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# Work Instruction

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WI No.: REDOX- 302-R02

Title: Serious Adverse Events Reporting: Research Sites

Referenced SOP: Serious Adverse Event Recognition and Reporting # 302-00

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Intended Audience: Participating Research Sites

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## Procedures

The purpose of this work instruction is to describe the process for identifying and processing serious adverse events reported for the REDOX<sup>®</sup> study.

Since the patient population in the REDOX<sup>®</sup> study is strictly critically ill patients with organ failures that have a high baseline mortality and given the complex nature and the diversified progress of the underlying critical illness, adverse events and adverse drug reactions attributed to the underlying clinical condition do not need to be reported to the Methods Centre (MC). Serious adverse events must be reported if they meet the following criteria.

For the Serious Adverse Event to be reported to the MC for the REDOX<sup>®</sup> study, the event has to meet both the following criteria i.e. it must be both **Serious and Unexpected**.

A **Serious Adverse Event** is any untoward medical occurrence that at any dose:

- Results in death
- Is life threatening
- Requires or prolongs in-patient hospitalization
- Results in persistent or significant disability/incapacity
- May require medical or surgical intervention to prevent one of the other outcomes serious outcomes listed above

An **Unexpected Serious Adverse Event** is one, the nature or severity of which is not consistent with information in the Investigators' Brochure/Product Monograph AND fits the above definition of serious. Since there are no known expected serious adverse events in the investigator's brochure/product monograph for the REDOX investigational products, an unexpected SAE can be defined as any adverse event not attributed to the progression of the underlying disease or co-morbid illnesses.

- (1) All Serious Adverse Events that are unexpected must be reported by the research site to the MC within 48 hrs of becoming aware of the, or as soon as possible.
- (2) The site is to do this by filling out the Serious Adverse Events Report (Initial) and faxing this to the Project Leader at 1-613-548-2428. (Appendix 1).
- (3) The Final Report (Appendix 2) must be completed by the site and faxed to Project Leader at whatever time occurs first:
  - end of study period day 30 (from admission to ICU)



- time of ICU d/c
- time of ICU death
- within 10 days from becoming aware of the event *if the event is fatal or life-threatening*

(4) The SAE Report Form will contain, at a minimum, the following fields:

- Study Name
- Participant ID (enrolment number, DOB, gender)
- Name of event being reported
- Seriousness and unexpectedness of event
- Date/time of onset
- Relationship to investigational product
- Treatment for the event
- Cause attributed to the event
- Outcome

(5) If applicable, the research site will also report the SAE to their local Research Ethics Board (REB) using established forms and policies at the local institution.

(6) All SAEs must have an assessment concerning the relationship to investigational product.

Definitions will be split into four groups: not related, unlikely related, possibly related and probably related. Since the products are nutrients, there are no known events that are related. The relationship of the events to the products is based on the judgment of the Qualified Investigator. In the absence of a relationship to investigational product determination, or if there is any doubt concerning the relationship assessment, the relationship should be considered "possibly related" to the investigational product.

(7) The Project Leader will report all serious and unexpected adverse events that are considered to be *possibly or probably related to the study supplements* to Health Canada and Fresenius Kabi, according to the established time frames and procedures specified.

(8) The Project Leader will compile a SAE Summary Report of all the reported SAEs and forward this to the sites at established intervals established by the MC.

(9) The participating sites will be asked to submit the SAE Summary Report to their REB and other regulatory bodies as necessary, and to fax a copy of their REB submission or acknowledgement to the Project Leader as proof of submission.

(10) Refer to SAE Reporting Algorithm (Appendix 3).

Appendix 1  
Serious Adverse Events Report (Initial)

