CONTRACT NUMBER: W81XWH-16-D-0024

TITLE: Cold Stored Platelet Early Intervention (CriSP) trial

PRINCIPAL INVESTIGATOR: Jason Sperry

CONTRACTING ORGANIZATION: University of Pittsburgh, Pittsburgh, PA

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

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6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

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University of Pittsburgh
Pittsburgh, Pennsylvania 15213

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

CriSP-HS is a proposed 3-year (2 years of enrollment), open label, multi-center, randomized trial designed to determine the feasibility, efficacy and safety of urgent release cold store platelets in hemorrhagic shock patients.

Specific aim one is to determine the feasibility, most appropriate study population and primary outcome that will lead to a large multicenter clinical trial designed to evaluate the effectiveness of cold stored platelet early intervention in patients with injury and hemorrhagic shock. Specific aim two is to determine whether early cold stored platelet infusion compared to standard care results in improved clinical outcomes and hemostatic function in injured patients with hemorrhagic shock in patients. Specific aim three is to determine if early cold stored platelet hemostatic function is similar at 1 through 7 days as compared to 8 through 14 days in patients with hemorrhagic shock in patients.

CriSP-TBI is a proposed 3-year open label, single center, randomized trial designed to determine the feasibility, efficacy and safety of urgent release cold stored platelets in blunt injured patients with traumatic brain injury requiring platelet transfusion.

Specific aim one is to determine the feasibility, most appropriate study population and primary outcome that will lead to a large multicenter clinical trial designed to evaluate the effectiveness of cold stored platelet early intervention in patients with TBI requiring platelet transfusion. Specific aim two is to determine whether early cold stored platelet transfusion compared to standard platelet transfusion results in improved hemostatic function and clinical outcomes in patients with traumatic brain injury requiring platelet transfusion. Specific aim three is to determine if early cold stored platelet hemostatic function is similar at 1 through 7 days as compared to 8 through 14 days in patients with TBI on antiplatelet therapy.

15. SUBJECT TERMS
Trauma; Platelets; Cold-Stored Platelets; Transfusion; Hemorrhagic Shock; Traumatic Brain Injury

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	15	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

CriSP-HS
CriSP-HS is a proposed open label, multi-center, randomized trial designed to determine the feasibility, efficacy and safety of urgent release cold stored platelets in patients in hemorrhagic shock. Subjects will receive an early infusion of urgent release cold stored platelets (CSP) (intervention) or receive resuscitation, blood and blood component transfusion per site standard care (control). The primary outcome for the trial is feasibility with the principal secondary clinical outcome will be 24-hour mortality. Trial will utilize 5 level-1 trauma centers from within the LITES network and will enroll approximately 200 subjects.
CriSP-TBI
CriSP-TBI is a proposed open label, single center, randomized trial designed to determine the feasibility, efficacy and safety of urgent release cold stored platelets in blunt injured patients with traumatic brain injury requiring platelet transfusion. Patients randomized to the intervention arm will receive an early infusion of urgent release CSP (intervention) or receive room temperature (RT) platelet transfusion per standard care (control). The primary outcome for this pilot trial will be feasibility and the principle secondary clinical outcome will be 6-month Extended Glasgow Outcome Scale (GOS-E). Trial will utilize UPMC Presbyterian Hospital and will enroll a total of 100 subjects.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Trauma; Platelets; Cold-Stored Platelets; Transfusion; Hemorrhagic Shock; Traumatic Brain Injury

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

CriSP-HS
The purpose of Task Order 0004 (CriSP-HS) is to compare urgent release cold-stored platelets to standard of care in hemorrhagic shock patients.
CriSP-TBI
The purpose of Task Order 0004 (CriSP-TBI) is to compare urgent release cold-stored platelets to standard of care in patients with traumatic brain injury.

