FROZEN AND DEGLYCEROLIZED RED BLOOD CELLS

Original Release/Approval		25 Jun 2008	Note: This CPG requires an annual review.
Reviewed:	Mar 2014	Approved for PACOM	DEC 2014
Supersedes:	N/A		
☐ Minor Changes ***(or)***		☒ Changes are substantial and require a thorough reading of this CPG ***(or)***	
☐ Significant Changes		No restrictions on number of units of DRBC transfused in 24 hr period, including use in MT; PI monitoring plan added	

1. **Goal.** To provide guidance for the use of frozen and deglycerolized red blood cells (DRBCs) in the combat theater.

2. **Background**

   a. Frozen and DRBCs are initially derived from 450 ml of blood collected in citrate/phosphate/dextrose/adenine (CPDA-1) collection bags. The RBCs are stored for 2 - 6 days at 1 – 6°C before being frozen in a cryoprotectant (40% m/v glycerol), and stored in the frozen state at minus 65°C or colder. Once it is determined there is a need to transfuse, the frozen RBCs are thawed. They are then deglycerolized by sequential washing with hypertonic (12%) saline followed by normal (0.9%) saline mixed with 0.2% glucose. Following deglycerolization, they are re-suspended with an AS-3 additive solution and stored at 1 – 6°C, until ready for transfusion. DRBCs with the AS-3 additive are Food and Drug Administration (FDA)-approved for transfusion up to 14 days when processed on the Haemonetics Automated Cell Processor ACP215, an FDA 510(k)-cleared, closed processing system device.

   b. The first operational frozen blood bank was established in 1956 at Chelsea Naval Hospital (Boston), in part to determine the practicality of frozen blood usage aboard Navy ships. In 1966, under Department of Defense direction (DoD), the Navy Bureau of Medicine and Surgery established the first frozen blood bank in a combat zone at Navy Station Hospital, DaNang, Republic of South Vietnam. Over a seven-month period, 465 previously frozen RBC units were transfused to severely injured casualties, both solo and in combination with liquid RBCs. In the 1980s, the DoD, under each branch Surgeon's General FDA license, froze 68,000 RBC units. Those units were pre-positioned throughout several geographic Combatant Commands (COCOMs) in direct support of current and future military medical expeditionary/contingency operations. FDA-approved frozen and deglycerolized red blood cells may be used at any Role/Role II and above Medical Treatment Facility with appropriate transfusion support within the CENTCOM AOR.

3. **Clinical Indications for Use.** Each unit of frozen and DRBCs:

   a. Should be considered equivalent to a fresh unit of RBCs since they are frozen within 6 days of collection and have a 14 day shelf-life upon deglycerolization.

   b. Contains more than 80% of the RBCs present in the original unit of blood;

   c. Provides the same physiologic benefits as liquid RBCs;

d. Carries the same post-transfusion survival expectation as liquid PRBCs.

e. Has significant decrease in proteins associated with non-hemolytic transfusion reactions.

f. **The primary indication for use of frozen and deglycerolized RBCs is as a supplement to liquid RBCs during surge periods of increased transfusion requirements in order to decrease casualty hemorrhagic morbidity and mortality.**

Frozen and deglycerolized RBCs may be used in lieu of liquid RBCs for all RBC transfusion requirements including massive transfusions. The Joint Trauma System Performance Improvement Division analyzed data from the Joint Theater Trauma Registry and Massive Transfusion database and found no statistically significant difference in outcomes or transfusion related complications between patients who received at least 1 unit of deglycerolized RBCs as part of their massive transfusion and those who received none (Table 1.)

Table 1

Massive transfusion with DRBC compared to standard massive transfusion		
	p value	
Overall Mortality	0.241	63 cases / 63 controls matched for age, ISS, total RBC w/in 24 hrs, patient category, gender
Complications	**p value**	
Transfusion Reaction	N/A	No cases in sample
Coagulopathy	0.271	63 cases / 63 controls matched for age, ISS, total RBC w/in 24 hrs, patient category, gender, initial Base deficit, initial temperature, initial INR
Renal Failure	0.57	60 cases / 60 controls matched for age, ISS, total RBC w/in 24 hrs, patient category, gender, initial systolic blood pressure
DVT	0.753	23 cases / 23 controls matched for age, ISS, total RBC w/in 24 hrs, patient category, gender, extremity injury
Respiratory Failure	N/A	No cases in sample
Sixty three patients in Afghanistan were identified between JAN 10 - SEP 11 as having a massive transfusion which included deglycerolized blood (DRBC). A control population of 525 patients with non-DRBC massive transfusion from the same time period and theater was found in the JTTR to provide comparison of overall mortality.		
CONCLUSION: With the data available, there appears to be no statistical difference in mortality outcome in theater for patients receiving deglycerolized blood (DRBC) as part of a massive transfusion when compared to patients receiving no DRBC as part of a massive transfusion. Additionally, there seems to be no significant difference between massive transfusions with DRBC and without DRBC in the development of complications for transfusion reaction, coagulopathy, renal failure, deep vein thrombosis (DVT), or respiratory failure.		
Completed 23 MAR 2012		

g. Transfusion monitoring:

1) Clinical: **Treat as a routine liquid RBC transfusion before, during, and after transfusion, and for a suspected/actual adverse event.**

2) Laboratory: Obtain pre- and post-transfusion Hgb/Hct and Base Excess/Deficit.

4. Documentation. Clinical documentation for a frozen and deglycerolized transfusion is the same as for a liquid transfusion. In addition:

a. The physician order should specify use of previously frozen and deglycerolized RBCs.

b. The Laboratory will establish/maintain a process to document previously frozen and deglycerolized RBC transfusions in a manner that will facilitate future evaluation of recipients, including but not limited to:

1) Blood component identifiers

2) Date of blood component receipt in frozen state

3) Date of thaw/deglycerolization/additive process and resulting expiration date

4) Casualty indentifiers (including nationality and ABO/Rh categorization)

5) Date of transfusion

6) Transfusion indication

7) Transfusion reaction, nature and outcome

5. Performance Improvement (PI) Monitoring.

a. Intent (Expected Outcomes).

1) All patients who receive DRBC transfusions have accurate documentation in the medical record of the quantity of transfused blood and any transfusion-related adverse events.

b. Performance/Adherence Measures.

1) In patients who were transfused DRBCs, there was accurate documentation in the medical record as to the quantity of blood transfused and any transfusion-related adverse events.

c. Data Source.

1) Patient Record

2) Dept of Defense Trauma Registry (DoDTR)

3) PACOM blood bank logs

4) TMDS

d. System Reporting & Frequency.

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed biannually; additional PI monitoring and system reporting may be performed as needed.

The system review and data analysis will be performed by the Joint Theater Trauma System (JTTS) Director, JTTS Program Manager, and the Joint Trauma System (JTS) Performance Improvement Branch.

6. **Responsibilities**. It is the combined responsibility of the trauma team leader and blood bank officer to ensure familiarity, appropriate compliance and PI monitoring at the local level with this CPG.

7. **References.**

[1] *Emergency War Surgery Handbook*

Approved by USPACOM JTTS Director, JTS Director and the USPACOM SG

Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the Services or DoD.

APPENDIX A,

ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGs

1. **Purpose**.

   The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of "off-label" uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

2. **Background**.

   Unapproved (i.e., "off-label") uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing "investigational new drugs." These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

3. **Additional Information Regarding Off-Label Uses in CPGs**.

   The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the "standard of care." Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

4. **Additional Procedures**.

   a. Balanced Discussion. Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

   b. Quality Assurance Monitoring. With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

   c. Information to Patients. Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.