<b>The REDOX<sup>®</sup> Study</b> <b>Initial Report</b> Complete and fax to CERU at 613-548-2428 attention: Project Leader REDOX <sup>®</sup> within 48 hrs of becoming aware of event.		<b>Serious Adverse Events (SAE) Report</b>		Page 1 of 2	
Complete one form for EVERY adverse event that is <i>Serious and Unexpected</i> . Report only those SAEs that occur from the time of randomization to the end of the study period (30 days from admission to ICU or until ICU d/c or death, whatever occurs first).					
<b>Patient Identification</b> Site # _____ Enrollment # _____ Initials _____ DOB _____ / _____ / _____ dd    mmm    yr  <input type="checkbox"/> Male <input type="checkbox"/> Female		<b>Name of Site Investigator</b>   <b>Person reporting SAE</b>		<b>SAE #</b> _____  <small>Record the sequential SAE # for this patient i.e.          For 1<sup>st</sup> SAE for this patient, write 01          For 2<sup>nd</sup> SAE for this patient, write 02</small>	
				<b>Date SAE reported</b> _____ / _____ / _____ dd    mmm    yr  <b>Date became aware of SAE</b> _____ / _____ / _____ dd    mmm    yr	
<b>Serious Adverse Event Reported (only one per form)</b>					
<b>Seriousness (select all that apply)</b> <input type="checkbox"/> Patient died → please document date in Outcomes <input type="checkbox"/> Life threatening <input type="checkbox"/> Requires or prolongs hospitalization <input type="checkbox"/> Results in persistent or significant disability/incapacity <input type="checkbox"/> May require medical or surgical intervention to prevent one of the other outcomes to defining serious			<b>Outcomes (at time of initial report)</b> <input type="checkbox"/> Complete recovery/return to baseline → Date of recovery dd ___ / mmm ___ / yr ___ <input type="checkbox"/> Alive with sequelae <input type="checkbox"/> Death → death date dd ___ / mmm ___ / yr ___ <input type="checkbox"/> SAE persisting <input type="checkbox"/> Unknown/lost to follow-up		
<b>Onset of SAE</b>  _____ / _____ / _____ dd    mmm    yr		<b>Admission to ICU</b>  _____ / _____ / _____ dd    mmm    yr		<b>Start of Study Supplements</b>  _____ / _____ / _____ dd    mmm    yr	
<b>Resolution of SAE</b>  _____ / _____ / _____ dd    mmm    yr		<b>Signature of Principal Investigator</b>  _____  <b>Date</b> _____ / _____ / _____ dd    mmm    yr			
<b>Action Taken</b> <input type="checkbox"/> None <input type="checkbox"/> Uncertain <input type="checkbox"/> Procedure or physical therapy <input type="checkbox"/> Blood or blood products <input type="checkbox"/> Prescription drug therapy <input type="checkbox"/> Non-prescription drug therapy <input type="checkbox"/> Hospitalization <input type="checkbox"/> IV fluids <input type="checkbox"/> Other , specify _____ _____		<b>Action taken with Study Supplements</b> <input type="checkbox"/> None (including not on study supplements) <input type="checkbox"/> Dose reduced, interrupted or therapy delayed <input type="checkbox"/> Study supplements stopped permanently due to SAE		<b>Relationship of SAE to Study Supplements</b> <input type="checkbox"/> Not related <input type="checkbox"/> Unlikely related <input type="checkbox"/> Possibly related <input type="checkbox"/> Probably related	
<b>Follow up with a Final Report (on page 2) within specified timelines.</b>					

Appendix 2  
Serious Adverse Events Report (Final)

<b>The REDOX<sup>®</sup> Study</b>		<b>Serious Adverse Events (SAE) Report</b>		page 2 of 2
<b>Final Report</b> Complete and fax to CERU at 613-548-2428 attention: Project Leader REDOX <sup>®</sup> at day 30, ICU d/c, death or within 10 days from becoming aware of SAE, whatever occurs first. To be completed by Site Investigator for EVERY Initial SAE that was reported to CERU.				
<b>Patient ID</b> Site # _____ Enrollment # _____ Initials _____  SAE # (from Initial Report) _____	<b>Past medical history, comorbid illnesses and reason for admission to hospital</b>	<b>Admitting diagnosis to ICU and chronological events leading to SAE</b>	<b>Chronological events preceding SAE until discharge from ICU (or day 30 or within 10 days of becoming aware of the event, whatever occurs first)</b>	
<b>Confirmation of Unexpected nature of SAE (not due to the progression of underlying disease)</b>	<b>Relationship of SAE to Study supplements vs. progression of underlying illness (based on timing of supplements, SAE)</b>		<b>Outcomes (at time of final report)</b> <input type="checkbox"/> Complete recovery/return to baseline → Date of recovery dd ___/ mmm ___/yr ___ <input type="checkbox"/> Alive with sequelae <input type="checkbox"/> Death → death date dd ___/ mmm ___/yr ___ <input type="checkbox"/> SAE persisting <input type="checkbox"/> Unknown/lost to follow-up	
<b>Action Taken</b> <input type="checkbox"/> None <input type="checkbox"/> Uncertain <input type="checkbox"/> Procedure or physical therapy <input type="checkbox"/> Blood or blood products <input type="checkbox"/> Prescription drug therapy <input type="checkbox"/> Non-prescription drug therapy <input type="checkbox"/> Hospitalization <input type="checkbox"/> IV fluids <input type="checkbox"/> Other , specify _____	<b>Action taken with Study Supplements</b> <input type="checkbox"/> None (including not on study supplements) <input type="checkbox"/> Dose reduced, interrupted or therapy delayed <input type="checkbox"/> Study supplements stopped permanently due to SAE	<b>Summary</b>	<b>Signature of Site Investigator</b> _____	
	<b>Relationship of SAE to Study Supplements</b> <input type="checkbox"/> Not related <input type="checkbox"/> Possibly related <input type="checkbox"/> Probably related <input type="checkbox"/> Unlikely related	<b>Date</b> _____ / _____ / _____ dd      mmm      yy		

Appendix 3  
SAE Reporting Algorithm

**SAE Reporting Algorithm**

\*Serious if:

- Results in death
- Is life threatening
- Requires or prolongs in-patient hospitalization
- Results in persistent or significant disability/incapacity
- May require medical or surgical intervention to prevent one of the other outcomes to defining serious

\*\* Unexpected if:  
not expected due to the progression of the underlying disease or co-morbid illnesses.

