AWARD NUMBER: W81XWH-20-2-0032

TITLE: Plasma Resuscitation Without Lung Injury (PROpOLIs)

PRINCIPAL INVESTIGATOR: Leopoldo Cancio, MD

CONTRACTING ORGANIZATION: Coalition for National Trauma Research, San Antonio, TX

REPORT DATE: October 2022

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2022	Annual	30Sep2021-29Sep2022

4. TITLE AND SUBTITLE

Plasma Resuscitation Without Lung Injury (PROpOLIs)

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-20-2-0032

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Monica Phillips, Leopoldo Cancio

E-Mail: monica@nattrauma.org

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Coalition for National Trauma Research
7970 Fredericksburg Road, Suite 101-60, San Antonio, TX 78229

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release, Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
This study evaluates the administration of plasma for resuscitation after burn injury and its effect on 24 hour and total resuscitation volumes and resuscitation related morbidities at five Burn Centers across the US. Institutional Review Board and HRPO approval for protocol and several centers has been achieved. Logistics to support the study are in place.

15. SUBJECT TERMS
Resuscitation, burn, injury, blood

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE		104	USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified		19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI

TABLE OF CONTENTS

	Page
1. Introduction	**4**
2. Keywords	**4**
3. Accomplishments	**4**
4. Impact	**7**
5. Changes/Problems	**7**
6. Products	**9**
7. Participants & Other Collaborating Organizations	**10**
8. Special Reporting Requirements	**11**
9. Appendices	**11**

1. INTRODUCTION:

This study evaluates the administration of pathogen reduced plasma for resuscitation after burn injury and its effect on 24 and total resuscitation volumes and resuscitation related morbidities at five Burn Centers across the US. Its aims include (1) To determine whether administration of plasma during burn resuscitation results in decreased total resuscitation volumes compared to standard-of-care crystalloid-based resuscitation. (2) To determine whether plasma administration during burn resuscitation reduces ARDS. (3) To determine the effect of plasma administration on inflammation and the endotheliopathy of burns. Ninety-four subjects will be enrolled.

2. KEYWORDS:

Resuscitation, burn, injury, blood, plasma

3. ACCOMPLISHMENTS:

PROPOLIS	Timeline (months)	Description of effort expended in this report period	Status
Major Task 1: Adapt PROPOLIS protocol for DoD Funded Status			
Coordinate with Sites for IRB agreement to use WIRB	1-3	University of Washington, DCC received WCG-IRB approval 12/11/2021. University of Alabama, Birmingham received WCG-IRB approval 1/26/2022.	5/6 complete (83% complete)
Coordinate with Sites for Military 2nd level IRB review (ORP/HRPO)	1	HRPO approval: UTSW - 11/29/2021 UAB – 2/17/2022 UWDCC – 1/6/2022 Continuing review submitted and approved by HRPO.	5/6 approved (83%)
Submit amendments, adverse events and protocol deviations as needed	As needed	Amendment#2: Protocol, ICF, and patient materials were amended to delete the USAISRS Coagulation laboratory analysis (one blue top tube from patient and 10 mL tube from plasma infused). Amendment approved by WCG-IRB 9/1/2022.	ongoing
Submit annual WIRB report for continuing review	Annually	Submitted in 1/2022.	
Prepare and submit quarterly progress report to DoD	Quarterly	Quarterly reports were submitted for quarter 1, 2, and 3.	ongoing
Milestone Achieved: Central IRB approval at all sites	3	Five of six sites approved	83%
Milestone Achieved: HRPO approval	6	Five of six sites approved	83%
Major Task 2: Subcontract with all Study Sites			

Verify subaward documents: budget, budget justification, salary verification	1-3	Subaward documents have been reviewed for all site subawards.	100%
Issue and execute subaward documents	3	All subawards are fully executed.	100%
Submit quarterly progress reports	Quarterly	The monthly teleconference is currently serving as the quarterly report from sites.	ongoing
Review quarterly progress reports	Quarterly	Sites progress in submitting to WCG-IRB, HRPO, etc is monitored monthly.	ongoing
Milestone Achieved: Subawards issued for all sites	3		100%
Major Task 3: Patient Enrollment			
Educate and train research staff on study protocol and data collection procedures	1-6	• Monthly meetings are held via teleconference. A study webpage on the CNTR webpage has been created and has all study related resource documents and trainingshttps://www.nattrauma.org/research/research-policies-templates-guidelines/propolis-project-page/ To see the PROPOLIS Staff pages of the website – the password is PROPOLIS1. • Work to coordinate plasma centers (4) in each state of enrollment was undertaken. • Lab kits were assembled and sent to enrolling sites. • Work with blood banks to provide education and ensure readiness to receive plasma product. • Plasma product received at four of five enrolling centers. • Staff education materials, manual of procedures was edited and revised to account for plan changes (i.e four plasma centers rather than one; 2.7 ml blue top tubes rather than 44.5mL, etc). and revised again to delete the USAISR Coagulation lab samples and role. • Training plan and all training materials were developed and implemented. • Site initiation presentation created, and meetings were held with UW and USAISR. • Burn Navigator incorporated the PROPOLIS resuscitation in their software and educated sites as to update.	ongoing
Identify patients for study inclusion and collect initial data	1-6	Site Initiation Notifications issued: UW 8/17/2022 – screened 3 patients USAISR 9/27/2022 – screened 4 patients	Ongoing 2/5 sites open to enrollment
Validate data collected quarterly	1-6	First quarter of enrollment has not ended	Ongoing
Follow-up data collection	1-6		
Coordinate with Sites & CNTR for monitoring data	1-16		

collection rates and data quality			
Milestone Achieved: Completion of study; 94 patients enrolled	24		
Major Task 4: Data Analysis and Knowledge Translation			
Perform all analyses according to specifications, share findings with all investigators	24-29	Have not started.	
Comprehensive analysis of enrolled patients with intended publication	30-33	Have not started	
Dissemination of results, MHSRS, journal publications, electronic/print broadcasts through NTI	34	Have not started	
Milestone Achieved: Complete National Trauma Research Action Plan incorporating *findings from Aims 1-4*	36	Have not started	
Milestone Achieved: Identify optimal metrics to assess long term functional outcomes (Aim 2)	36	Have not started	
Milestone Achieved: Develop the NTRAP investigator toolkit	36	Have not started	

What opportunities for training and professional development has the project provided?

Nothing to report

How were the results disseminated to communities of interest?

Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?

1. Obtain WCG-IRB approval for Vanderbilt.
2. Obtain HRPO approval for Vanderbilt.
3. Conduct site initiation presentation/meeting with UAB, UTSW, and VUMC.
4. Enroll patients

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:
Changes in approach and reasons for change

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

Participating Sites:

a. Vanderbilt: This institution requested a 6-month delay because they were implementing a new resuscitation process and using that timeframe for American Burn Association verification. STATUS: VUMC working through internal coordination and submission to WCG-IRB.
b. UTSW: This institution has identified blood bank personnel issues The Department of Surgery is committed to provide funding for staff. Blood Bank staff is concerned the implementation of the product requires software code changes. The original Blood Bank leadership that supported the study has left. STATUS: Ms. Phillips is coordinating a meeting between UTSW blood bank personnel and UW and/or UAB to provide guidance as to implementation of plasma and answer questions. Anticipate this will resolve the issue and we will move swiftly to site initiation activities.
c. University of Texas Medical Branch, Galveston: UTMB is undergoing research coordinator staffing challenges. They will be unable to participate until they have hired staff. This issue remains. It is unknown at this time when it will be resolved. UTMB is a sixth site. It's ability to participate will not affect the study.

Plasma Availability:

Plasma is available to all enrolling centers via Plasma Centers in those states. Additionally, there are two centers in the US with approved BLAs. This issue is resolved.

Blue top blood specimen tubes:

Availability of commercial blue top and purple top tubes has improved. We have plenty to assemble additional lab

Changes that had a significant impact on expenditures

None

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

None

Significant changes in use or care of vertebrate animals

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

Nothing to report

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers and presentations.

Nothing to report

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name	Project Role	Nearest person month worked	% Effort	Contribution to the project
Leopoldo Cancio	Principal Investigator	0.3	10%	Oversight and leads all aspects of the study.
Amy Flores	Controller	0.3	10%	Contract management, tracking grant expenditures
Monica Phillips	Project Manager	2.1	50%	Performing administrative support for the study. Schedules and supports monthly meetings. Works with all sites regarding human subjects protection, site initiation, education and training, and data collection.
Joel Baker	Research Coordinator	1.0	50%	Research Coordinator at ISR to support this study at the ISR.
Michelle Price	Co-Investigator	0.3	10%	Oversee/supervise CNTR staff, participates in all monthly meetings and adhoc meetings.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Dr. Cancio:
Additional closed studies: Ex vivo Heparin-Free ECLS.
Current studies added:

a) Title: Vitamin C in Thermal injury: The VICToRY Trial. A Phase III Multi-Center Randomized Trial

b) Title: Compensatory Reserve Measurement (CRM) during Burn Shock Management

c) Title: Restoring Immune Function to Critically-ill Burn Patients.

Pending studies include:

a. Title: The Burn Medical Assistant (BURNMAN): An Automated Burn Identification and Classification Tool
b. Title: Commercialization and Clinical Assessment of Large Surface Area Burn Treatment for Prolonged Field Care and Long-Term Care
c. Title: Burns for Prehospital Providers Program
d. Title: Use of Low-Flow Extracorporeal Life Support in Burned Patients as Ultra-Lung Protective Method
e. Title: Clinical Evaluation of Field Shield Spray on Wound Dressing with Antimicrobial silver and Lidocaine for Mass Casualty and Abnormal Burn Wound Management

What other organizations were involved as partners?

Organization	Location	Contribution to Project
Institute of Surgical Research and US Army Burn Center	3698 Chambers Pass, JBSA Fort Sam Houston, TX 78234-6315	Dr. Leopoldo Cancio (Study PI)
University of Washington	325 9th Ave, Seattle, WA 981014-2420	Dr. Barclay Stewart (Site PI)
University of Washington	325 9th Ave, Seattle, WA 981014-2420	Dr. Dagmar Amtmann (DCC PI)
University of Alabama, Birmingham	1720 2nd Avenue South, Birmingham, AL 35294.0111	Dr. Jan Jensen (Site PI)
Vanderbilt University Medical Center	3319 West End Avenue, STE 970, Nashville, TN 37203-6856	Dr. Robel Beyene (Site PI)
University of Texas Medical Branch	815 Market Street, Galveston, TX 77550-2725	Dr. Steven Wolf (Site PI)
University of Texas Southwestern	5323 Harry Hines Blvd E6.202, Dallas, TX 75390	Dr. Samuel Mandel (Site PI)
University of Maryland	800 West Baltimore Street, Baltimore, MD 21201-1100	Dr. Rosemary Kozar (Site PI)
Cerus Corporation	1220 Concord Avenue, Concord, CA 94520	Dr. Larry Corash, Consultant

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS:
A QUAD chart is included as an appendix.

9. APPENDICES:

a. Quad Chart
b. Site Initiation Presentation
c. Updated Plasma Policy
d. Updated Specimen Handling Policy
e. PROPOLIS Training Plan
f. PROPOLIS Training Log
g. PROPOLIS Site Initiation Attendance Log
h. Burn Navigator software changes presentation
i. Blood Bank Plasma Center Meeting presentation
j. Support Document – Dr. Cancio

Plasma Resuscitation WithOut Lung Injury (PROpOLIs)

DM090167
W81XWH2020032

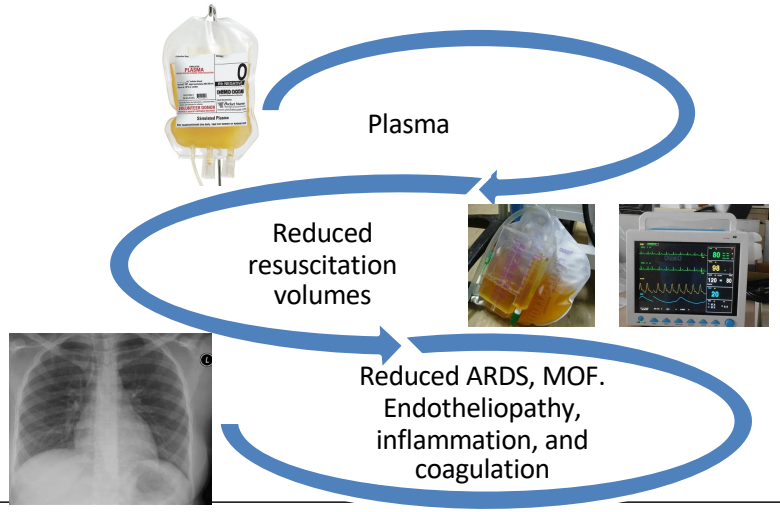
PI: Dr. Leopoldo Cancio **Org: Coalition for National Trauma Research (CNTR)** **Award Amount: 2,485,163**

Study/Product Aim(s)

- To determine whether administration of Pathogen-Reduced Plasma during burn resuscitation results in decreased total resuscitation volumes compared to standard-of-care crystalloid-based resuscitation
- To determine whether Pathogen-Reduced Plasma administration during burn resuscitation reduces ARDS
- To determine the effect of Pathogen-Reduced Plasma administration on the endotheliopathy, inflammation and coagulation of burns.

Approach

This is an open-label, phase IV, multicenter, randomized controlled prospective clinical trial in patients with burns. The study model is parallel (between-patient). The intervention to be tested is Pathogen-Reduced Plasma for burn shock resuscitation vs. standard-of-care resuscitation.



Accomplishment:. Plasma centers in place for four states. Site initiation meetings held for UW & USAISR. Blood Bank/Plasma meetings held for 3 sites. Training plan finalized. Specimen handling video recorded. Burn Navigator software updated.

Timeline and Cost

Activities CY	21	22	23
Adapt Protocol			
Issue Subawards			
Patient Enrollment			
Data Analysis and Dissemination			
Estimated Budget ($K)	**$769**	**$874**	**$841**

Updated: October 30, 2022

Goals/Milestones

CY21 Goal – Adapt Protocol
☐ IRB approval at all sites
☐ HRPO approval

CY21 Goals – Subcontracts
☒ Subawards issued for all sites

CY21 and CY 22 Goal – Patient Enrollment
☐ Subject enrollment goal of 94

CY23 Goal – Data Analysis and Dissemination
☐ Analyze Data
☐ Disseminate findings

Comments/Challenges/Issues/Concerns

- Blue and purple top tube issue solved.

Budget Expenditure to Date

Projected Expenditure: $2,485,163
Actual Expenditure: $980,468

PROpOLIs

PLASMA RESUSCITATION WITHOUT LUNG INJURY

June 21, 2022

Agenda

- Sites – Dr. Cancio
- Study objectives and design – Dr. Cancio
- Informed consent and enrollment – Dr. Cancio
- Study procedures – Dr. Cancio
- Safety Reporting – Monica Phillips
- Data collection – Monica Phillips
- Monitoring – Monica Phillips
- Questions

Participating Sites

Clinical Sites

- US Army Burn Center, Leopoldo Cancio, MD
- University of Alabama at Birmingham, Jan Jansen, MBBS, PhD
- Vanderbilt University Medical Center, Robel Beyenne, MD
- University of Washington, Harborview Burn Center, Barclay Stewart, MD
- University of Texas Southwestern, Sam Mandell, MD
- University of Texas Medical Branch, Galveston, Steve Wolf, MD

