-36.

The web based data entry system has been programmed with various checks to simplify the query process. When proceeding with the data entry, please follow the order in which the forms appear. This will reduce the input warnings that you will encounter.

Locking Data and Finalizing Patients
The web based data entry system has been programmed with a data locking process to help determine when the first stage of data entry has been completed. Similarly a process has been built into the last data entry that will finalize the patient. Refer to the section on Locking of Data and Investigator Confirmation and Finalizing Patient for more details.

REDOXS© Study Website

The REDOXS© website will be the gateway for accessing the web application's login page. Users (SC or Pharmacist) will go to the website for the REDOXS© study www.criticalcarenutrition.com or directly to https://ceru.hpcvl.queensu.ca/REDOXS_RCT

- The SC will then choose the site Login option from the drop down box on the left column of the web page to access the login page.

Regular updates and useful information regarding the REDOXS© study will also be posted on this website so please check it regularly.

www.criticalcarenutrition.com / REDOXS / Resources

Delegation of Authority Logs and Web Access Signature Log

Investigator Delegation of Authority Log

- All research site personnel with a material effect on the REDOXS© Study should sign the ***Site Investigator Delegation of Authority Log (Appendix 1)***. This is to confirm that the Site Investigator has delegated tasks to reasonably qualified individuals. The completed log and subsequent updates to the log is to be faxed to the Clinical Evaluation Research Unit (CERU) at (613)548-2428 by the Research Coordinator.

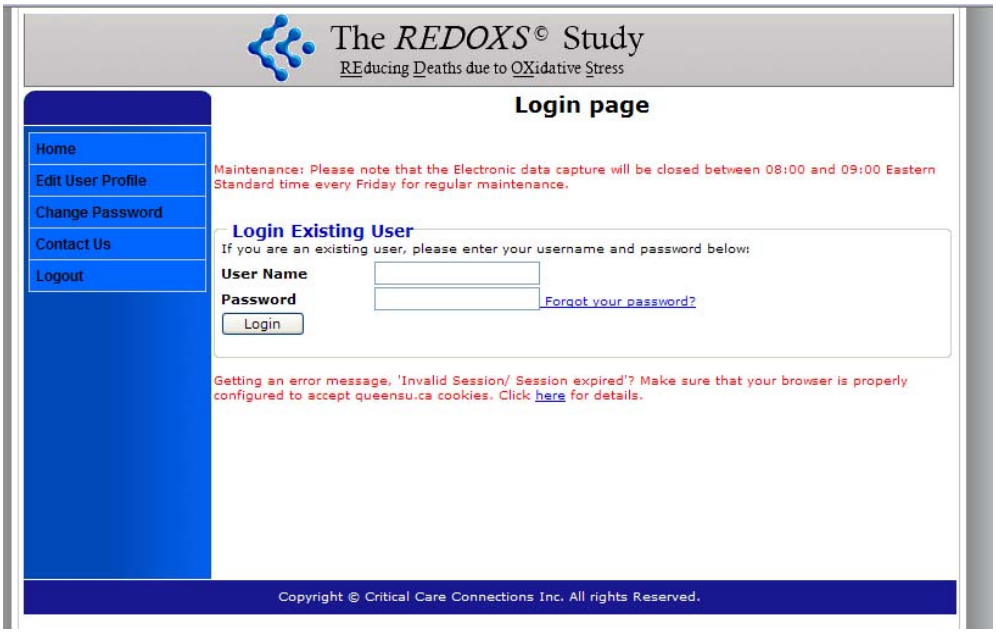
Web Access Signature Log

- Research Coordinators (and those delegated the task of entering data on the EDCS) must sign the ***Web Access Signature Log (Appendix 2)*** provided by CERU (Clinical Evaluation Research Unit).
- Completed signature logs are to be faxed to the Project Leader at CERU at (613)548-2428 before a username and password to the web based system can be assigned.
- Web access will only be granted to those who have completed REDOXS© Study training.

The Research Coordinator will be responsible for notifying the CERU Project Leaders with any changes in personnel. Updates to the Delegation Logs are to be faxed to the CERU Project Leader at (613)548-2428.

Web Login Page

- You will be provided with a username and password once your regulatory paperwork has been completed. Keep this EDCS access information confidential.
- Enter username and password
- Click the “Login” button to access the web. If the login information is correct, the user will be brought to the Welcome Home Page.
- If you forget your password, click on ‘Forgot your password?’ tab. Enter your e-mail address and complete the human user verification. You will be sent an e-mail with your username and a temporary password. Please change this password when you next login to the web system.



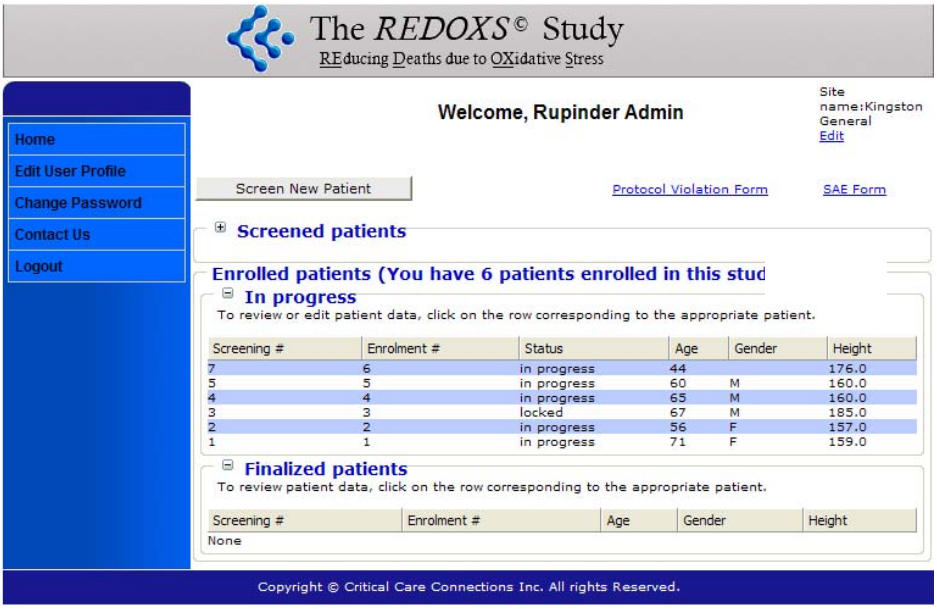
Welcome Home Page

Choose from one of the following options:

- **Screen new patients (click here to screen a new patient)**. Only enter patients that meet **ALL of the inclusion criteria.**
- **Screened Patients (DO NOT use this option to screen new patients).** Click on the '+' button to the left of 'Screened patients' to view all patients previously screened and entered. To review or edit patient information, click on the row corresponding to the appropriate patient.
- **Enrolled Patients (In progress).** Click on the '+' button to the left of 'In progress' to view patients for whom you are still collecting data. To enter, review or edit patient information, click on the row corresponding to the appropriate patient.
- **Enrolled Patients (Finalized):** Click on the '+' button to the left of 'Finalized patients' to view patients for whom all data (daily and outcomes) have been completed. To enter, review or edit patient information, click on the row corresponding to the appropriate patient.
- **Home.** To return to the web home page, click on 'Home' on the left hand side menu.
- **Contact Us.** On the left hand side of the menu click on 'contact us' to view the contact details of the Project Leader and Technical Support
- **Edit User Profile.** To change your personal or hospital specific information click on 'edit user profile' on the left hand side menu
- **Change password.** To change password, click on 'change password' on the left hand side menu. You will be asked to enter your old password, select and confirm a new password.
- **Log Out.** To log out of the web system and return to the login page click on "Log out' on the left hand side menu
- **SAE (Serious Adverse Events) and Protocol Violation Forms** can be downloaded from this page and must be filled in and faxed to the PL within the specified timelines.

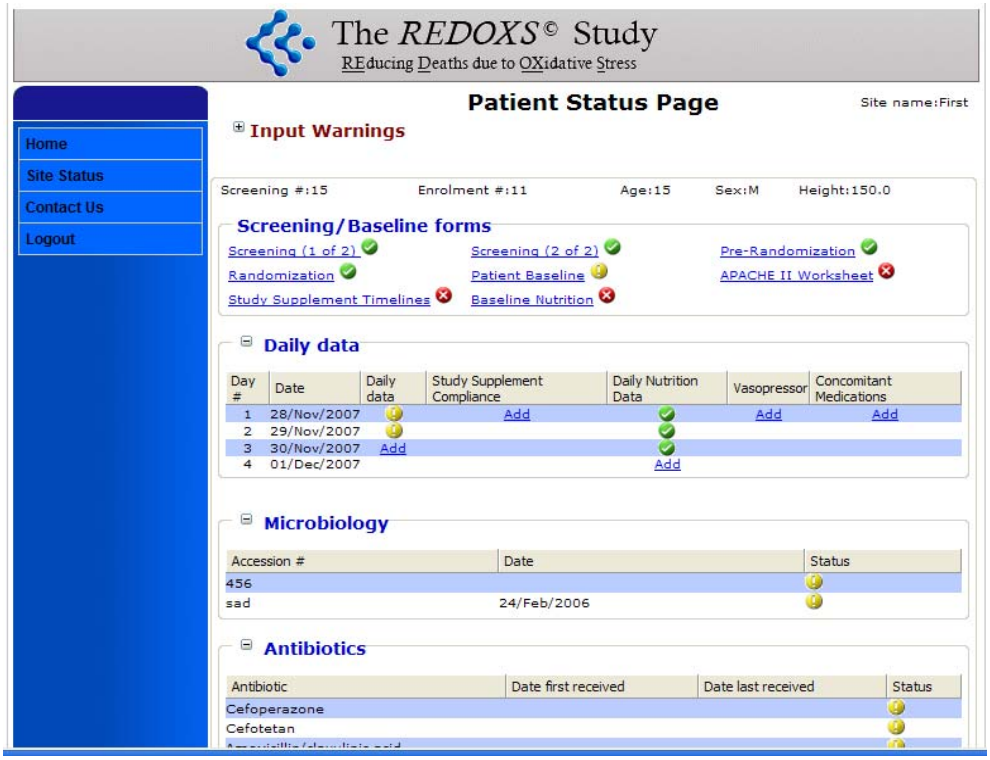
This page can also be accessed via the 'Site Status' link on the various Patient pages.

Welcome Home Page



Patient Status Page

- After clicking on a screened or enrolled patient on the Welcome Home Page you will be directed to the Patient Status page.
- From this page you can view, enter data, or edit information for all REDOXS© study related eCRFs.
- If you 'save' any eCRF, you will be directed back to this page.
- Traffic light symbols next to each eCRF link indicate the status of each from (pending)
  - If no data has been entered and saved on an eCRF it will be marked with a red .
  - If there is still outstanding data on an eCRF it will be marked with an amber .
  - If all data fields have been completed on an eCRF it will be marked with a green



Screening

Screen patients admitted to your ICU daily to see if they meet the inclusion criteria or exclusion criteria as listed below.

The screening data **must** be entered onto the web in a timely manner in order to randomize the patient and start study supplements soon after ICU admission.

- **Enter only** patients who meet **ALL** the inclusion criteria.
- The site number will automatically be entered.
- The patient's screening number will automatically be entered.
- Enter date and time of screening
- Provide patients age (round off to the nearest age).

Inclusion Criteria

1) Patient **must be** mechanically ventilated, ≥ 18 years old and admitted to ICU

AND

2) Must have **2 or more** organ failures related to their **acute illness**.
If you have any questions about whether the organ failure is related to the patient's acute illness or not, please discuss this with your Site Investigator (SI).

- As a general guideline, if an organ failure has occurred > 72 hours prior to admission to ICU, this is considered **not** to be acute. This patient may not be appropriate for inclusion and this should be discussed this with your SI.
- Organ Failures may have started before ICU admission **but have to be present in ICU**. Example: An organ failure that was present in the emergency room that has resolved by the time ICU admission occurs, does **not** meet the inclusion criteria.
- Organ failures may have resolved at time of screening or randomization.
- Patients re-admitted to ICU with new organ failures are eligible as long as new organ failures are acute relative to the reason for the re-admission.

- Record **ALL** organ failures.
- Provide the date DD/MMM/YYYY and time using a 24-hour clock for the onset of each individual organ failure:
  - Respiratory failure
  - Hypoperfusion failure
  - Renal dysfunction
  - Low platelet count

- Table 1 provides definitions for each organ failure & timing of onset of organ failures.

Table 1: Organ Failure Definitions & Timing

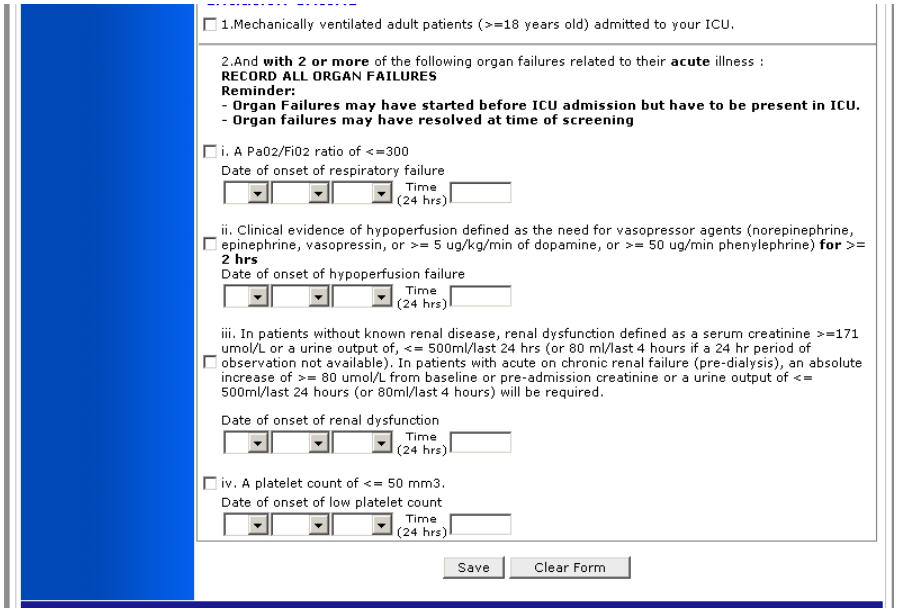
Organ Failure	Definition
Respiratory Failure	Date and time of onset of respiratory failure is when the $PaO_2/FiO_2 \leq 300$ **Note:** Use the time the ABG was drawn. PaO_2/FiO_2 ratio **must** be calculated on a patient who is receiving mechanical ventilation **i.e.** intubation with mechanical ventilation **or** tracheostomy with mechanical ventilation.
Hypoperfusion Failure	Date and time of onset of hypoperfusion is the **start of** vasopressor / inotrope agents: o Norepinephrine (any dose) for ≥ 2 hrs o Epinephrine (any dose) for ≥ 2 hrs o Vasopressin (any dose) for ≥ 2 hrs o Dopamine (≥ 5 µg/kg/min) for ≥ 2 hrs o Phenylephrine (≥ 50 µg/min) for ≥ 2 hrs Note: When assessing for eligibility, once you have verified that a patient has been receiving vasopressor/inotrope agents, as per the above list, go back and use the date/time of the start of infusions for the documented time of onset of hyperperfusion.
Renal Dysfunction	In patients **without known renal disease**,date and time of onset of renal dysfunction is: o Serum creatinine* ≥ 171 umol/L **OR** o Urine output* ≤ 500mls/last 24 hours (**or** 80 ml/last 4 hrs if a 24 hr period of observation is not available). ***If elevated serum creatinine used**, enter date and time of laboratory report. If using **decreased urine output** over 24 hours **or** over 4 hours, enter date and time of the start (not end) of the time window. If patient qualifies for both elevated serum creatinine or decrease urine output, enter serum creatinine date and time of laboratory report.* In patients with **acute on chronic** renal failure (predialysis): o an absolute increase of ≥ 80 umol/L from baseline or preadmission creatinine **or** o urine output of ≤ 500 ml/last 24 hours (**or** 80 ml/last 4 hrs) will be required. ***In patients with acute on chronic renal failure**, baseline or preadmission creatinine is defined as the normal or pre hospitalization creatinine for this patient. It is not the creatinine at Study Day 1 or admission to ICU value. Please check hospital records for this information.*
Platelet Count	Date and time of onset of low platelet count is when: o the platelet count ≤ 50 mm^3 *NOTE: Patients with chemo induced- or chronic thrombocytopenia are not considered acute in terms of the organ failure.*

For patients previously admitted to the ICU, discharged and then re-admitted to the ICU, they may be considered eligible for the study ONLY if the organ failures are considered to

be acute at this current ICU admission (and are NOT a continuation from a previous ICU admission).

Web shot of Screening Form

Inclusion Criteria



Exclusion Criteria

- Choose **only <u>one</u>** exclusion criteria i.e. the most pertinent. If the patient meets more than one exclusion, the MD must determine which exclusion criteria is to be entered. As a general guideline, the criteria are listed in the order of importance. The exclusion criteria are as follows:

Exclusion Criteria	Description
1	>24 hours from admission to ICU. This refers to the time from ICU admission to <u>time of consent.</u> *For patients that have been transferred from another ICU, the 24 hours pertains to the TOTAL time in the intensive care unit setting. For example, if a patient was in another ICU for 4 hours and then gets transferred to your ICU, this time becomes 20 hours from the admission to your ICU.* *A step-down unit is <u>not</u> considered an ICU.*
2	Patients who are moribund (not expected to be in ICU for more than 48 hours due to imminent death).
3	A lack of commitment to full aggressive care (anticipated, withholding or withdrawing treatments in the first week). *Example: A patient with an isolated DNR is eligible as long as there is a commitment to ongoing medical treatment.*
4	Absolute contraindication to enteral nutrients (i.e., GI perforation, obstruction or no GI tract access for any reason). *Distended abdomen and/or high gastric residuals are <u>not</u> exclusion criteria.* *Patient who has undergone GI surgery shortly before or after admission to ICU is eligible.* *The study supplements are nutrients that are infused at low rates; they are very well absorbed even in patients that are not tolerating enteral nutrition.*
5	Patients with **<u>acute</u>** Severe acquired brain injury. ▪ Significant head trauma (defined as an injury in the opinion of the investigator to represent a severe, disabling, or fatal brain injury) ▪ Grade 4 or 5 subarachnoid hemorrhage (subdural hemorrhage is eligible) ▪ Stroke resulting in coma and intubation ▪ Post-cardiac arrest with suspected significant brain injury *Patients with a past history of head injury may be included if they experience a reasonable level function at home.*
6	Routine elective cardiac surgery (patient's with complicated peri-operative course requiring pressors, IAPB, ventricular assist devices can be included).
7	Seizure disorder requiring anticonvulsant. This refers to a pre-existing history of seizure disorder requiring anticonvulsants. Patients with acute seizures that occur in the ICU requiring anticonvulsants, where there is NO documented history of seizures needing anticonvulsants prior to this illness, are eligible.
8	Patients with primary admission diagnosis of burns (≥30% BSA). This refers to patients with "active" burns.
9	Weight less than 50 kg or greater than 200 kg.
10	Pregnant or lactating with the intent to breast-feed.
11	Previous randomization in this study.
12	Enrolment in a related ICU interventional study. *Co-enrolment in REDOXS and PROTECT or ABLE or OSCILLATE is allowed. Contact the Project Leader if you have any questions regarding co-enrolling in another study.*
13	Cirrhosis Child's Class C Liver Disease- click on "Explain" and the criteria to determine Child- Pugh scoring will appear (see below).
14	Cancer metastatic cancer Stage IV Lymphoma with life expectancy < 6 months.

Patients with Expected ICU Length of Stay < 5 Days

If a patient is expected to be in the ICU < 5 days because they are expected to be extubated and discharged to the floor, this should be entered as an eligible patient who is NOT randomized. Refer to the Pre-Randomization form for further data entry details.

Child's Class C Liver Disease Classification

The child-Pugh score is obtained by adding the points for all 5 criteria. Any patient having a score of 10 – 15 falls into Group C (severe hepatic impairment), which would be considered exclusion for this study.

Criteria	**Points assigned**		
	1	**2**	**3**
Total Bili Conventional SI units	 < 2 mg/dl < 34 µmol/L	 2.0 – 3.0 mg/dL 34 – 51 µmol/L	 > 3 mg/dL > 51 µmol/L
Serum Albumin Conventional SI units	 > 3.5 g/dL > 35 g/L	 2.8 – 3.5 g/dL 28 – 35 g/L	 < 2.8 g/dL < 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.			

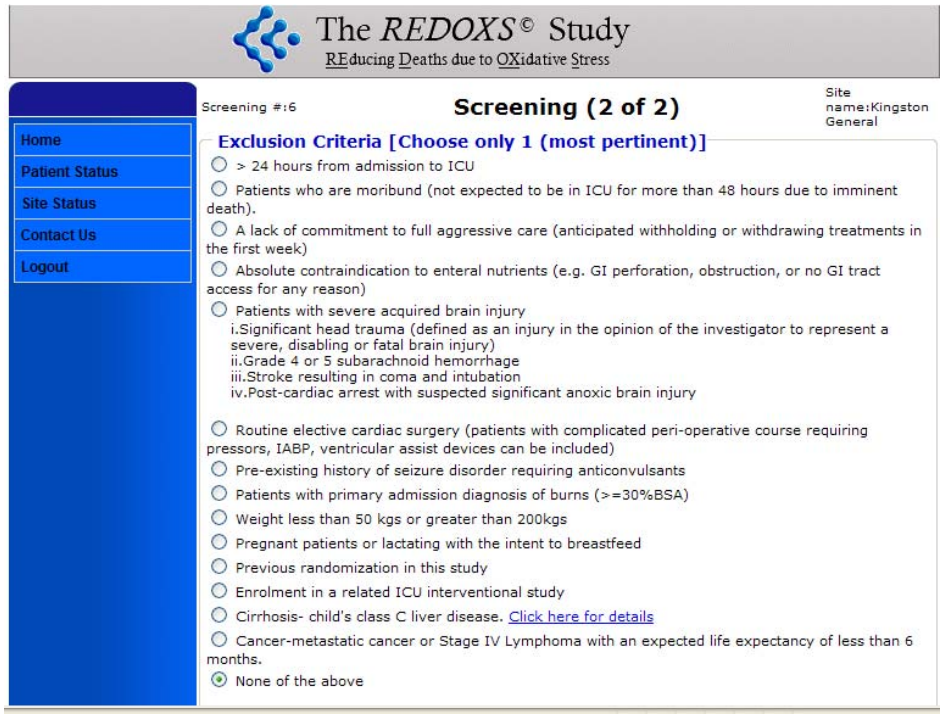
- If any 1 of the 14 exclusion criteria is met the patient is **NOT ELIGIBLE for the study.** After you click the save button, you will automatically be taken back to the home page.
- If no exclusion criteria are met, choose the last criteria, "None of the above", save the form and the patient is eligible for the study. You will be directed to the Pre-Randomization Page.
- If any questions regarding the screening form arise, contact your Site Investigator first. If questions cannot be resolved contact the PL or Study Chair at CERU.

Please print off the web page showing the inclusion/exclusion criteria met by the patient and have this signed and dated by the Site Investigator for confirmation that the criteria were met at the time. Alternatively, a worksheet can be used or progress notes must be made in the medical chart. If using a worksheet, this MUST be kept at your site for source documentation.

Once you have randomized a patient, you are unable to make changes to the screening criteria or dates and times. Please contact the Project Leader with the corrections that need to be made.

Webshot of Screening Form

Exclusion Criteria



Randomization

Note: Refer to Randomization Process on Web Appendix 3 for algorithm.

Pre-Randomization

- If **no exclusion** criteria are met the patient is considered eligible for randomization into the study. Once you click "Save", you will be directed to Pre-Randomization Page.
- When the web prompt states "Eligibility has been confirmed with MD", you **must** click on the box to continue.
- The name of MD who confirmed eligibility for the study must be typed into the text box provided.
- You must confirm that informed consent has been obtained to proceed.
    - After clicking **'yes'** you will be prompted to enter patient's height in cms. See "conversion table" to convert feet/inches into cms (see appendix 2). Record the height in the patient's chart/ICU flowsheet as this will need to be source-verified later.
- Click on "CLICK HERE TO RANDOMIZE PATIENT".
- You will be directed to the Randomization page. The top of the web page reads "**You have successfully randomized this patient! Randomization #X. Please print off this page for your records".**
- Print the page and notify the study pharmacist of the following:
    - Patient randomization number (= enrollment number)
    - Height in cm
    - Patient initials and DOB
- The patient's height and randomization date/time will automatically be completed for you (from the Pre-randomization form).
- Enter the date and time you contacted your site pharmacist.
- The pharmacist upon notification will then proceed with the web-based randomization process.
- You must click on the save button at the bottom of the form to save entered information.
- You will be directed to the Patient Baseline Form and subsequent forms.

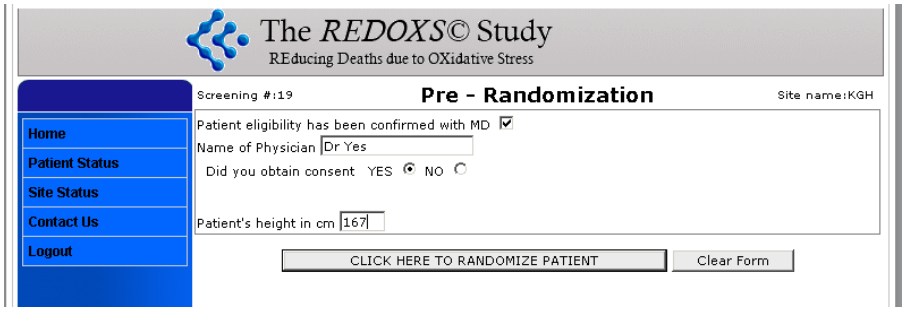
If no consent was obtained the patient CANNOT be randomized into the study

- After Clicking 'no' to this question you will be prompted to choose the most important reason the patient wasn't randomized.
- After you click the save button, you will be taken back to the home page.

