



Work Instruction

WI No.: REDOXS- 204-01

Title: Review of Informed Consent Forms

Referenced SOP: Development and Administration of Informed Consent # 204-00

Author: Rupinder Dhaliwal, Project Leader **Signature:** _____ **Date:** _____

Intended Audience: Methods Centre, Research Sites

Procedures

The purpose of this work instruction is to ensure that the informed consent forms (ICF)s used for the REDOXS study are accurate and comply with the ICH, GCP section 4.8.10

1. The Methods Centre will develop a written ICF template according to the REDOXS study protocol that will contain the essential elements of GCP 4.8.10 (see appendix 1). An electronic version of the template will be filed under the Q drive>REDOXS>START UP>CONSENT. A French version of the template will also be filed here.
2. The ICF template will be forwarded to Health Canada along with the Clinical Trial Application or amendment as needed.
3. The Project Leader/delegate will send an electronic version of a consent template to the research coordinator (RC) at the participating site.
4. The research site will adapt the ICF template to meet the requirements of their local Research Ethics Board (REB).
5. The research site will provide the locally adapted ICF to the Project Leader/delegate for review prior to submission to their REB.
6. The Project Leader/delegate will review the site specific ICF to ensure the following:
 - a. accuracy
 - b. all essential elements of ICH, GCP section 4.8.10 are included
7. The Project Leader/delegate will document the review of the ICF by completing the ICF checklist (see appendix 2).
8. If changes to the ICF are needed, the Project Leader/delegate will inform the research site of the changes by sending the tracked version of the ICF/email and the completed ICF checklist.
9. If no changes to the ICF are needed, the completed ICF checklist will be sent to the research site.
10. The research site will submit the ICF reviewed by the Project Leader/delegate to their REB for review and approval. They may also choose to submit the completed ICF checklist.



11. If the local REB requests changes to the ICF, the research site will inform the Project Leader/delegate who will then review the revised ICF before the re-submission to the REB. Steps 7-11 may need to be repeated as needed.
12. In the event that a site does NOT submit their ICF to the Project Leader/delegate before approval by the local REB, the Project Leader/delegate will review the approved ICF upon receipt from the research site. The Project Leader/delegate will inform the research site of essential elements that are missing and will advise the site to make the necessary changes to the ICF and re-submit to their REB.
13. All documentation with the site will be filed by the Project Leader/delegate under the "REB communication" section of the CERU Site Binder. The approved ICF will be filed under the "REB approval" section of the CERU Site Binder.
14. The Project Leader/delegate will request a copy of the approved version of the ICF from the research site. This must be received before the site starts recruitment and will be filed under the REB approval section of the CERU Site Binder.
15. In the event that ICFs are in any language other than English or French, the research site will be asked for a version that has been translated into English or French along with proof of translation by an authorized individual.
16. During Site Monitoring visits, the Project Leader/delegate will ensure that the correct version of the approved consent form is used for enrolled study participants and is present in the study files at the site.



Appendix 1. Template of Informed Consent

The REDOX[®] Study
A Randomized Trial of Glutamine and
Antioxidant Supplementation in Critically ill Patients

Dr. <<insert name here>>
<<insert hospital address here>>

Substitute Decision Maker Information and Consent Form

You _____ are invited to consider allowing the voluntary participation of your family member in a research (essential element a) study of nutritional supplementation in critically ill patients. The supplements consist of Glutamine and antioxidants. The purpose and nature of these supplements will be explained in further detail later on. You are being asked to give consent because your family member is critically ill and cannot personally consent.

In order to decide whether you wish your family member to participate in this research study you should understand the risks and benefits in order to be able to make an informed decision. This process is known as informed consent. This consent form provides detailed information about the research study. The doctor or a member of the study staff will discuss the study with you. Once you understand the study, you will be asked to sign this form if you wish to allow your family member to participate in this study. You will be given a signed copy of the consent to keep as a record.

This study is to be conducted at multiple centers in Canada and is supported by the Canadian Critical Care Trials Group. Dr. <<insert name here>> will be supervising this study at the <<insert name of hospital here>>

Fresenius Kabi makes the Glutamine and antioxidant supplements that will be used in this study. These supplements are not currently registered or for sale in the Canadian Market. This study is funded by the Canadian Institutes for Health Research and Fresenius-Kabi provides the study supplements.



Description/Purpose of the Study

The relationship between nutrient deficiency and impaired function of the immune system has been recognised for years. Critically ill patients often have conditions that will create or worsen a nutrient deficiency and therefore weaken their immune system's ability to prevent or fight infections. This may also lead to a worsening of the function of organs and ultimately cause death.

There have been many studies conducted over the last few decades that have tested various nutrients in order to determine if there was an improvement in the immune system's ability to fight infection, and/or improve patient outcome in general. None of these studies have been conclusive and nutrient supplementation is not done routinely in the ICU. Reviews of these studies are suggestive but not conclusive that the provision of Glutamine and antioxidants to critically ill patients will result in an improvement in survival.