Data Coordinating Center

- University of Washington, Dagmar Amtmann, PhD

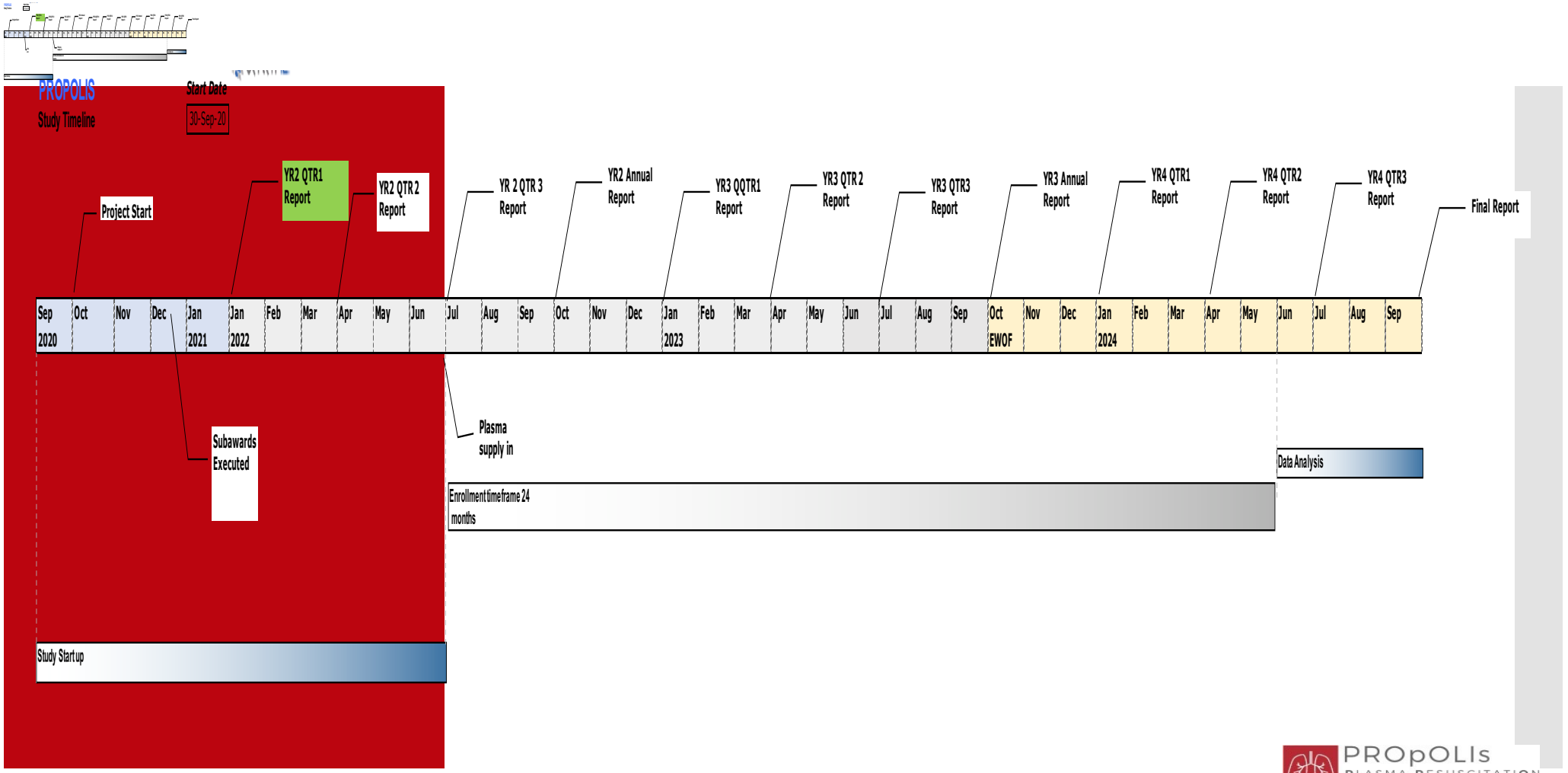
Laboratory Sites

- University of Maryland, Rosemary Kozar, MD
- Cerus, Larry Corash, MD

Coordinating Center

- CNTR, Monica Phillips

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY



PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Study Objectives

Hypothesis: Administration of plasma for resuscitation after burn injury will 1) reduce 24-hour and 48-hour resuscitation volumes and 2) reduce the incidence of acute respiratory distress syndrome, multi-organ failure and other resuscitation-related morbidities

Objectives:

Specific aim 1: To determine whether administration of Pathogen-Reduced Plasma during burn resuscitation results in decreased total resuscitation volumes compared to standard-of-care crystalloid-based resuscitation.

Specific Aim 2: To determine whether Pathogen-Reduced Plasma administration during burn resuscitation reduces ARDS.

Specific Aim 3: To determine the effect of Pathogen-Reduced Plasma administration on the endotheliopathy of burns

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Study design

Research design:

- This is an open-label, phase IV, multicenter, randomized controlled prospective clinical trial.
- The study model is parallel (between-patient)

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Primary Endpoints

Primary endpoint

- Total volume of **all** resuscitation fluids delivered between **hours 0-24 postburn**, in ml/kg

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Secondary Endpoints – Specific Aim 1

Resuscitation Volumes

- The total volume of all resuscitation fluids delivered between hours **0-48 postburn**, in ml/kg
- The total volume of all resuscitation fluids delivered between hours **0-24** and **0-48 postburn**, in ml/kg/TBSA
- Severity and duration of hemodynamic instability during hours 0-48 postburn (norepinephrine equivalents)
- Severity and duration of metabolic acidosis during hours 0-48 postburn (arterial lactate levels)
- Incidence of "rescue," defined as any of the following:
  - Initiation of extracorporeal therapy, i.e. continuous renal replacement therapy or therapeutic plasma exchange, during the first 48 hours postburn
  - Infusion of high-dose ascorbic acid (66 mg/kg/hr) during the first 48 hours postburn
  - Initiation of a continuous infusion of albumin before hour 24 postburn

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Secondary Endpoints– Specific Aim 2

Acute Respiratory Distress Syndrome (ARDS)

- Incidence and severity of ARDS using Berlin criteria
- Duration of mechanical ventilation in survivors
- Ventilator-free days in the first 30 days
- Multi-organ failure (Sequential Organ Failure Assessment Scores)
- Length of ICU and hospital stays
- In-hospital mortality
- Patient-reported outcomes 6 months after injury
- Incidence of transfusion-related acute lung injury (TRALI; consensus definition)
- Incidence of venous thrombo-embolic events

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Secondary Endpoints – Specific Aim 3

Endotheliopathy of Burns

- Syndecan-1 levels
  - Sera from purple top tubes
  - Analysis performed by University of Maryland
- Cytokines IL-6, TNFα , IL-1β , and IL-10
  - Sera from purple top tubes
  - Analysis performed by University of Maryland
- Thrombin generation
  - Sera from blue top tubes
  - Analysis performed by Cerus

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Inclusion criteria

- Age ≥ 18 years
- Weight ≥ 40 kg
- Thermal injury size ≥ 20% TBSA
- Admitted to the Burn Center and enrollable within 8 hours of injury
- Expected to receive intravenous resuscitation fluids for at least 24 hours after injury
- Expected to live > 24 hours after injury

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Exclusion Criteria

Target total enrollment = 94

- Chemical injury
- Deep electric injury
- Severe non-thermal injuries
  - Major surgery prior to enrollment (laparotomy, thoracotomy, craniotomy, major amputation
  - Transfusion of > 2 units of packed red blood cells prior to enrollment
  - Considered by attending MD to have life-threatening traumatic (non-thermal) injuries
- Inability to obtain informed consent
- Decision not to treat due to injury severity or other factors
- Patient >65 years or < 18 years
- Presence of anoxic brain injury that is not expected to result in complete recover
- Patient already receiving plasma infusion, or judged to be likely to require plasma infusion
- Patient already receiving rescue procedures" (albumin infusion, CRRT, TPE, or high-dose ascorbic acid)
- Existence of pre-morbid conditions (congenital heart failure, end-stage kidney disease, cirrhosis of the liver, oxygen-dependent chronic obstructive pulmonary disease
- Malignancy currently under treatment, history of thromboembolism

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Informed consent

- Informed consent must be obtained within **8 hours** of burn injury
- Legally Authorized Representative consent approved
- eConsent through REDCap approved
- Scan signed consent forms and attach to subject file in REDCap if REDCap eConsent is not used

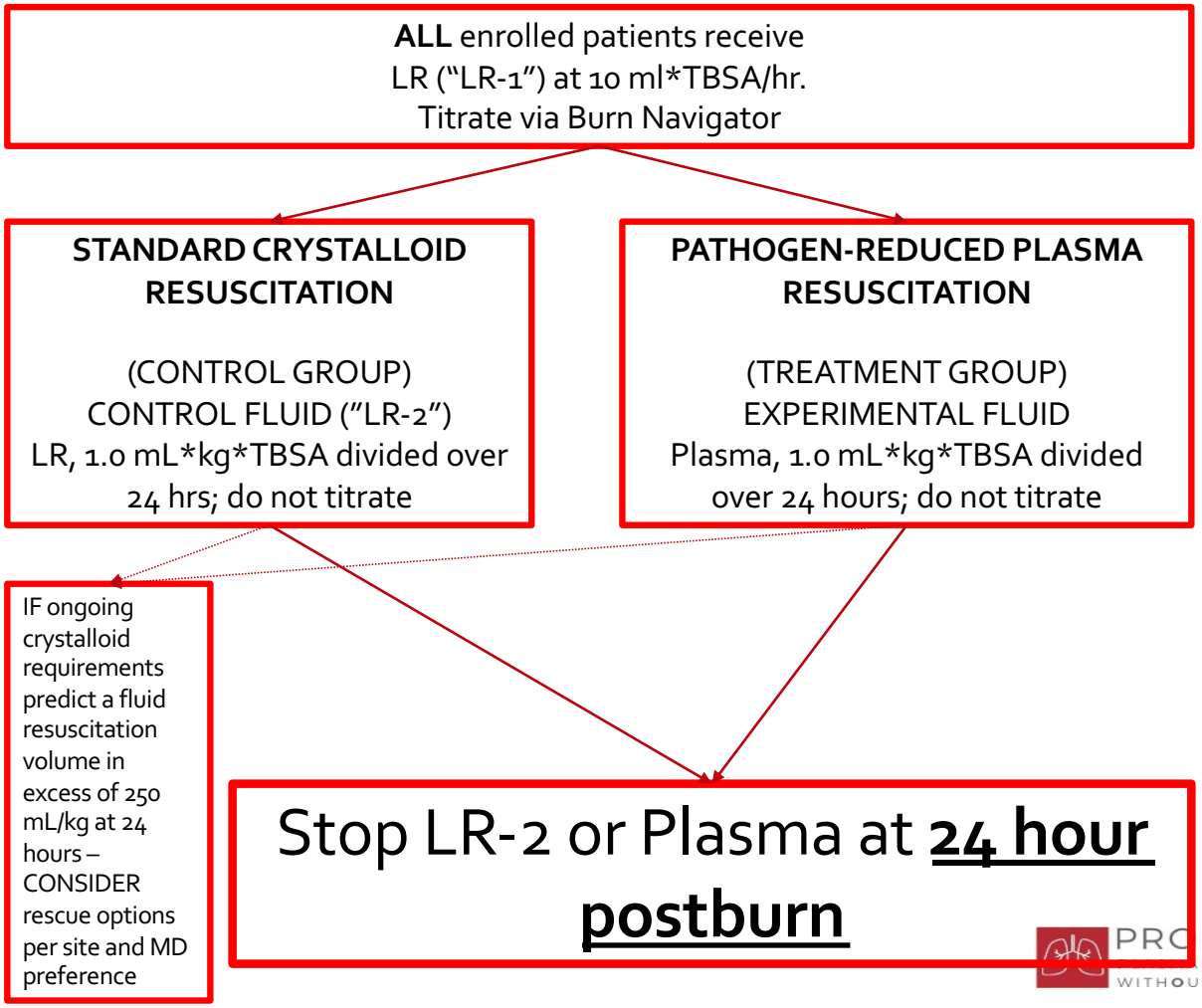
PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Randomization

- Subjects will be randomized into one of two study resuscitation conditions – control OR plasma (treatment group)
- Block randomization stratified on TBSA categories
  - TBSA 20-34%
  - TBSA 35-59%
  - TBSA 60+%
- If the patients TBSA is found to change they will remain in their original randomization group
- If the patients TBSA changes from 20% to less than 20%, they remain in the study in their original randomization category even if they are receiving plasma.

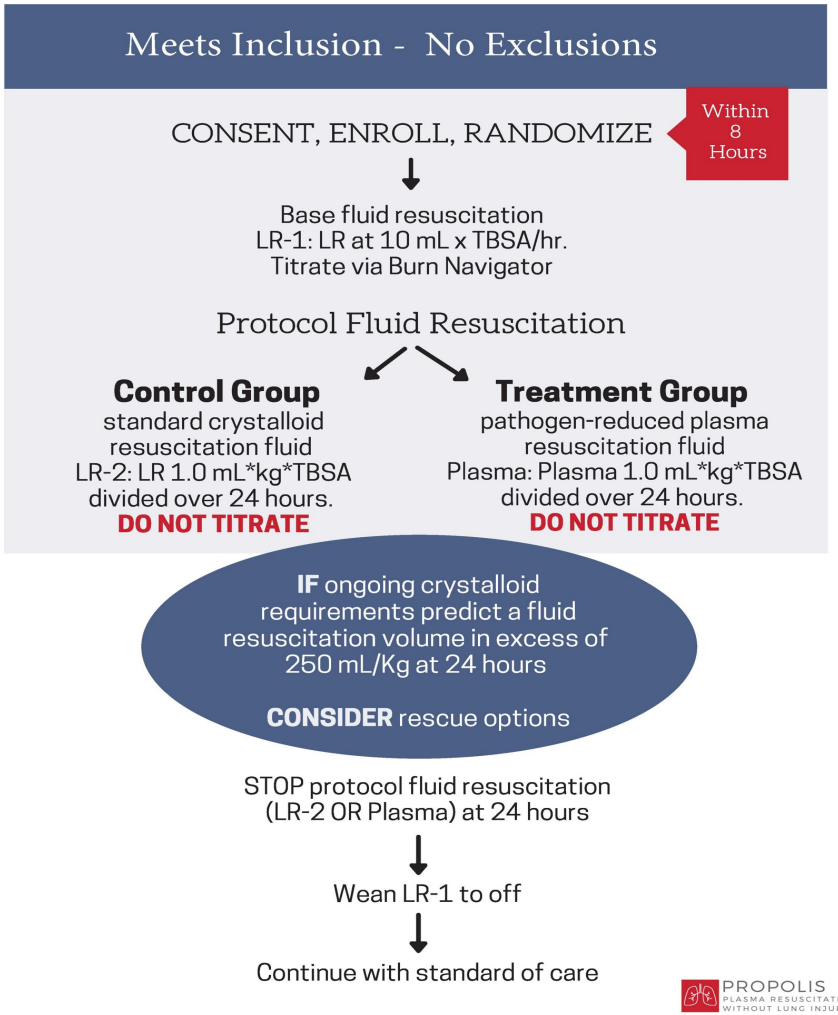
PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Resuscitation



PRCpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

First 24 Hours



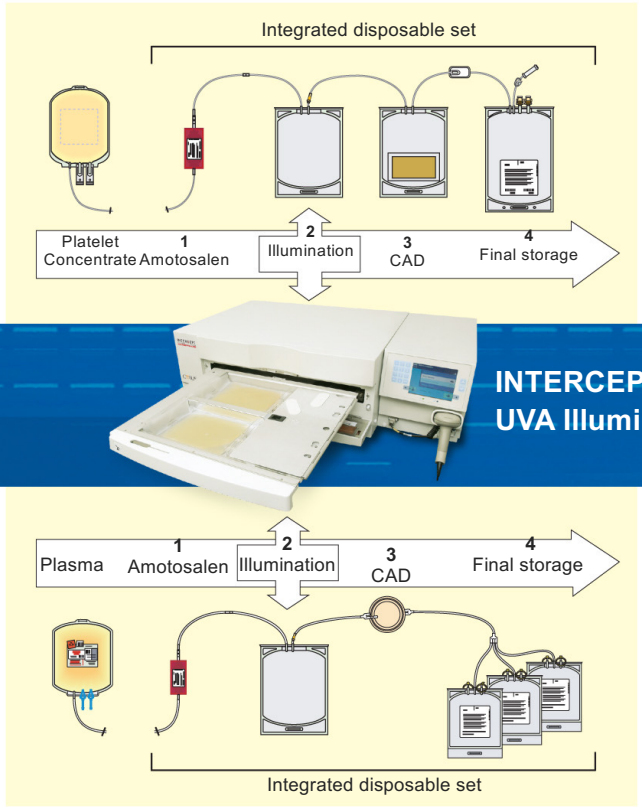
PROPOLIS PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROpOLIs PLASMA RESUSCITATION WITHOUT LUNG INJURY

INTERCEPT Blood System

Intended to be used for the ex vivo preparation of pathogen-reduced, whole blood derived or apheresis plasma to reduce the risk of transfusion-transmitted infection, and as an alternative to gamma irradiation for prevention of transfusion-associated graft versus host disease.