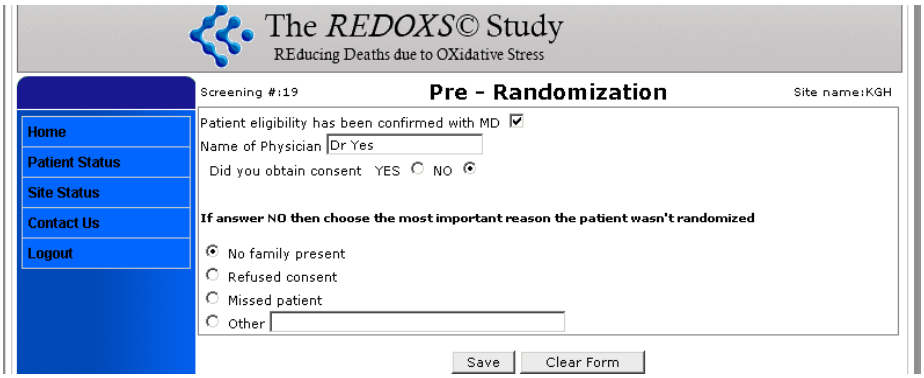
Once you have randomized a patient, you CANNOT go back and add an exclusion criterion to make this patient "not eligible". In the event of an error in the screening, you MUST contact the Project Leader immediately.

Webshot of Pre-Randomization Form

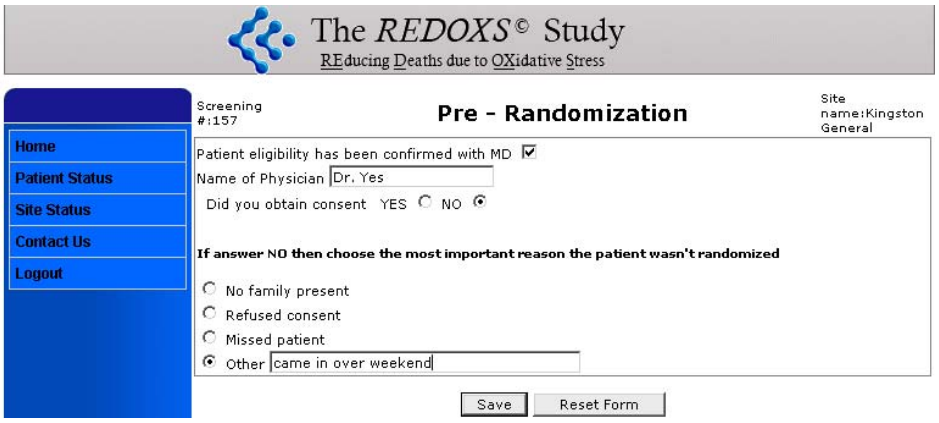
Consent obtained



Consent Not Obtained

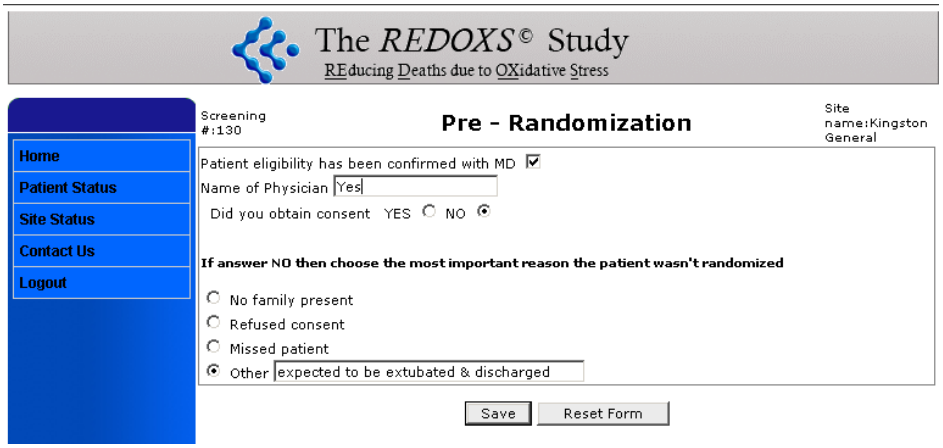


Eligible but not Randomized

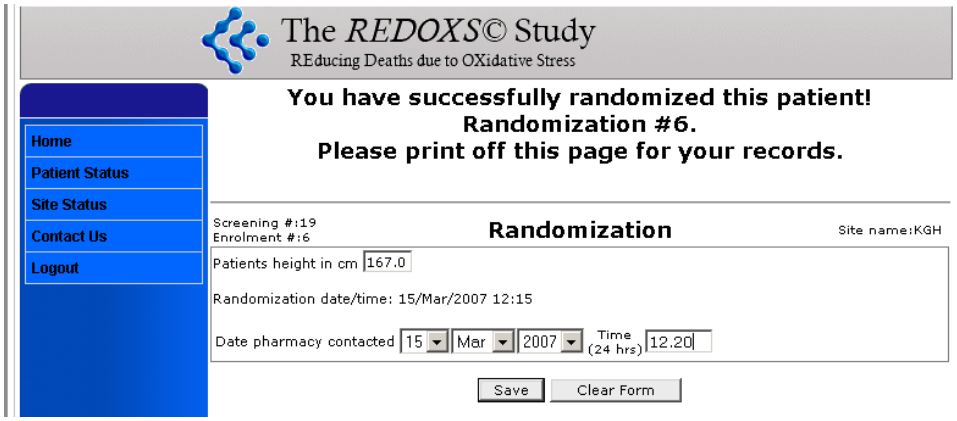


Patients with Expected ICU Length of Stay < 5 Days

For patients NOT expected to be in the ICU for at least 5 days, this should be entered as an eligible patient who is NOT randomized. Complete the Pre-Randomization form. Use the "other" category in the consent section to document that the patient is expected to be discharged from the ICU before 5 days.



Webshot of Randomization Form



Patient Baseline Form

- Enter the patient's admission weight in kilograms (kg). Weight in pounds divided by 2.2 = weight in kilograms. Record the weight in the patient's chart/flow sheet as this will need to be source-verified later.
- Please indicate patient's sex by ticking appropriate box.
- Please indicate the patient's ethnicity using taxonomy provided (see below).

Ethnicity
White
Black or African American
Hispanic
Asian or Pacific Islander
Native
Other

- Indicate by yes/no if patient is diabetic. If yes, indicate if Type I or Type II.
  - Type I is defined as being a juvenile diabetic or insulin dependent.
  - Type II is defined as non-insulin dependent diabetes, adult onset or insulin resistant diabetes
- For admission category choose either medical, elective surgery or emergency surgery.
- For Primary ICU Admission Diagnosis please use the taxonomy provided on the web (see appendix 3).
  - Primary admission diagnosis is the diagnosis that resulted in the patient's admission to ICU.
  - Choose only one diagnosis that is **most** pertinent.
  - The taxonomy for Medical diagnoses (Non-Operative conditions) is different from that for Surgical diagnoses (Operative Conditions).
- Click on '+' next to the diagnostic category to reveal the specific conditions.
- If a Primary ICU Diagnosis is not present in the taxonomy, look for the appropriate category (based on systems) i.e. Cardiovascular/Vascular, use "Other CV disease" option and type in the diagnosis in the text box provided.
- **Correct Example:**
  - If Primary Diagnosis is SARS, choose "Other Respiratory Disease". Type in SARS in the text box provided.

The following should not be entered as Primary diagnoses as these are conditions caused by the primary diagnoses: Hypotension, Respiratory Failure, Renal Disease, Coronary angiogram-stenting.

- Comorbidities (Please enter ALL that apply from the taxonomy provided, see appendix 4).
- Comorbidities that do not appear in the taxonomy do **not** need to be documented.
- For etiology of shock, select only one that applies from the taxonomy provided. If the shock is of uncertain origin, please check the appropriate box and provide an explanation in the Comment box at the bottom of the page.

Definition of shock: end organ dysfunction secondary to hypoperfusion.

Etiology of Shock Taxonomy

- Cardiogenic
- Septic
- Neurogenic
- Anaphylactic
- Hemorrhagic
- Other
- Uncertain Origin
- Not in Shock

For cases where the patient is considered to be in hypovolemic shock, please determine the cause of the hypovolemia: Is it hemorrhagic in nature or due to something else?

For cases where the patient is considered to be in distributive shock, you should determine the most responsible reason for the shock: Is the disruptive shock primarily anaphylactic, neurogenic or septic in nature? Is there some other reason (e.g. drug overdose).

You may need to wait to get a better understanding of the etiology of shock so this field on the Baseline form may be completed later.

Logic Alert

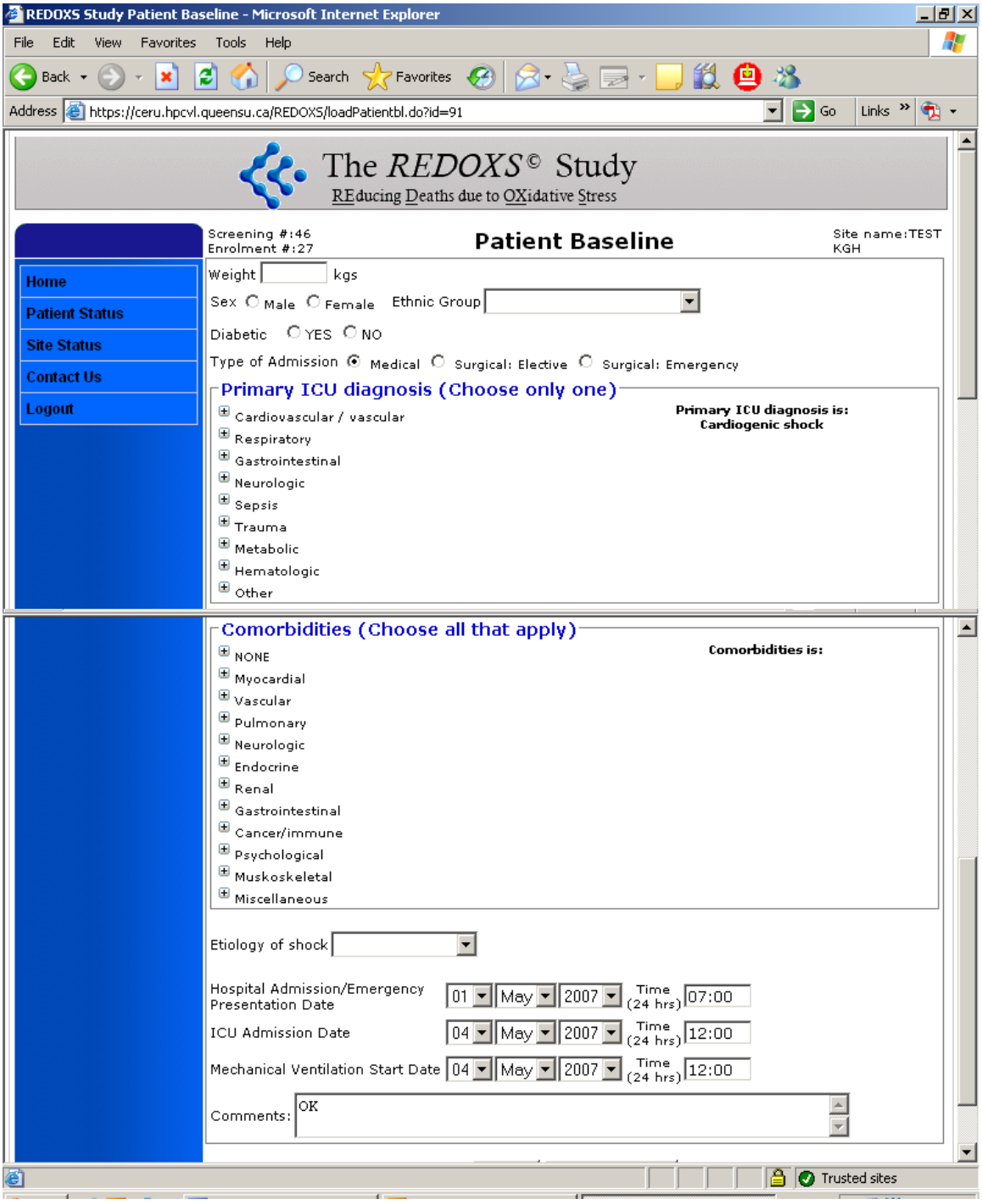
If you have chosen a type of shock here that is not consistent with the inclusion criteria 2ii (evidence of hypoperfusion), you will be asked to correct this.

- Hospital admission/Emergency presentation:
  - For the patient that is admitted to the hospital through emergency, this is same as the date and time of admission to emergency.
  - For the patient admitted to hospital directly, this is same as the date and time of admission to hospital.
- ICU admission date/time: enter admission date/time to your ICU. This **must** be entered to be able to proceed with data entry.
- Mechanical Ventilation start date and time:
  - This refers to ***invasive mechanical ventilation*** i.e. intubation with mechanical ventilation or tracheostomy with mechanical ventilation. This includes ***any*** positive pressure delivered via an endotracheal tube or a tracheostomy.
  - For the patient that is mechanically ventilated prior to admission to your hospital, this is the same as the admission date and time to your hospital, including patients undergoing outpatient surgery.
  - This **does not** refer to ***non-invasive*** methods of ventilation such as BI-PAP or mask-CPAP.

Logic Alert

- Dates must be in a logical sequence (i.e. hospital admission must be before ICU admission, etc)
- Start of Mechanical Ventilation cannot be more than 1 day before ICU admission and cannot be more than 1 day after ICU admission.

Webshot of Patient Baseline Form



APACHE II

Note: Use values from the first 24 hours of admission to ICU.

- When you first enter this form you will be asked **"Does this patient have an APACHE II score available (from first 24 hrs admission to ICU)?**" If yes, you will be prompted to enter the score. If no, you will be directed to complete the worksheet.
- Enter the ***lowest and highest value*** recorded in the source documentation within the first 24 hours from admission to ICU. The worst value that generates the highest severity score will be selected by the web application.
- When you enter the values in the right-hand columns, the severity score will be automatically calculated.
- **Note**: If variables are not available from the first 24 hrs, go outside the 24-hour window and use the data closest to ICU admission. Use the Comment Box to indicate that you used data outside the 24-hour window.
- Age will be automatically transferred from previous web page.
- Temperature: Enter the value and indicate, core, oral, axilla or tympanic listed in the second drop box.
    - The program will re-calculate to the appropriate core temperature.
    - Rectal, tympanic, temporal, and bladder temperatures are considered as core temperature.
    - For manual calculations of APACHE: To obtain the core temperature: if oral temperature is reported, add 0.5 °C to oral temperature; if axilla temperature is reported, add 1.0°C.
- Enter the systolic and diastolic blood pressures in the appropriate box. Once these values have been entered the Mean Arterial Pressure (MAP) value will automatically be calculated and entered in the right-hand column.
- Heart Rate: enter the highest and lowest value.
- Respiratory rate: (either ventilated, or non-ventilated)
- Oxygenation: When determining the highest and lowest oxygenation values, determine the highest or lowest FiO_2, then obtain the pH, $PaCO_2$ and PaO_2 from the same blood gas.
    - If the **FiO_2 is $\geq$ 0.5**, the **$PaCO_2$**, and the **PaO_2 boxes appear.** Enter the values into the appropriate boxes. Again, the program will calculate the A-a$D0_2$ and enter the value in the right-hand column. For the purposes of this trial the barometric pressure value will be standardized at **713.** In the event that the Fi02 is greater than or equal to 0.50 and multiple gases are available, you will need to calculate the A-aD02 (alveolar arterial gradient) manually to obtain the highest and lowest scores. To calculate the A-aD02, you must use the variables from the same gas.
    - If the **FiO_2 is < 0.5**, only the **PaO_2** box will appear. Enter the value.
    - If **no ABGs** available, tick the appropriate box and enter the HCO_3 in place of arterial pH. Serum HCO3 should **only** be used if there are no ABGs available in the previous 24 hours.
- Arterial pH.
- Serum Sodium: the unit of measure is mmol/L.
- Serum Potassium: the unit of measure is mmol/L.
- Serum Creatinine: the unit of measure is umol/L**.** If you require a definition of Acute Renal Failure, click on **"Explain"** and definitions will be provided.

- Hematocrit: enter this value as a percentage.
- White Blood Cells (total/mm^3)(in 1000's).
- Glasgow Coma Score (GCS): To determine the GCS choose the best response from each of the **3** categories for the **previous 24 hours** from screening. If the patient is sedated, then go back to the period when the patient was not receiving sedation or approximate what the score would be if the sedation where to be removed. Enter the values in the 3 separate categories and the GCS will automatically be calculated.

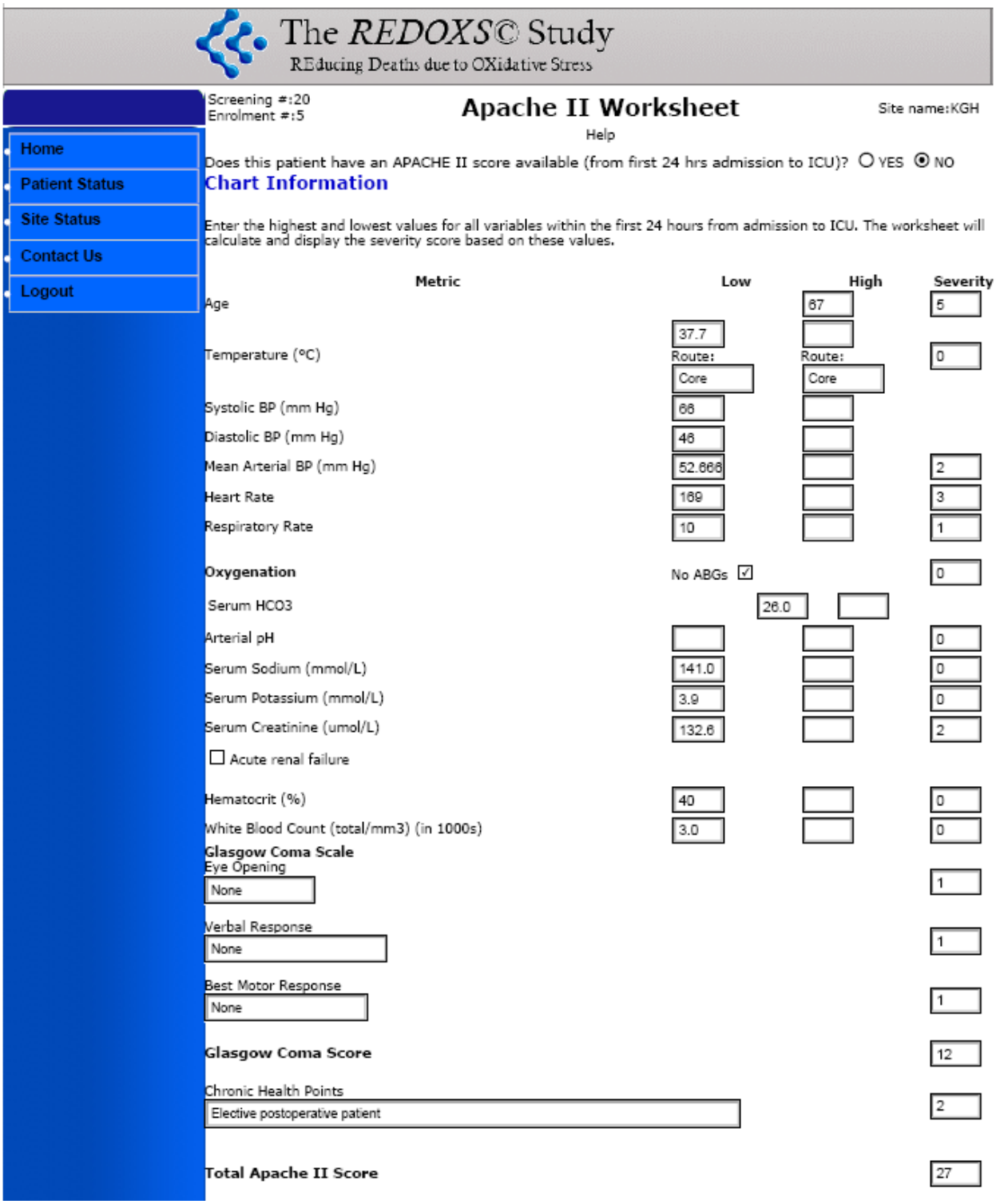
  Eye Opening:
  1- None
  2- To Pain
  3- To speech
  4-Spontanous

  Verbal Response:
  1- None
  2- Incomprehensible words
  3- Inappropriate words
  4- Confused
  5- Oriented

  Best Motor Response:
  1- None
  2- Extension
  3- Abnormal flexion
  4- Withdraws from pain
  5- Localizes to pain
  6- Obeys commands

- Chronic Health Points: Choose one of the 3 categories for patients with a history of severe organ system insufficiency or immunocompromised – Click "Explain" box on the left hand side of the screen for definitions.
- When all the categories are completed, click on the box labeled **"Save Apache II Form"** and the system will automatically save and calculate your Apache Score.

Apache II Form



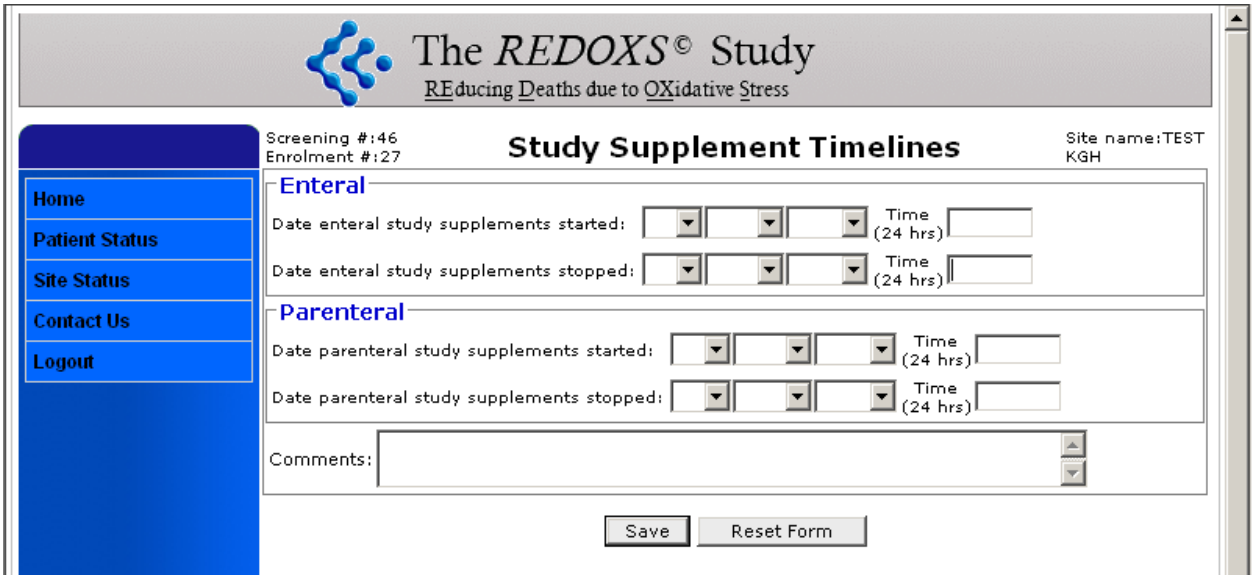
Study Supplement Timelines

Every effort should be made to start both enteral and parenteral study supplements within 2 hours of randomization and within 24 hours from admission to ICU.

THE DURATION OF THE STUDY SUPPLEMENTS SHOULD NOT EXCEED A TOTAL OF 28 DAYS FROM RANDOMIZATION. *Study supplements will be discontinued in the event that the patient is discharged from ICU or dies before 28 days (exception: patients with ICU stay < 5 days and transferred to ward, the duration of study supplements should be 5 days in total = 120 hours).*

On this page record the following:

- Actual date and time enteral/parenteral study supplements started.
- Actual date and time enteral/parenteral study supplements were permanently stopped.
  - Do not enter dates on which study supplements were held and restarted. Do NOT add study days to make up for interruptions. The volumes of the supplements received will be captured on the Study Supplement Compliance page.



Baseline Nutrition

- For the prescribed energy and protein intake, **contact the ICU dietitian to obtain this information**. This will need to be calculated by the dietitian once at baseline as below:
    - the prescribed energy and protein intake is the kilocalories and grams of protein provided by the **goal regimen** (i.e. maximum rate/volume determined at the initial assessment) for EN/PN according to the dietitian's recommendation.
        - For eg. If the dietitian recommends a starting rate of 25 mL/hr on day 1 with a final rate of 75 mL/hr by day 3, calculate the calories and protein that the **final rate** = 75mL/hr X 24 would provide.
    - Include calories from protein.
    - If the patient is on enteral nutrition and parenteral nutrition at the same time, the prescribed energy and protein intake will still be the FINAL amount as assessed by the dietitian.
    - **If the prescription changes over the days of observation, calculate the average prescribed calories and protein.**
- **The SC will record the information obtained from the dietitian on to the web.**

Enteral Nutrition

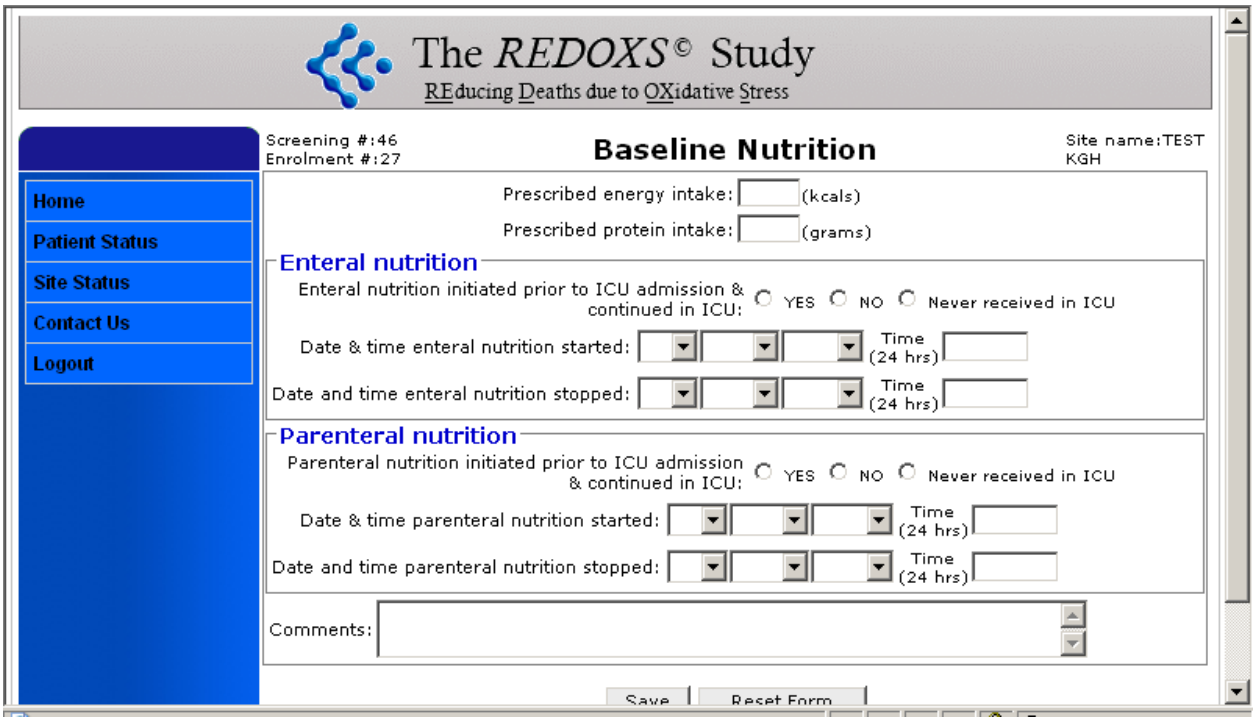
- Indicate if enteral nutrition was started prior to ICU admission and continued in ICU, "Yes" or "No" or whether it was never received in ICU.
    - If Yes, date and time of enteral nutrition started will become ICU admission date/time.
    - If No, record the date and time enteral nutrition was started in ICU.
    - Record the date and time that enteral nutrition was discontinued (permanently) in ICU.
    - If enteral nutrition is continued beyond ICU discharge, record the ICU discharge as the date and time enteral nutrition was stopped, even if the study supplements are continued beyond ICU discharge (in patients that are in ICU < 5 days). Enter the actual EN stop date, if known, in the comments field.
    - If "Never received in ICU" is chosen, the rest of the fields on this page will become disabled.