Glutamine is one of the building blocks for proteins and it plays an important role in the body's essential metabolic functions. Normally, our bodies produce large amounts of glutamine, however, studies have shown that glutamine is depleted after major surgery and during critical illness. Lower levels of Glutamine appear to alter the effectiveness of our immune system.

Antioxidants, in the form of trace elements (minerals present in small quantities) and vitamins are naturally occurring substances that the human body needs to overcome serious illness. Again, during critical illness, the levels of these nutrients are very low in the body and current scientific evidence suggests that by replacing these trace elements and vitamins, we may help the body deal with the stress of critical illness.

The purpose ^(essential element b) of this study is to find out if giving Glutamine and antioxidant supplements to critically ill patients will improve their chances of survival.

Study Procedures and Duration ^(essential element d)

Patients who enter this study will be divided into four groups as listed below. Each group will receive standard ICU care plus nutrient supplementation or placebo. Your family member will be assigned to one of the four experimental ^(essential element e) treatment groups listed below by a random selection process (*like flipping a coin*) ^(essential element c)

Group A. Standard ICU care plus both Glutamine and Antioxidant therapy, simultaneously given through an intravenous and through a feeding tube into the stomach.

Group B. Standard ICU care plus Glutamine given through an intravenous and Glutamine therapy given through a feeding tube into the stomach.

Group C. Standard ICU care plus Antioxidant therapy given through an intravenous and Antioxidant therapy given through a feeding tube into the stomach.

Group D. Standard ICU care plus a Placebo given through an intravenous and through a feeding tube into the stomach.



The dose of Glutamine provided intravenously will be 0.35 gm/kg/day and the amount given through a feeding tube dose will be 30 grams. The intravenous dose of antioxidant will be Selenium 500 ug; the antioxidants given through a feeding tube will consist of Selenium 300ug, Zinc 20mg, Beta Carotene 10mg, Vitamin E 500mg, and Vitamin C 1500mg.

The intravenous supplements will be given as a continuous infusion for a minimum of 5 days even if your family member has been transferred out of the intensive care unit. While in the intensive care unit your family member will receive the intravenous supplements up to a maximum of 28 days. (essential element s)

The supplements given through a feeding tube as a continuous infusion will continue for a minimum of 5 days even if your family member has been transferred out of the intensive care unit. While in the intensive care unit your family member will receive these supplements up to a maximum of 28 days or until nutritional support is discontinued, if this occurs before day 28. (essential element s)

This is a blinded study, which means that, neither yourself, your family member and medical staff will not know what treatment group your family member has been assigned to. This blinding procedure is necessary to assess the true effects of glutamine and the antioxidants. Placebo is made up of material that does not have any effect, but looks exactly like the nutrients/antioxidant therapy. The bedside nurse and research nurse will monitor your family member closely while they are receiving the study supplements. There will be no other study procedures performed.

At 3 months and 6 months from the time of ICU admission, your family member will be contacted by a member of the research team to conduct a quality of life questionnaire, either in person if still admitted to the hospital or by telephone. (essential element e,s)

There will be 1200 patients (essential element t) from approximately 30 sites in Canada and other countries participating in this study.

Risks and Benefits Associated with the Study

There is strong but not conclusive evidence to suggest that these supplements will reduce the development of infections, reduce length of hospital stay, improve overall organ function, and improve chances of survival. (essential element h)

The Glutamine and antioxidant supplements provided in this study are generally regarded as safe for use in critically ill patients. There are no known serious adverse events or risks related the administration of these supplements given through an intravenous or feeding tube. As with any study, there may be other risks or side effects that we do not know about, however your family member will be monitored closely during administration of these supplements. (essential element g)

A feeding tube and intravenous catheters are routinely placed as part of care in the ICU. The Glutamine and antioxidants will be delivered through these.



The study nutrients/antioxidants have not been tested in pregnant women or children therefore your family member may not take part in this research study if she is pregnant or is breast-feeding a child. As with any study drug, there may be other risks or side effects that we do not know about (essential element g). You will be informed in a timely manner of any information that becomes available relevant to your family member's willingness to continue participation (essential element p).

Alternative Therapy (essential element i)

You may decide not to allow your family member to participate in this study. Your family member will continue to receive the best medical therapy, without prejudice, whether or not you choose for him or her to take part in this study. These nutrients are not routinely administered or available outside of clinical studies in Canada and will not be made available to your family member if they do not participate in the study. If you are a First Nations person, or an indigenous person who has contact with spiritual "elders" you may want to talk with them before you proceed with being part of this study.

Voluntary Participation (essential element m)

Participation in this study is entirely voluntary. You are free at any time to stop your family member's involvement in the study. This will not affect your family member's medical care in any way. If you decide to withdraw your family member from this study, we request that you contact Dr. <<insert name here>> at <<insert phone number here>> or one of the research nurses at <<insert phone number here>>.

Stopping the Study

Dr. << insert name here>> or Fresenius-Kabi may stop this study, or your family member's participation in this study at any time without your or your family member's consent. Usually this happens if in the judgment of the investigator, the benefits of continuing on in the study are outweighed by the risks either secondary to a possible reaction that your family member has had or that new information has become available as to the safety and effectiveness of the nutrients and antioxidants (essential element m).