INTERCEPT Blood System for Platelets



INTERCEPT Blood System for Plasma

SOLIS PLASMA RESUSCITATION WITHOUT LUNG INJURY

INTERCEPT PLASMA

Indications

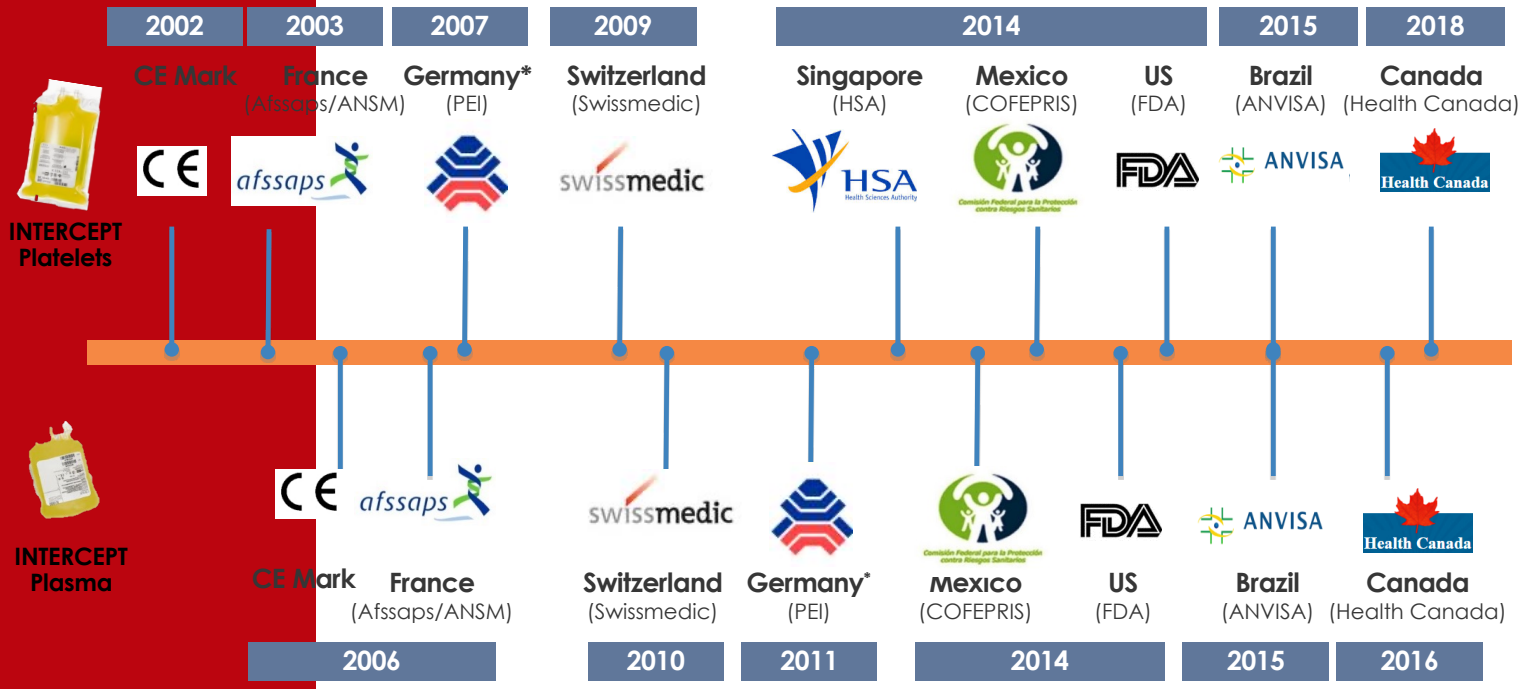
- Management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors (eg, liver disease, DIC).
- Patients undergoing massive transfusion who have clinically significant coagulation deficiencies.
- Patients taking warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect or who need only transient reversal of warfarin effect.
- Transfusion or plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP).
- Management of patients with selected coagulation factor deficiencies, congenital or acquired, for which no specific coagulation concentrates are available.
- Management of patients with rare specific plasma protein deficiencies, such as C1 inhibitor, when recombinant products are unavailable.

Contraindications

- Contraindicated for preparation of plasma intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens.
- Contraindicated for preparation of plasma intended for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm, or have a lower bound of the emission bandwidth 375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Regulatory Approvals



Approvals shown do not represent a comprehensive list

* For first center approval

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Pathogen-reduced Plasma

Blood Bank

- Each bag may contain up to 200 mL of plasma
- Units will be shipped frozen using dry ice
- Stored at or below -18°C for up to 12 months
- Track receipt and distribution via REDCap
- Keep par level at 40 units

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Pathogen reduced plasma

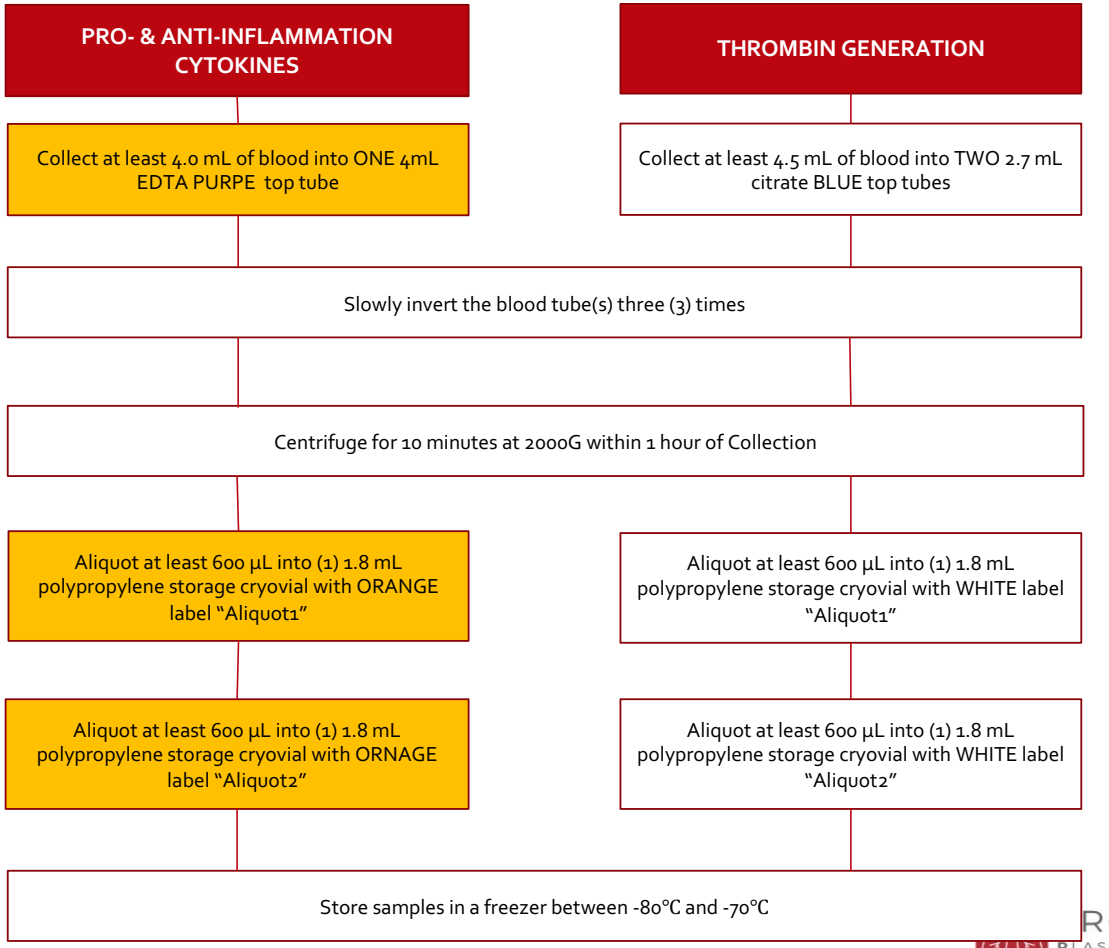
Patient/clinical

- Communication to blood bank as to need for study plasma
- Administer per local policy for blood product administration
- Use same blood tubing as traditional blood products
- Change blood tubing per local policy

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Research Labs - Patient specimens

At Admit, 12, 24, & 48 hours Post-Burn

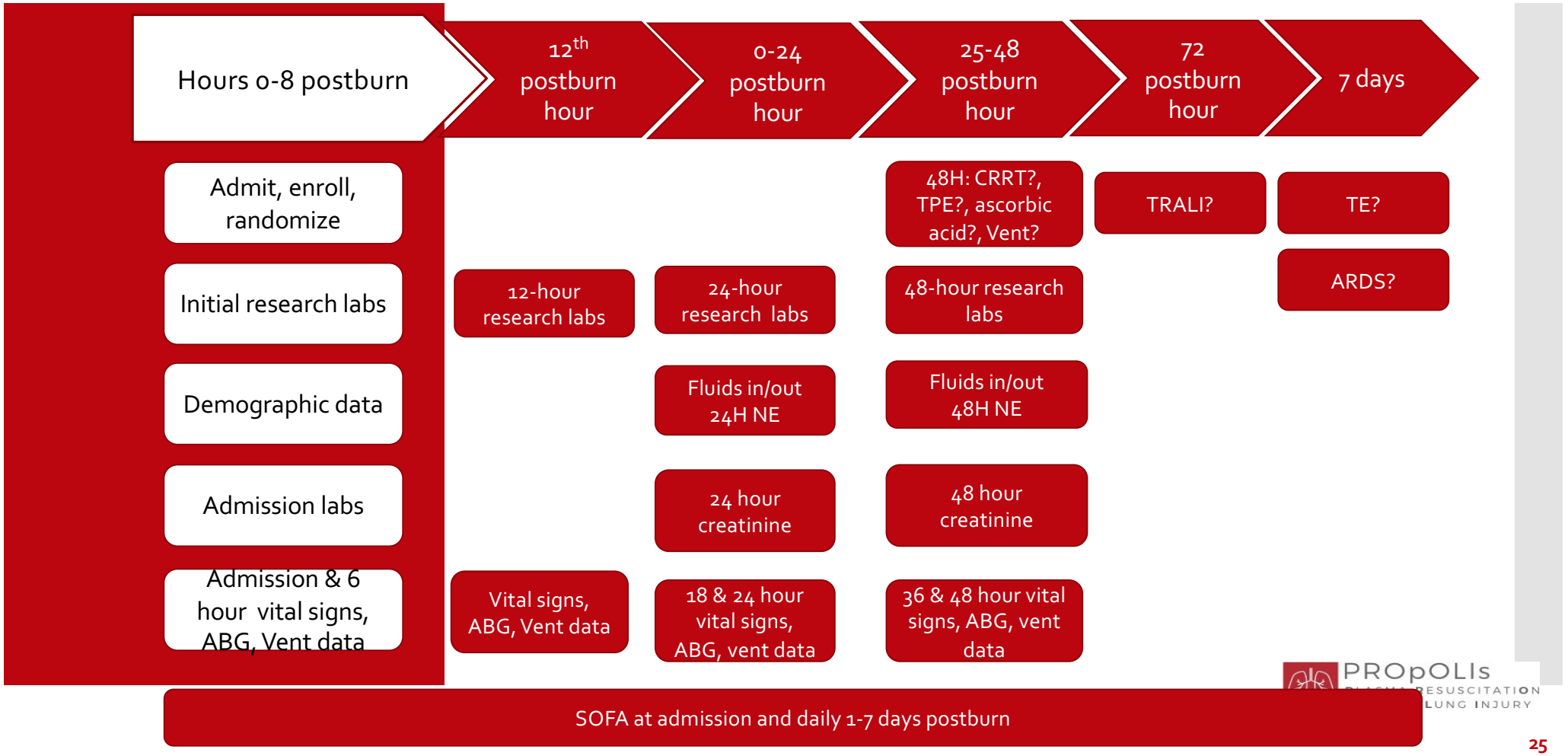


ROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Research Labs- Plasma sample

- Plasma samples from the purple top tube are shipped to:
  - University of Maryland
- Plasma samples from the blue top tube are shipped to:
  - Cerus
- Refer to Site Specific Specimen Handling and Shipping Manual

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY



PROpOLIs
PLASMA RESUSCITATION
LUNG INJURY

Schedule of Activities

Schedule of Activities												
Timelines	0 - 8 hours postburn	12 hours postburn	18 hours postburn	24 hours postburn	36 hours postburn	48 hours postburn	72 hours posburn	Day 4	Day 5	Day 6	Day 7	Day 60
Type of Visit	Inpatient	Inpatient	Inpatient	Inpatient	Inpatient	Inpatient	Inpatient	Inpatient	Inpatient	Inpatient	Inpatient	Outpatient/phone
Initiation Procedures												
- Eligibility criteria	x											
- Informed consent	x											
- Randomize	x											
- Initiate LR-2 OR Plasma	x											
- End LR-2 OR Plasma				x								
Data Collection												
- Demographic	x											
- Admission Labs	x											
- VS, ABG	x	x	x	x	x	x						
- Ventilator data	x	x	x	x	x	x						
- Creatinine	x			x		x						
- Platelets	x											
Research labs												
- patient specimens	x	x		x		x						
- plasma sample		x										
Assessments												
- SOFA	x			x		x	x	x	x	x	x	
- CRRT?						x						
- Ascorbic acid?						x						
- Ventilated?						x						
- TPE?						x						
- TRALI?							x					
- TE?											x	
- ARDS?											x	
- PROMIS 10												x
Adverse Events	x	x	x	x	x	x						

Data Collection

REDCap

REDCap is a web-based data entry platform managed by the PROPOLIS Data Center at the University of Washington.

The PROPOLIS REDCap website is:
https://rc.burndata.washington.edu/

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

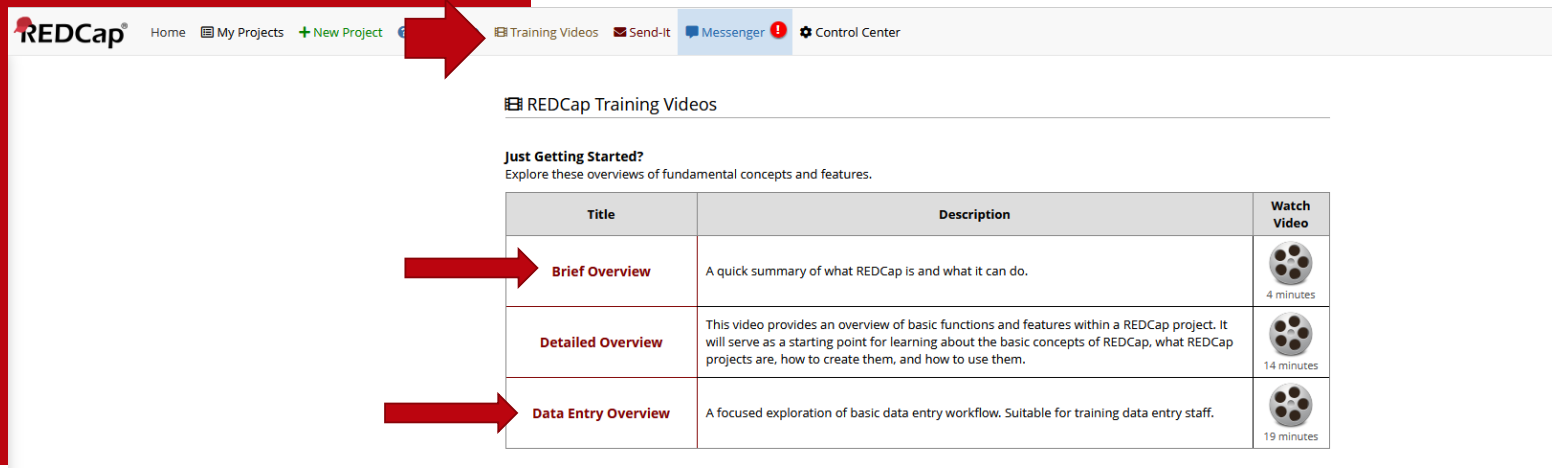
REDCap Account

- All PROPOLIS study staff will need to have a REDCap account set up, even if you use REDCap for other studies (the PROPOLIS database is run on a separate, secure instance of REDCap that we fully manage at the University of Washington)
- Please contact Kara with the list of names (first and last) and email addresses of everyone at your site who will need REDCap access (mcmulk@uw.edu)
- REDCap usernames will be assigned so that they map to your email address (for example, my REDCap username is mcmulk)

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

REDCap training

- REDCap has training videos—if you are new to REDCap, please watch at least the *Brief Overview* Video and the *Data Entry Overview* Video
- These can be found by clicking the Training Videos tab at the top of the REDCap Projects page:



PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROPOLIS Databases

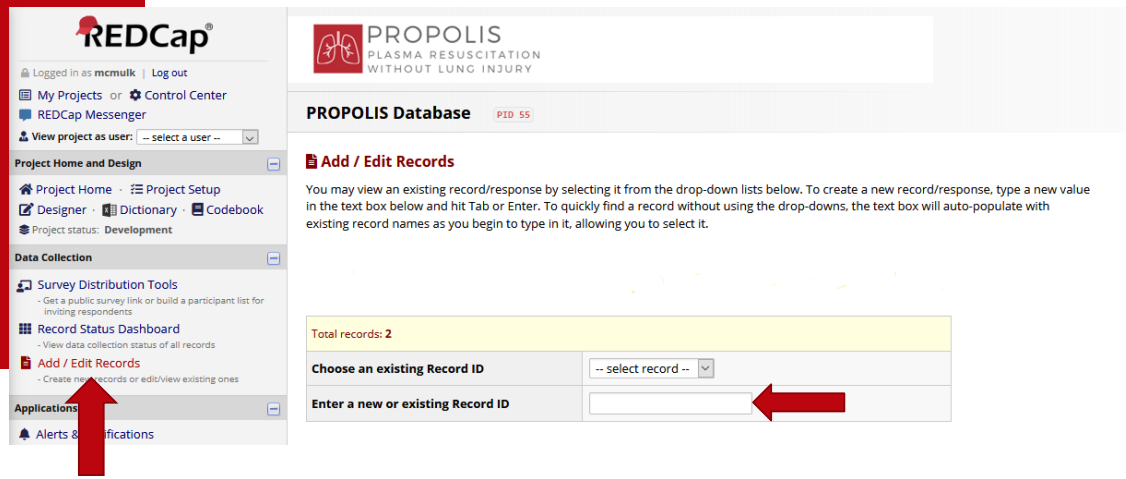
There are three REDCap databases for PROPOLIS:

- PROPOLIS Database
  - main database for data entry
- PROPOLIS Plasma tracking database
  - Cerus tracks plasma shipped
  - Enrolling center tracks plasma received and distributed
- PROPOLIS Shipment Tracking database
  - Track specimen shipping
- Participant tracking at the local level – excel template at PROPOLIS webpage (data center is NOT approved to manage personal identifying information such as name, address, phone number, etc.)