Parenteral Nutrition

- Indicate if parenteral nutrition was started prior to ICU admission and continued in ICU, "Yes" or "No" or whether it was never received in ICU.
    - If Yes, date and time of parenteral nutrition started will become ICU admission date/time.
    - If No, record the date and time parenteral nutrition was started in ICU.
    - Record the date and time that parenteral nutrition was discontinued (permanently) in ICU.
    - If parenteral nutrition is continued beyond ICU discharge, record the ICU discharge as the date and time parenteral nutrition was stopped, even if the study supplements are continued beyond ICU discharge (in patients that are in ICU < 5 days).
    - If "Never received in ICU" is chosen, the rest of the fields on this page will become disabled.

If the patient is still in the ICU past study day 30 and is still receiving feeds, the EN or PN stop date = Day 30 date. The stop time is the time your ICU flow sheet ends. Enter the actual the stop date, if known, in the comments field.

Webshot of Baseline Nutrition



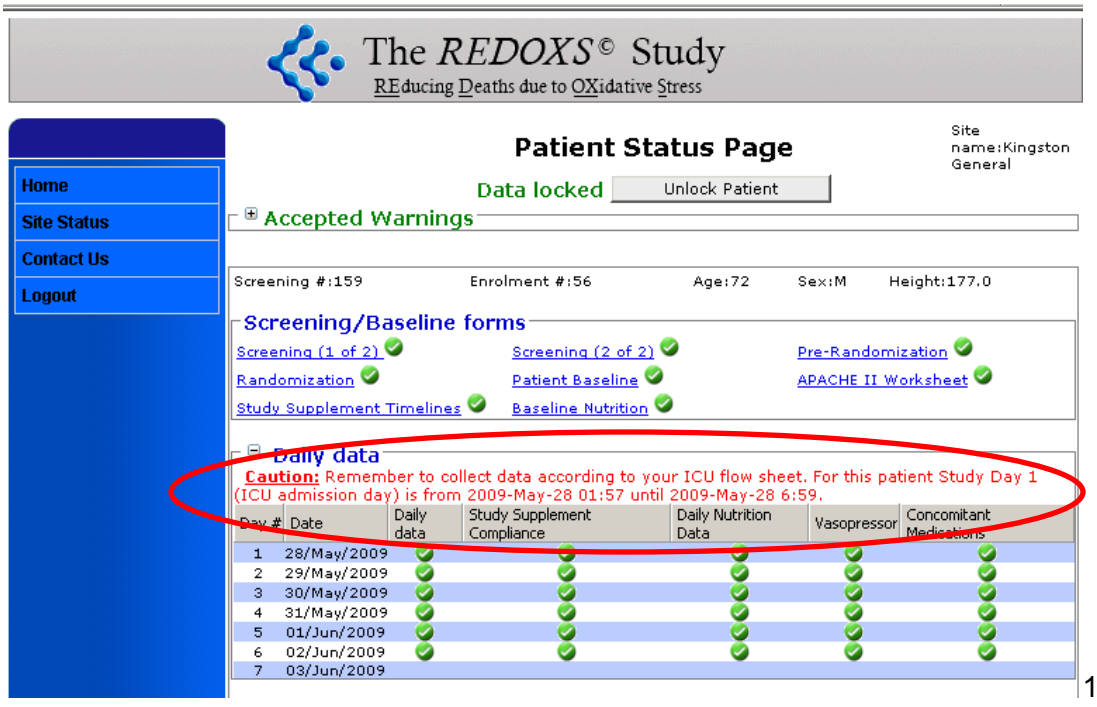
Determining Study Days

Study Day 1 is from ICU admission to the end of your 24 hr ICU flow sheet.
Study Day 2 and subsequent days are the 24 hr period according to your ICU flow sheet.

For sites with an ICU flow sheet other than 12-12, if the patient is admitted to the ICU after midnight but before the start of the next flow sheet the EDCS generates a reminder message to facilitate correct data collection. For example, if a site has a flow sheet that runs from 7-7 and the patient was admitted to the ICU on 28-May-09 @ 0157 hours, the study days are represented in the table below:

Study Day	Date Range	Date Listed on EDCS
1	28-May-09 @ 0157 hrs to 28-May-09 @ 0659 hrs	28-May-09
2	28-May-09 @ 0700 hrs to 29-May-09 @ 0659 hrs	29-May-09
3	29-May-09 @ 0700 hrs to 30-May-09 @ 0659 hrs	30-May-09
etc	etc	Etc

The screen shot below illustrates the caution message regarding the correct time frames for daily data collection.



1

All daily data should be collected from study day 1 and each day following until the end of day 30 unless ICU discharge (actual) or death occurs before day 30 (except blood sugars, see below).

Use the following rules:

Variable	Description
Heart rate (HR)	Record highest HR.
Blood Pressure (BP)	Record the lowest systolic BP and the corresponding diastolic BP.
Temperature (Temp)	Units = ˚C Record the most aberrant temperature recorded from midline 37.0 ˚C, not the highest. This means the temperature that deviates either above or below the midline the most. Rectal, tympanic, temporal, and bladder temperatures are considered as core temperatures. For manual calculations: To obtain the core temperature: if oral temperature is reported, add 0.5 °C to oral temperature; if axilla temperature is reported, add 1.0 °C.
Urine Output (U/O)	Units = mL Record total volume in 24 hours using the drop-down menu. • 0-199 mL/day • 200-499 mL/day • ≥ 500 mL/day For study day 1, record the volume from ICU admission until the end of your 24 hr flow sheet.
Dialysis	Record if the patient received any type of dialysis (e.g. hemodialysis, chronic renal replacement therapy), Yes or No. If 'yes', on the first day, you will be prompted to answer the question, "Did dialysis start due to acute renal failure?" Yes or No.
Respiratory rate (RR)	Record highest RR, either mechanical/spontaneous or both.
Mechanically Ventilated	Yes or No. Select 'yes' if patient was invasively mechanically ventilated at any point during the course of the study day. ***Invasive mechanical ventilation*** i.e. intubation with mechanical ventilation or tracheostomy with mechanical ventilation. This includes ***any*** positive pressure delivered via an endotracheal tube or a tracheostomy. This **does not** refer to ***non-invasive*** methods of ventilation such as BI-PAP or mask-CPAP.
PF ratio ($PaO_2/Fi0_2$) worst	Using the patient's arterial blood gases (ABGs), record the worst P/F ratio *regardless of ventilation status*. Click on the "See Table" link for help with determining the worst value.
†White Blood Count (WBC)	Units = $x10^9$/L Record the highest and lowest WBC. If there is only one value for the day, record this as both the highest and the lowest.
†Platelets	Units = $x10^9$/L Record the lowest platelets.
†Blood Sugar (BS)	Units = mmol/L Record first blood sugar reading closest to 08:00 hrs**.** This can be either serum or capillary. *Daily data is collected for the 24 hr period according to your flow sheet. The exception to this requirement is blood sugar reading. We ask you to record the first blood sugar reading closest to 08:00. We would like to clarify that the*

	reading can be 08:00 ± 6 hours. A reading between 02:00 and 14:00 is acceptable regardless of study day.
†Creatinine (Cr)	Units = µmol/L Record the highest creatinine.
†Urea	Units = mmol/L Record the highest urea. *For US sites, BUN should be converted to urea:* • *BUN mg/dL → urea mmol/L multiply by 0.357* • *BUN g/L → urea mmol/L multiply by 35.7*
†Bilirubin (Bili)	Units = µmol/L Record the highest total bilirubin.
†Albumin	Units = g/L Record the highest albumin.
Gastric residual volume	Units = mL Record total gastric residual volume (GRV) and the total volume of gastric residuals discarded. The total volume of gastric residual volumes is equal to the total volume measured regardless of whether you discard it or re-feed it. GRV discarded can be equal to but can **never be greater** than the total gastric residual volume (i.e. Volume measured). GRV are to be recorded even if the patient is not being tube feed; but if they are not measured click 'N/A'. For NG drainage (to low gomco/drainage tube), do not record as gastric residual volumes. GRVs are recorded when you are actually aspirating and checking to see how much residual is left in the stomach. Emesis is not captured as GRV, please add as a comment.
Location of feeding tube	Pick one of the options from the drop down box to indicate the location of feeding tube (refers to **any** oro/naso-gastric or feeding tube): • "Gastric confirmed" if placement was confirmed by an X-ray on that day • "Gastric presumed" if placement was confirmed by an X-ray earlier but not on that day • "Post-pyloric duodenal confirmed" if placement was confirmed by an X-ray on that day • "Post-pyloric duodenal presumed" if placement was confirmed by an X-ray earlier but not on that day • "Post-pyloric jejunal confirmed" if placement was confirmed by an X-Ray on that day • "Post-pyloric jejunal presumed" if placement was confirmed by an X-ray earlier but not on that day • No tube in place on that day If the feeding tube is confirmed by X-ray to be in the esophagus, and the patient was fed, please select "Gastric presumed". If the patient was not fed, use the "no tube in place" option to enter the data. *Remember that you are recording the location of the feeding tube (confirmed/presumed) rather than the type of feeding tube used*. Record the location of the feeding tube according to the location of the tip of the tube. E.g. you may be using a small bowel feeding tube but the actual location of the tip of the tube may be coiled in the stomach and hence the location should be recorded as gastric. If the location of the feeding tube changes within the day, please choose the location that was used for the majority of the day. If gastric was used for half the day and post-pyloric for the other half, choose post-pyloric. If the feeding tube is confirmed by X-ray to be in the esophagus, please select

	"Gastric presumed".
Diarrhea	Indicate by choosing Yes or No if patient has diarrhea. **Note:** Definition of diarrhea is **>5 bowel movements/day or >750ml/day.**

† Refer to the Unit Conversions Calculator to convert results reported in units different than those outlined above. (Worksheet found at www.criticalcarenutrution.com > REDOXS© Study > Resources > Study Procedures Manual).

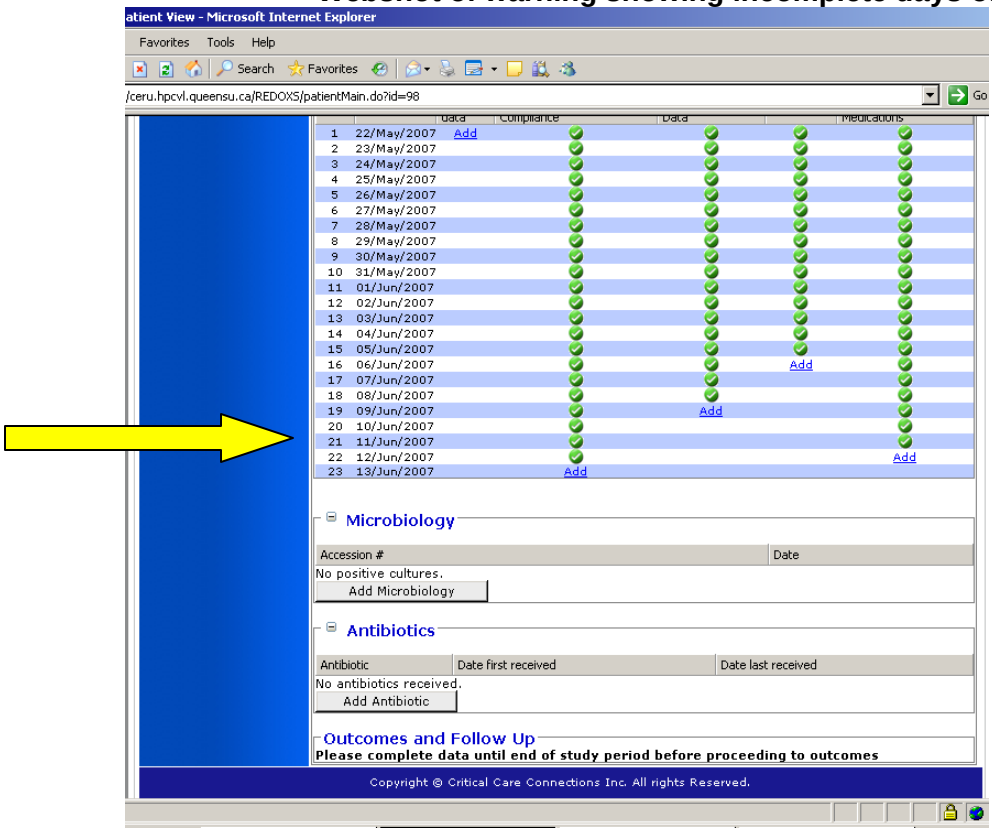
Click on '**save**' to save the form and return to the patient status page, or click on **'New Day'** to save the form and continue entering daily data for this patient for the next consecutive day.

Logic Alert

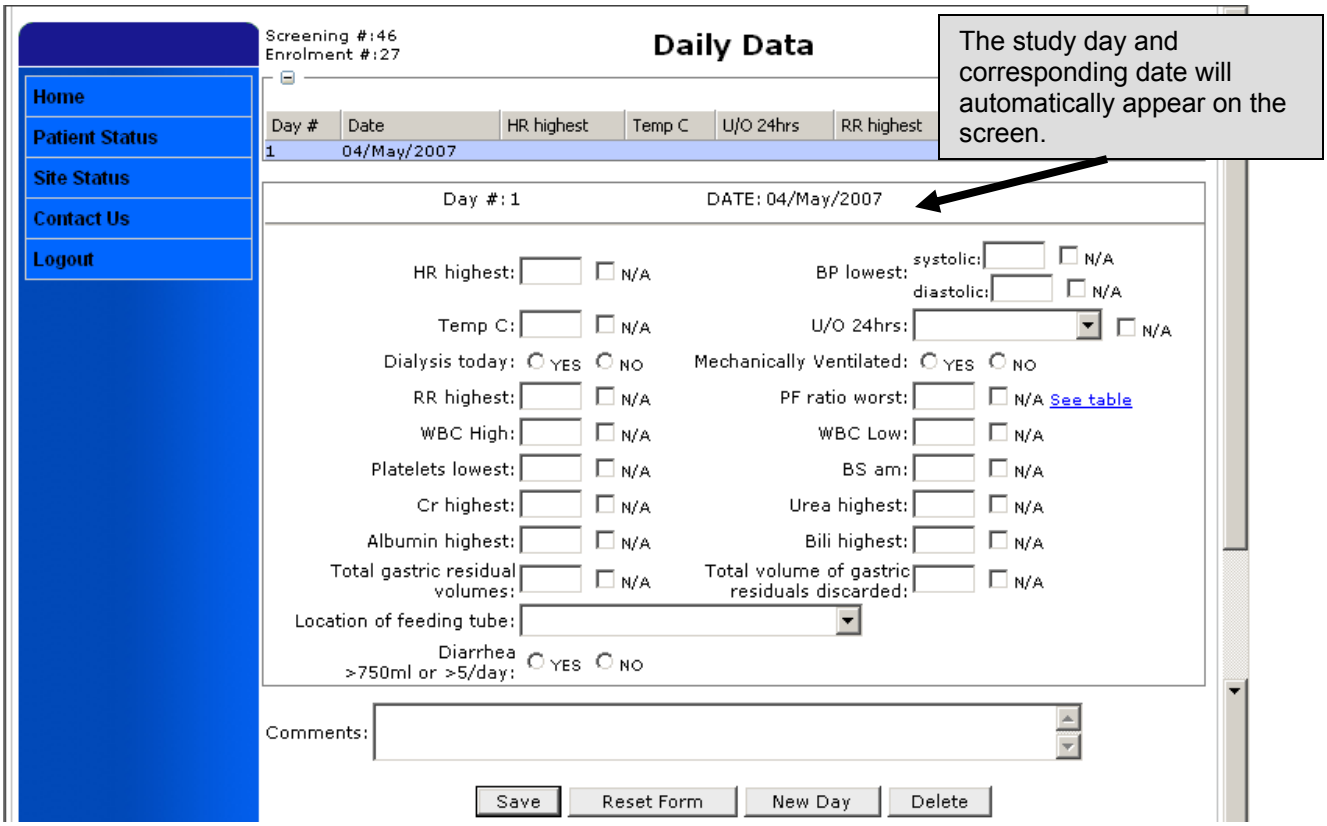
If you do not have enough days of daily data entered, a message will appear at the bottom of the Patient Status page that says "Please complete data until the end of the study period" (see web shot below).

Proceed with entering data for the missing days.

Webshot of warning showing incomplete days of daily data



Webshot of Daily Data Page



If you have accidentally entered an extra day, you may go ahead and delete this day by clicking on the DELETE button that will appear on the last day that you have entered. The DELETE button appears on the last day on the following pages: daily data, study supplement compliance, daily nutrition data, vasopressor, concomitant medications, microbiology and antibiotic pages.

Study Supplement Compliance

THE DURATION OF THE STUDY SUPPLEMENTS SHOULD NOT EXCEED A TOTAL OF 28 DAYS FROM RANDOMIZATION. Data should be collected up to the end of the day 28 flow sheet.
Study supplements will be discontinued in the event that the patient is discharged from ICU or dies before 28 days (exception: patients with ICU stay < 5 days and transferred to ward, duration of study supplements should be 5 days in total = 120 hours).

The volumes of supplements actually received are to be collected DAILY (not retrospectively) to ensure that the patient receives the adequate volumes of study supplements. It is encouraged that you use the provided Daily Monitoring Log or other checklist/worksheet to record the volumes received.

The prescribed volume of Enteral Study Supplement is **480mls/day (20 mL/hr X 24 hrs)** for all patients. The prescribed infusion rate for Parenteral Study Supplement is **240mL/day** (**10 mL/hr X 24 hrs)** in most cases. In rare cases, if the patient is extremely tall, the parenteral study supplements may need to run at a faster rate. Refer to the label on the parenteral bag for the infusion rate.

- Record the volume of Enteral/Parenteral Study supplement **actually received** daily in mL from the nursing flow sheet.
- If the volumes received are **lower** than that prescribed, you will be prompted if a protocol violation or protocol deviation has occurred. Follow the prompts on the screen to proceed.

Protocol Violation for Enteral Supplements

- **A protocol violation** is defined as receiving < 80% of the prescribed volume in one day.

Protocol Violation for Parenteral Supplements

- **A protocol violation** is defined as receiving < 90% of the prescribed volume in one day.

All protocol violations need to be reported to the Project Leader within 24 hours of becoming aware of the violation. *Refer to form that can be downloaded from the Welcome Home Page.*

- Please refer to the ***Protocol Violation/Deviation section*** of your study binder for detailed information and instructions regarding reporting and completing the appropriate forms.
- Every attempt should be made to make up for the deficit in the prescribed volume of study supplements. Refer to ***Administration of Study Supplements section*** for instructions on how to do this.

	Parenteral SS	Enteral SS
Protocol Violations	0-215 mL	0-383 mL
Protocol Deviations	216-239 mL OR > 300 mL	384-479 mL OR > 500 mL

A Protocol Violation does NOT need to be completed on the following days:

- Day of randomization
- Day of ICU discharge (unless patient has received less than 5 days of study supplements)
- Day of death

Protocol <u>Deviation</u> for Enteral Supplements

- **A protocol deviation** occurs when the volume received ≥ 80% but <100% of the prescribed volume.
- For example, the prescribed volume is 20mL/hr x 24hrs= 480mL per day. If the volume actually received is ≥ 80% but < 100% of 480mL (384mL per day) but is < 480 mL, this is a **protocol deviation**.

Protocol <u>Deviation</u> for Parenteral Supplements

- **A protocol deviation** occurs when the volume received ≥ 90% but <100% of the prescribed volume.
- For example, the prescribed volume is 10mL/hr x 24hrs= 240mL per day. If the volume actually received is ≥ 90% of 240mL (216-239 m**L** per day) but is < 240 mL, this is a **protocol deviation.**

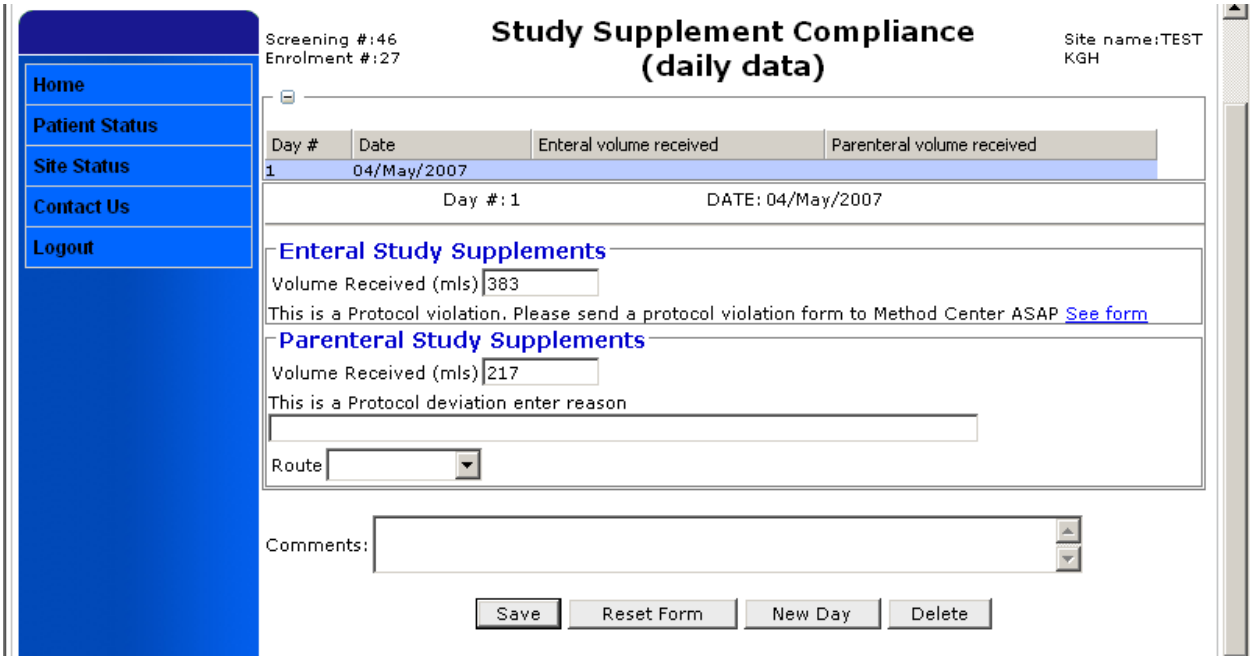
Provide a detailed explanation in the comments box every time a Protocol Deviation occurs.

- If the volumes received are **higher** than that prescribed (> 500 mL for the enteral supplements and > 300 mL of the parenteral supplements), this will be flagged and you will be asked to write an explanation in the text box provided.

- Record if the parenteral supplement was given via central line (C) or peripheral line (P).
    - If the IV access changes from peripheral to central within the same day, choose the access used for the majority of the day and provide an explanation in the Comments box at the bottom of the page.
- If given peripherally, record if any signs of phlebitis/extravasations by indicating with a "Yes" or "No" and provide an explanation in the Comments box at the bottom of the page. See below for **definition of Phlebitis:**
    - "Inflammation of a vein, which tends to lead to the formation of a thrombus. The symptoms are: pain, swelling, and redness along the course of the vein, which is felt later as a hard, tender cord."

- Click on **'save**' to save the form and return to the patient status page, or click on **'New Day'** to save the form and continue entering study supplement compliance data for this patient for the next consecutive day.
- A summary of study supplement compliance for each day will be displayed at the top of the webpage.

Webshot of Study Supplement Compliance Page



Daily Nutrition Data

This page is for recording Enteral or Parenteral nutrition formulas and is separate from the *Study Supplement Forms*.

All daily nutrition data should be collected from study day 1 and each day following until the end of day 30 unless ICU discharge (actual) or death occurs before day 30.

Enteral Nutrition

- For each study day, indicate "Yes" or "No" to indicate if patient received enteral nutrition.
- If patient is on both enteral and parenteral nutrition on the same day, click the 'yes' response in both places "Enteral nutrition" and "Parenteral nutrition".
- For the total energy intake received from the enteral nutrition or parenteral nutrition: **contact the ICU dietitian to obtain this information**. The total calories will need to be calculated by the dietitian **daily** as follows:
    - Include calories from protein
    - Include calories from other supplements.
    - Include calories from propofol if continuous infusion ≥ 6 hrs (within a particular study day). Do NOT include intermittent doses of propofol.

If propofol is running < 6 consecutive hours (within a study day) those propofol calories are NOT included in total energy.

If propofol is running ≥ 6 consecutive hours (within a study day) there are four possible scenarios:

1. *If pt is receiving both PN & EN, then propofol calories are added to PN total energy*
2. *If pt is receiving only PN, then propofol calories are added to PN total energy*
3. *If pt is receiving only EN, the propofol calories are added to EN total energy*
4. *If pt is not receiving any nutrition (no EN, no PN), then do not record calories from propofol.*

Note: Calories from propofol should only be calculated if the patient is receiving enteral and/or parenteral nutrition.