Payments and Costs

Your family member will not receive any compensation, royalty, or other financial benefits for being in this study or as a result of products developed from data obtained from research conducted under this study (essential element k). Neither you nor your family member will incur any additional costs as the result of participating in this study (essential element L).



Treatment and Compensation for Injury

In the event that your family member is injured as a result of taking study medication or the study procedures, medical care will be provided to him/her until resolution of the problem (essential element j). By signing this consent form, you do not waive your family member's legal rights nor release the investigator(s) and sponsors from their legal and professional responsibilities

Questions

If you have any questions concerning this study, contact Dr. <<insert name here>> at <<insert phone number here>>. If you think your family member may have experienced a research-related injury, and if you have any questions concerning the availability of medical care, contact Dr. <<insert name here>> at <<insert phone number here>> or Dr. <<insert name here>>, the Head of the Department of Medicine, at <<insert phone number here>> (essential element q). If you have any questions about your family member's rights as a research subject, you may call <<insert name here>>, the chair of the Research Ethics Board at <<insert phone number here>> (essential element q).

Permission for Review of Records/Confidentiality

Your family member's medical information will be kept confidential by the study doctor and staff and will not be made publicly available unless disclosure is required by law.

Data obtained from this study that does not identify your family member individually will be given to the sponsor and/or its representatives and may be published or given to regulatory authorities in the United States, Canada or other countries (essential element o).

Your family member's original medical records may be reviewed by the sponsor and/or its representatives, the Ethical Review Board for this study, and regulatory authorities for the purpose of verifying clinical trial procedures and/or data. His/her medical information may be held and processed on a computer. By signing this consent form, you authorize the record review, information storage and data transfer described above (essential element n).



To allow your family member to participate in this study, you must sign this page. By signing this page, you are confirming the following:

- You have read and understood all of the information in this Substitute Decision-maker Information and Consent Form, and you have had time to think about it.
- All of your questions have been answered to your satisfaction. If you did not understand any of the words, you asked the study doctor or a staff member to explain them to you.
- You voluntarily agree to allow your family member to be part of this research study, to follow the study procedures, and to provide necessary information to the doctor, nurses, or other staff members, as requested.
- You understand that you may freely choose to withdraw your family member from this study at any time.
- You have received a signed copy of this Substitute Decision-maker Information and Consent Form to keep for yourself.

Subject/Patient Name (Print or Type)

Patient Initials and
Number

Signature of [Subject/Patient] or Legal Representative

Date and Time

Name of Individual Conducting Informed Consent
Discussion

Signature of Individual Conducting Informed Consent
Discussion

Date and Time

I, or one of my colleagues, have carefully explained to the subject, the nature of the above research study. I certify that to the best of my knowledge, the subject understands clearly the nature of the study and demands, benefits and risks involved in participating in this study.

Signature of Investigator (if investigator did not sign above)

Date/Time



Informed Consent Form (ICF) Essential Elements Checklist

Site: _____

ICF version being reviewed: _____

Reviewer: _____

Date reviewed: _____

As per ICH: Good Clinical Practices section 4.8.10, the following essential elements are required to be incorporated into the Informed Consent Form for the REDOXSM Study.

GCP Reference (4.8.10)	Essential Element	Location (ICF pg #)
a	The trial involves research	
b	The purpose of the trial	
c	The trial treatment and the probability of for random assignment to each treatment	
d	Description of all study procedures (including invasive procedures)	
e	The patient's responsibilities	
f	The aspects of the trial that are experimental	
g	Reasonably foreseeable risks and inconveniences to the patient	
h	Reasonably expected benefits. When there is no intended clinical benefit to the patient, the patient is made aware of this.	
i	Alternative treatments and procedures available to the patient, including any potential benefits or risks.	
j	Compensation and/or treatment available to the patient in the event of a trial related injury	
k	Any anticipated payment or compensation for participation in the trial.	
l	Any anticipated expenses to the patient for participation in the trial	
m	The patient's participation in the study is completely voluntary. The patient may refuse to participate or withdraw from the trial at any time, without any loss of benefits to which the patient is otherwise entitled.	
n	Monitors, auditors, REBs, regulators may be granted direct access to the subject's original medical records for verification of clinical trial procedures/data without violating the confidentiality of the patient, to the extent permitted by the applicable laws. Signing the consent form is authorizing such access.	
o	Records identifying the patient will be kept confidential. Any publications resulting from this trial will not reveal the patient's identity, confidentiality will be maintained.	
p	The patient will be informed in a timely manner of any information that becomes available relevant to the patient's willingness to continue participation.	
q	The person to contact regarding patient rights and in the event of a trial related injury (usually REB chair)	
r	Foreseeable circumstances in which the patient's participation in the trial may be terminated.	
s	The expected duration of the patient's participation in the trial	
t	The approximate number of patients involved in the trial.	

Complete this checklist every time the ICF for your site is updated.

File this checklist with the ICF documentation in your site Regulatory Binder.

This checklist can be forwarded to the REB along with the ICF to ease review.

Reviewer Signature: _____

Date: _____