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Assigning a Participant ID

1) The record ID convention in PROPOLIS is “site_id number”, where site is the PROPOLIS center site number and ID number is the number assigned at each site. **REDCap will not automatically assign an ID to a record for you**, so this is the first step.
   a. Site numbers are:
      1. US Army Burn Center
      2. UAB
      3. UW
      4. VU
      5. UTMB
      6. UTSW/Parkland
   b. For the ID number, use sequential numbers starting with 1. So, the first UAB patient screened will be numbered 2_1. The third UTSW/Parkland patient screened will be 6_3, and so on.
   c. **It’s important to assign an ID and enter demographic and inclusion/exclusion criteria for every patient screened, even if they end up not consenting**. We want to ensure that we can describe the population of eligible patients from which the PROPOLIS sample was drawn.
2) To enter a new patient, first select “Add/Edit Records.”
3) Enter the record ID (named based on the rules described above) into the blank field.



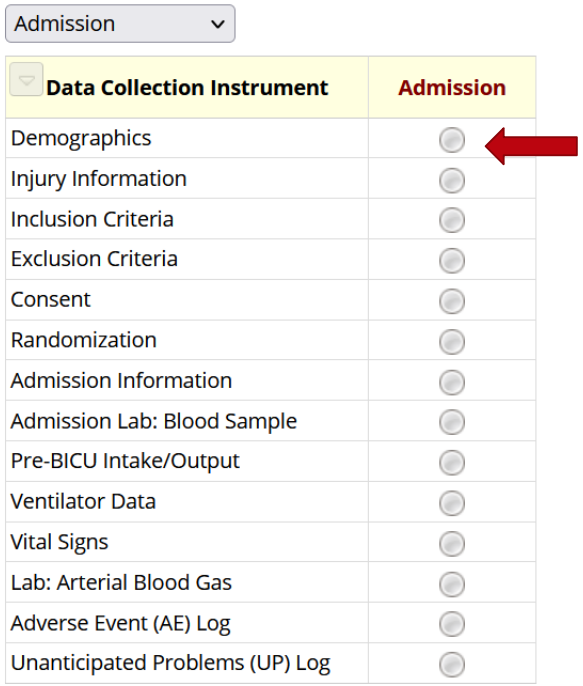
PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Entering Participant Info

The grid that appears once you've created a new record for each patient is called the Record Dashboard. On each patient's record dashboard, you can pick the following:

a. The timepoint you want to enter information for. When you first set up a record, you will only see the Admission timepoint. Using this dropdown, you can pivot to whatever timepoint you want to access for each record.

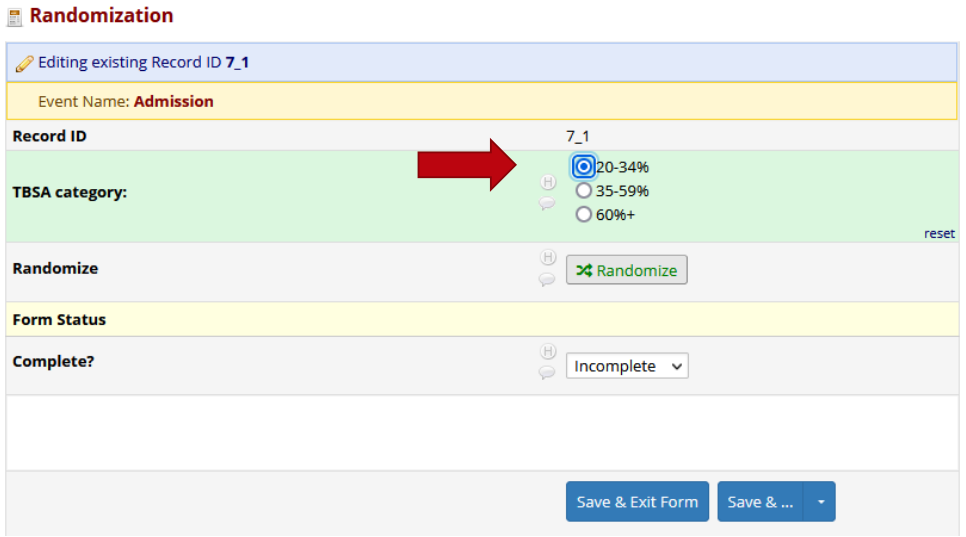
b. The form you want to enter information for. When you start a new record, you will start with demographics.



PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Randomization

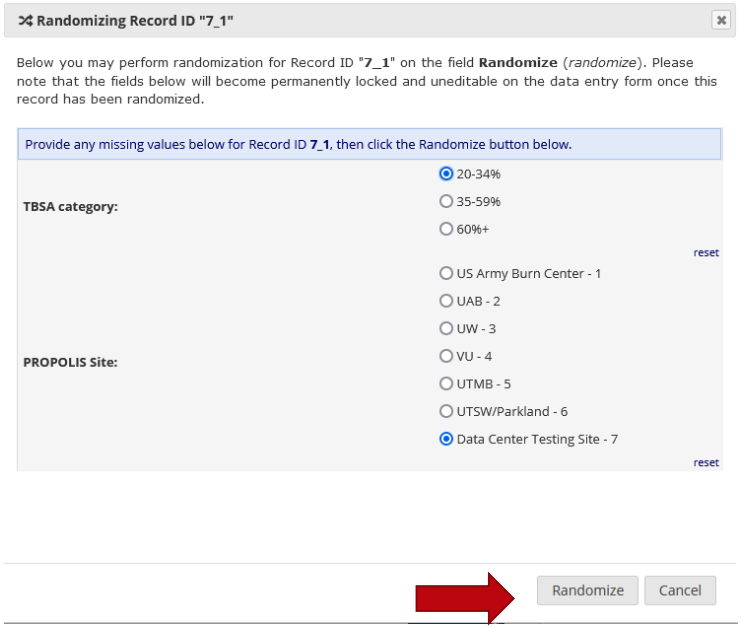
If the patient is eligible and has consented (or a LAR has consented), it's time to randomize! Go to the "Randomization" form on the Record Dashboard. Because we're randomizing by TBSA category, you need to select which category the patient belongs to.



PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Randomization, cont…

Once you've entered that, on the "Randomization" form select the "RANDOMIZE" button. The next screen will ask you to make sure the information about TBSA category and your site is correct. If site and TBSA category are correct, select the "Randomize" button:

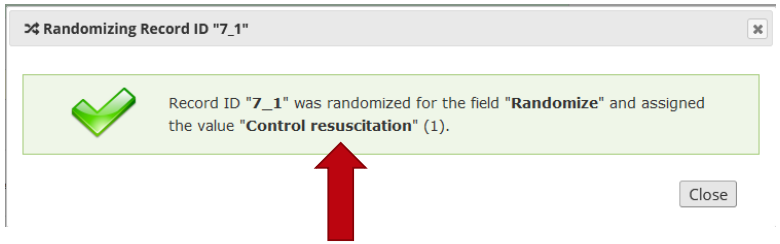


PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Randomization, cont...

REDCap will then perform the randomization and assign the participant to a treatment group. Mark the “Randomization” form as complete and save the form. The form will always show the patient’s randomized group, and you can also print the “Randomization” form for your paper records.

After you’ve randomized the participant, mark the form as “Complete” and “Save and Exit” the form. If you have more data to enter, you can continue entering it by selecting the appropriate form and entering the data as indicated on the paper data collection form.



PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

REDCap Training for PROPOLIS

- The PROPOLIS Data Center has developed PROPOLIS specific training documents and videos
  - How to Assign a Participant ID and Randomize a Patient in REDCap
  - How to do Data Entry in REDCap
  - How to use the PROPOLIS Plasma Tracking Database (Plasma Centers)
  - How to use the PROPLIS Plasma Tracking Database (Enrolling Centers)
  - How to do e-Consent in REDCap
- These can be found at: https://www.nattrauma.org/propolis-training-resources/
- Please complete all training videos and review the documents
- Once you've finished the trainings, we can set up a meeting for the data center and each site to cover any questions that came up or clarify any REDCap/randomization/data entry procedures

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Safety Reporting within REDCap

REDCap Forms

- Adverse Event (AE)Log
- Unanticipated Problem (UP) Log
- Protocol Deviation (PD) Log
- If there is an AE or a UP, log it in REDCap at the timepoint nearest to which the issue occurred
- REDCap will send an automated email to the Site PI, Dr. Cancio and others as appropriate when an AE or a UP is logged

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Safety Reporting: Expected Serious Adverse Events

This study population is expected to have unrelated serious adverse events including:

- compartment syndrome
- multi-organ failure (MOF)
- acute respiratory distress syndrome (ARDS)
- Pneumonia
- wound infection
- urinary tract infection (UTI)
- blood stream infection (BSI)
- acute kidney injury (AKI) requiring hemodialysis
- Death (Baux Score > 100)

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Safety Reporting: Unexpected Serious Adverse Events

Unexpected serious adverse events are possible and include:

- potential transfusion-related acute lung injury
- thromboembolic events
- transfusion reactions
- Death (Baux Score < 100)

These events will be reportable during the first 48 hours post burn.

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Safety Reporting

- AEs will be identified by research staff and entered into the AE log in REDCap
- Site PI is responsible for classifying all adverse events as to a) Severity (mild, moderate, severe); b) expected vs unexpected; and c)related vs unrelated and document ratings in REDCap
- AEs that are deemed to be ***severe, unexpected, and related*** to the study are considered **unanticipated problems** and will be promptly reported through the UP log in REDCap

- **Unrelated** adverse events, either expected or unexpected (as determined by the PI) will **not** be recorded on the eCRF. Only study-related adverse events or ancillary outcomes measures of interest that occurred during the study period (after randomization until study conclusion) will be recorded on the eCRF.

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Safety Reporting: Unanticipated Problems

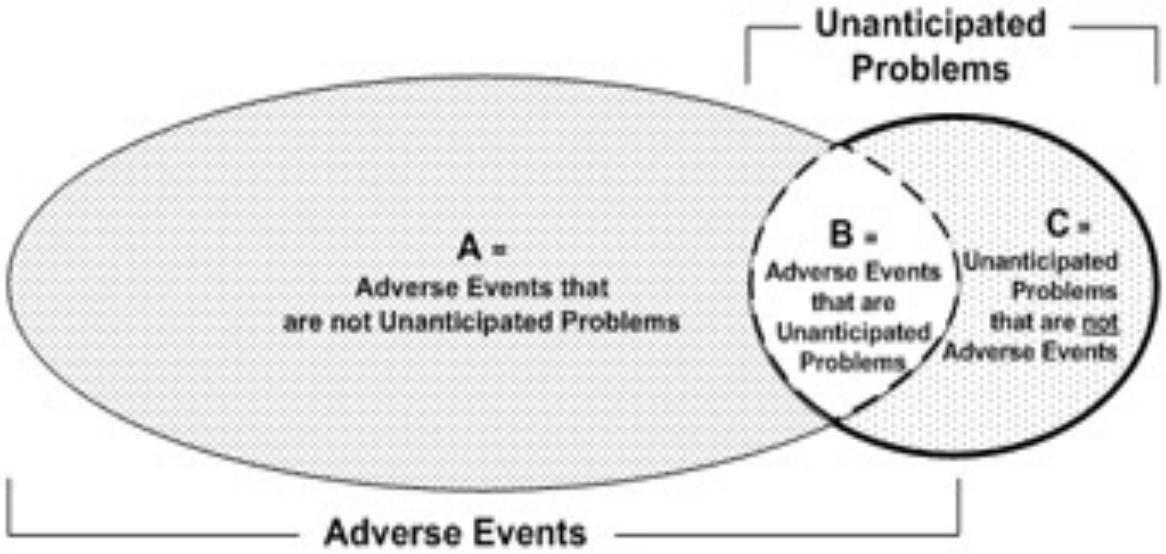
The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

- UPs will be promptly reported through REDCap to Dr. Cancio, Research Monitor, DCC, WCG-IRB, and HRPO.

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

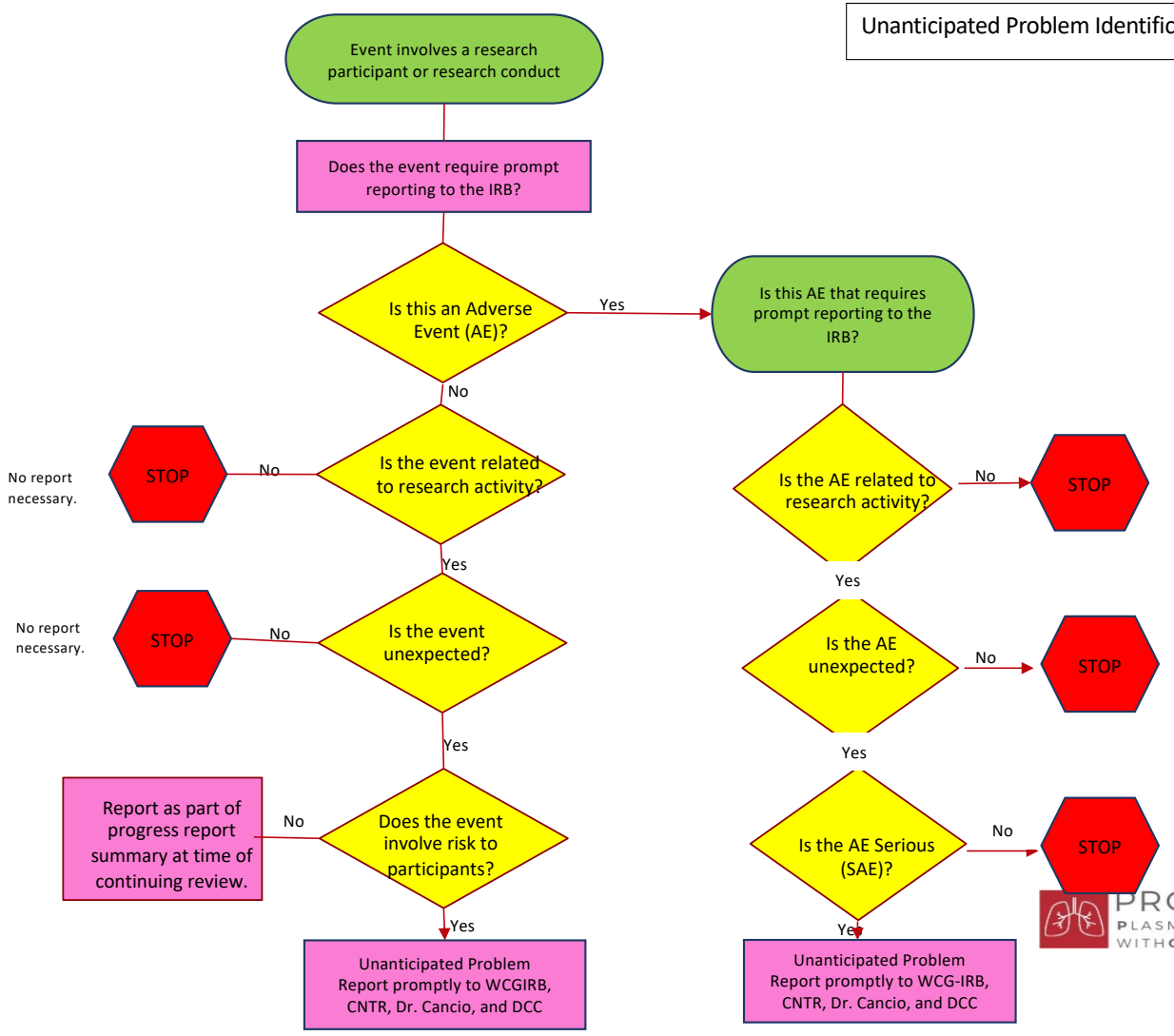
Safety Reporting: Unanticipated Problems



Under 45 CFR part 46: Do not report A, Do report (B+C)

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Safety Reporting: Unanticipated Problem Identification schematic

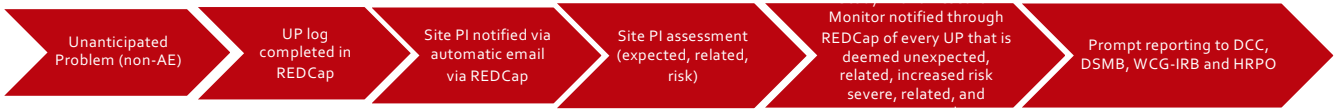


PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Safety Reporting: Reports flow

Adverse Event Reporting Flow

Unanticipated Problem Reporting Flow



PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Safety Reporting: Protocol Deviations

Protocol Deviations are assessed to be:

- Minor Deviation: An occurrence that does not adversely affect subject safety, will not compromise the validity of the study results, and does not violate local, State, or Federal laws.
- Major Deviation: An occurrence that jeopardizes subject safety, may compromise the validity of study results, or violates local, State, or Federal laws.
- Unanticipated Events: occurrences beyond the control of research personnel and not meeting the criteria for minor and major deviations defined above, such as hurricane, blizzard, earthquake - preventing screening/enrollment or follow-up of subjects.