    - Do NOT include calories from oral feeding (i.e. PO feeds).
    - Do **NOT** include calories from IV solutions.
    - Do **NOT** include calories from the study supplements.
- For the total protein intake received from the enteral formula or parenteral nutrition: **contact the ICU dietitian to obtain this information**. The total protein will need to be calculated by the dietitian **daily** as follows:
    - Include protein from supplements.
    - Do **NOT** include the grams of protein from the study supplements.
- If patient is on a combination of Enteral Nutrition and Parenteral Nutrition, please calculate the calories received from each separately.
- The SC will record the information obtained from the dietitian on to the web.
- Using taxonomy provided on the web, please record enteral formula(s) received (hold the control key to select more than one formula). See appendix 7 for list of formulas.
    - You may select up to 3 formulas per day. In the event that the patient receives more than 3 formulas, select the 3 that provided the largest volumes.

- If on enteral nutrition, indicate Yes or No if enteral nutrition was **ever** interrupted **due to feeding intolerance.** Feeding intolerance is defined as the presence of any one of the following:
    - High gastric residual volumes
    - Emesis
    - Aspiration of enteral nutrition
- If enteral nutrition is interrupted due to high urea or fluids concerns, indicate Yes or No in the appropriate boxes provided.
    - If Yes (Y), please provide a comment in the comment box.
- An **interruption** in enteral feeding is defined as a reduction in the rate of delivering the feed **or** stopping the feed.

Patients that are enrolled in this study should NOT be on enteral formulas, parenteral solutions or supplements that have elevated levels of glutamine, antioxidants or selenium, vitamin A,C,E, beta-carotene, zinc, arginine or omega 3 fatty acids. A patient enrolled in the study should NOT be placed on the following:

- Vivonex Plus/T.E.N
- Oxepa
- Optimental
- Impact/Impact 1.5
- Perative
- Peptamen AF
- Pivot 1.5
- Probiotics
- Glutamine supplements

The following are exceptions and are allowed:

- Thiamine, folic acid
- Standard multivitamin/mineral preparations (maximum of 5 mg zinc)
- Standard amounts of vitamins and minerals already present in enteral or parenteral solutions (maximum of 5 mg zinc; 60 µg/L selenium, if intravenous)
- Vitamin K

In patients on long term parenteral nutrition, supplementation may be necessary and can be started after notifying the Project Leader.

If the patient has been on any of these formulas/supplements prior to enrolment in the study (either at home or in a hospital), these should be discontinued once the patient is enrolled.

For clarification regarding the use of European formulas, please contact the Project Leader.

Parenteral Nutrition

- For each study day, indicate “Yes” or “No” to indicate if patient received parenteral nutrition.
- If on parenteral nutrition, indicate the type of lipids received (see below). **You will have to obtain this information from the dietitian/pharmacist.**
  If the patient does NOT receive lipids, you should select OTHER from the Type of Lipids taxonomy. Please type in NONE RECEIVED in the available field.

Type of lipids

1. Soybean oil based (LCTs)
2. MCT/LCT physical mixture
3. MCT/LCT structured form
4. Olive Oil based
5. Fish Oil based (10-20% of total lipid emulsion)
6. Mixture of soy oil, MCTs, and fish oil
7. Mixture of soy oil, MCTs, olive oil, and fish oil (SMOF)
8. Other, specify _____

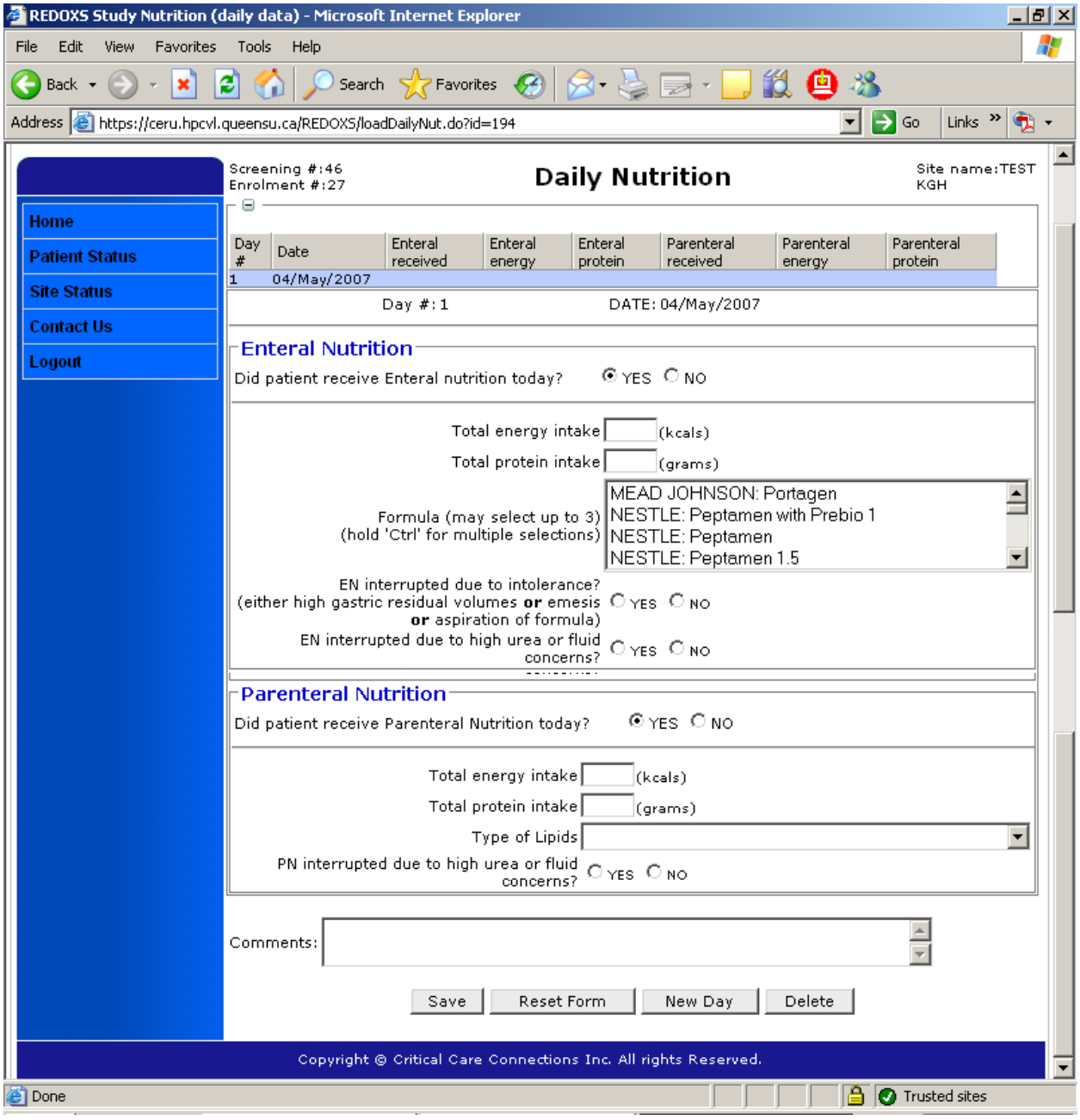
- If parenteral nutrition is interrupted due to high urea or fluids concerns, indicate “Yes” or “No” in the appropriate boxes provided.
    - If “Yes”, please provide a comment in the comment box.
- Click on **‘save**’ to save the form and return to the patient status page, or click on **‘New Day’** to save the form and continue entering daily nutrition data for this patient for the next consecutive day.
- A summary of nutrition for each day will be displayed at the top of the webpage.

If the patient has renal failure, has an elevated urea of concern and is not going to be dialyzed, refer to Appendix B in the Administration of Study Supplements section.

If a patient is feeding orally, you do not need to include calories from oral feeding in your calculations.

If nutrition is ongoing at study day 30, record the date corresponding to study day 30 as the stop date on the Baseline Nutrition Form. Use the your flow sheet end time as the stop time. Make a note in the comments field that nutrition was ongoing at study day 30.

Webshot of Daily Nutrition Data

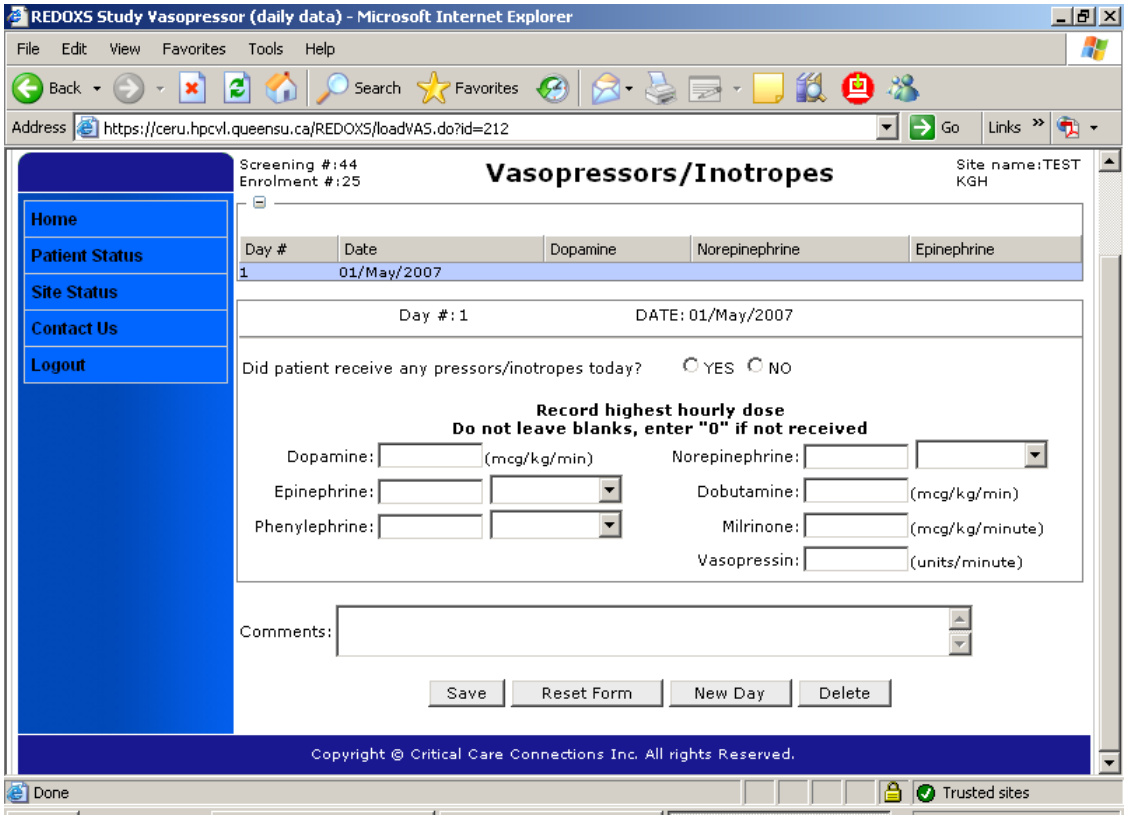


Vasopressors/Inotropes

All vasopressor/inotrope data should be collected from study day 1 and each day following until the end of day 30 unless ICU discharge (actual) or death occurs before day 30.

You will be asked **"Did patient receive any pressors/inotropes today?"**

- If No', no further questions need to be answered, either click 'Save' to save the form and be directed to the patient status page or "New day" to complete the vasopressor form for the same patient for the next consecutive day.
- If 'Yes' Record the highest hourly dose infused of the following pressors / inotropes only:
  - Dopamine, Norepinephrine, Epinephrine, Dobutamine, Phenylephrine, Vasopressin, Milrinone.
  - For **Dopamine, Dobutamine and Milrinone** record in **mcg/kg/min**
  - For **Norepinephrine, Epinephrine, Phenylephrine** select the appropriate units from the drop-down box (i.e. **mcg/kg/min** or **mcg/min)**
  - For **vasopressin,** record in **units/min.**
  - Do not record single injections (eg. one-time doses ephedrine etc.)
  - Do NOT leave blanks, enter zero, if not received.
- Click on **'save**' to save the form and return to the patient status page, or click on **'New Day'** to save the form and continue entering daily data for this patient for the next consecutive day.

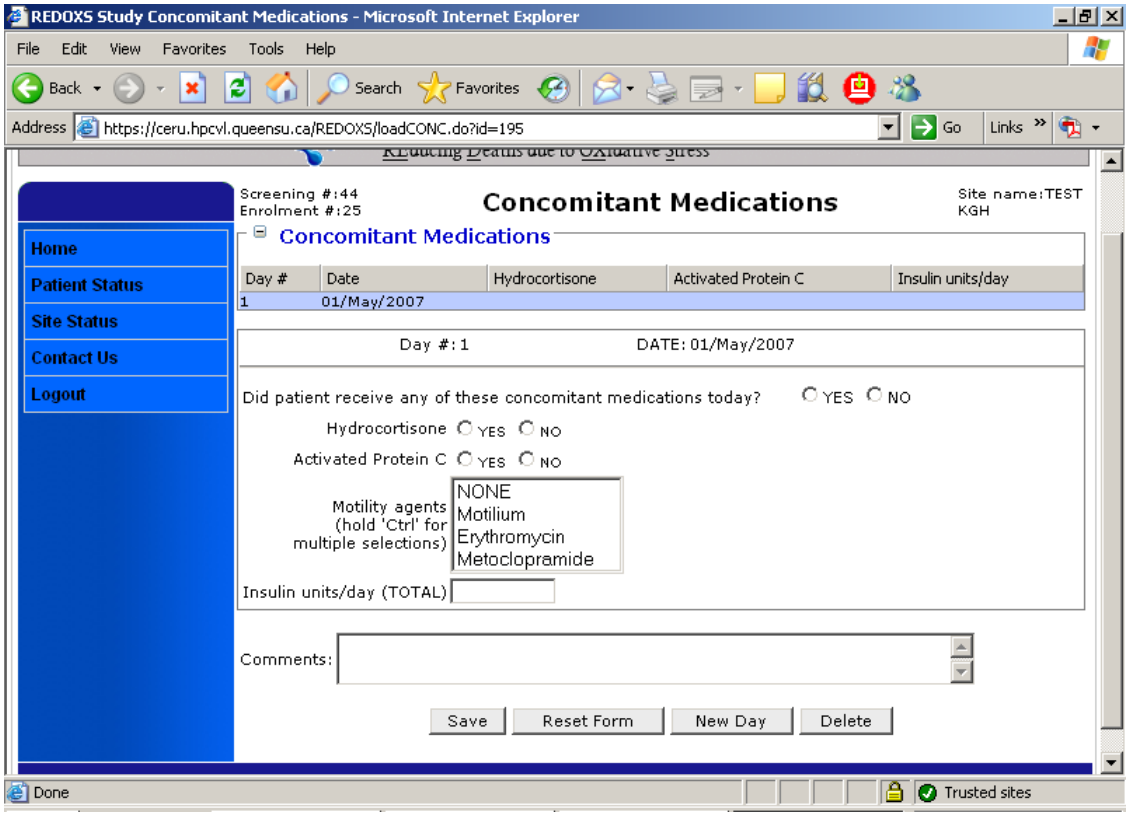


Concomitant Medications

All concomitant medications should be collected from study day 1 and each day following until the end of day 30 unless ICU discharge (actual) or death occurs before day 30.

You will be asked **"Did patient receive any of these concomitant medications today?"**

- If 'No', no further questions need to be answered, either click 'Save' to save the form and be directed to the patient status page or "New day" to complete the vasopressor form for the same patient for the next consecutive day.
- If 'Yes', record whether the following medications were given by indicating "Yes" or "No".
    - **Hydrocortisone** (dexamethasone and predisone should NOT be included here, Solucortef if okay)
    - **Activated Protein C**
    - **Motility agents**- choose one of these:
        - Motilium, Erythromycin, Metoclopromide (Maxeran) or None.
- For **insulin**, record the daily cumulative units given every day (includes subqutaneous, drip/IV routes). If no insulin is given on a particular day, record this as a zero.
- Click on **'save**' to save the form and return to the patient status page, or click on **'New Day'** to save the form and continue entering daily data for this patient for the next consecutive day.



Microbiology

The period of data collection for this page starts with any cultures taken 7 days prior to ICU admission until ICU discharge.

This form only pertains to the following:

- All positive cultures from 7 days prior to ICU admission until the end of day 30, unless ICU discharge (actual) or death.
  - **Do not record cultures if they are reported as "No Growth" or "Common/Mixed Flora".**
  - **Do not record cultures that are considered to be a contaminant.**
- On the **Patient Status Page** click on '+' next to **Microbiology**. A grey 'Add Microbiology' Tab will appear, click here to be directed to the Microbiology page.
- You will be asked "Did the patient have any positive cultures from 7 days prior to ICU admission until ICU discharge?"
  - If "No", click on 'Save microbiology' and you will be directed back to the Patient Status Page. You will note the phrase "no positive cultures" under Microbiology.
  - If "Yes", provide the Accession Number also known as the laboratory requisition number.
  - Record date and time the culture is taken.
  - For sample type, select a type from the drop down menu. If sample type is "other" (not listed in taxonomy), select 'other' and write sample type in the box provided.

Sample Type taxonomy:
- Blood
- Endotracheal Aspirate
- BAL or PBC Specimen
- Wound
- Cath tip/line
- Urinary
- Stool
- Other

Note: A simple bronchial wash should be recorded as an endotracheal aspirate (ETA) aspirate. This is different than bronchoalveoar lavage (BAL) with quantitative cultures.

For BAL or bronchial washings with no quantitative results, choose sample type OTHER and write in comments "bronchial washings, no quantitative growth".

  - For Organism, click on '+' next to Organism select the category, species and subspecies from the organism taxonomy provided in the drop-down boxes (see appendix 6).
    - Organism Taxonomy (appendix 6) is organized into 4 categories, which are bacteria, fungi/yeast, virus, and mycobacteria. Species in each category are listed alphabetically.

- If the sub-species for the corresponding species are not listed, record the number of the appropriate "other" in the Organism column**.** You **must** write the "other" sub-species in the text box provided.

Example #1
If species is Enterobacter, and sub-species is Enterobacter Cloacae, choose this from sub-species box (24a) If sub-species is Enterobacter Aerogenes, choose "Other Specify" (24b) and write "Aerogenes" in the box.
Example #2
If species is Enterococcus, need to specify if Vancomycin Resistant Fecalis (25a) or Vancomycin Resistant Foecium (25b), Vancomycin Sensitive Fecalis (25c), Vancomycin Sensitive Foecium (25d) or Other (and specify in text box).
Example #3
For Staph Aureus, need to specify if Methicillin Resistant Staph Aureus (52a), Methicillin Sensitive Staph Aureus (52b), Coagulase negative (epidermatitis) (52c) or Other (and specify in box) (52d)

- Record Quantitative results using the same units as reported on the microbiology reports i.e. CFU, CFU/mL or CFU/L if available.

Record **all** susceptibilities for **each individual** organism by selecting the appropriate antibiotic from the taxonomy. The selected antibiotic will be highlighted in blue. Click on the **Sensitive, Intermediate**, or **Resistant** tab and the susceptibilities will be listed automatically in the box on the right hand side of the screen. Repeat for each antibiotic.

- If an error is made, highlight the susceptibility and click on the **delete** tab.
- If no susceptibilities reported, click on button to the right of the Susceptibilities box.
- To add another organism, click on '+' next to Add Organism and the taxonomies will appear.

If a quantitative value is not available for a positive culture, you will need to enter this micro data as follows: Click on <Sample type>, and select <Other>. In the empty field that appears, type in the sample type (ie urinary etc). This will remove the quantitative results field and you will be able to continue progressing through the eCRF.

If toxin for C. difficile present, consider this as a positive culture and choose C. difficile from the taxonomy.

ICU Acquired Infection?

If there are positive cultures after 72 hours from ICU admission (ICU admission to date of culture taken), you will be prompted to answer Yes or No to the following questions:

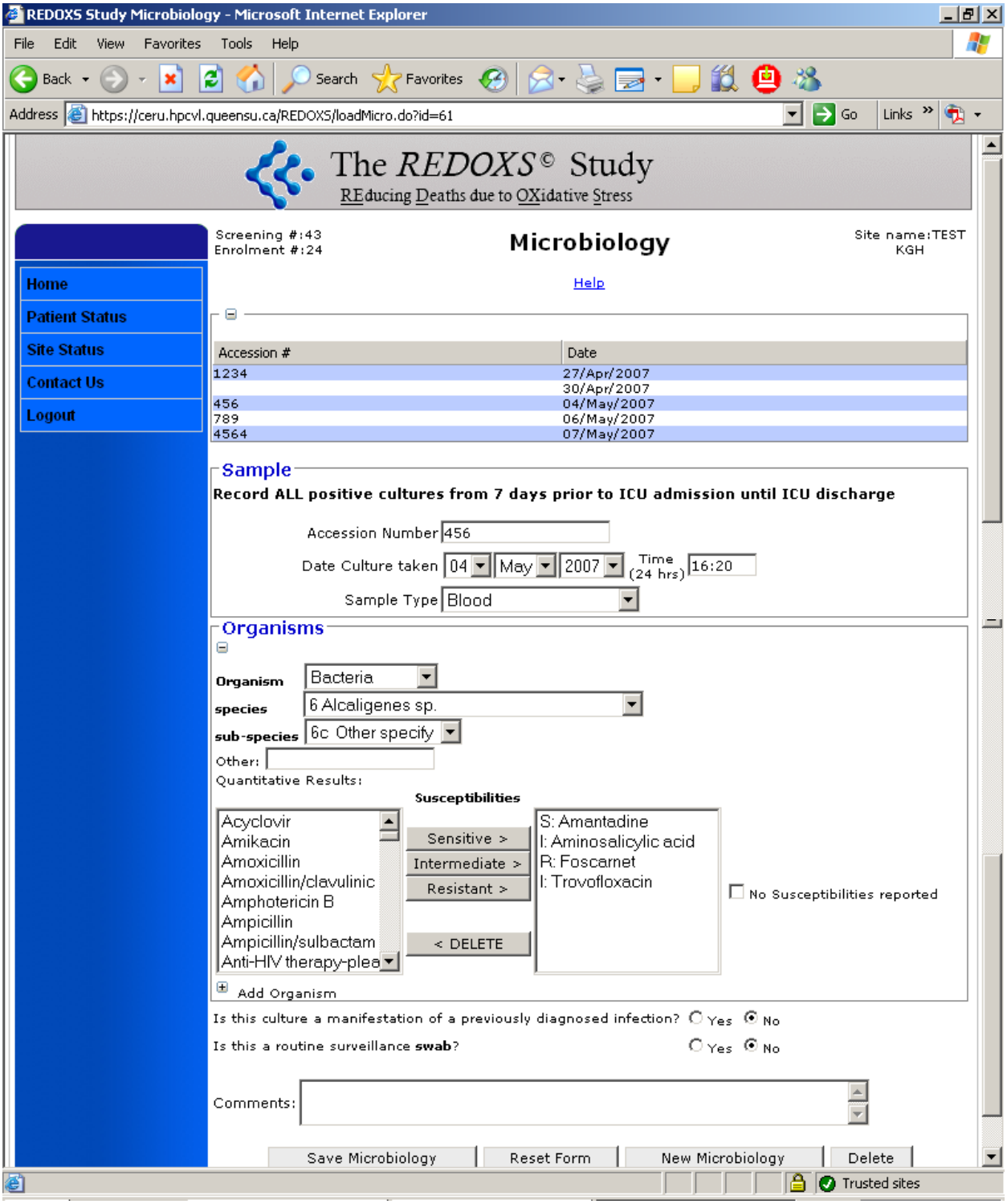
- Is this culture a manifestation of a previously diagnosed infection?
- Is this a routine surveillance swab?

**It is important to collaborate with your Site Investigator when responding to these questions.

Examples of routine surveillance cultures: nasal swabs for MRSA, rectal swabs for VRE.
Note: A cath tip/line swab is not a surveillance swab.

- Click on **'Save microbiology**' to save the form and return to the patient status page, or click on **'New microbiology'** to save the form and continue entering cultures for this patient.

Webshot of Microbiology Page



Antibiotics

The period of data collection for this page starts with all antibiotics initiated 7 days prior to ICU admission, even if stopped prior to ICU admission, and may extend <u>beyond</u> ICU discharge.

This page only pertains to the following:

- All antibiotics started within the period of 7days (current hospital stay) prior to admission to the ICU even if stopped prior to ICU admission
- All antibiotics started prior to ICU admission **AND** continued in the ICU.
- All antibiotics started in the ICU and continued beyond ICU discharge.
- For patients that are in the ICU beyond 30 days:
    - If an antibiotic is started in ICU before day 30 and continues after day 30, you need to collect the stop date/time.
    - If the antibiotic is started after 30 days, you do NOT need to collect data.
- ***Do NOT record any antibiotics started after ICU discharge.***
- ***Do NOT record any antibiotics that were ordered but never received.***

- On the **Patient Status Page** click on '+' next to **Antibiotics**. A grey 'Add Antibiotic' Tab will appear, click here to be directed to the Antibiotic Form.
- You will first be asked 'Did the patient receive antibiotics 7 days prior to ICU admission until ICU discharge? '.
    - If 'No' click 'save' and you will be directed back to the Patient Status Page.
    - If 'Yes' you will be prompted to record all antibiotics. Select the generic name of the antibiotic from the drop down box (see appendix 7 for taxonomy).
    - **Note:** Antibiotics are listed alphabetically.
    - Record the dose, the route (IV or PO/NG) and the frequency of all antibiotics (OD, BID, TID,QID or q_hrs).
      Enter a single stat dose as OD; the start and stop date/time will be the same.
        - For antibiotics received pre/post dialysis, record these as OD.
    - Record the date and time the antibiotic was **ordered**. In the event that the time is not available, record the date and click 'no time available'
    - Record the date and time the antibiotics were first **received.**
    - Record start date and time the antibiotics were actually **stopped** even if this occurs beyond ICU discharge. If the patient switches from IV to PO vancomycin, please enter the last dose given via the IV route as the stop date.
    - <u>Do not</u> record any changes in dose/route/frequency as a separate entry.
    - If antibiotics are held for > 48 hours and then restarted, then enter as a separate entry, except if drug levels are high.

ICU Acquired Infection?

If antibiotics were started <u>after 72 hours from ICU admission</u>, (ICU admission to date of antibiotics received), you will be prompted to answer Yes or No the following questions:

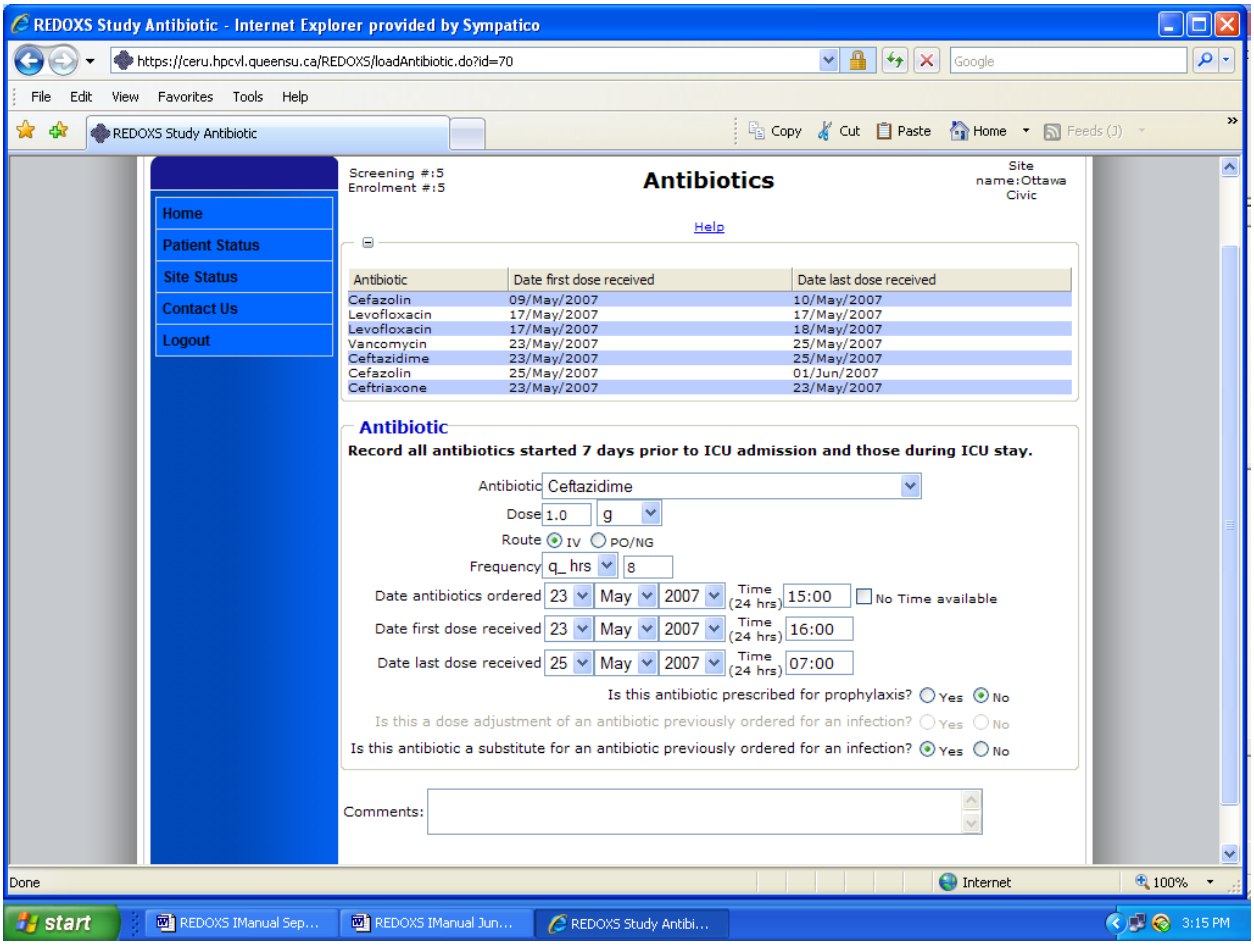
- Is this antibiotic prescribed for prophylaxis?
- Is this antibiotic a substitute for an antibiotic previously ordered for an infection?

<u>**It is important to collaborate with your Site Investigator when responding to these questions.</u>

Examples of Prophylaxis antibiotics: patient undergoing lung resection received Ancef pre and post-op.

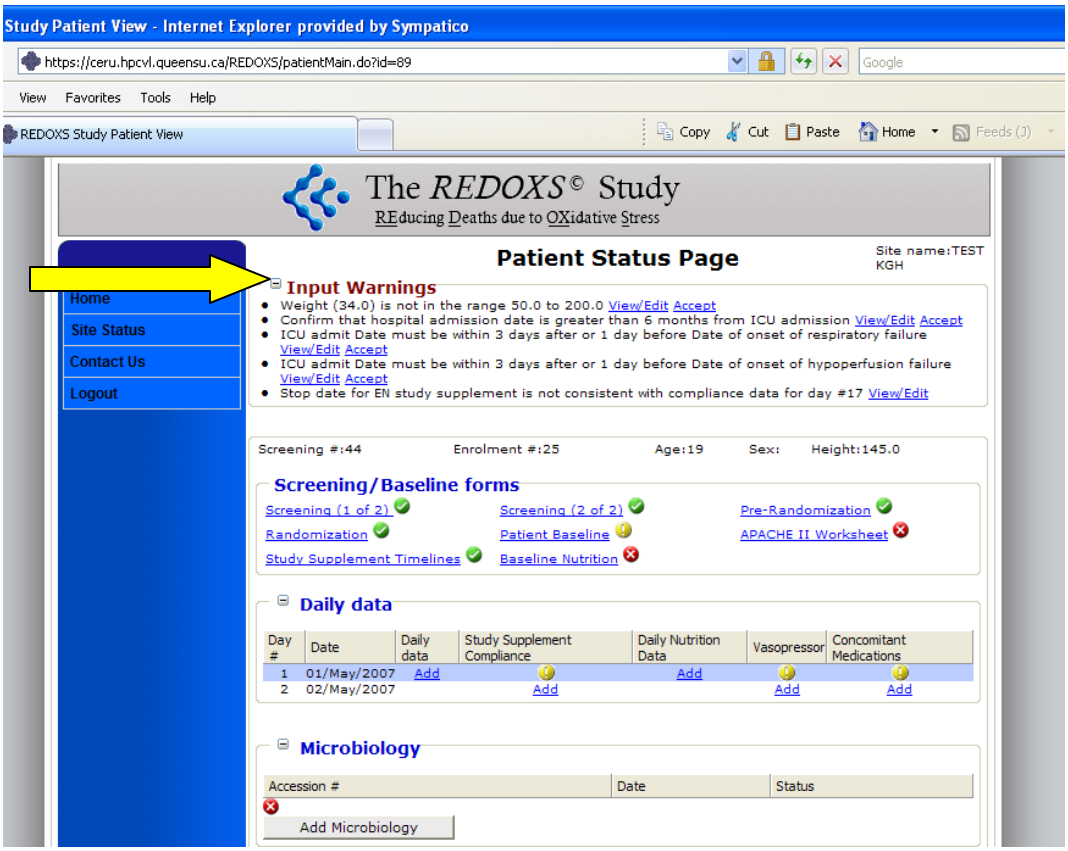
- Click on **'save antibiotic**' to save the form and return to the patient status page, or click on **'New antibiotic'** to save the form and continue entering antibiotics for this patient.

Webshot of the Antibiotics Page



ICU Outcomes

All input warnings must be addressed before you can access this page. The input warnings will appear at the top of the Patient Status Page (see webshot below).



The ICU Outcomes page must be completed when patient is discharged from ICU or dies in the ICU.

- On the Patient Status Page under Outcomes and Follow-up select **'ICU Outcome Information'.** You will be directed to the ICU Outcomes page.

- "Did patient die in ICU?" "Yes" or "No"
  - **If "Yes":**
  - You will be prompted to provide date and time of actual death. **Note:** Death date & time will be same as Hospital & ICU discharge date and time, therefore you **do not** complete Hospital Outcomes Form.
  - Is the date and time of **final ventilation discontinuation** the same as death date & time? "Yes" or "No"

- If "**Yes**", Date and time of actual death will be final ventilation discontinuation date and time.
- If "**No**", provide date and time of final ventilation discontinuation.

IF a patient is reintubated within 48 hours, this is considered a continuation of the previous intubation.

If patient is discharged from ICU while still ventilated (for example, transfer to step-down unit), you must follow the patient to obtain the actual discontinuation date and time of ventilation. In addition, please make a comment in the Comment Box describing the situation. If patient is transferred to another hospital ventilated, the actual discharge date and time will become the ventilation discontinuation date and time, please add a comment.

- If "**No**" to "Did patient die in ICU?"

Provide date and time of actual ICU discharge.

For patients awaiting a bed to be transferred out of the ICU, the ICU discharge date/time should be the "actual" date/time of discharge, not the time when the patient would have been discharged if a bed was available.
For patients being transferred to a rehabilitation facility, use the date/time they are discharged from the acture care facility to the rehabilitation facility as the ICU discharge date/time.

Provide date and time of final ventilation discontinuation.

- "Is the patient still on dialysis as they leave ICU": "Yes" or "No". This question is only asked if patient had acute renal failure according to the Daily data.

- Click 'Save' to save the form and be directed back to the patient status page.

Logic Alert

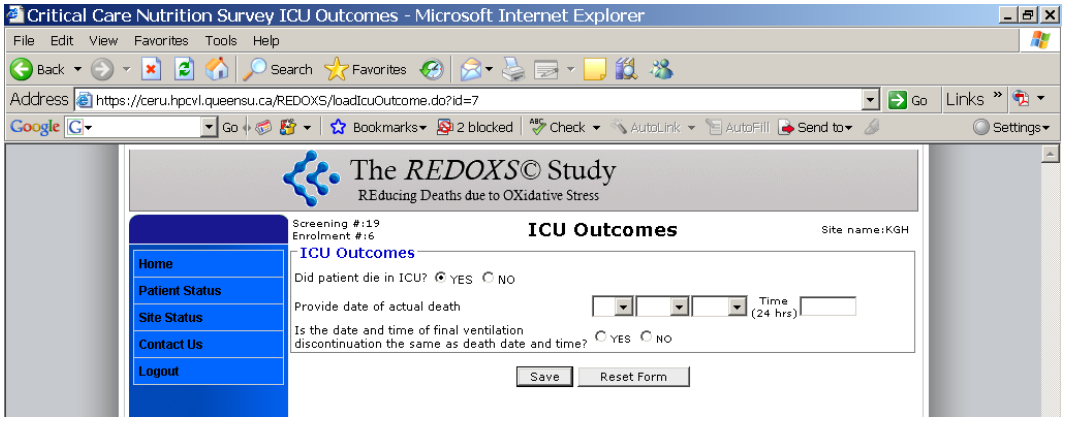
If ICU discharge date is not consistent with the duration of the daily data that you have entered, an input warning will be generated, as follows
"ICU discharge date is not consistent with daily data entered. Please enter daily data until ICU discharge"
You may either correct the ICU discharge date or enter additional daily data to the end of the study period

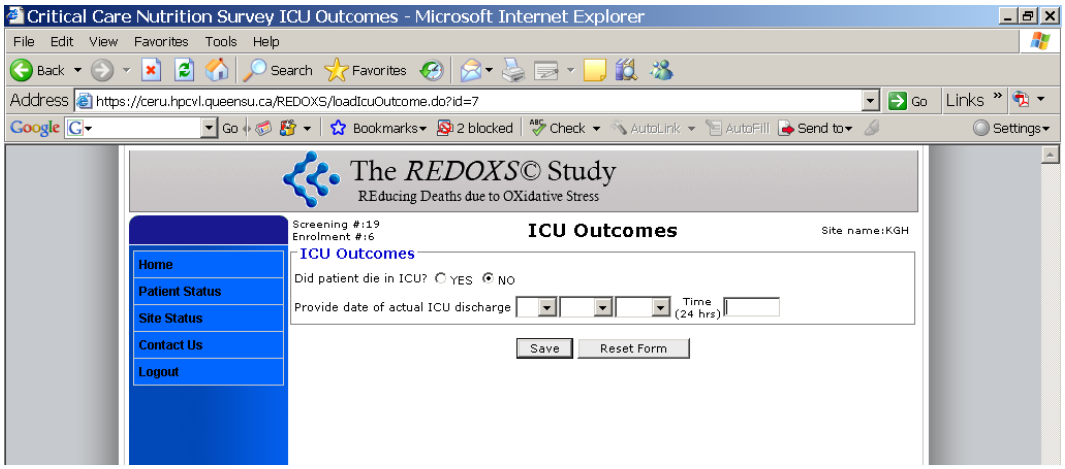
The ICU Outcomes page MUST be completed before you can proceed to the remaining pages i.e. Infection Adjudication, Hospital Outcomes, 3 and 6 month follow up and the Investigator's Confirmation.

If there is no suspicion of infection (based on the microbiology and antibiotic data), once you have entered the ICU outcomes data, you will be prompted to LOCK the data.

Once the data has been locked, access to the entered data can only granted by CERU. The administrators at CERU can unlock the data if needed. Please make sure that the data you have entered is accurate to the best of your knowledge.

Webshot of ICU Outcomes





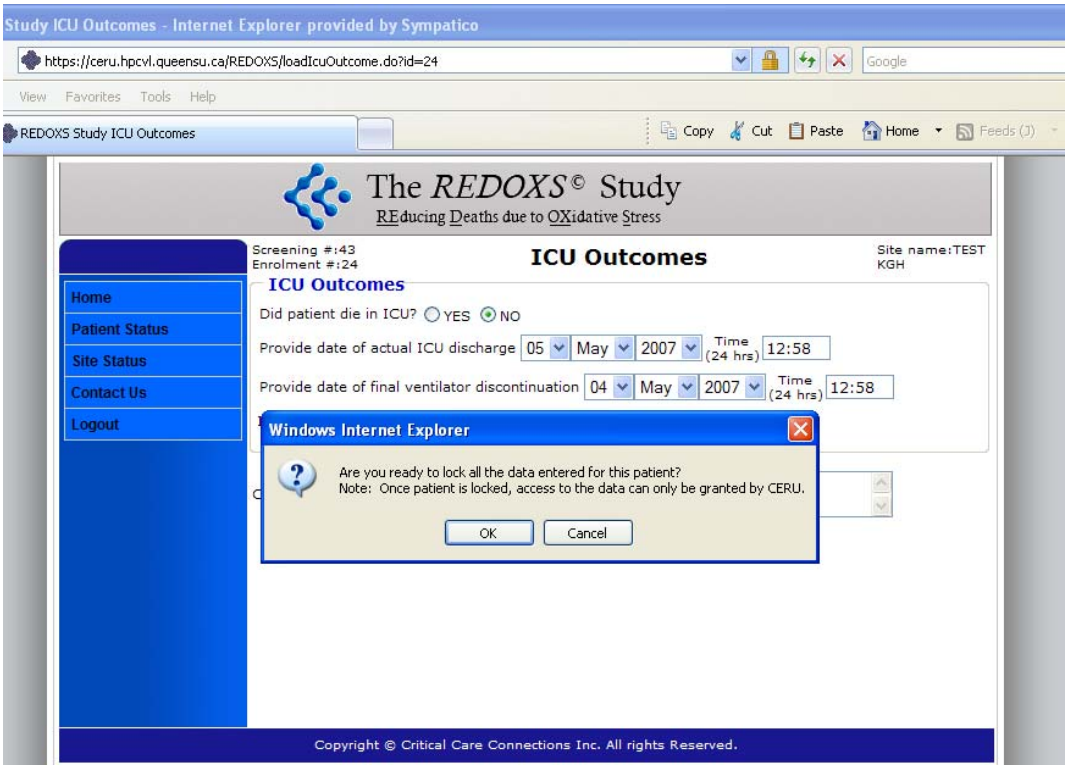
Locking Data

To determine when the first stage of data entry has been completed, a data locking process has been incorporated into the web based data entry system.

You will be prompted to lock the data at either one of the following 2 stages:

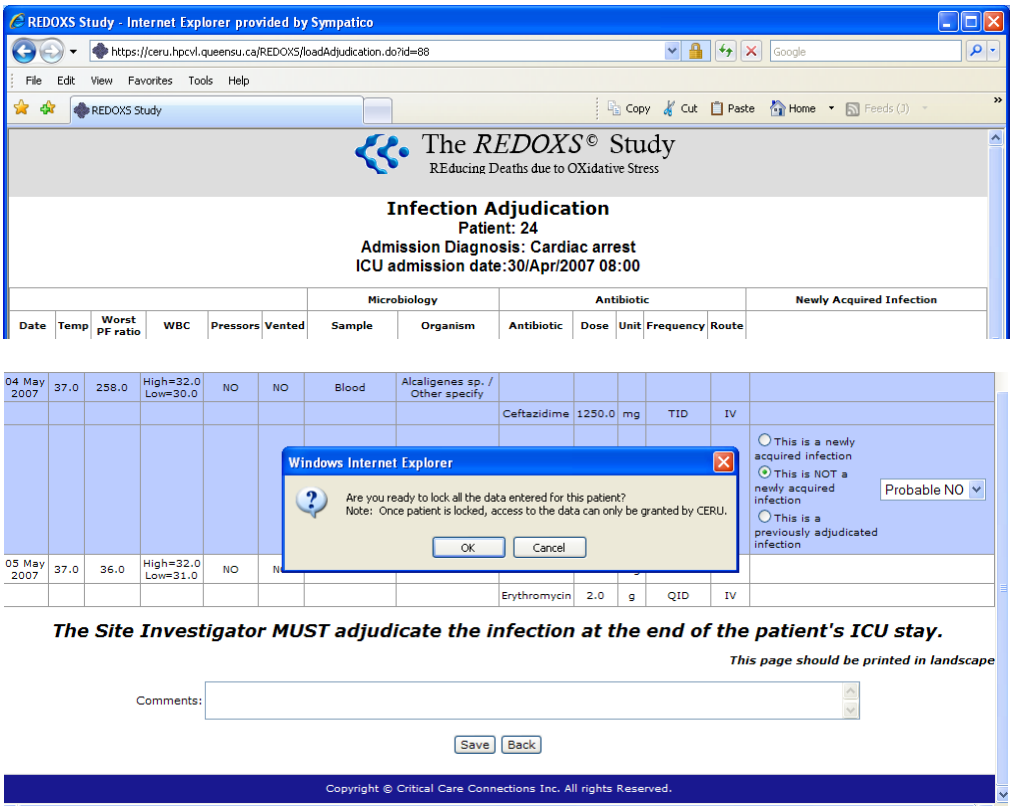
- If there is no infection adjudication form (based on the microbiology and antibiotic data), you will be prompted to LOCK the data once you have entered the ICU outcomes data.

Webshot of locking prompt (at ICU Outcomes)



- If there is an infection adjudication form (based on the microbiology and antibiotic data), you will be prompted to LOCK the data once you have completed the infection adjudication. See web shot below.

Webshot of locking prompt (at Infection Adjudication)



Once the data has been locked, you cannot make any changes to the data that you have entered. Access to the entered data can only granted by CERU.

Make sure that the data you have entered is accurate to the best of your knowledge before you lock the data.

After you lock the data, you can still access the Hospital Outcomes, 3 & 6 month and SF-36 pages (if applicable).

ICU Acquired Infection Adjudication

All input warnings must be addressed before you can access this page. The input warnings will appear at the top of the Patient Status Page.

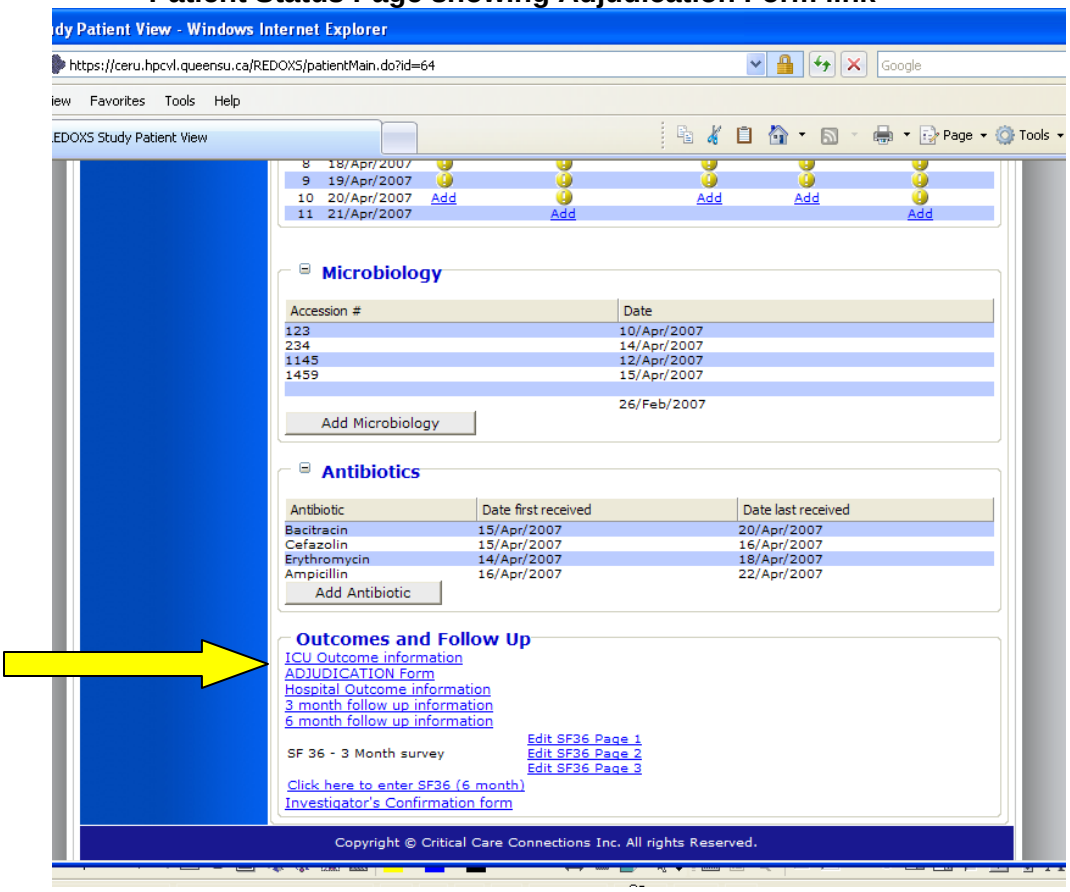
The electronic data capture system has been programmed to automatically generate a listing of relevant clinical data (microbiology. antibiotics, daily data) that will enable the Site Investigator to adjudicate newly acquired ICU infections.

1. Before determination of ICU acquired infection can be made by the SI, the SC **must** enter **ALL** daily data and ICU outcomes.

2. If there is **no** suspicion of infection (based on the microbiology and antibiotic data entered) or if the SC has not entered daily data or ICU Outcomes data, an ADJUDICATION FORM will NOT appear on the Patient Status Page (under ICU Outcomes).

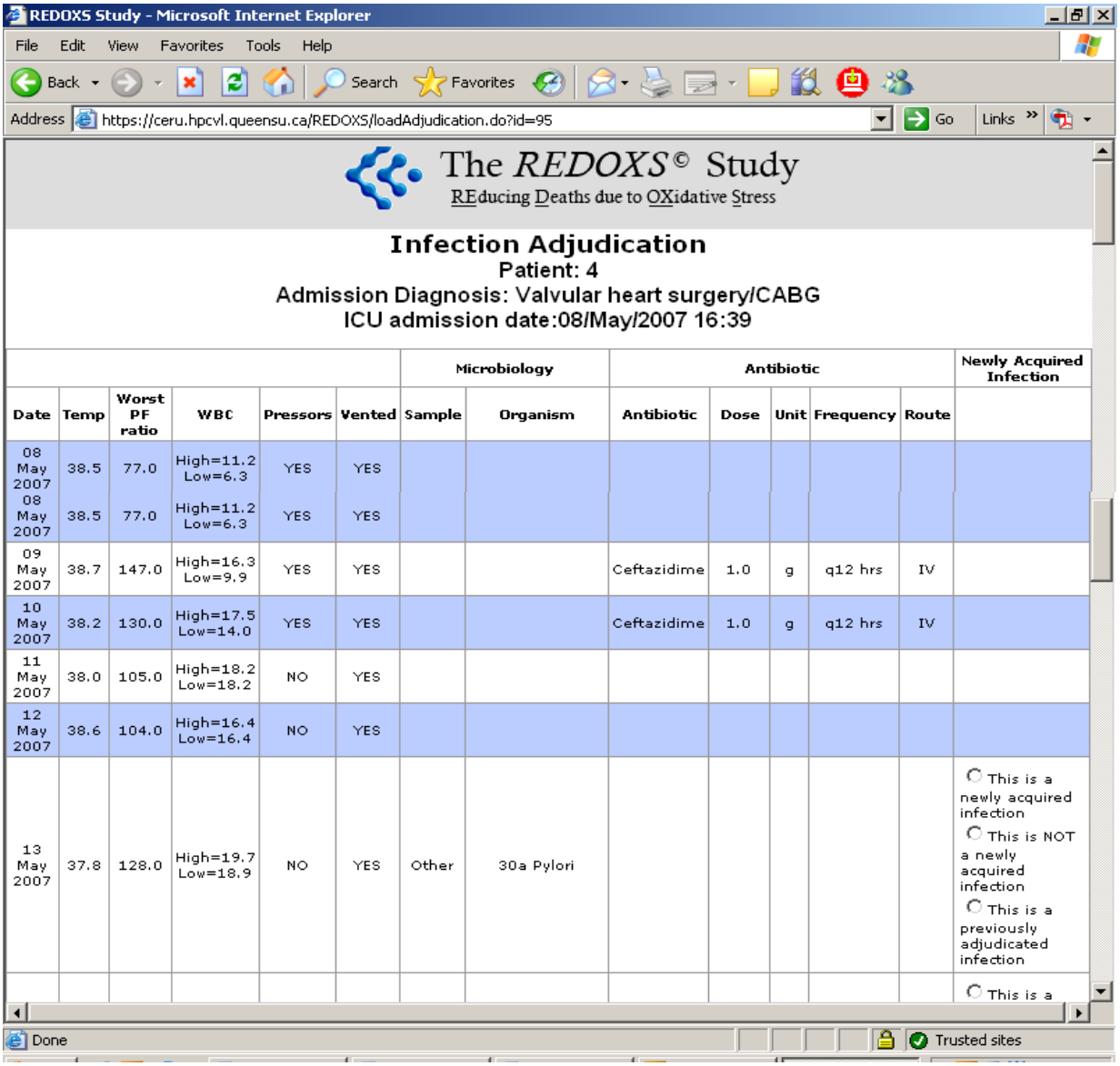
3. If there **is** a suspicion of infection (based on the microbiology and antibiotic data entered) and the SC has entered all the daily data and ICU Outcomes, an ADJUDICATION FORM will appear. See webshot below.

Patient Status Page showing Adjudication Form link



4. On the Patient Status Page under Outcomes and Follow-up, if you click on the “Adjudication Form”, this page will be automatically populated with the relevant data. See webshot below.