All protocol deviations will be reported via the Protocol Deviation log in REDCap

Protocol deviations that harm a participant or place a participant at risk of harm will be reported as an unanticipated problem.

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Protocol Deviation examples

Examples of Occurrences to Report: (Not Inclusive List)

Protocol

- Lack of baseline LR
- Incorrect dose of treatment fluid
- Titration of treatment fluid
- Treatment fluid given beyond 24 hours post burn hour
- Research blood specimen not drawn
- Research blood specimen not drawn on time

Informed Consent

- Incorrect Informed Consent: Unapproved Version
- Incorrect Informed Consent: Wrong Approved Version
- Incorrect Informed Consent: Wrong Study
- Informed Consent Not Properly Signed or Dated by Subject/LAR
- Informed Consent Not Properly Signed or Dated by Person Obtaining Consent
- Informed Consent Given by Someone Other Than the Subject's Legally Authorized Representative
- Informed Consent Without Required Witness (if required by local IRB)
- Unable to Locate Informed Consent Document (obtained but lost)

Enrollment

- Ineligible Subject Enrolled
- Screening for Eligibility Procedures Not Followed
- Subject Randomized Late
- Subject Randomized Prior to Screening Eligibility Procedures Completed
- Randomization Procedures Not Followed

Data Collection

- Data Incorrect – Not Supported by Source Documents
- Data Missed – Noted in Source Documents but Not Reported
- No Source Documents Found to Support Recorded Data
- Window for Data Collection Missed (too early/too late)
- Data obtained by Unauthorized Individual
- Data Correction Procedures Not Followed

AE/SAEs

- SAEs Reported Late
- SAE Reporting Procedures Not Followed
- SAE Reported with Incorrect Data
- SAE Reported with Missing Data
- Local IRB Reporting Requirements Not Followed

SITE REGULATORY ISSUES

- Failure to Maintain IRB Approval
- Failure to Maintain Regulatory Documents Binder (CV, License, Human Subjects Training)
- Noncompliance with Monitored Visit Procedures (Visits Cancelled at Last Minute, Coordinator Not Available, Medical Record or Other Source Documents Not Available)
- Study Records Unsecured/Missing
- Research Lab Equipment Unsecured/Missing

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Clinical Monitoring Strategy

- Risk based strategy:
  - High risk to patient or study conduct mitigated and monitored.
  - Low risk may be mitigated but not monitored.
- Central monitoring primarily
- On-site monitoring for
  - a) activities determined to be high risk and not amendable to remote monitoring strategies and
  - b) sites that are having difficulty conducting the study or quality issues AFTER remote/virtual monitoring techniques

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Clinical Monitoring: Critical elements

- Items below are considered to be critical data and study procedures that will be monitored:
  - Informed consent
  - Adherence to protocol eligibility criteria
  - Procedures for documenting appropriate accountability and administration of the investigational product
  - Conduct and documentation of procedures and assessments related to:
    - Study endpoints
    - Protocol required safety assessments
    - Evaluating, documenting, and reporting serious adverse events and unanticipated problems, subject deaths, and withdrawals
    - Conduct and documentation of procedures essential to trial integrity

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Clinical Monitoring: Participant level risks

Participant level risks identified

- Potential issues with consent process include multiple languages, consent/enrollment timeline of 8 hours from burn injury, eConsent process
  - translated consents; eConsent process; LAR; site specific enrollment strategies to support enrollment timeline
  - hard copy consents uploaded into REDCap for monitoring
- Confidentiality
  - User based access; secure patient logs locally; DCC de-identified data only

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Clinical Monitoring: Trial level risks

Trial level risks identified

- Protocol violations/adherence ** resuscitation algorithm followed**
  - Training
  - Monitoring total volumes infused
- Potential recruitment issues (subject identification, enrollment timeframe, LAR consent)
  - Local strategies; eConsent
  - Monitor screened and enrolled numbers
- Safety
  - AE, SAE, UP reporting
- Plasma distribution and management
  - Central tracking of plasma shipped and received
- Data Collection
  - Internal validity checks, eCRFS, MOP, DD, training

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Clinical Monitoring: Trial level risks

Trial level risks continued

- Unreliable outcomes assessments of primary and main secondary outcomes
  - Data collection training; scores as individual raw components
  - Paper eCRF uploaded to REDCap
- Research laboratory specimen handling and shipping
  - Training, central laboratory assessment of receipts
- Staff training issue due to small number of subjects per site
  - Staff trainings available on webpage; study training/refresher every 6 months during enrollment period

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROPOLIS webpage resources

https://www.nattrauma.org/propolis-training-resources/

Data

- Data Dictionary
- Data Collection Forms
- Hourly Spreadsheet (help determine individual patient hour post burn schedule)

Training

- PROPOLIS Protocol First 24 Hours infographic
- Specimen processing infographic
- REDCap data entry instructions and videos (assign ID, randomize, data entry, eConsent)
- REDCap plasma tracking instructions and videos (Cerus, enrolling center)

Policies

- Clinical Monitoring Plan
- PR Plasma Storage and Handling Policy
- Safety Reporting Policy
- Specimen Handling & Shipping Policy

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROPOLIS webpage resources

Documents

- Current approved protocol documents
- Current approval certificates

Study Administration

- Study timeline
- Enrollment dashboard – pending
- REDCap login link
- Tracking database template

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Training

- Training will be conducted using various methods
- All research staff and clinical staff involved in the research will complete the trainings and document per the Training log

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Training Grid

Topic	CRS	P	BB	CS	Tool
Screening and enrollment	x	x			SI PPT Protocol MOP
Resuscitation algorithm	X	X	X	X	SI PPT PROPOLIS First 24 Hours Infographic
eConsent	X				REDCap eConsent training documents/video
Randomization	X	X			SI PPT REDCap Randomization training document/video
Pathogen-Reduced Plasma Storage and Handling			X		PR Plasma Storage and Handling Policy
Pathogen-Reduced Plasma Administration	X	x		x	SI PPT
Pathogen-Reduced Plasma REDCap tracking			X		REDCap Plasma Tracking training document/video
Research sample collection, processing, shipping	x				Specimen Handling and Shipping Policy Specimen Preparation video Specimen Preparation Infographic
Safety Reporting	X	X			Safety Reporting Policy Unanticipated Problem Identification Schematic
Data Entry	X				REDCap Assigning ID and Randomization training document/video REDCap Data Entry training document/video
Clinical Monitoring	X	X			SI PPT Clinical Monitoring Policy

SI = Site Initiation; CRS = Clinical Research Staff; P = Physicians; BB = Blood Bank Personnel; CS = Clinical Staff

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Questions?

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Pathogen Reduced Plasma Storage & Handling

1. Introduction

1.1. This standard operating procedure provides hospital transfusion services personnel with directions for receipt, storage, thawing, and dispensing of Pathogen Reduced Plasma.

2. General Information

2.1. The INTERCEPT Blood System for Plasma is intended to be used for the ex vivo preparation of pathogen-reduced, whole blood derived or apheresis plasma in order to reduce the risk of transfusion-transmitted infection (TTI), and as an alternative to gamma irradiation for prevention of transfusion-associated graft versus host disease (TA-GVHD).

2.2. The INTERCEPT Blood System inactivates a broad spectrum of viruses, gram-positive and gram-negative bacteria, spirochetes, parasites and leukocytes.

2.3. The final product may contain up to 200 mL of plasma.

3. Receiving Pathogen Reduced Plasma

3.1. Shipping Facilities:

3.1.1. Each Blood Center will be responsible for manufacturing and shipping Pathogen Reduced Plasma units.

3.1.2. Pathogen Reduced Plasma units will be shipped using blood center standard operating procedures for shipping frozen blood components.

3.1.3. Units will be shipped in a validated shipping container with dry ice.

3.1.4. Facility Addresses:

Name	Address 1	City	State	Zip Code	Phone No.	FDA registration	Facility Identification
LifeSouth	4139 Carmichael Road	Montgomery	AL	36106	334-260-0803	FEI:3000203326	W1151
West Tennessee Regional Blood Center dba Lifeline Blood Services	183 Sterling Farms Drive	Jackson	TN	38305	731-427-4431	1071200	W0408

Vitalant	424 South Mesa Hills Dr.	El Paso	TX	79912	915-544-6601	2071464	W044
Vitalant	210 W. Cataldo Ave.	Spokane	WA	99201	509-624-0151	207464	W0685

3.2. Follow your institutional procedures for receiving frozen blood components shipped with dry ice.

3.3. Pathogen Reduced Plasma units are placed in individual cardboard sleeves to create a flat, uniform shape during freezing and to protect the frozen units during storage and shipping.

3.3.1. Inspect units upon receipt to ensure there is no evidence of thawing or breakage.

3.4. Pathogen Reduced Plasma units will be labeled with the following product code:

Parent	Division Codes	Product Description
E9003	E9003VA0, E9003VB0, E9003VC0	POOLED PLASMA | CP2D/XX/<=-18C | Frozen<=24h | Psoralen-treated | From 3 donors
E9004	E9004VA0, E9004VB0, E9004VC0	POOLED PLASMA | CP2D/XX/<=-18C | Frozen<=24h | Psoralen-treated | From 2 donors
E9006	E9006VA0, E9006VB0, E9006VC0	POOLED PLASMA | CPD/XX/<=-18C | Frozen<=24h | Psoralen-treated | From 3 donors
E9007	E9007VA0, E9007VB0, E9007VC0	POOLED PLASMA | CPD/XX/<=-18C | Frozen<=24h | Psoralen-treated | From 2 donors

3.5. Thawed codes:

Product code	Product description
E9013	Thawed POOLED PLASMA|CP2D/XX/refg|Frozen <=24h|Psoralen-treated|From 3 donors
E9014	Thawed POOLED PLASMA|CPD/XX/refg|Frozen <=24h|Psoralen-treated|From 3 donors
E9015	Thawed POOLED PLASMA|CPD/XX/refg|Frozen <=24h|Psoralen-treated|From 2 donors
E9023	Thawed POOLED PLASMA|CP2D/XX/refg|Frozen <=24h|Psoralen-treated|From 2 donors

3.6. Apheresis codes:

Frozen Code		Thaw Code	
E8733	Apheresis FRESH FROZEN PLASMA|ACD-A/XX/<=-18C|Psoralen-treated	E8872	Thawed Apheresis FRESH FROZEN PLASMA|ACD-A/XX/refg|>=200mL<400mL|Psoralen-treated
E8734	Apheresis FRESH FROZEN PLASMA|ACD-A/XX/<=-18C|1st container|Psoralen-treated	E8873	Thawed Apheresis FRESH FROZEN PLASMA|ACD-A/XX/refg|>=200mL<400mL|1st container|Psoralen-treated
E8735	Apheresis FRESH FROZEN PLASMA|ACD-A/XX/<=-18C|2nd container|Psoralen-treated	E8874	Thawed Apheresis FRESH FROZEN PLASMA/ACD-A/XX/refg|>=200mL<400mL|2nd container||Psoralen-treated
E8736	Apheresis FRESH FROZEN PLASMA|ACD-A/XX/<=-18C|3rd container|Psoralen-treated	E8875	Thawed Apheresis FRESH FROZEN PLASMA|ACD-A/XX/refg|<=200mL<400mL|3rd container|Psoralen-treated

NOTE: Final product received will be labeled with one of the listed division codes.

3.7. Follow your institutional procedures for entering blood component inventory into the Laboratory Information System (LIS).

4. Storing Pathogen Reduced Plasma

4.1. Pathogen Reduced Plasma must be stored in the plasma storage containers provided in the INTERCEPT INT3130 processing sets.

4.2. Pathogen Reduced Plasma may be stored at or below -18°C for up to 12 months.

4.3. Follow your institutional procedures for storing frozen blood components.

4.4. Pathogen Reduced Plasma units should be segregated from non-pathogen reduced FFP and PF24 inventory.

4.4.1. Refer to applicable study protocols and procedures for storing study products.

5. Thawing Pathogen Reduced Plasma

5.1. Following frozen storage at or below -18°C, thaw Pathogen Reduced Plasma according to current license requirements and institutional procedures for thawing and labeling thawed plasma components.

5.2. Infuse within 24 hours if held at 1° to 6°C.

6. Dispensing Pathogen Reduced Plasma

6.1. Refer to your institutional procedures for dispensing blood components.

6.2. Refer to applicable study protocols and procedures for dispensing blood components to enrolled study subjects.

7. Documenting Pathogen Reduced Plasma

7.1. The receipt and disposition of Pathogen Reduced Plasma wll be document in REDCap

7.2. The following elements will be recorded:

7.2.1. Donation Identification Number (DIN)

7.2.2. Product Code

7.2.3. Expiration date

7.2.4. Shipment date

7.2.5. Receving hospital

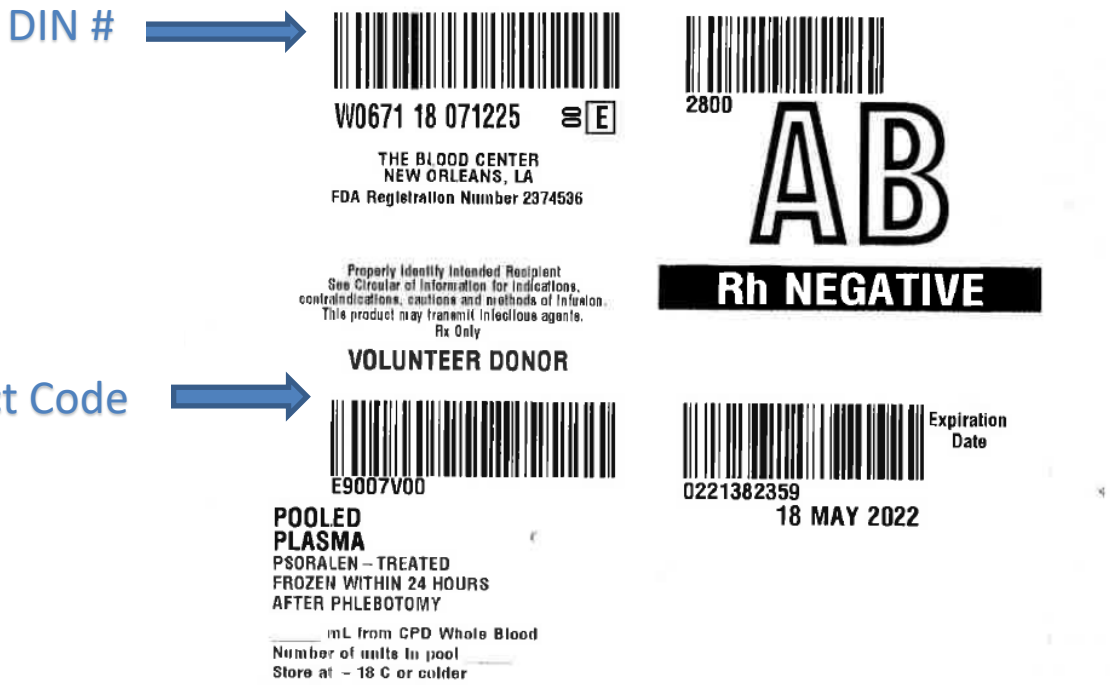
7.2.6. Final disposition (expired, transfused, discarded)

7.2.7. Date of final disposition

7.3. REDCap Database How-to: Use the PROPOLIS Plasma Tracking Database (PROPOLIS Center)

PROPOLIS REDCap Database How-to:
Use the PROPOLIS Plasma Tracking Database (PROPOLIS Center)

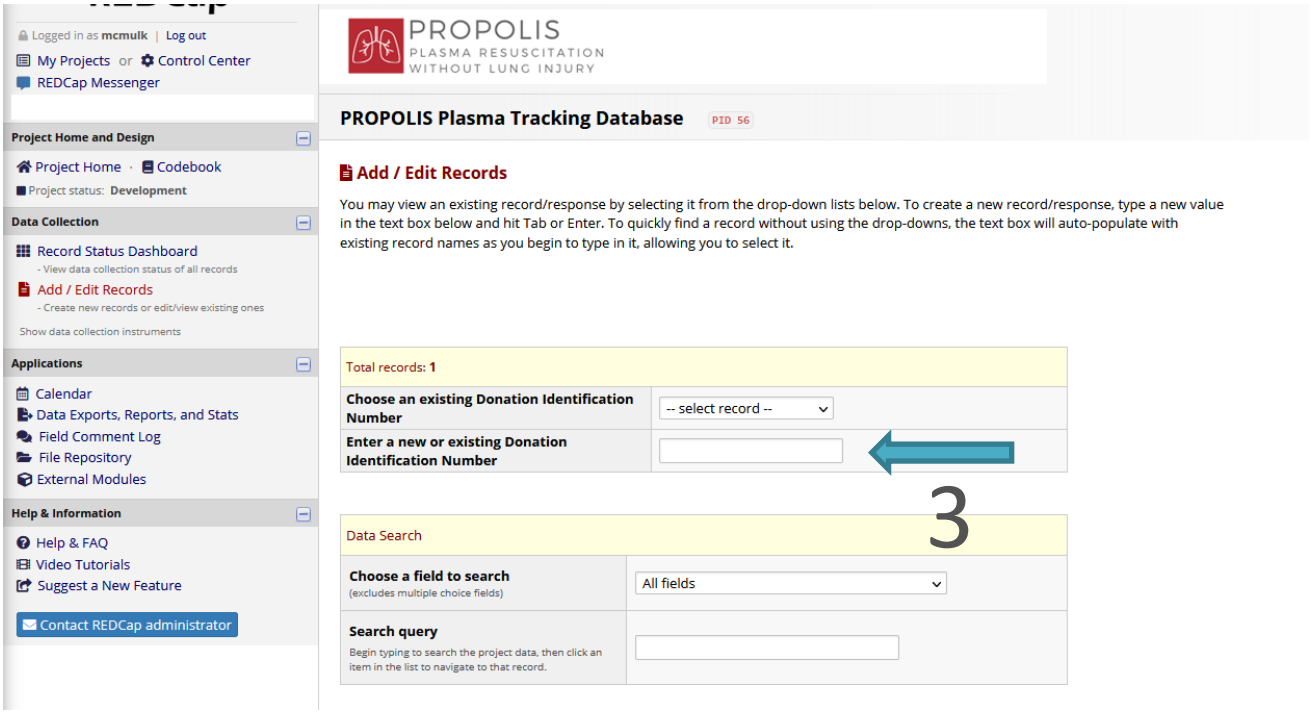
1) The record ID convention in PROPOLIS is “site_id number”, where site is the PROPOLIS center site number and ID number is the number assigned at each site. For the plasma tracking database, we will use the same convention, where the record ID is “site _Donation Identification Number_product code”. **When you receive plasma units, they will already be entered by Cerus into the PROPOLIS Plasma Tracking Database.**
    a. Site numbers are:
        1. US Army Burn Center
        2. UAB
        3. UW
        4. VU
        5. UTMB
        6. UTSW/Parkland
    b. For the ID number, the DIN on the plasma unit AND the product code are used. If this plasma unit was received at UAB (site 2), the record ID in the tracking database should be 2_W067118071225_E9007V00. Look for that record already entered into the database.