Sample Infection Adjudication form for patient with suspicion of infection



REDOXS Study - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites

Address https://ceru.hpcvl.queensu.ca/REDOXS/loadAdjudication.do?id=95 Go Links

The *REDOXS*© Study

REducing Deaths due to OXidative Stress

Infection Adjudication

Patient: 4

Admission Diagnosis: Valvular heart surgery/CABG

ICU admission date:08/May/2007 16:39

						Microbiology		Antibiotic					Newly Acquired Infection
Date	Temp	Worst PF ratio	WBC	Pressors	Vented	Sample	Organism	Antibiotic	Dose	Unit	Frequency	Route	
08 May 2007	38.5	77.0	High=11.2 Low=6.3	YES	YES								
08 May 2007	38.5	77.0	High=11.2 Low=6.3	YES	YES								
09 May 2007	38.7	147.0	High=16.3 Low=9.9	YES	YES			Ceftazidime	1.0	g	q12 hrs	IV	
10 May 2007	38.2	130.0	High=17.5 Low=14.0	YES	YES			Ceftazidime	1.0	g	q12 hrs	IV	
11 May 2007	38.0	105.0	High=18.2 Low=18.2	NO	YES								
12 May 2007	38.6	104.0	High=16.4 Low=16.4	NO	YES								
13 May 2007	37.8	128.0	High=19.7 Low=18.9	NO	YES	Other	30a Pylori						○ This is a newly acquired infection ○ This is NOT a newly acquired infection ○ This is a previously adjudicated infection
													○ This is a

Done Trusted sites

5. The SC MUST print off the Adjudication Form WITHOUT choosing Yes or NO to Newly acquired infection. This form should be printed in landscape.

6. The SC **must** ask the SI to determine if the suspicion is a Newly acquired infection and is to provide the SI with the following documentation to assist in making the determination:
    a. **Complete Infection ADJUDICATION FORM** (printed off the web with the relevant daily data)
    b. **Algorithm for ICU acquired Infection appendix 10.1**
    c. **Categories 1-12 appendix 10.2** (available on web page, click "details")
    d. **Definition of No Infection appendix 10.3**

7. The SI needs to determine if there is a newly acquired infection based on the information above and if needed, a review of the patient's chart. **The SI must pick one of these options for every newly acquired infection listed on the adjudication form:**

    Option #1: There is a newly acquired ICU infection. If so, the SI must pick one of the 12 Categories and then determine if this is either "definite", "probable" or "possible" yes (see appendix 10.2)

    Option #2: There is no infection. If so, the SI must determine is it is "probable" or "possible" no (see appendix 10.3).

    Option #3: This is a previously adjudicated infection. If so, indicate what category of Infection (appendix 10.2)

8. Once the SI has determined the presence, the type of infection and the certainty of this determination in conjunction with the SC, the SC returns to the ADJUDICATION FORM for that patient and transfers the information on to the web. To make the process smoother, it is **strongly encouraged** that the SI make this determination in conjunction with the SC online.

9. If there are any changes to the microbiology or antibiotic data after the SI has adjudicated the infection, you may need to have your SI re-adjudicate the infection.

The Study Coordinator MUST ensure that the Site Investigator is responsible for determining the presence of a newly acquired infection, the type of infection and the certainty of this determination.

Refer to Algorithm for ICU acquired Infection appendix 10.1 for more details.

After data entry on ALL pages has been completed, the SI is required to sign the Investigator's Confirmation form that will attest that the ICU acquired infection adjudication, are complete and accurate to the best of his/her knowledge.

It is strongly recommended that the infection adjudication process be completed close to the time of the antibiotics and as soon as ICU outcomes have been collected.

You are strongly encouraged to use the Comments box to record any issues or concerns regarding the adjudication.

All ICU Acquired Infection Forms will be reviewed by the Study Chair and designated staff at CERU. Any additional information including worksheets kept by the SC must be kept for source documentation.

For details on the process used for generating a suspicion of ICU acquired infection, contact the REDOXS© Project Leader.

Hospital Outcomes

This form must be completed when patient is discharged from hospital or dies in the hospital.

- On the Patient Status Page under Outcomes and Follow-up select **'Click here to enter Hospital Outcome Information'.** You will be directed to the Hospital Outcomes Form.

- Did patient die? "Yes" or "No"
  - **If "Yes":**
    - You will be prompted to provide date and time of actual death.
    - Is the patient still on dialysis as they leave Hospital": "Yes" or "No". This question is only asked if patient had acute renal failure according to the Daily data.
      - If no, provide the date of last known dialysis in hospital.

  - **If "No**":
    - Provide date and time of actual Hospital discharge.

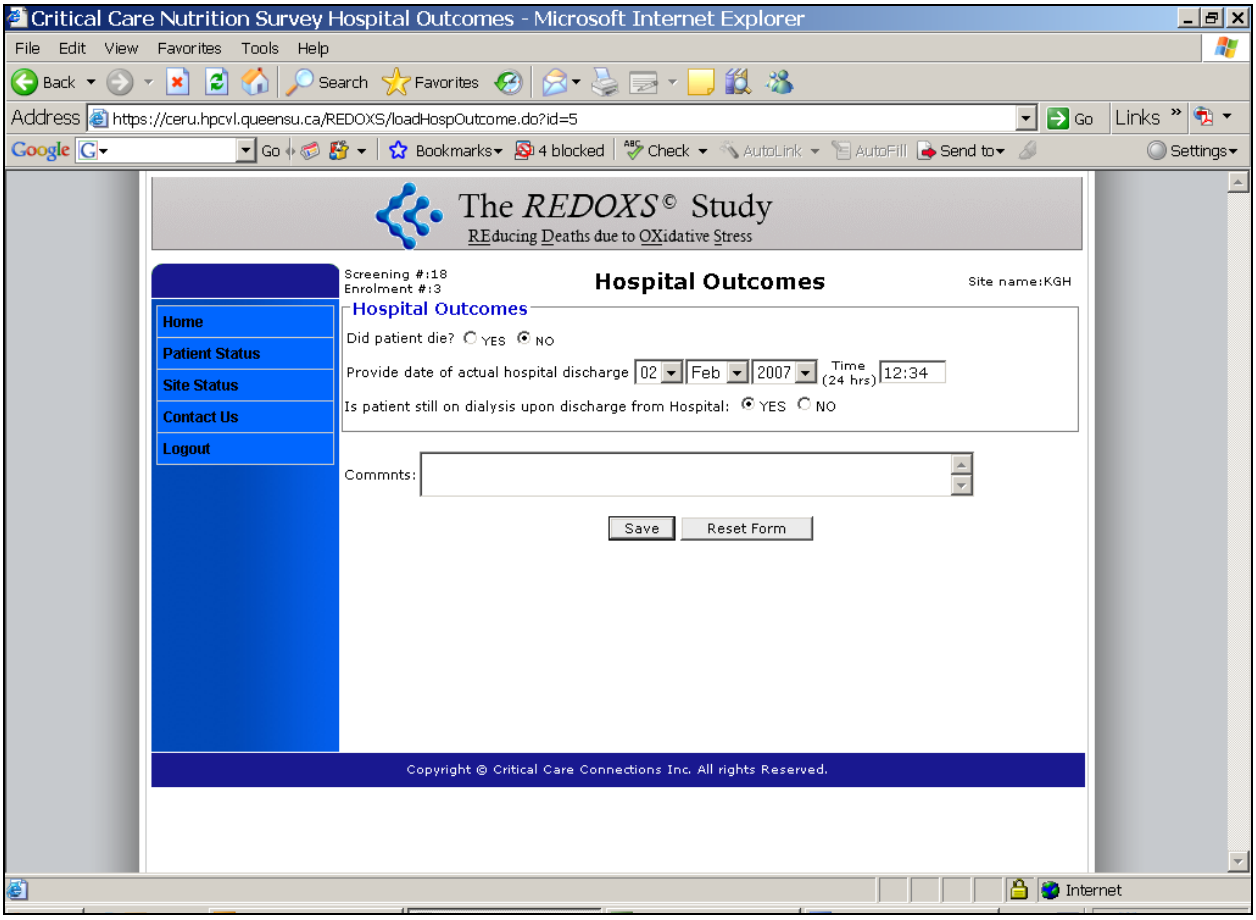
      If the patient is being discharged to a rehabilitation facility, enter the date the patient was transferred from the acute care facility to the rehabilitation facility as the discharge date. If it is an internal transfer (e.g. the rehabilitation facility is part of the hospital), please enter this transfer date as the discharge date.

      For patients who are still in hospital 6 months following randomization (i.e. not discharged to a rehab or palliative floor and status not changed to 'alternative level of care') then the hospital discharge should be recorded as the date/time at 6 months post randomization. Please make a note in the comments field of the Hospital Outcome form that the patient was still in the hospital at the 6 month follow-up.

    - "Is the patient still on dialysis as they leave Hospital": "Yes" or "No". This question is only asked if patient had acute renal failure according to the Daily data.
      - If no, provide the date of last known dialysis in Hospital.

- Click 'Save' to save the form and be directed back to the patient status page.

Webshot of Hospital Outcomes



3 and 6 Month Follow-up

In the event the patient dies in ICU or hospital, this page will become disabled as you will not need to complete it.

The follow-ups should be completed 3 and 6 months from the date of ICU admission.

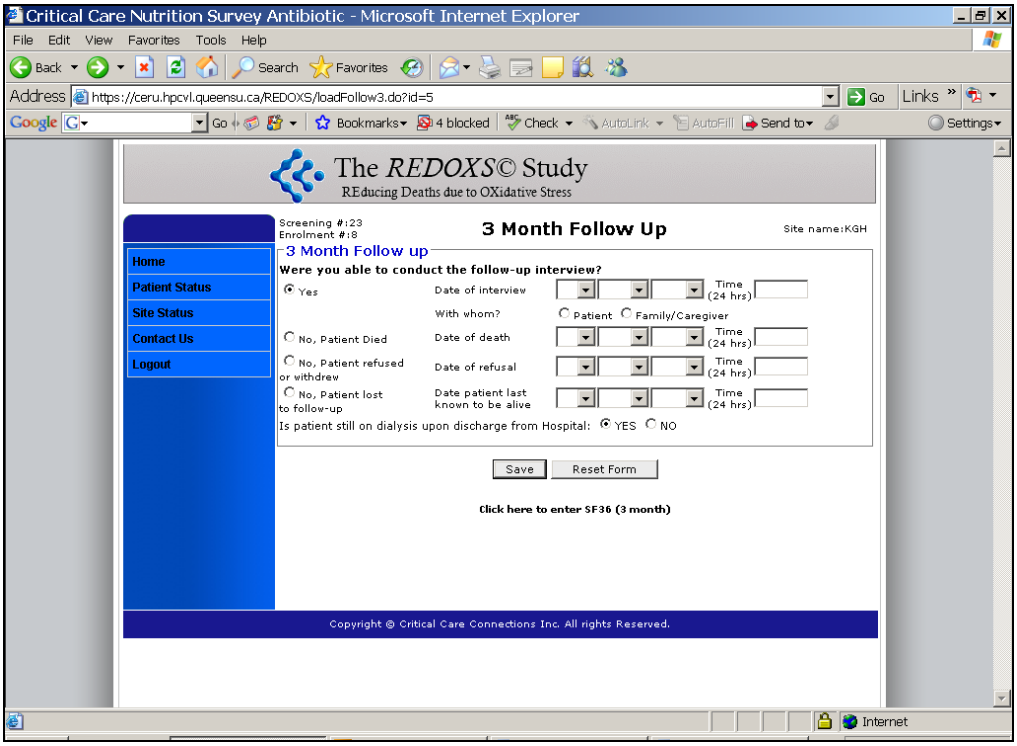
- On the Patient Status Page under Outcomes and Follow-up select **'Click here to enter 3/6 Month Follow-up Information'.** You will be directed to the 3/6 months follow-up Form.
- Were you able to conduct the follow-up interview?
    - If Yes, record date of the interview.
        - If Yes, indicate with whom the interview was conducted, patient or family/caregiver.
        - If family/caregiver is being interviewed, ensure that they respond in a manner that they believe that the patient would respond.
    - If No, choose one of the 4 options:
        - Patient died – provide date of death. Please obtain from a family member. If unknown, enter the date patient was last known to be alive.
        - Patient refused or withdrew - provide date of refusal.
        - Patient lost to follow up (f/u) - provide date patient last known to be alive.

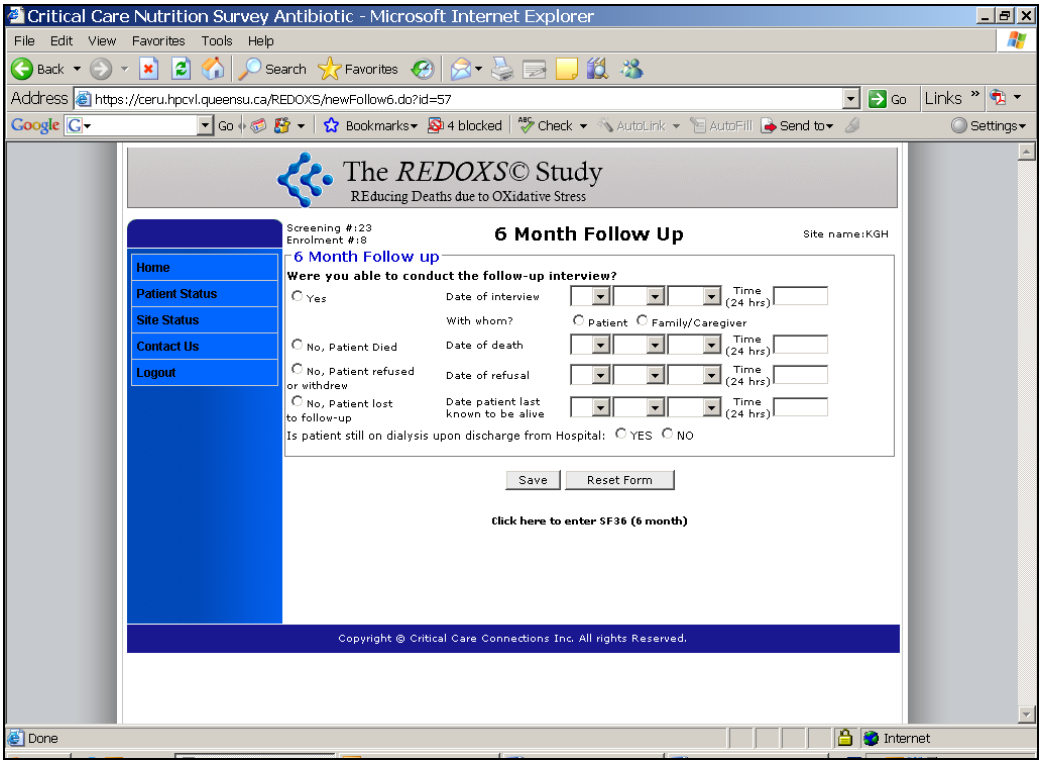
- If unable to contact the patient within the acceptable timeframe outlined above, make notes in the comment box provided at the bottom of the form. For example, document the date and time of attempts made to contact patient.

- For patients who developed acute renal failure only, provide the date of last known dialysis or check the box to confirm that patient was still on dialysis at 3/6 months.

- Click 'Save' to save form and return to the Patient Status page or 'Click here to enter SF36 (3/6 months)'.

Webshot of 3 and 6 Month Follow-up Form





SF-36 Survey (3 and 6 months)

In the event the patient dies in ICU or hospital, this page will become disabled as you will not need to complete it.

- To conduct the SF-36 survey, a telephone interview must be completed at 3 and 6 Months from ICU admission date. Do **not** give this survey to the patients to fill out as this is to be conducted in a telephone interview.
- The SF-36 Survey must be administered ± 2 weeks from the designated time points.
- Every attempt should be made to complete the interview within the given timeframe; however we will accept interviews outside the timeframe provided. If in doubt do not hesitate to contact the PL to confirm if the timeframe is still acceptable.
- Schedule reminders for the 3 and 6 month long term follow-up for each REDOXS© patient.
- For instructions on conducting the SF-36 survey, refer to the Script for Personal Interview SF-36 Administration (appendix 9).

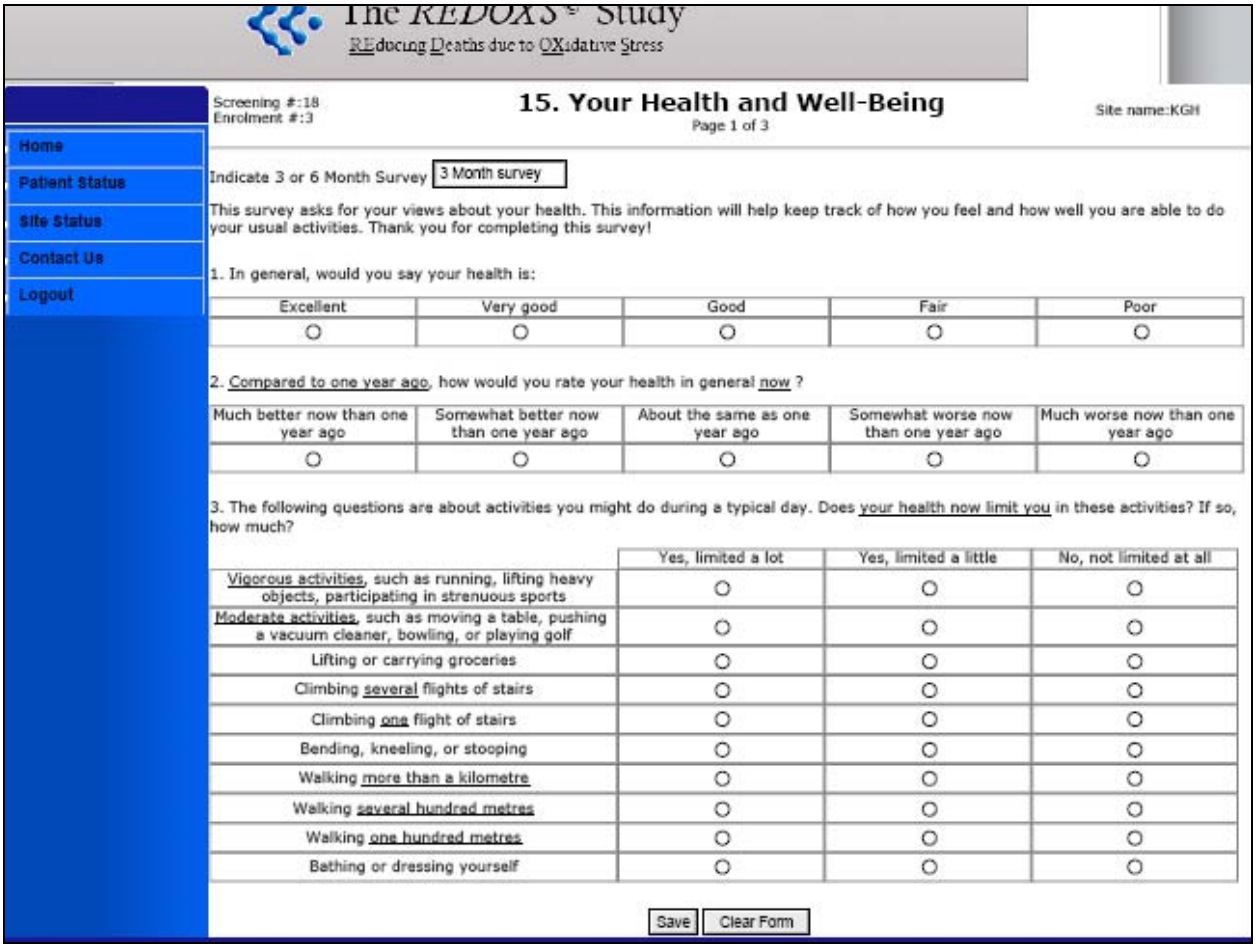
Ideally, the SF36 should be administered to the patient; however if the patient is not able to participate a substitute may respond on their behalf. A substitute respondent should be an individual who knows the patient's condition the best. This may be a family member or a health care professional (i.e. assigned bedside nurse).

Please note in the SF-36 for questions 3(g) - 3(i), the questions reference miles or yards. Please substitute kilometres or metres as needed.

- The SF36 Survey can also be accessed directly from the link under Outcomes and Follow-up section on the Patient Status page.
    - If the patient is still in the ICU/hospital at 3 and/or 6 months, the online version of the SF-36 will not appear on the Patient Status Page. In these cases, the research coordinator will need to administer the survey manually and enter the data into the eCRF retrospectively.

- Use a paper copy of the SF36 survey to interview the patient and keep this as **source documentation.** Then transfer the responses to the web.

Webshot of SF36



The REDOXS Study
REducing Deaths due to OXidative Stress

Home
Patient Status
Site Status
Contact Us
Logout

Screening #:18
Enrolment #:3

15. Your Health and Well-Being

Page 1 of 3

Site name:KGH

Indicate 3 or 6 Month Survey: 3 Month survey

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!

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

Excellent	Very good	Good	Fair	Poor
○	○	○	○	○

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

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
○	○	○	○	○

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
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	○	○	○
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	○	○	○
Lifting or carrying groceries	○	○	○
Climbing several flights of stairs	○	○	○
Climbing one flight of stairs	○	○	○
Bending, kneeling, or stooping	○	○	○
Walking more than a kilometre	○	○	○
Walking several hundred metres	○	○	○
Walking one hundred metres	○	○	○
Bathing or dressing yourself	○	○	○

Save | Clear Form

Investigator's Confirmation and Finalizing Patient

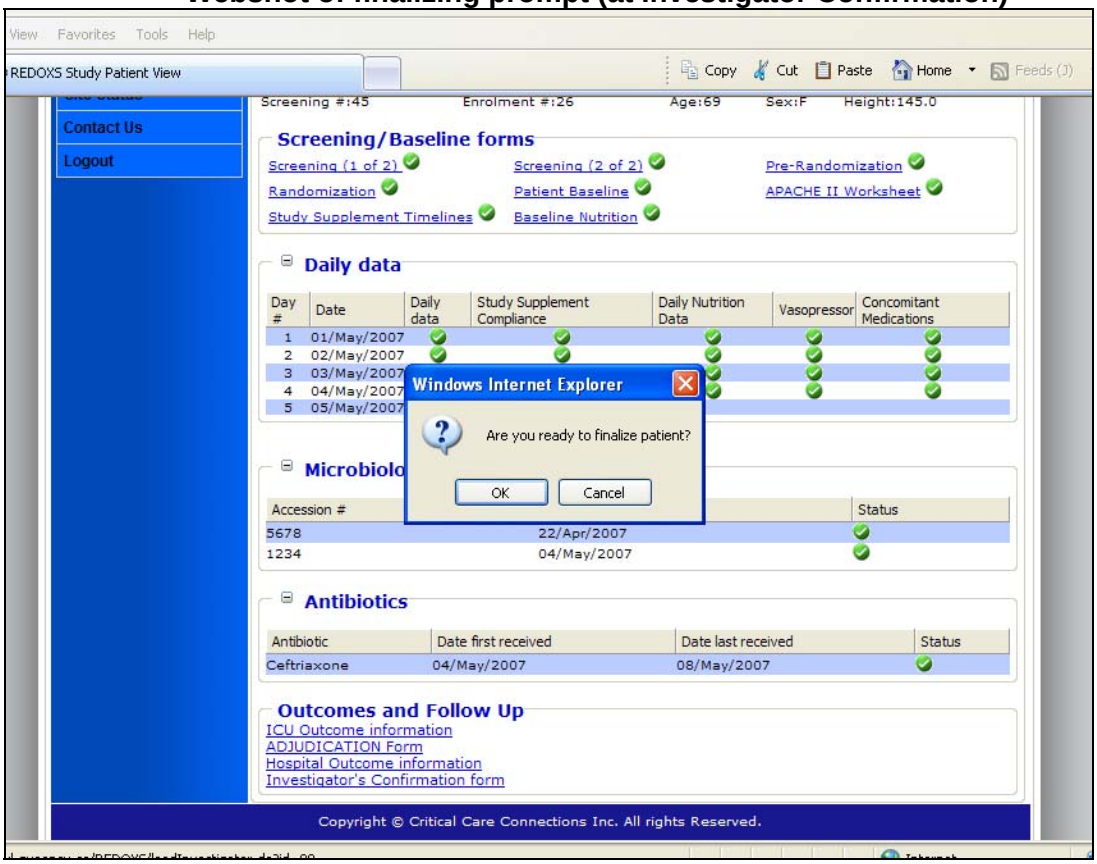
The Investigator's Confirmation form will only appear on the Patient Status Page once the ICU and Hospital outcomes have been completed and all input warnings have been resolved.

- After completion of all eCRFs and resolution of all input warnings, the investigator's confirmation must be obtained. This is to be done at the end of ALL data collection i.e. when the last outcome data has been entered (Hospital Outcomes or 3, 6 month follow up or SF 36 data).

- Click on 'Investigator's Confirmation' under Outcomes and Follow-up on the Patient Status Page.

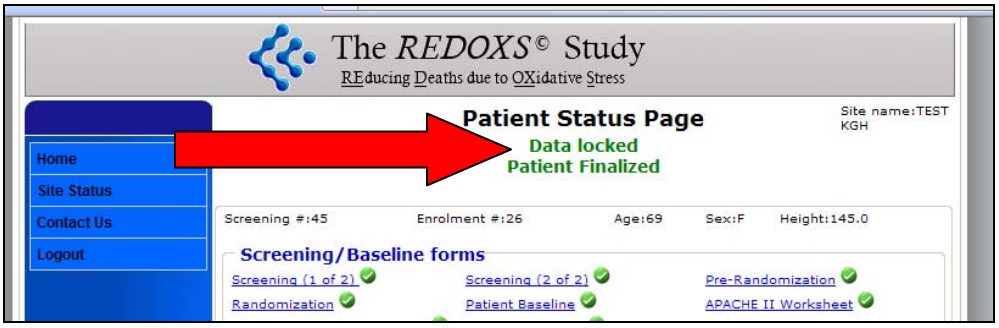
- To determine when the final stage of data entry has been completed, a patient finalizing process has been incorporated into the web based data entry system. This occurs as soon as the last outcomes have been entered and you click on the Investigator Confirmation Form. You will be prompted to finalize the patient.

Webshot of finalizing prompt (at Investigator Confirmation)



Make sure that the data you have entered is accurate to the best of your knowledge before you finalize the patient. You will not be able to make any changes to the data once patient has been finalized and subsequent changes can only be performed by the database manager at CERU.

Once the patient is finalized, the patient status changes to “Data Locked, Patient Finalized” (see webshot below).



- The SC must print this form (Appendix 10). The form will automatically be populated with the site number, patient enrollment number, and enrollment date. See web shot below.

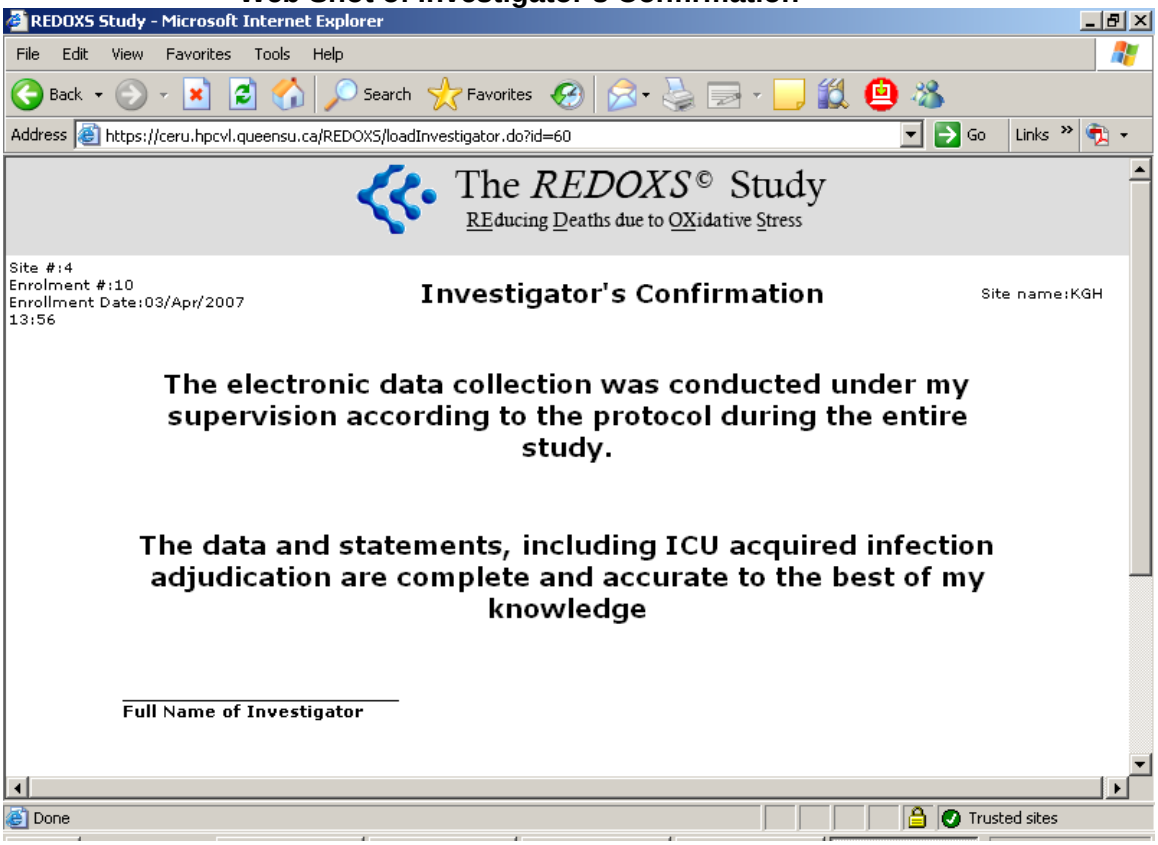
- The Site Investigator is then asked to sign and date the form, to attest the following:
  - The electronic data collection was conducted under his / her supervision according to the protocol during the entire study.
  - The data and statements, including ICU acquired infection adjudication, are complete and accurate to the best of their knowledge.

Please fax the completed form to the PL as soon as possible after the signature is obtained. Keep the original as **source documentation.**

To complete the patient finalization process, the completed Investigator Confirmation Form must be received at CERU.

IF changes are made to a finalized patient during a source verification visit, a new Investigator Confirmation **Form must be signed and sent to CERU.**

Web Shot of Investigator's Confirmation



Appendix 1 – Site Investigator Delegation of Authority Log

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 (see next page)	Dates	
					Start	End

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

Appendix 2 – Web Access Signature Log

The *REDOXS*® Study
REducing Deaths due to OXidative Stress

Electronic Data Capture Signature Sheet

INSTITUTION:	**SITE NUMBER:**
INVESTIGATOR:	

Please complete the Electronic Data Capture (EDC) System Access Signature Sheet for each study coordinator at your site who will be entering study data into the electronic forms. A signature and email address is required to create user accounts for the EDC system for the REDOXS® Study.

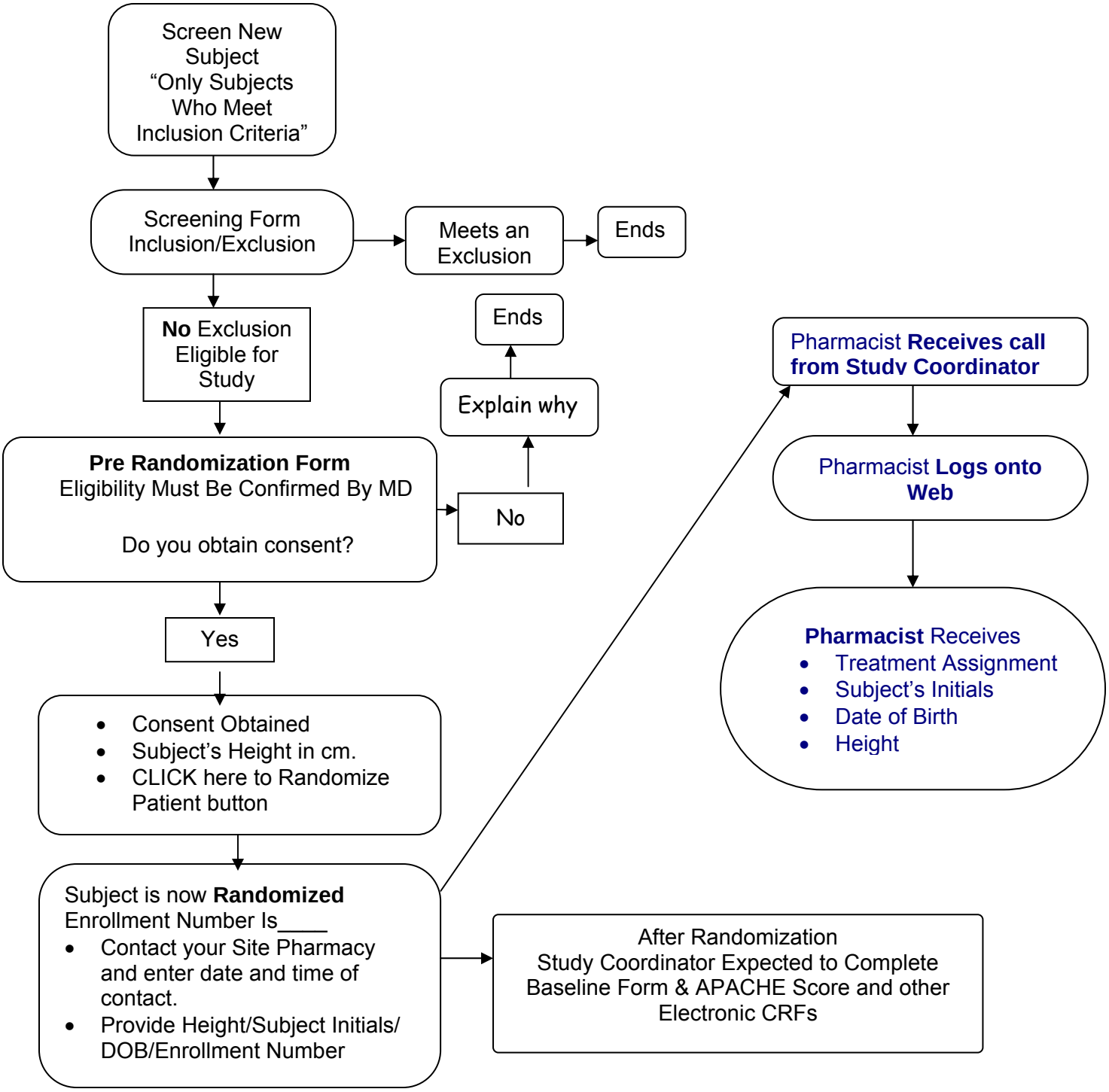
NAME	TITLE	SIGNATURE	EMAIL	DATE

NOTE:
By completing the information in the table above, the individual confirms they have been delegated the responsibility of entering confidential study information into the electronic data capture system for the REDOXS® Study.

The individual agrees to keep their password confidential to prevent unauthorized access to the data.

Reference: ICH GCP 5.5.3

Appendix 3 - Randomization Process on Web



Appendix 4 - Height Conversion Table

One foot = 12 inches
One inch = 2.54 cms

Feet/Inches	Inches	Centimeters	Feet/Inches	Inches	Centimeters
4ft 6 inch	54	137	5ft 10 inch	70	178
4ft 7 inch	55	140	5ft 11 inch	71	180
4ft 8 inch	56	142	6 ft	72	183
4ft 9 inch	57	145	6ft 1 inch	73	185
4ft 10 inch	58	147	6ft 2 inch	74	188
4ft 11 inch	59	150	6ft 3 inch	75	191
4ft 12 inch	60	152	6ft 4 inch	76	193
5ft 1 inch	61	155	6ft 5 inch	77	196
5ft 2 inch	62	157	6ft 6 inch	78	198
5ft 3 inch	63	160	6ft 7 inch	79	201
5ft 4 inch	64	163	6ft 8 inch	80	203
5ft 5 inch	65	165	6ft 9 inch	81	206
5ft 6 inch	66	168	6ft 10 inch	82	208
5ft 7 inch	67	170	6ft 11 inch	83	211
5ft 8inch	68	173	7ft	84	213
5ft 9inch	69	175	7ft 1 inch	85	216

Appendix 5 - ICU Admission Diagnosis Taxonomy

NON-OPERATIVE CONDITIONS
Choose from this list if admission category is medical

Cardiovascular / vascular:
1. ☐ *Cardiogenic shock*
2. ☐ *Cardiac arrest*
3. ☐ *Aortic aneurysm*
4. ☐ *Congestive heart failure*
5. ☐ *Peripheral vascular disease*
6. ☐ *Rhythm disturbance*
7. ☐ *Acute myocardial infarction*
8. ☐ *Hypertension*
9. ☐ *Other CV disease: _____*

Respiratory:
10. ☐ *Parasitic pneumonia (ie.pneumocystis carinii)*
11. ☐ *Aspiration pneumonia*
12. ☐ *Respiratory neoplasm (inc. larynx, trachea)*
13. ☐ *Respiratory arrest*
14. ☐ *Pulmonary edema (non-cardiogenic)*
15. ☐ *Bacterial / Viral pneumonia*
16. ☐ *Chronic obstructive pulmonary disease*
17. ☐ *Pulmonary embolism*
18. ☐ *Mechanical airway obstruction*
19. ☐ *Asthma*
20. ☐ *Other respiratory disease: _____*

Gastrointestinal:
21. ☐ *Hepatic failure*
22. ☐ *GI perforation/obstruction*
23. ☐ *GI bleeding due to varices*
24. ☐ *GI inflammatory disease (ulcerative colitis, crohn's disease)*
25. ☐ *GI bleeding due to ulcer/laceration*
26. ☐ *GI bleeding due to diverticulosis*
27. ☐ *Pancreatitis*
28. ☐ *Other GI disease: _____*

Neurologic:
29. ☐ *Intracerebral hemorrhage*
30. ☐ *Subarachnoid hemorrhage*
31. ☐ *Stroke*
32. ☐ *Neurologic infection*
33. ☐ *Neurologic neoplasm*
34. ☐ *Neuromuscular disease*
35. ☐ *Seizure*
36. ☐ *Other neurologic disease: _____*

Sepsis:
37. ☐ *Sepsis (other than urinary tract)*
38. ☐ *Sepsis of urinary tract origin*

Trauma:
39. ☐ *Head trauma (with/without multiple trauma)*
40. ☐ *Multiple trauma (excluding head trauma)*

Metabolic:
41. ☐ *Metabolic coma*
42. ☐ *Diabetic ketoacidosis*
43. ☐ *Drug overdose*
44. ☐ *Other metabolic disease:_____*

Hematologic:
45. ☐ *Coagulopathy //neutropeniathrombocytopenia*
46. ☐ *Other hematologic condition: _____*

Other:
47. ☐ *Renal disease:_____*
48. ☐ *Burns*
49. ☐ *Other medical disease: _____*

POST-OPERATIVE CONDITIONS:
Choose from this list if admission category is surgical

Vascular / cardiovascular:
50. ☐ *Dissecting/ruptured aorta*
51. ☐ *Peripheral vascular surgery (no bypass graft)*
52. ☐ *Valvular heart surgery/CABG*
53. ☐ *Elective abdominal aneurysm repair*
54. ☐ *Peripheral artery bypass graft*
55. ☐ *Carotid endarterectomy*
56. ☐ *Other CV disease: _____*

Respiratory:
57. ☐ *Respiratory infection*
58. ☐ *Lung neoplasm*
59. ☐ *Respiratory neoplasm (mouth, sinus, larynx, trachea)*
60. ☐ *Other respiratory disease: _____*

Gastrointestinal:
61. ☐ *GI perforation/rupture*
62. ☐ *GI inflammatory disease*
63. ☐ *GI obstruction*
64. ☐ *GI bleeding*
65. ☐ *Pancreatitis*
66. ☐ *Liver transplant*
67. ☐ *GI neoplasm*
68. ☐ *GI cholecystitis / cholangitis*
69. ☐ *Other GI disease: _____*

Neurologic:
70. ☐ *Intracerebral hemorrhage*
71. ☐ *Subdural/epidural hematoma*
72. ☐ *Subarachnoid hemorrhage*
73. ☐ *Laminectomy/other spinal cord surgery*
74. ☐ *Craniotomy for neoplasm*
75. ☐ *Other neurologic disease: _____*

Trauma:
76. ☐ *Head trauma (with/without multiple trauma)*
77. ☐ *Multiple trauma (excluding head trauma)*

Renal:
78. ☐ *Renal neoplasm*
79. ☐ *Other renal disease: _____*

Gynecologic:
80. ☐ *Hysterectomy*

Orthopedic:
81. ☐ *Hip or extremity fracture*

Bariatric Surgery:
82. ☐ *Laparoscopic Banding*
83. ☐ *Laparoscopic Gastric Bypass*
84. ☐ *Open Gastric Bypass (Roux-en-Y)*
85. ☐ *Vertical Banded Gastroplasty*

Other:
86. ☐ *Other surgical condition:_____*

Appendix 6 - Comorbid Taxonomy

0. ☐ **NONE**

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

PULMONARY

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

NEUROLOGIC

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

ENDOCRINE

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

RENAL

18. ☐ Moderate or severe renal disease

GASTROINTESTINAL

19. ☐ Mild liver disease
20. ☐ Moderate or severe liver disease
21. ☐ GI Bleeding
22. ☐ Inflammatory bowel
23. ☐ Peptic ulcer disease
24. ☐ Gastrointestinal Disease (hernia, reflux)

CANCER/IMMUNE

25. ☐ Any Tumor
26. ☐ Lymphoma
27. ☐ Leukemia
28. ☐ AIDS
29. ☐ Metastatic solid tumor

PSYCHOLOGICAL

30. ☐ Anxiety or Panic Disorders
31. ☐ Depression

MUSKOSKELETAL

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

MISCELLANEOUS

36. ☐ Visual Impairment (cataracts, glaucoma, macular degeneration
37. ☐ Hearing Impairment (very hard of hearing even with hearing aids)

Appendix 7 - Formula Taxonomy

Code	Formula Name
1.	MEAD JOHNSON: Portagen
2.	NESTLE: Peptamen with Prebio 1
3.	NESTLE: Peptamen
4.	NESTLE: Peptamen 1.5
5.	NESTLE: Peptamen VHP
6.	NESTLE: Peptamen AF
7.	NESTLE: Nutren 2.0
8.	NESTLE: Nutren 1.5
9.	NESTLE: Nutren VHP
10.	NESTLE: Nutren VHP fibre
11.	NESTLE: Nutren Fibre with Prebio 1
12.	NESTLE: Nutren Fibre with Prebio 1.5
13.	NESTLE: Nutrihep
14.	NESTLE: Supplements - Caloreen
15.	NESTLE: Resource Beneprotein Powder
16.	NOVARTIS: Compleat
17.	NOVARTIS: Impact
18.	NOVARTIS: Impact 1.5
19.	NOVARTIS: Isosource HN
20.	NOVARTIS: Isosource HN with fibre
21.	NOVARTIS: Isosource VHN
22.	NOVARTIS: Isosource 1.5
23.	NOVARTIS: Novasource Renal
24.	NOVARTIS: Peptinex
25.	NOVARTIS: Peptinex DT
26.	NOVARTIS: Resource 2.0
27.	NOVARTIS: Resource Plus
28.	NOVARTIS: Resource Standard
29.	NOVARTIS: Resource Diabetic
30.	NOVARTIS: Tolerex
31.	NOVARTIS: Trauma-cal

Code	Formula Name
31	NOVARTIS: Vivonex TEN
32	NOVARTIS: Vivonex Plus
33	NOVARTIS: Supplements- Instant Protein Powder
34	NOVARTIS: Supplements - Microlipid
35	NOVARTIS: Supplements - MCT oil
36	NOVARTIS: Supplements-Resource Glutasolve
37	ROSS: Jevity 1 kcal
38	ROSS: Jevity 1.2 kcal
39	ROSS: Osmolite HN Plus
40	ROSS: Osmolite HN
41	ROSS: Promote
42	ROSS: Glucerna
43	ROSS: Nepro
44	ROSS: Suplena
45	ROSS: Pulmocare
46	ROSS: Perative
47	ROSS: Vital HN
48	ROSS: TWO Cal HN
49	ROSS: Oxepa
50	ROSS: Optimental
51	ROSS: Ensure
52	ROSS: Ensure High Protein
53	ROSS: Ensure Plus
54	ROSS: Ensure Fibre
55	ROSS: Supplements -Polycose powder
56	ROSS: Supplements -Polycose Liquid
57	Hormel Health: Immun-Aid
58	Hormel Health: Hepatic-Aid
59	Other:

Appendix 8 - Organism Taxonomy

	SPECIES	SUB-SPECIES
	Acinetobacter sp.	Baumani
		Other specify
	Actinomyces sp.	Other specify
	Aeromonas sp.	Aerogenes
		Other specify
	Aerococcus sp	Other specify
	Alcaligenes sp.	Dentrificans
		Foecalis
		Other specify
	Bacillus sp.	Anthracis
		Other specify
	Bacteroides sp.	Fragilis
		Thetaiotamicron
		Other specify
	Babesia sp.	Other specify
	Bartonella sp.	Other specify
	Borrellia sp.	Burgdoferi
		Other specify
	Bortetella sp.	Pertussis
		Other specify
	Burkholderia sp.	Cepacia
		Mallei
		Pseudomallei
		Other specify
	Campylobacter sp.	Jejuni
		Fetus
		Other specify
	Capnocytophaga sp.	Other specify
	Chlamydia sp.	Pneumoniae
		Trachomatis
		Other specify
	Citrobacter sp.	Freundii
		Koseri
		Other specify
	Clostridium sp	Botulism
		Difficile
		Perfringes
		Tetani
		Other specify
	Corynobacteria sp.	Other specify
	Coxiella sp.	Burnetti
		Other specify
	Diphteroids sp.	Other specify
	Eikenella sp.	Corrodens
		Other specify
	Ehrlichia sp.	Other specify
	Enterobacter sp.	Cloacae
		Other specify

	Enterococcus	Vancomycin Resistant Fecalis
		Vancomycin Resistant Foecium
		Vancomycin Sensitive Fecalis
		Vancomycin Sensitive Foecium
		Other specify
	Escherichia sp.	Coli
		Other specify
	Erysipelothrix sp.	Rhusiopatheia
		Other specify
	Francisella sp.	a Tularensis
		Other specify
	Fusobacterium sp.	Other specify
	Hafnia Alvei	
	Helicobacter sp.	Pylori
		Other specify
	Hemophilus Influenza	Other specify
	Klebsiella sp.	Pneumonia
		Oxytoca
		Other specify
	Legionella sp.	Pnemophillia
		Other specify
	Listeria sp.	Monocytogenes
		Other specify
	Moraxella sp.	Catarrhalis
		Other specify
	Morganella sp.	Other specify
	Mycoplasma sp.	Other specify
	Neisseria sp.	Gonorrhoeae
		Other specify
	Nisseria sp.	Meningitidis
		Other specify
	Nocardia sp.	Asteroides
		Other specify
	Other bacteria specify	Other specify
	Pasteurella sp.	Moltocida
		Other specify
	Peptostreptococcus/ Peptococcus sp.	Prevotti
		Other specify
	Porphyromonas sp.	Other specify
	Prevotella sp.	Melaningogenica
		Other specify
	Proteus sp.	Other specify
	Providencia sp.	Other specify
	Pseudomonas sp.	Aeruginosa
		Other specify
	Rhodococcus sp.	Equi

		Other specify
	Ralstonia	Other specify
	Rickettsia sp.	Ricketsii
		Other specify
	Salmonella sp.	Other specify
	Serratia sp.	Marcescens
		Other specify
	Shigella sp.	Dysenteriae
		Other specify
	Staph sp.	Methicillin Resistant Staph Aureus (MRSA)
		Methicillin Sensitive Staph Aureus (MSSA)
		Coagulase Negative (epidermatitis)
		Other specify
	Stenotrophomas sp.	Maltophillia
		Other specify
	Strep sp.	Agalactiae (Group B Strep)
		Anginosus
		Bovis
		Pneumoniae
		Pyogenes (Group A Strep)
		Viridans
		Other specify
	Streptobacillus	Moniliformis
		Other specify
	Yersinia sp.	Pestis
		Other specify
	Vibrio sp	Cholerae
		Other specify
	Fungi/Yeast	
	Aspergillus sp.	Other specify
	Bipolaris sp.	Other specify
	Blastomyces sp	Dermatitidis
	Candida sp.	Albicans
		Torulopsis
		Glabrata
		Tropicalis
		Other specify
	Coccidiomycosis sp.	Other specify
	Pneumocystis sp.	Carinii or Jiroveci
	Not specified	Not specified
	Virus	
	Adenovirus	
	Cytomegalovirus	
	Herpes sp.	Simplex 1
		Simplex 2
	HIV	
	Hepatitis sp.	A

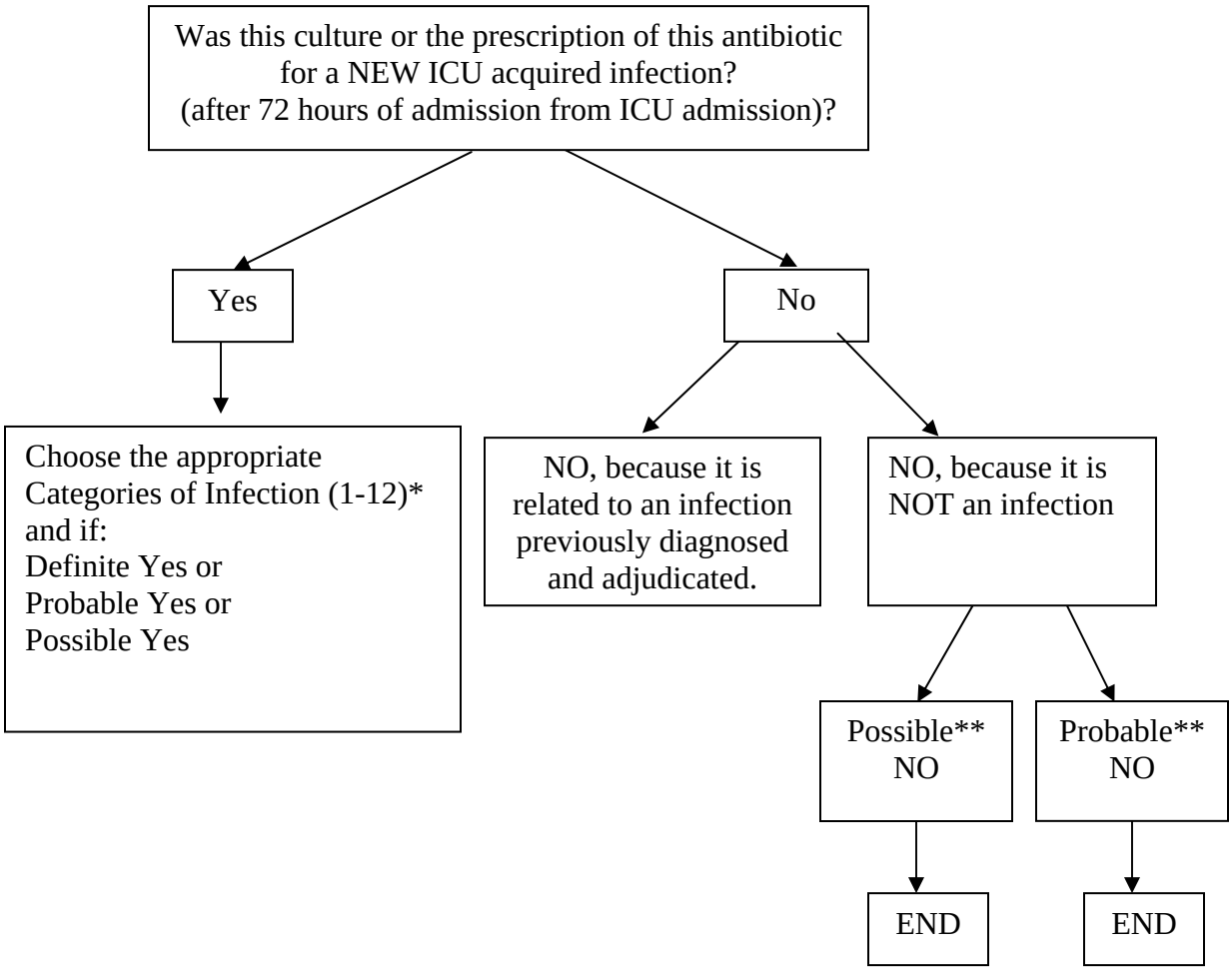
		B
		C
		Other specify
	Influenza	A
		B
	Other Virus specify	
	Mycobacteria	
	Avium-Intracellulare (MAI)	
	Tuberculosis	
	Other Mycobacteria specify	