PROPOLIS
PLASMA RESUSCITATION
WITHOUT LUNG INJURY

PROPOLIS REDCap Database How-to:
Use the PROPOLIS Plasma Tracking Database (PROPOLIS Center)

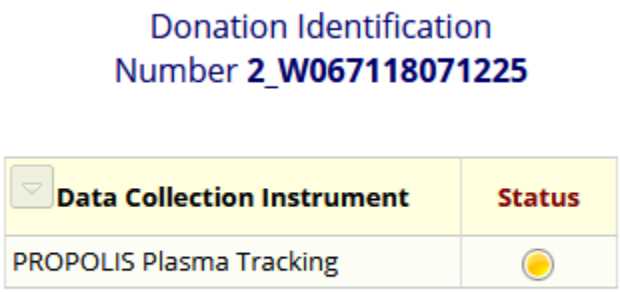
2) To update information for each plasma unit you have received, first select “Add/Edit Records.”
3) Enter the record ID into the blank field.



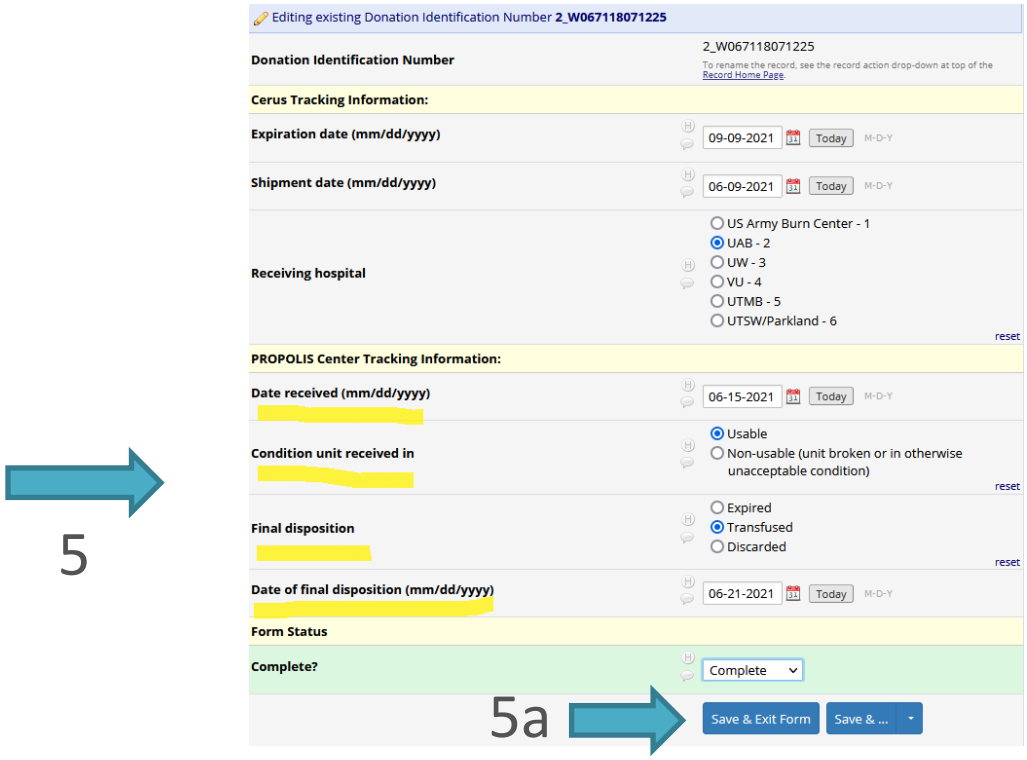
PROPOLIS
PLASMA RESUSCITATION
WITHOUT LUNG INJURY

PROPOLIS REDCap Database How-to:
Use the PROPOLIS Plasma Tracking Database (PROPOLIS Center)

4) The record dashboard will appear. To update the information needed from your center, hit the yellow radio button.



5) Some of the information on the form ("Expiration date", "Shipping date", and "Receiving hospital") has already been filled out by Cerus. As the PROPOLIS Center, you need to enter "Date received", "Condition received in", "Final disposition", and "Date of final disposition". **When you've finished entering that info, mark the Form Status as "Complete."** <u>If the unit arrives damaged, mark "Non-usable" for condition and "Discarded" for final disposition.</u>
   a. Finally, hit the "Save and Exit Form" button.
   b. The database will trigger Cerus to send more plasma units when you have used 20 units and marked them in the database.



PROPOLIS
PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROPOLIS Training Plan

The PROPOLIS Training plan will be conducted through various mediums to include teleconference meetings and self-paced learning tools.

All research staff associated with the study will complete the trainings and document per the Training Log

Clinical Research Staff Training

All clinical research staff involved with PROPOLIS must be trained to:

- Screen all eligible patients
- Obtain informed consent
- Randomize subjects using REDCap
- Understand the process to notify the blood bank
- Knowledgeable about the research sample collection process
  - Timepoints for research sample collection
  - Procedure for sample collection, processing, storage, and shipping
- Identify protocol deviations
- Understand plasma administration process
- Complete data collection
- Knowledgeable about database use and data entry

Physician Training

All physicians involved in the resuscitation of burn patients should be informed of the PROPOLIS protocol:

- Understand the process of screening for potential patients and timeline for enrollment
- Understand the resuscitation protocol and timeline for administration of plasma
- Understand the purpose of the research lab samples

Blood Bank Personnel

All personnel in the blood bank must be trained to:

- Understand the storage and preparation of the plasma
- Understand the process for notification of patient receiving study plasma
- Understand how to document plasma unit distribution
- Understand the process to reorder plasma product to maintain par level

Clinical Staff Training

Inservices need to be included for all clinical staff who may be involved in the care of PROPOLIS patients:

- Understand the PROPOLIS resuscitation protocol
- Understand the process of screening for potential patients

- Understand how to administer the study plasma and timeline for administration
- Understand the need for research specimen collection

Tools to use for training

All centrally developed training tools are available on the study webpage at https://www.nattrauma.org/research/research-policies-templates-guidelines/propolis-project-page/

The Resources for Study Staff section is password protected.

- PROPOLIS Power point presentation
- Study conduct (First 24 hours) infographic
- REDCap Randomization education document and/or video
- REDCap Data Entry education document and/or video
- REDCap eConsent education document and/or video
- Specimen Preparation video
- Specimen Handling and Shipping Policy
- Specimen preparation infographic
- Safety Reporting Policy and graphic
- REDCap Plasma tracking education document and/or video

Recommendations

- Recommend frequent and ongoing training prior to and throughout subject enrollment due to low number of subjects to be enrolled
- Document attendance at training meetings – use training log
- Train new staff as rotations occur

Training Grid

Clinical Research Staff (CRS); Physician (P); Blood Bank personnel (BB); Clinical Staff (CS)

Topic	CRS	P	BB	CS	Tool
Screening and enrollment	x	x			SI PPT Protocol MOP
Resuscitation algorithm	X	X	X	X	SI PPT PROPOLIS First 24 Hours Infographic
eConsent	X				REDCap eConsent training documents/video
Randomization	X	X			SI PPT REDCap Randomization training document/video
Pathogen-Reduced Plasma Storage and Handling			X		PR Plasma Storage and Handling Policy
Pathogen-Reduced Plasma Administration	X	x		x	SI PPT

Pathogen-Reduced Plasma REDCap tracking			X		REDCap Plasma Tracking training document/video
Research sample collection, processing, shipping	x				Specimen Handling and Shipping Policy Specimen Preparation video Specimen Preparation Infographic
Safety Reporting	X	X			Safety Reporting Policy Unanticipated Problem Identification Schematic
Data Entry	X				REDCap Assigning ID and Randomization training document/video REDCap Data Entry training document/video
Clinical Monitoring	X	X			SI PPT Clinical Monitoring Policy

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROPOLIS Training Log

Investigator Name: Leopoldo Cancio MD	**Protocol: Plasma Resuscitation without Lung Injury**	**Protocol version 2.0, 12/27/2020** **IRB Study ID:1311838**	**Site Number:** 1 US Army Burr

Training Topics:

#	Topic	#	Topic	#	Topic
1	Screening & enrollment	5	PR Plasma Storage & Handling	9	DataEntry
2	Resuscitation algorithm	6	PR Plasma REDCap tracking	10	Clinical Monitoring
3	eConsent	7	Research sample collection, processing, shipping	11	
4	Randomization	8	Safety Reporting	12	

Training Tools:

Tool ID:	Tool Name	Tool ID:	Tool Name	Tool ID:	Tool Name	Tool ID:	Tool Name
a.	Site Initiation powerpoint	e.	REDCap eConsent training documents/video	i.	Specimen Handling and Shipping Policy	m.	Unanticipated Problem Identification Schematic
b.	Protocol	f.	REDCap Randomization training documents/video	j.	Specimen Preparation video	n.	REDCap Assigning ID and Randomization training documents/video
c.	Manual of Procedures	g.	PR Plasma Storage and handling Policy	k.	Specimen Preparation Inforgraphic	o.	REDCap Data Entry training documents/video
d.	PROPOLIS First 24 Hours Inforgraphic	h.	REDCap Plasma Tracking training documents/video	l.	Safety Reporting Policy	p.	Clinical Monitoring Policy

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

PROPOLIS Training Grid					
Topic	**CRS**	**P**	**BB**	**CS**	**Tool**
Screening and enrollment	x	x			SI PPT Protocol MOP
Resuscitation algorithm	X	X	X	X	SI PPT PROPOLIS First 24 Hours Infographic
eConsent	X				REDCap eConsent training documents/video
Randomization	X	X			SI PPT REDCap Randomization training document/video
Pathogen-Reduced Plasma Storage and Handling			X		PR Plasma Storage and Handling Policy
Pathogen-Reduced Plasma Administration	X	x		x	SI PPT
Pathogen-Reduced Plasma REDCap tracking			X		REDCap Plasma Tracking training document/video
Research sample collection, processing, shipping	x				Specimen Handling and Shipping Policy Specimen Preparation video Specimen Preparation Infographic
Safety Reporting	X	X			Safety Reporting Policy Unanticipated Problem Identification Schematic
Data Entry	X				REDCap Assigning ID and Randomization training document/video REDCap Data Entry training document/video
Clinical Monitoring	X	X			SI PPT Clinical Monitoring Policy

CRS = Clinical Research Staff; P = Physician Staff; BB = Blood Bank Staff; CS = Clinical Staff

PROpOLIs
PLASMA RESUSCITATION WITHOUT LUNG INJURY

Trainee Printed Name	Trainee Signature	Topic #	Tool ID	Training Date	Trainer Signature & Date

Agenda – Study Initiation Meeting

Meeting Date and Start Time: June 16th, 2022 11:00 am (PT) – 12:00 pm (PT)

Study: Plasma Resuscitation without Lung Injury (IRB Protocol Version 2)
Site Investigator: Barclay Stewart, MD
Site: University of Washington, Harborview

Attendees: See separate sheet

Topic	Presenter	Duration/Total Time in minutes
I. Participating Sites/roles a. Clinical sites b. DCC c. Laboratory Sites d. Coordinating Center	Leopoldo Cancio	3 min
II. Protocol Overview a. Study design and objectives b. Endpoints c. Key inclusion/exclusion criteria d. Enrollment/Informed Consent e. Randomization f. Study procedures i. Resuscitation ii. Pathogen reduced plasma iii. Research laboratory specimens iv. Schedule of activities	Leopoldo Cancio	30 min
III. Data a. Data collection b. eCRF REDCap c. REDCap randomization d. REDCap trainings	Kara McMullin	5 min
IV. Safety Reporting a. EXPECTED Serious Adverse Events b. UNEXPECTED Serious Adverse Events c. Unanticipated Problems d. Protocol Deviations	Monica Phillips	5 min
V. Clinical Monitoring a. Critical elements b. Participant level risks c. Trial level risks	Monica Phillips	5 min

Topic	Presenter	Duration/Total Time in minutes
VI. PROPOLIS resources	Monica Phillips	2 min
VII. Training Plan a. Methods b. Grid c. Frequency	Monica Phillips	5 min
VIII. Closing/Review of Action Items	All	5 min

Training Log

Training: *Plasma Resuscitation without Lung Injury (PROPOLIS)*

Date: June 16, 2022
Presented by (Trainer): *Various – See agenda*

Investigator Name: *Barclay Stewart*	**Protocol:** **Plasma Resuscitation without Lung Injury (PROPOLIS)**	**Protocol Version & Date:** 2.0, 20July2022	**Site Number:** UW 3

Printed Name	Training Date	Signature	Signature Date

Training Log (Page 2)

Training: *Plasma Resuscitation without Lung Injury (PROPOLIS)*

Date: June 16, 2022
Presented by (Trainer): *Various – See agenda*

Investigator Name: Barclay Stewart, MD	**Protocol:** Plasma Resuscitation without Lung Injury (PROPOLIS)	**Protocol Version & Date:** 2.0, 20July2022	**Site Number:** UW 3

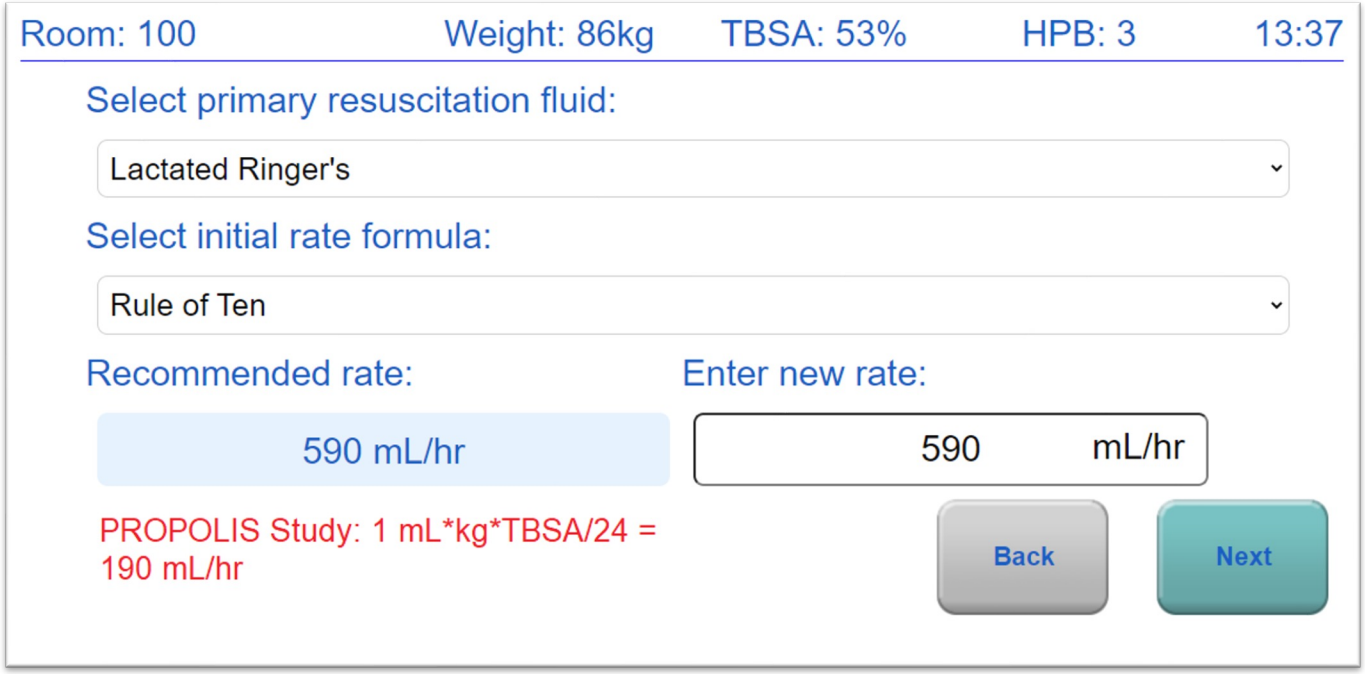
Printed Name	Training Date	Signature	Signature Date