Appendix 9 - Antibiotic Taxonomy

1	Acyclovir	35	Clofazimine	69	Nyastatin
2	Amantadine	36	Cloramphenicol	70	Ofloxacin
3	Amikacin	37	Cloxacillin	71	Olsetamivir
4	Aminosalicylic acid	38	Cycloserine	72	Oxacillin
5	Amoxicillin	39	Dicloxacillin	73	Penicillin
6	Amoxicillin/clavulinic acid	40	Dimenocycline	74	Pentamidine
7	Amphotericin B	41	Doxycycline	75	Pipercillin
8	Ampicillin	42	Ertapenem	76	Pipercillin/Tazobactem
9	Ampicillin/sulbactam	43	Erythromycin	77	Polimyxin B
10	Anti-HIV therapy-please name:	44	Ethambutal	78	Primaquin
11	Azithromycin	45	Ethionamide	79	Pyrazinamide
12	Aztreonam	46	Fluconazole	80	Quinopristin+ Dalfopristin
13	Bacitracin	47	Flucytosine	81	Ribavirin
14	Capreomycin	48	Foscarnet	82	Rifabutin
15	Carbenicillin	49	Ganciclovir	83	Rifampin
16	Caspofungin	50	Gatifloxacin	84	Rimantadine
17	Cefaclor	51	Gentamicin	85	Spectinomycin
18	Cefamandole	52	Imipenem/Cilastatin	86	Streptomycin
19	Ceftazidime	53	Isoniazid	87	Sulfadiazine
20	Cefazolin	54	Itraconazole	88	Sulfamethoxazole
21	Cefepime	55	Kanamycin	89	Sulfisoxazole
22	Cefixime	56	Ketoconazole	90	Teicoplanin
23	Cefoperazone	57	Levofloxacin	91	Tetracycline
24	Cefotaxime	58	Linezolid	92	Ticarcillin
25	Cefotetan	59	Meropenem	93	Ticarcillin/clavulinic acid
26	Cefoxitin	60	Metronidazole	94	Tobramycin
27	Cefprozil	61	Mezlocillin	95	Trimethoprim
28	Ceftriaxone	62	Minocycline	96	Trimethoprim-Sulfamethoxazole (Cotrimoxazole)
29	Cefuroxime	63	Moxyfloxacin	97	Trovofloxacin
30	Cephalexin	64	Nafcillin	98	Vancomycin
31	Cephalothin	65	Nalidixic Acid	99	Voriconazole
32	Ciprofloxacin	66	Netilmycin		
33	Clarithromycin	67	Nitrofurantoin		
34	Clindamycin	68	Norfloxacin		

Appendix 10.1 - Algorithm for ICU Acquired Infection Adjudication

To be determined by the Site Investigator after review of Infection Adjudication Form and patient's chart



* See Appendix 8.2 for categories and definitions of YES
** See appendix 8.3 for definitions of NO

Appendix 10.2
Categories of Infection

This document outlines the categories of infection that may be considered "outcomes" in a clinical trial. We have attempted to operationalize the definitions developed by the International Sepsis Forum Consensus Conference (CCM 2005;33:1538-1548) and in doing so, have made modifications to those definitions. Furthermore, given the uncertainty around the diagnosis of infection, we have consistently used the terminology, 'Definite'(a), 'Probable'(b), and 'Possible'(c) for each type of infection. The categories of infection are as follows:

Category 1	**Deep surgical wound infection**
Category 2	**Incisional (or superficial) surgical wound infection**
Category 3	**Skin and soft-tissue infection (non-surgical) (SSTS)**
Category 4	**Catheter-related blood stream infections (CRI)**
Category 5	**Primary blood stream infections (BSI)**
Category 6	**Lower urinary tract infection**
Category 7	**Upper urinary tract infection**
Category 8	**Intra abdominal infection**
Category 9	**Sinusitis**
Category 10	**Lower respiratory tract infection** (excluding pneumonia)
Category 11	**ICU Acquired Pneumonia**
Category 12	**Other**

Category 1

Deep surgical wound infection must meet the following criterion:

Infection occurs at operative site within 30 days after surgery if no implant is left in place or within 1 year if implant is in place **AND** infection appears related to surgery **AND** infection involves tissues or spaces at or beneath fascial layer or a deeper anatomical space opened during the surgical procedure. In all categories, signs and symptoms suggestive of surgical site infection must be present. These include wound erythema and blanching, tenderness, pain, purulent discharge, fever, and leukocytosis.

a) Definite Infection ☐

An abscess or other evidence of infection seen on direct examination, during surgery or by histopathologic examination.

OR

Organism isolated from culture of fluid obtained during open procedure or aspiration

b) Probable Infection ☐

Purulent drainage from drain placed beneath fascial layer (no microbial confirmation or Gram stain positive but negative culture).

c) Possible Infection ☐

Wound spontaneously dehisces or is deliberately opened by surgeon (no pus or microbial confirmation).

Comments:

_____

_____

_____

_____

Category 2

Incisional (or superficial) surgical wound infection must meet the following criterion:

Infection occurs at incision site within 30 days after surgery **AND** involves skin and subcutaneous tissue above the fascial layer. In all categories, signs and symptoms suggestive of surgical site infection must be present. These include wound erythema and blanching, tenderness, pain, purulent discharge, fever, and leukocytosis.

a) Definite Infection ☐

Organism(s) isolated from culture of fluid from wound closed primarily

b) Probable Infection ☐

Purulent drainage from incision or drain located above fascial layer (no microbial confirmation or Gram stain positive but no positive culture).

c) Possible Infection ☐

Surgeon deliberately opens wound

Comments:

_____

_____

_____

_____

Category 3

Skin and soft tissue infection (non-surgical) must meet the following criterion:

Infection occurs in skin or soft tissue structures (SSTS) NOT associated with surgical procedures.

a) Definite Infection ☐

Compelling clinical and laboratory evidence (such as spreading cutaneous erythema and blanching, or drainage or purulent material, with or without lymphangitis, in association with fever and leukocytosis) of the presence of SSTS infection based on clinical, radiographic, or surgical findings
AND
Organism isolated from culture from a skin lesion that has drained pus or from a skin aspirate or biopsy of subcutaneous tissues of an erythematous skin lesion (not a simple skin swab).

b) Probable Infection ☐

Compelling clinical and laboratory evidence (such as spreading cutaneous erythema and blanching, or drainage or purulent material, with or without lymphangitis, in association with fever and leukocytosis) or the presence of SSTS infection based on clinical, radiographic, or surgical findings
AND
No microbial confirmation or only positive Gram stain but negative culture.

c) Possible Infection

Some clinical evidence of infection, such as mild cutaneous erythema associated with fever, some laboratory evidence (leukocytosis), some radiographic but insufficient evidence to confirm a diagnosis.
AND ☐
No microbial confirmation

Comments:

_____

_____

_____

_____

Category 4

Catheter-related blood stream infections (CRI) must be associated with an indwelling central line/arterial line (usually placed more than 5-7 days ago) and have an organism isolated from the bloodstream that is not related to infection as some other site (lungs, GI tract, etc.). In addition, patients must have signs of sepsis (fever, chills, hypotension, etc.):

a) Definite Catheter-related Infection ☐

1. In association with a central line or arterial line, recognized pathogen (defined as a pathogen not usually regarded as a skin contaminant) isolated from one or more blood culture
AND
Catheter tip positive (>15 CFU/mL) or hub or exit site culture positive with the same organism

OR

2. In association with a central line or arterial line, a common skin contaminant[1] isolated from two or more blood cultures (at least one from a venipuncture)
AND
Catheter tip positive (>15 CFU/mL) or hub or exit site culture positive with the same organism

b) Probable Infection ☐

1. In association with a central line or arterial line, recognized pathogen (defined as a pathogen not usually regarded as a skin contaminant) isolated from one or more blood culture
OR

2. In association with a central line or arterial line, a common skin contaminant isolated from two or more blood cultures (at least one from a venipuncture)

c) Possible Infection ☐
One of the following: fever (core temp >38^{0}C), chills, or hypotension in association with a central line or arterial line (with or without a positive catheter tip (>15 CFU/ml) or positive hub or exit site positive)[2]
AND
Patient's clinical course improves with removal or change of the central line or arterial line and institution of appropriate antibiotic therapy.

Comments:
_____
_____
_____
_____

[1] Skin contaminants include diptheroids, Bacillus species, Propionibacterium, coagulase-negative Staphylococci, or micrococci)
[2] A positive catheter tip culture (>15 CFU/mL) or positive exit site culture without systemic symptoms and improvement with removal or change of the central/arterial line and institution of appropriate antibiotic therapy is not considered to be indicative of a central/arterial line infection.

Category 5

Primary blood stream infections (BSI) must NOT be associated with a indwelling vascular device or related to infection as some other site (lungs, GI tract, etc.). In addition, patients must have signs of sepsis (fever, chills, hypotension, etc.):

a) Definite Blood Stream Infection ☐

1. A recognized pathogen (defined as a pathogen not usually regarded as a skin contaminant) isolated from one or more blood culture
OR
2. A common skin contaminant[3] isolated from two or more blood cultures drawn on separate occasions (from venipunctures; must not be associated with a indwelling vascular device)

{there is no definition of 'probably infection' for this category}

c) Possible Infection ☐

A common skin contaminant isolated from a blood culture that does not fulfill the definition of 'Definite" BSI.
AND
Patients clinical course improves with institution of appropriate antibiotic therapy.

Comments:
_____
_____
_____
_____

[3] Skin contaminants include diptheroids, Bacillus species, Propionibacterium, coagulase-negative Staphylococci, or micrococci)

Category 6

Lower urinary tract infection (LUTI)

a) Definite
Symptoms (fever - core temp > 38^{o}C), hypotension) and Pyuria ($\geq$10 white blood cells {WBC}/ml
AND
a positive urine culture of $\geq 10^5$ colonies/ml urine with no more than two species of organisms
AND
No other sources of the patient's signs and symptoms are identified

b) Probable

Symptoms (fever - core temp > 38^{o}C), hypotension)
AND
A urine culture of $\geq 10^5$ colonies/ml urine with no more than two species of organisms

c) Possible*
A urine culture of $\geq 10^5$ colonies/ml urine with no more than two species of organisms

Comments:

_____

_____

_____

_____

* Candida isolated in the urine may be considered indicative of a possible UTI if the attending physician feels that it is significant and institutes management for it (either/both changes the catheter or institutes antifungal therapy)

Category 7

Upper Urinary Tract Infection includes infections of the urinary tract (kidney, ureter, bladder, urethra, or perinephric spaces).

☐

a) Definite:
Organism isolated from culture of fluid (other than urine) or tissue from affected site
OR
An abscess or other evidence of infection seen on direct examination, during surgery, or by histopathologic examination.

b) Probable ☐

Two of the following: fever (core temp >38^{0}C), urgency, localized pain, or tenderness at involved site

AND any of the following:

(a) Purulent drainage from affected site

(b) Positive Gram stain from fluid from affected site

(c) Organism isolated from urine or blood culture

(d) Radiographic evidence of infection

c) Possible ☐

Two of the following: fever (core temp >38^{0}C), localized pain, or tenderness at involved site

a. Physician's diagnosis

b. Physician institutes appropriate antimicrobial therapy and patient responds appropriately.

Comments:

_____

_____

_____

_____

Category 8

Intra abdominal infection includes gallbladder, bile ducts, liver [other than viral hepatitis], spleen, pancreas, peritoneum, subphrenic or subdiaphragmatic space, pelvis or other intra abdominal tissue or area not specified elsewhere, and must meet the following criteria:

a) Definite ☐

1. Organism(s) isolated from culture of purulent material from intra abdominal space/structure obtained during surgery or needle aspiration.

OR

2. Abscess or other evidence of intra abdominal infection (such as soilage of the peritoneal cavity after intestinal perforation) seen during surgery or by histopathologic examination.

OR

3. Pseudomembranous colitis- Direct visualization of pseudomembranes during sigmoidoscopy or on examination of surgically removed specimens of the colon.

b) Probable ☐

1. In the appropriate clinical setting, **organism isolated from blood culture** and:
   Radiographic evidence for intra-abdominal infection
   OR
   Clinical evidence of intra-abdominal infection (Abdominal Pain, Systemic leukocytosis, tenderness, jaundice)
   OR
   Laboratory evidence of intra-abdominal infection (inflammatory ascitic fluid i.e. > 500 PMN/ml, evidence of billiary obstruction, positive gram stain of fluid from abdominal cavity but negative cultures).

2. Organisms seen on Gram stain of drainage or tissue obtained during surgery or needle aspiration but cultures are negative.

3. Pseudomembranous colitis- Toxin isolated from the stool in the setting of clinical illness compatible with Pseudomembranous colitis (exposure to antibiotics, diarrhea, colonic dilation, toxic megacolon, etc.)

c) Possible: one of the following: ☐

1. Upper Gastro-intestinal perforation or penetrating abdominal trauma that is surgically repaired without further evidence of microbiologic confirmation or clinical signs or symptoms supportive of a diagnosis of bacterial or fungal peritonitis
2. Clinical evidence of intra-abdominal infection with an inflammatory peritoneal fluid (> 500 leucocytes/ml for primary peritonitis and >100 leukocytes/ml for peritoneal dialysis related peritonitis) in the absence of a positive culture (in peritoneal fluid or blood) or gram stain
3. Organism isolated from culture of drainage from surgically placed drain (e.g., closed suction drainage system, open drain or T-tube drain).
4. Clinical evidence of intra-abdominal infection with persistent signs of systemic inflammation but without clear documented evidence of persistent inflammation within the peritoneal space following secondary bacterial peritonitis.
5. Clinical evidence of intra-abdominal infection with signs of systemic inflammation which improves with the institution of systemic antibiotics (e.g. cholecystitis treated with antibiotics only)
6. Pseudomembranous colitis- Pseudomembranous colitis suspected on clinical grounds but toxin not sent or negative, colonoscopy not done and therapy instituted.

Comments:

_____

Category 9

Sinusitis

a) Definite ☐

Organism isolated from culture of purulent material directly obtained from sinus cavity by antral puncture.

b) Probable ☐

One of the following: fever (core temp >38^{0}C), pain or tenderness over the involved sinus, headache, purulent exudate, or nasal obstruction

AND

Radiographic evidence of infection

c) Possible ☐

Two of the following: fever (core temp >38^{0}C) or pain or tenderness over the involved sinus, headache

AND

purulent nasal exudate,

Comments:

_____

_____

_____

_____

Category 10

Lower respiratory tract infection (excluding pneumonia) includes infections such as bronchitis, tracheobronchitis, bronchiolitis, tracheitis, lung abscess, and empyema.

a) Definite: ☐

Organism seen on smear or isolated from culture of lung tissue or fluid, including pleural fluid.

b) Probable: ☐

1. Lung abscess or empyema seen during surgery or by histopathologic examination but no microbiological confirmation.

2. For bronchitis, tracheobronchitis, bronchiolitis, tracheitis, without evidence of pneumonia, must meet the following criterion:

Patient has no clinical or radiographic evidence of pneumonia but has fever (core temp >38 C) and increased sputum production

AND

Organism isolated from culture obtained by deep tracheal aspirate or bronchoscopy.

c) Possible ☐

Abscess cavity seen on radiographic examination of lung.

Comments:

_____

_____

_____

_____

Category 11

ICU-Acquired Pneumonia includes HAP and VAP. It must be associated with a clinical suspicion of pneumonia defined as new, progressive, or persistent infiltrates on CXR and be associated with signs and symptoms of infection (fever, leukocytosis, worsening oxygenation, purulent secretions, etc.).

a) Definite Pneumonia ☐

1. Radiographic evidence of pulmonary abscess and positive needle aspirate

OR

2. Histological proof on open lung biopsy or at post mortem (abscess formation, or consolidation with PMN accumulation).

b) Probable Pneumonia ☐

Must be associated with a positive culture of a pathogen known to cause pneumonia. For example, positive cultures for Coagulase Negative Staph. Species or normal oral flora would not be considered as positive since they do not usually cause VAP/HAP. The positive cultures need to come from 1 of the following:

1. A sputum or an endotracheal aspirate specimen.
2. A culture of bronchial washings, BAL or PSB regardless of quantitation (if done).
3. A blood culture of an organism found within 48 hours of the clinical suspicion of VAP/HAP.
4. A positive pleural fluid culture.

c) Possible Pneumonia ☐

No microbial confirmation in the setting of a clinical suspicion for pneumonia as described above, and a clinical course compatible with VAP/HAP including the institution of appropriate antimicrobial therapy.

Comments:

_____

_____

_____

Category 12

If the patient developed an infection which does not fall into any of the previous categories. Please describe below.

a) Definite ☐

Clinical evidence of infection and one of the following:

The culture of an organism(s) or positive Gram stain or positive viral cultures from a normally sterile bodily fluid or tissue in the absence of previous surgical intervention (e.g. organism isolated from CSF or synovial fluid).

OR

Positive antigen/RNA/DNA test for pathogens from a normally sterile bodily fluid

OR

Positive viral/bacterial serology.

b) Probable ☐

Clinical evidence of infection and of one the following:

The culture of a pathogenic organism(s) or positive Gram stain positive or positive viral culture from a body site that is not normally sterile or a specimen obtained from an indwelling drain or catheter placed into a normally sterile body site (e.g. intra-abd. drain)

OR

Positive antigen/RNA/DNA test for pathogens from a body site that is not normally sterile.

c) Possible ☐

Clinical evidence of infection but no microbiologic, smear or serological confirmation of infection

Please describe infection:

_____

_____

_____

_____

Appendix 10.3 - Definitions of "No" Newly acquired ICU infection

If **"No"** to infection, choose either one, Probable No or Possible No

Probable No:

With greater certainty, the Investigator feels the patient is NOT infected. Clinical story is clearly consistent with no infection supported by lack of physiologic response (SIRS), or no positive cultures, or no treatment with antibiotics (short-term prophylaxis OK), and patient gets better.

Examples:

1) Patient with ischemic heart disease (IHD) admitted to ICU in cardiogenic shock. No positive cultures, no treatment with antibiotics, and patient gets better. Even if the patient dies, if there is no suggestion of infection or no treatment with antibiotics, the patient could still be "probably not infected".
2) Patient with multiple traumas admitted to ICU on ventilator. Has SIRS for 24-48 hours (probably related to trauma), no organ dysfunction, no positive cultures, only short-term antibiotic prophylaxis, and gets better in a few days.
3) Clear cut cases related to "colonization" or "contamination" should be categorized here (i.e., cultures that are positive secondary to organisms likely to reflect contamination or colonization that get better with no treatment).

Possible No:

Investigator believes the patient is not infected but with some degree of uncertainty. Investigator cannot comfortably rule out infection but thinks it is not likely. Patient may manifest SIRS and organ dysfunction secondary to some other process but was treated with antibiotics.

Examples:

1) Patient admitted to ICU with severe necrotizing pancreatitis. Patient had SIRS and MODS and is treated with antibiotics from the beginning despite the lack of positive cultures. (prophylaxis for secondary pancreatitic complications).
2) Patient with ischemic heart disease admitted to ICU in cardiogenic shock. CXR shows a bilateral process compatible with pulmonary edema. Patient receives treatment of IHD and cardiogenic shock and seems to improve. On Study Day 1 while in ICU, patient spikes a fever and is started on antibiotics. No positive cultures, but patient gets better.

Appendix 11 - SF-36 v2 Script

SCRIPT FOR INTERVIEW ADMINISTRATION

These first questions are about your health now and your current daily activities.

Please try to answer every question as accurately as you can.

1. **In general, would you say your health is . . .** *[READ RESPONSE CHOICES]*
(Circle one number)

Excellent 1
Very good 2
Good 3
Fair 4
Poor? 5

2. **Compared to one year ago, how would you rate your health in general now? Would you say it is . . .** *[READ RESPONSE CHOICES]*
(Circle one number)

Much better now than one year ago 1
Somewhat better now than one year ago 2
About the same as one year ago 3
Somewhat worse now than one year ago 4
Much worse now than one year ago? 5

Now I'm going to read a list of activities that you might do during a typical day. As I read each item, please tell me if your health now limits you a lot, limits you a little, or does not limit you at all in these activities.

3a. **First, vigorous activities, such as running, lifting heavy objects, participating in strenuous sports. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Circle one number)

Yes, limited a lot 1
Yes, limited a little 2
No, not limited at all 3

3b. **. . . moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. Does your health now limit you a lot, limit you a little, or not limit yo at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?] (Circle one number)

Yes, limited a lot 1
Yes, limited a little 2
No, not limited at all 3

3c. **. . . lifting or carrying groceries. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?] (Circle one number)

Yes, limited a lot 1
Yes, limited a little 2
No, not limited at all 3

3d. **. . . climbing several flights of stairs. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?] (Circle one number)

Yes, limited a lot 1
Yes, limited a little 2
No, not limited at all 3

3e. **. . . climbing one flight of stairs. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?] (Circle one number)

Yes, limited a lot 1
Yes, limited a little 2
No, not limited at all 3

3f. **. . . bending, kneeling, or stooping. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Circle one number)

Yes, limited a lot 1

Yes, limited a little 2

No, not limited at all 3

3g. **. . . walking more than a mile. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Circle one number)

Yes, limited a lot 1

Yes, limited a little 2

No, not limited at all 3

3h. **. . . walking several hundred yards. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Circle one number)

Yes, limited a lot 1

Yes, limited a little 2

No, not limited at all 3

3i. **. . . walking one hundred yards. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Circle one number)

Yes, limited a lot 1

Yes, limited a little 2

No, not limited at all 3

3j. **. . . bathing or dressing yourself. Does your health now limit you a lot, limit you a little, or not limit you at all?** *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]

(Circle one number)

Yes, limited a lot 1

Yes, limited a little 2

No, not limited at all 3

The following four questions ask you about your physical health and your daily activities.

4a. **During the past four weeks, how much of the time have you had to cut down on the amount of time you spent on work or other daily activities as a result of your physical health?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

or None of the time? 5

4b. **During the past four weeks, how much of the time have you accomplished less than you would like as a result of your physical health?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

or None of the time? 5

4c. **During the past four weeks, how much of the time were you limited in the kind of work or other regular daily activities you do as a result of your physical health?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

or None of the time? 5

4d. **During the past four weeks, how much of the time have you had difficulty performing work or other regular daily activities as a result of your physical health, for example, it took extra effort?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

or None of the time? 5

The following three questions ask about your emotions and your daily activities.

5a. **During the past four weeks, how much of the time have you had to cut down the amount of time you spent on work or regular daily activities as a result of any emotional problems, such as feeling depressed or anxious?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

or None of the time? 5

5b. **During the past four weeks, how much of the time have you accomplished less than you would like as a result of any emotional problems, such as feeling depressed or anxious?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

or None of the time? 5

5c. **During the past four weeks, how much of the time did you do work or other regular daily activities less carefully than usual as a result of any emotional problems, such as feeling depressed or anxious?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
or None of the time? 5

6. **During the past four weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? Has it interfered . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Not at all 1
Slightly 2
Moderately 3
Quite a bit 4
or Extremely? 5

7. **How much bodily pain have you had during the past four weeks? Have you had . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

None 1
Very mild 2
Mild 3
Moderate 4
Severe 5
or Very severe? 6

8. **During the past four weeks, how much did pain interfere with your normal work, including both work outside the home and housework? Did it interfere . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Not at all 1
A little bit 2
Moderately 3
Quite a bit 4
or Extremely? 5

The next questions are about how you feel and how things have been with you during the past four weeks.

As I read each statement, please give me the one answer that comes closest to the way you have been feeling; is it all of the time, most of the time, some of the time, a little of the time, or none of the time?

9a. **How much of the time during the past four weeks . . . did you feel full of life?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
None of the time 5

9b. **How much of the time during the past four weeks . . . have you been very nervous?** *[READ RESPONSE CHOICES]*

(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
None of the time 5

9c. **How much of the time during the past four weeks . . . have you felt so down in the dumps that nothing could cheer you up?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
None of the time 5

9d. **How much of the time during the past four weeks . . . have you felt calm and peaceful?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4

None of the time 5

9e. **How much of the time during the past four weeks . . . did you have a lot of energy?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

None of the time 5

9f. **How much of the time during the past four weeks . . . have you felt downhearted and depressed?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

None of the time 5

9g. **How much of the time during the past four weeks . . . did you feel worn out?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

None of the time 5

9h. **How much of the time during the past four weeks . . . have you been happy?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

(Circle one number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

None of the time 5

9i. **How much of the time during the past four weeks . . . did you feel tired?** *[READ RESPONSE CHOICES ONLY IF NECESSARY]*
(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
None of the time 5

These next questions are about your health and health-related matters.

Now, I'm going to read a list of statements. After each one, please tell me if it is definitely true, mostly true, mostly false, or definitely false. If you don't know, just tell me.

10. **During the past four weeks, how much of the time has your physical health or emotional problems interfered with your social activities like visiting with friends or relatives? Has it interfered . . .** *[READ RESPONSE CHOICES]*
(Circle one number)

All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
or None of the time? 5

11a. **I seem to get sick a little easier than other people. Would you say that's . . .** *[READ RESPONSE CHOICES]*
(Circle one number)

Definitely true 1
Mostly true 2
Don't know 3
Mostly false 4
Definitely false? 5

11b. **I am as healthy as anybody I know. Would you say that's . . .** *[READ RESPONSE CHOICES]*
(Circle one number)

Definitely true 1
Mostly true 2
Don't know 3
Mostly false 4
Definitely false? 5

11c. **I expect my health to get worse. Would you say that's . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Definitely true 1
Mostly true 2
Don't know 3
Mostly false 4
Definitely false? 5

11d. **My health is excellent. Would you say that's . . .** *[READ RESPONSE CHOICES]*

(Circle one number)

Definitely true 1
Mostly true 2
Don't know 3
Mostly false 4
Definitely false? 5

Appendix 12
Investigator's Confirmation

Site ____ Site Name

Enrolment # _____
Enrollment Date:

The *REDOXS*© Study
REducing Deaths due to OXidative Stress

Investigator's Confirmation

The electronic data collection was conducted under my supervision according to the protocol during the entire study.

The data and statements, including ICU acquired infection adjudication are complete and accurate to the best of my knowledge.

_____
Full Name of Investigator

_____ | | | | __ __: ___ __
Signature of the Investigator **dd** **mmm** **yyyy** **24 hr clock**

Please fax signed form to REDOXS© Project Leader at 613-548-2428 **AS SOON AS POSSIBLE**