Burn Navigator®
Planned Changes for PROPOLIS

May 2022

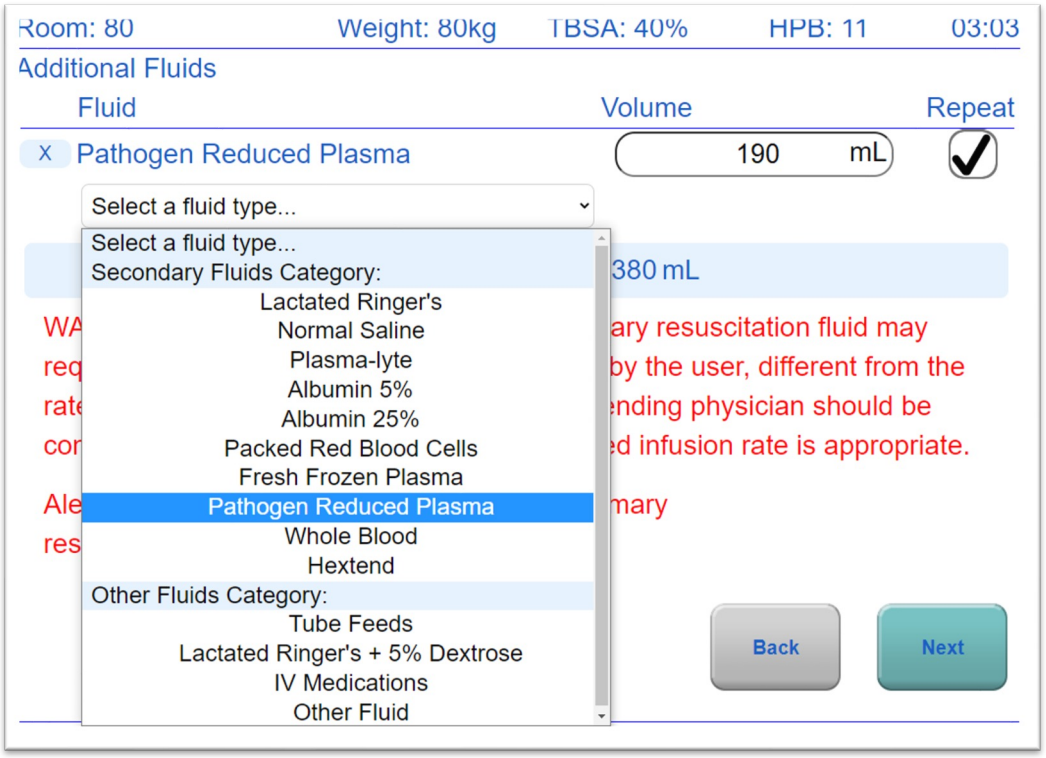
New Patient Wizard

- Include the PROPOLIS calculation on the initial recommendation screen



Hourly Fluid Wizard – Additional Fluids Screen

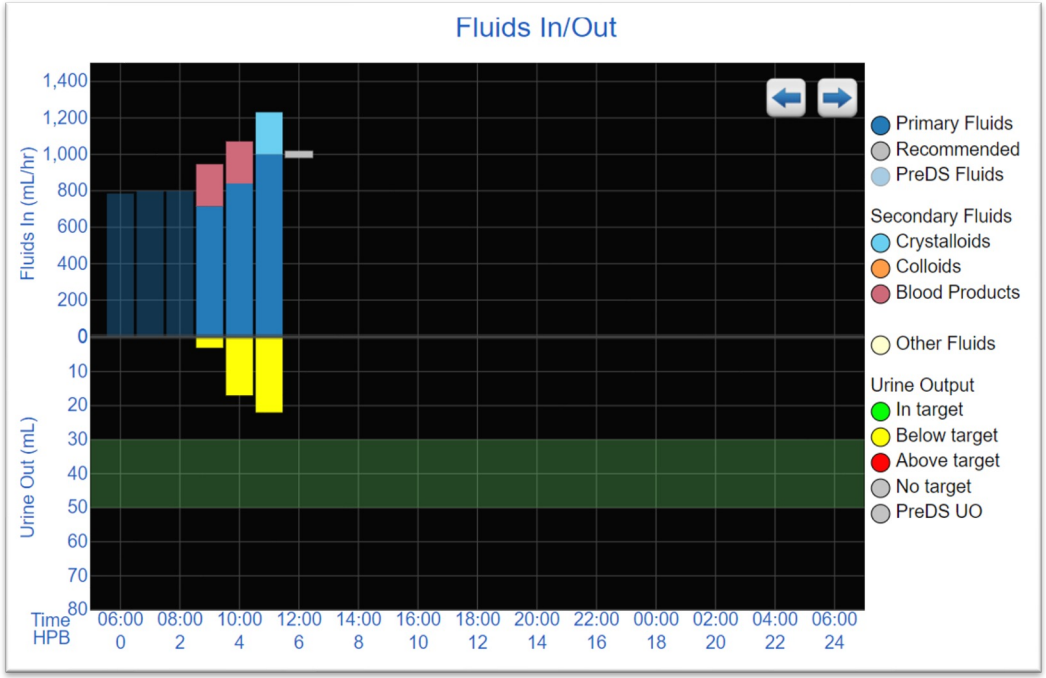
- PRP Added to the Additional Fluids drop down list
- Expecting users to enter
  - *either* PRP or LR
  - as an Additional Fluid
  - repeated hourly



Hourly Fluid Wizard – Fluids In/Out

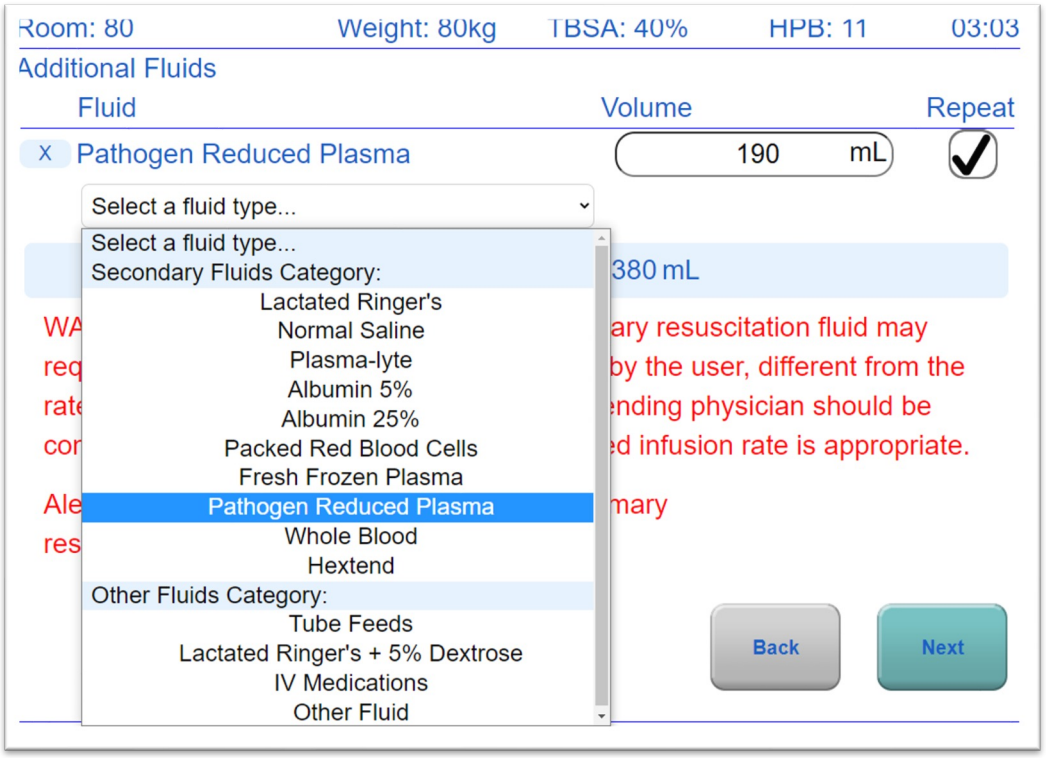
- The PROPOLIS fluid (*<u>either</u>* PRP or LR) would show as an additional fluid on the Fluids In/Out graph
  - *Picture to right shows both:*
    - PRP in salmon color
    - PROPOLIS LR in light blue
  - The titrated primary fluid (LR) will be shown in dark blue

- Whether PRP or LR, these values will be added to the **Volume Graph** and used in the 24-hour volume projection



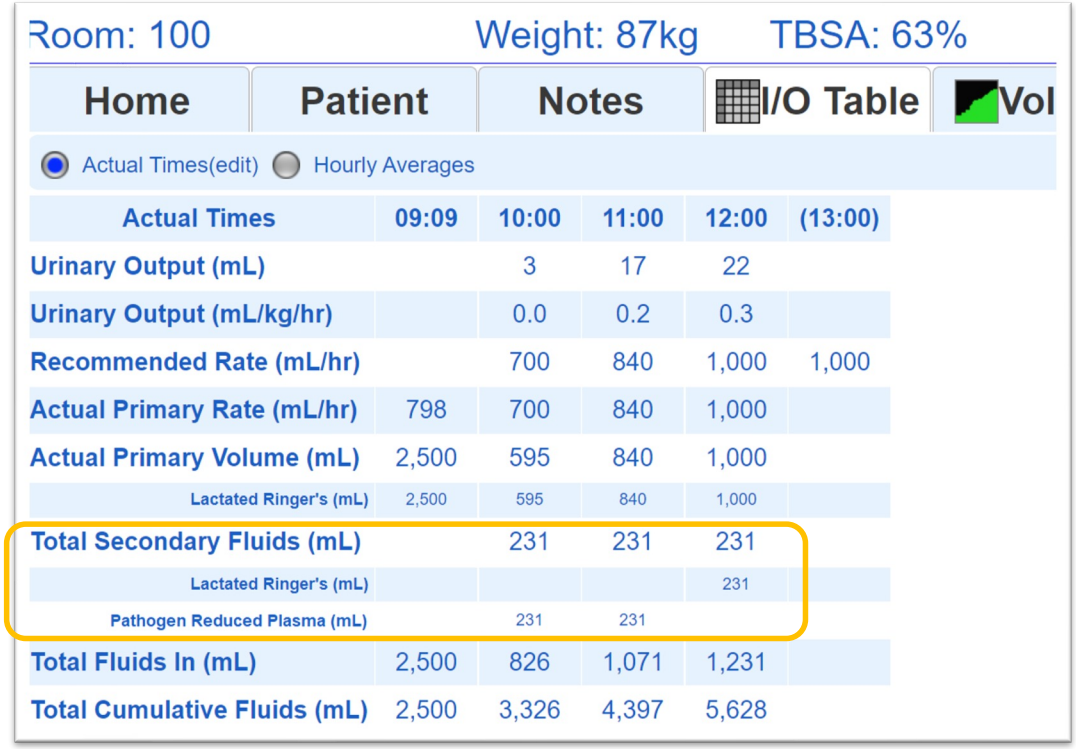
I/O Table

- Expecting users to enter
  - *<u>either</u>* PRP or LR
  - as an Additional Fluid
  - repeated hourly



I/O Table

- The PRP or LR fluid will show as a **Secondary / Additional Fluid** on the I/O Table and in the CSV data output file



Room: 100 Weight: 87kg TBSA: 63%

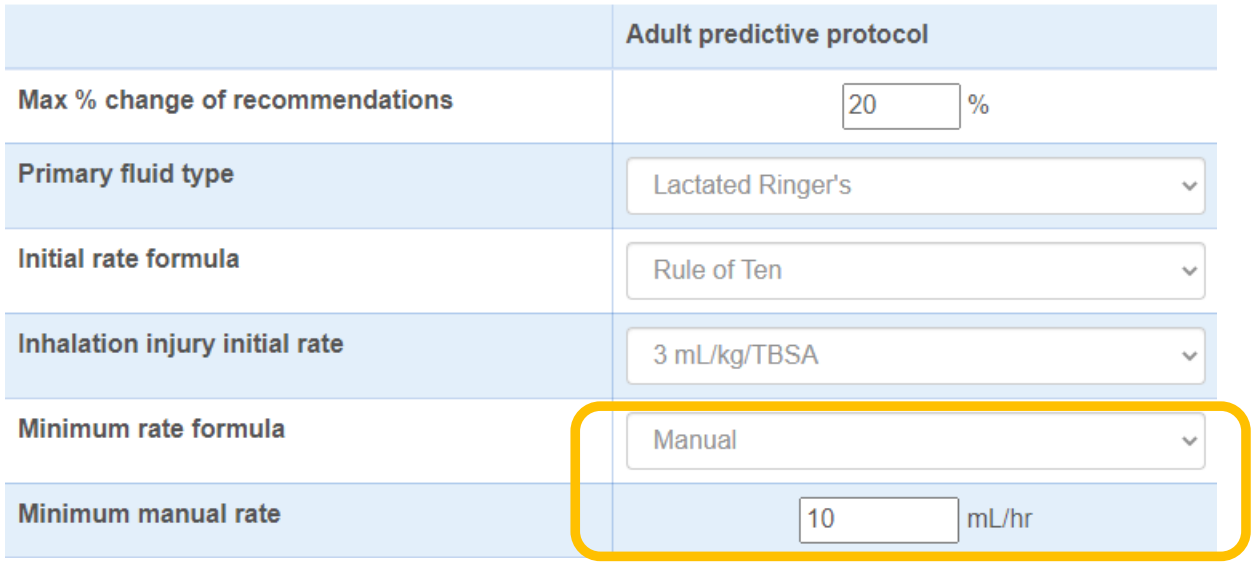
Home | Patient | Notes | I/O Table | Vol

Actual Times(edit) Hourly Averages

Actual Times	09:09	10:00	11:00	12:00	(13:00)
Urinary Output (mL)		3	17	22	
Urinary Output (mL/kg/hr)		0.0	0.2	0.3	
Recommended Rate (mL/hr)		700	840	1,000	1,000
Actual Primary Rate (mL/hr)	798	700	840	1,000	
Actual Primary Volume (mL)	2,500	595	840	1,000	
Lactated Ringer's (mL)	2,500	595	840	1,000	
Total Secondary Fluids (mL)		231	231	231	
Lactated Ringer's (mL)				231	
Pathogen Reduced Plasma (mL)		231	231		
Total Fluids In (mL)	2,500	826	1,071	1,231	
Total Cumulative Fluids (mL)	2,500	3,326	4,397	5,628	

Primary Fluid minimum recommendation

1. Set the Primary Fluid minimum recommendation rate to 10 mL/hr.
   - The PROPOLIS fluid rate (e.g., 86 kg, 53%TBSA = 190 mL/hr) could easily be greater than the common minimum rate (e.g., 100 mL/hr).
   - 10 mL/hr is the current Burn Nav minimum (a Keep-Vein-Open rate).



The changes will be made for both Burn Nav Web and Burn Nav Active tablets

PROPOLIS

Sites w/ Burn Nav Active tablets

- U.S. Army Burn Center (soon)
- Harborview Univ of Washington
- Parkland UTSW

Sites w/ Burn Nav Web

- UAB
- Vanderbilt (pending)
- UTMB

Arcos™

Burn Navigator®

Contact us!

+1 877.542.8025

info@arcosmedical.com

PROpOLIs

PLASMA RESUSCITATION WITHOUT LUNG INJURY

May 25, 2022

Study Objectives

Hypothesis: Administration of plasma for resuscitation after burn injury will 1) reduce 24-hour and 48-hour resuscitation volumes and 2) reduce the incidence of acute respiratory distress syndrome, multi-organ failure and other resuscitation-related morbidities

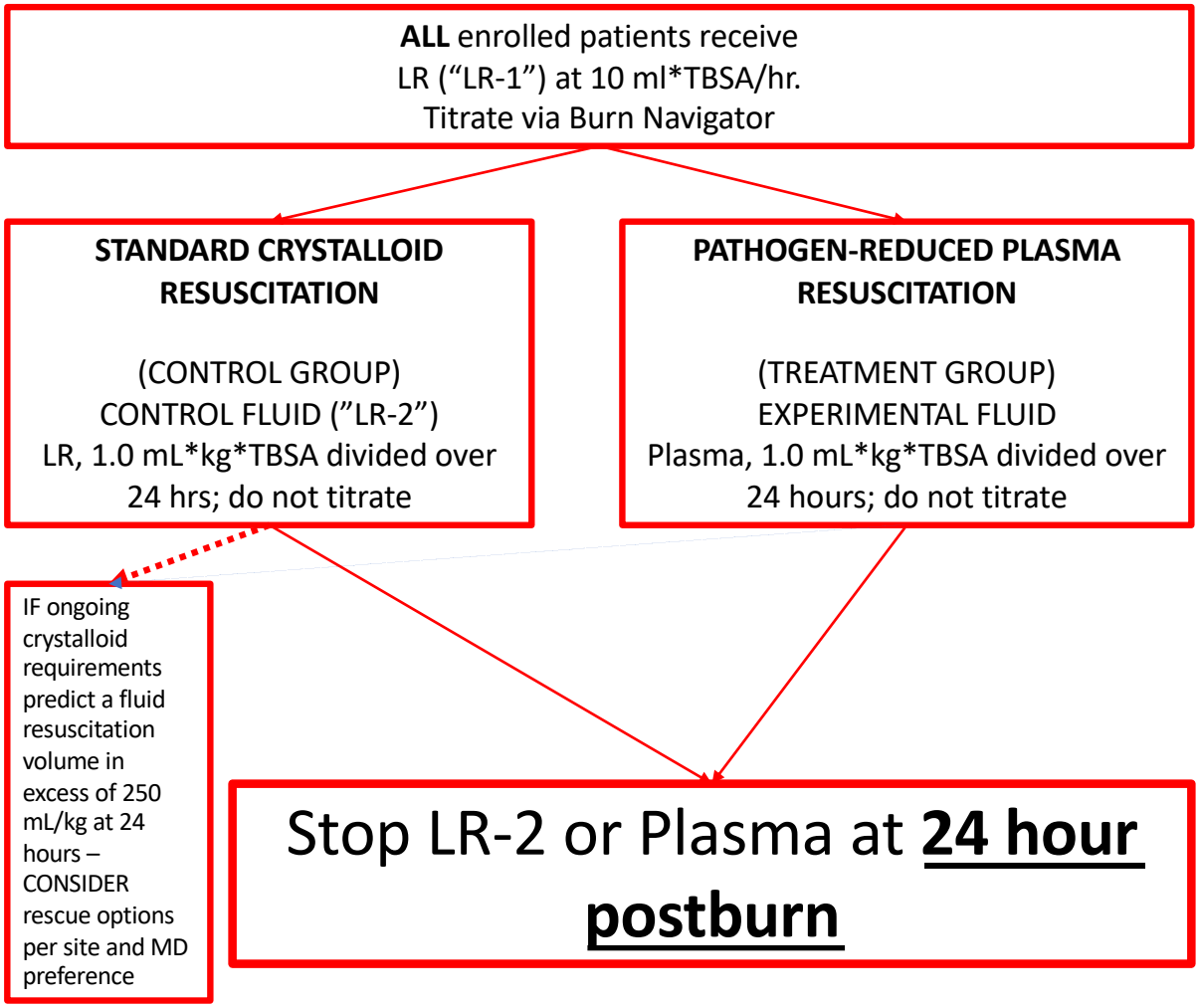
Objectives:

Specific aim 1: To determine whether administration of Pathogen-Reduced Plasma during burn resuscitation results in decreased total resuscitation volumes compared to standard-of-care crystalloid-based resuscitation.

Specific Aim 2: To determine whether Pathogen-Reduced Plasma administration during burn resuscitation reduces ARDS.

Specific Aim 3: To determine the effect of Pathogen-Reduced Plasma administration on the endotheliopathy of burns

Resuscitation



Pathogen-reduced Plasma

Blood Bank

- Each bag may contain up to 200 mL of plasma
- Units will be shipped frozen using dry ice
- Stored at or below -18℃ for up to 12 months
- Track receipt and distribution via REDCap
- Keep par level at 40 units

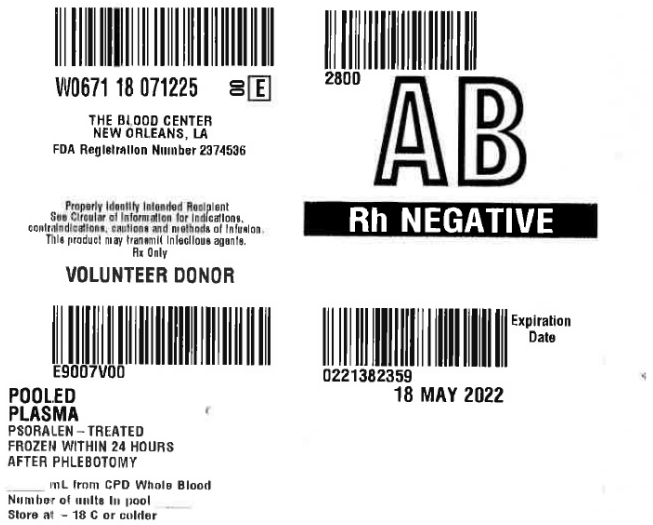
Pathogen reduced plasma

Patient/clinical

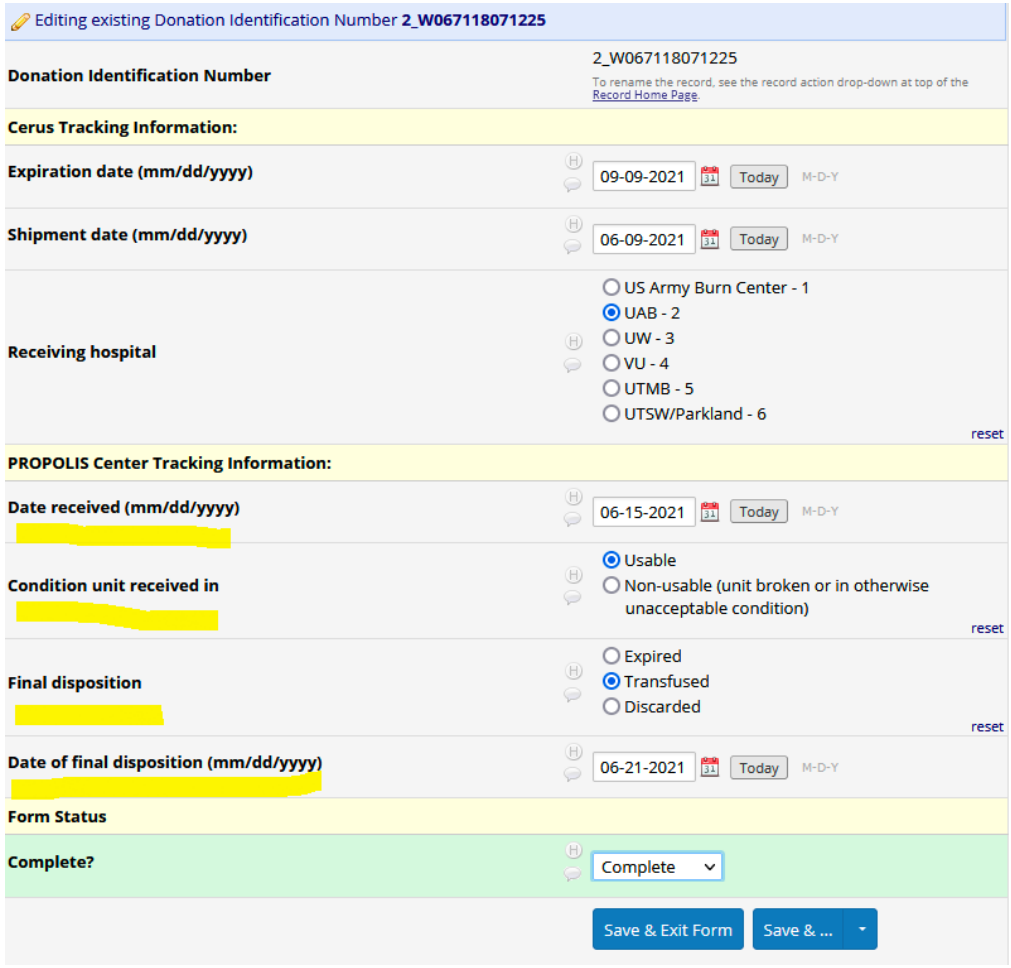
- Communication to blood bank as to need for study plasma
- Administer per local policy for blood product administration
- Use same blood tubing as traditional blood products
- Change blood tubing per local policy

REDCap Tracking Database

- When the Blood Bank receives plasma, those units will already be entered into the database by Cerus.
- Each unit is logged into REDCap with receiving entity number _ (underscore) DIN. Such as a unit to UW would be 5_W067118071225



- Look up each unit by Donor ID Number.
- Tracking form will be available
- Some information for that unit will be completed by Cerus.
- Enrolling blood bank will enter
  - Date received
  - Condition received
  - Final disposition
  - Date of final disposition
  - Hit save
- When your plasma level hist 20 units an email will be sent via REDCap to Cerus to initiate plasma shipment.



Past, Current, and Pending Support
Leopoldo C. Cancio, MD
10 April 2022

Previous Support (Last 5 Years)

Principal Investigator: Mauricio Rojas, MD (University of Pittsburgh)
Title: Combination of extracorporeal life support and mesenchymal stem cell therapy for treatment of ARDS in combat casualties and evacuation of service members with ARDS
Supporting Agency: USAMRAA
Period of Performance: 01/01/2015-12/31/2017
Funding:
Role: Associate investigator

Principal Investigator: Leopoldo C. Cancio, MD
Title: Efficacy of permissive-hypotension REBOA (pH-REBOA) in a porcine model of exsanguination
Supporting Agency: U.S. Army Medical Research and Materiel Command, Combat Casualty Care Research Program (CCCRP)
Period of Performance: FY17
Funding: /1 year
Role: Principal investigator

Principal Investigator: Ben Antebi, PhD (USAISR)
Title: Comparative evaluation of bone-marrow-derived and adipose-derived stem cells in swine model of prolonged field care
Supporting Agency: CCCRP
Period of Performance: FY 17-19
Funding: /3 years
Role: Associate investigator

Principal Investigator: Arezoo Mohammadipoor, PhD (USAISR)
Title: Preclinical Production and Characterization of Extracellular Vesicles Derived from Mesenchymal Stem Cells
Time Commitment: 5%
Supporting Agency: CCCRP
Period of Performance: FY 2018-2020
Funding: over 3 years
Goal: Produce, characterize, and evaluate extracellular vesicles derived from mesenchymal stem cells for use following combat injury.
Role: Associate investigator

Principal Investigator: Andriy I. Batchinsky, MD (USAISR and University of the Incarnate Word)
Title: Ex vivo Heparin-Free ECLS
Time Commitment: 5%
Supporting Agency: CCCRP
Period of Performance: FY 2020-2022
Funding: over 3 years
Goal: Develop and evaluate novel antithrombogenic coatings for extracorporeal devices which obviate the need for systemic anticoagulation.
Role: Associate investigator

Current Support

Principal Investigator: Adit Ginde, MD (University of Colorado-Denver)
Title: Multicenter Implementation Trial of Targeted Normoxia Strategy to Define Oxygen Requirements for Combat Casualty Care**:** An Approach to Reduce Warfighter Morbidity, Deployed Logistical Burden of Oxygen, and Readiness Costs
Time Commitment: 2%
Supporting Agency: Medical Technology Enterprise Consortium (MTEC-19-08-MuLTI)
Period of Performance: 2019-2022
Funding:
Goal: Determine the feasibility, safety, and effectiveness of the targeted normoxia approach to conserve oxygen and improve clinical outcomes in major burn patients.
Role: Site principal investigator

Principal Investigator: Leopoldo C. Cancio
Title: PROPOLIS (Plasma Resuscitation WithOut Lung Injury)
Time Commitment: 10%
Supporting Agency: Defense Medical Research and Development Program (DMRDP), Joint Program Committee-6 (JPC-6)/CCCRP Multi-Domain Lifesaving Trauma Innovations (MuLTI) Award, W81XWH-19-S-CCC1.
Period of Performance: 2019-2022
Funding: over 3 years (for all sites)
Goal: Randomized controlled multicenter clinical trial of plasma (Pathogen-Reduced Plasma) vs. crystalloid solution for burn shock resuscitation.
Role: Principal investigator

Principal Investigator: Soman Sen, MD (University of California, Davis)
Title: STAT – Standard Therapy plus Active Therapy to Improve Mobility, Long-term Activity and Quality of Life for Severely Burn Injured Patients after Skin Graft Surgery
Time Commitment: n.a.
Supporting Agency: Military Burn Research Program
Period of Performance: FY 2019-22
Funding: (overall); /patient (our site)
Goal: In burn patients, compare a standardized approach to rehabilitation (STAT protocol, which emphasizes four active components--mobility, strengthening, cardiovascular fitness and functional training), to standard of care
Role: Site principal investigator

Principal Investigator: Darren Heyland (Queen's University, Kingston, ON)
Title: VItamin C in Thermal injuRY: The VICToRY Trial. A Phase III Multi-Center Randomized Trial
Time Commitment: 5%
Supporting Agency: Military Burn Research Program (W81XWH-21-MBRP-CTRA)
Period of Performance: 2022-6
Funding:
Goal: Multicenter randomized controlled trial of high-dose vitamin C in burn patients
Role: Site principal investigator

Principal Investigator: Garrett Britton (USAISR)
Title: Compensatory Reserve Measurement (CRM) during Burn Shock Management
Time Commitment: 2.5%
Supporting Agency: Military Burn Research Program (W81XWH-21-MBRP-CTRA)
Period of Performance: 2022-6
Funding:
Goal: Single-site evaluation of the CRM in patients presenting in burn shock and undergoing resuscitation
Role: Associate investigator

Principal Investigator: Isaiah Turnbull (Washington University at St. Louis)
Title: Restoring Immune Function to Critically-Ill Burn Patients
Time Commitment: 5%
Supporting Agency: Military Burn Research Program (W81XWH-21-MBRP-CTRA)
Period of Performance: 2022-6
Funding:
Goal: Determine the ability of clinically available immune adjuvants to restore ex-vivo immune function to immunosuppressed burn sepsis patients
Role: Site principal investigator

Pending Support (proposals under review):

Principal Investigator: Jeffrey Carter, MD (Louisiana State University)
Title: Burns for Prehospital Providers Program (BPPP).
Time Commitment: 5%.
Supporting Agency: MTEC-22-01-BurnTraining, W81XWH-15-9-0001.
Period of Performance: TBD.
Funding: TBD.
Goal: Develop a curriculum and simulators to teach personnel how to take care of burns in an austere environment.
Role: Site principal investigator

Principal Investigator: Kerriann Greenhalgh, Ph.D. (KeriCure Medical)
Title: Commercialization and Clinical Assessment of Large Surface Area Burn Treatment for Prolonged Field Care and Long-Term Care
Time Commitment: 5%.
Supporting Agency: Joint Warfighter Medical Research Program, W81XWH-22-S-JWMRP
Period of Performance: TBD.
Funding: TBD.
Goal:.Clinically evaluate the efficacy of Field Shield Wound Dressing (FSWD) as a treatment for 10-30% TBSA burn wounds in a randomized crossover study vs a standard of care silver dressing.
Role: Co-Investigator/Site principal investigator

Principal Investigator: Kerriann Greenhalgh, Ph.D. (KeriCure Medical)
Title: Clinical Evaluation of Field Shield Spray on Wound Dressing with Antimicrobial silver and Lidocaine for Mass Casualty and Abnormal Burn Wound Management
Time Commitment: 5%.
Supporting Agency: Military Burn Research Program, W81XWH-22-MBRP-CTRA
Period of Performance: TBD.
Funding: TBD.
Goal:.Clinically evaluate the efficacy of the Field Shield Wound Dressing (FSWD) as an effective treatment for ubrn wounds in a mass casualty event where various size/shape/severeiteis of burs are experienced for a large number of patients in austere, degraded, or field care scenarios.
Role: Co-Investigator/Site principal investigator

Principal Investigator: Linda Sousse, Ph.D. (Coalition for National Trauma Research)
Title: Use of Low-Flow Extracorporeal Life Support in Burned Patients as Ultra-Lung Protective Method
Time Commitment: 5%.
Supporting Agency: Military Burn Research Program, W81XWH-22-MBRP-CTRA
Period of Performance: TBD.
Funding: TBD.
Goal:.Demonstrate the safety and efficacy of low-flow ECLS as a treatment for multiple respiratory conditions before and in conjunction with mechanical ventilation in burns.
Role: Co-Investigator/Site principal investigator

Principal Investigator: Christopher Argenta, Ph.D. (Applied Research Associates)
Title: Burn Digital Assistant
Time Commitment: 5%
Supporting Agency: MTEC-22-08-BDA
Period of Performance: TBD
Funding: TBD
Goal: Develop and test an advanced prototype system that cpatures burn casualty images and automatically generates an enhanced burn diagram (EBD) with burns objectively annotated by depth.
Role: Co-Investigator/Site principal investigator