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

CriSP	
▪ Successful virtual In Progress Review (IPR) meeting held on 13-DEC-2022! - CCC/DCC worked on/finalized the PPT presentation in preparation for the DEC IPR meeting. ▪ The IDSMB review was conducted on 25-OCT-2022 and the board voted to allow CriSP (HS & TBI combined) to continue as is – final letter received 08-DEC-2022. ▪ DCC continued regular database maintenance. ▪ CCC/DCC continued responding to help tickets. ▪ Request for a No Cost Extension (NCE) was submitted to USAMRAA on 09-JUN-2023 – fully executed contract modification was received on 05-JUL-2023. - Period of Performance was extended to 30-SEP-2024. ▪ IDSMB review meeting was conducted on 22-AUG-2023 and the board voted to allow CriSP (HS & TBI combined) to continue as is. Awaiting final letter. - This meeting was extended to include interim and 6-month analysis for TBI.	
CriSP-HS	CCC/DCC conducted monthly site coordinator calls.
	The Annual IND Report for CriSP-HS (IND Number: 19467) covering MAR-2022 through MAR-2023 was submitted to the FDA on 24-MAR-2023.
	CCC finalized the process to wind down enrollment and notified sites of the general plan via email on 30-JUN-2023.
	IRB Continuing Review was submitted on 14-JUL-2023. ▪ Committee review date: 25-JUL-2023 – approval was granted on 25-JUL-2023.
	OHRO Continuing Review documents were submitted via eBRAP on 01-AUG-2023. ▪ Continuing review acceptance memo was received on 12-SEP-2023.
	Enrollment goal reached on 07-SEP-2023! ▪ Enrollment was projected to take 2 years and the goal was reached in 14 months!
	Data Entry and Query Resolution: ▪ DCC identified IDs to be included in the interim analysis, generated Data Compliance reports, and worked with sites to make sure data was entered and edits were addressed in preparation for the interim analysis data freeze. ▪ Sites were instructed to have all remaining data entered and queries/edits cleaned by 01-NOV-2023 for final analysis.
	Reallocation request submitted to the DoD for CSP costs. ▪ Approved obtained on 21-SEP-2023.
UCSF	Nothing to report.
Mississippi	Three months after commencing enrollment, site surpassed UCSF in total enrollments and maintained status of highest enrolling site throughout the remainder of the study.
	A minor modification was submitted 09-FEB-2023 and approved 14-FEB-2023 for Spanish translations of approved UMMC consent forms.
Baylor	The site was activated on 24-OCT-2022! ▪ Enrollment commenced on 03-NOV & their first patient was enrolled 15-NOV-2022.
	Reportable New Information (RNI2212001886) submitted to the Pitt IRB on 22-DEC-2022. ▪ 17-MAR-2023 IRB Determination: Committee has determined this event to represent serious noncompliance for administration of a study product to a patient not enrolled in the study. ▪ Full details outlined below in the following section: *Actual or anticipated problems or delays and actions or plans to resolve them*
	During the initial monitoring visit, the CCC investigated new processes and procedures following the RNI submitted DEC-2023. CCC noted new labeling at the ED fridge the contains the investigational product is highly visible and clearly indicated.
	On 08-DEC-2022, CCC notified OHRO of the prisoner status of one enrolled subject. OHRO

	acknowledged receipt 08-DEC-2022. ▪ No IRB determination is available as this event does not meet the definition of reportable to the sIRB. ▪ Per enrollment guidelines under EFIC, the data for this subject will be retained.
UT Houston	The site was activated on 27-SEPT-2022! ▪ Enrollment commenced on 27-SEP & their first patient was enrolled on 01-OCT-2022.
	Reportable New Information (RNI2306002050) submitted to the Pitt sIRB on 20-JUN-2023. ▪ 28-JUL-2023 sIRB Determination: The IRB reviewed response and closed the RNI with no further action required ▪ Full details outlined below in the following section: *Actual or anticipated problems or delays and actions or plans to resolve them*
USC	Site struggled to finalize blood bank procedures. Discussions with San Diego blood bank stalled throughout the study.
	Site investigated using Vitalant as their supplier, but Vitalant was unwilling to provide product due to limited availability of platelets.
	In APR-2023, the site confirmed that they will be unable to open to enrollment. ▪ San Diego Blood Bank has not moved forward, and no other blood supplier has been willing to provide product to them for the study.

Monitoring/Closeout Schedule

Remote Consent Monitoring:
- Reviews are conducted quarterly, and reports are distributed to sites upon completion.
  - Individual site calls are being held to discuss finding and provide additional guidance.
- Final Consent Review – site uploads will be due 30-NOV-2023.

Interim Monitoring Visit (IMV):
- Continued conducting remote IMVs with participating sites/trauma centers (schedule below).
  - Post IMV calls are being held with the PI and lead CRC to discuss findings.
- Close-Out Visits
  - Due to the LITES CCC monitoring requirements, Mississippi will need another IMV prior to their close-out. At this time, we are unsure if we will be able to combine these.

Items	Mississippi	UT Houston	Baylor	UCSF	USC
IMV-01	29-30-NOV-2022	09-FEB-2023	07-09-FEB-2023	01-12-AUG-2022	N/A
IMV-02	17-18-MAY-2023	25-29-SEP-2023	14-18-AUG-2023	20-24-FEB-2023	N/A
IMV-03	TBD: NOV-2023	N/A	N/A	21-25-AUG-2023	N/A
Closeout	TBD	TBD	TBD	TBD	N/A

CriSP-TBI	
Pittsburgh	CCC, Neuro, and MACRO continued to hold monthly meetings to discuss study logistics.
	CCC/Neuro submitted a minor modification on 03-OCT-2022 clarifying the process for using the notification letter for deceased subjects and cover letter for discharged subjects. ▪ IRB approval received 05-OCT-2022.
	IRB Continuing Review was submitted 18-OCT and approval was granted on 01-NOV-2022.
	OHRO continuing review documents were submitted on 04-NOV-2022. ▪ Acknowledgment memo received on 29-NOV-2022.
	Reached 50% enrollment milestone on 30-JAN-2023.
	Data Entry and Query Resolution: ▪ DCC identified IDs to be included in the interim analysis, generated Data Compliance reports, and worked with site to make sure data was entered and edits were addressed in preparation for the interim analysis data freeze.
	CCC/Neuro submitted a modification on 06-FEB-2023 to add the use of videoconferencing & DocuSign for the informed consent process, a brief letter to LAR for Remote Notification, and GOAT language for consent capacity evaluation was edited to clarify that

	the standard GOAT assessment will be utilized. ▪ IRB approval received 22-FEB-2023.	
	Monitoring visit with the University of Pittsburgh's Education and Compliance Support personnel was conducted 03-11-AUG-2023.	
	Enrollment hit 90% complete on 04-SEPT-2023.	
Monitoring Note	The University of Pittsburgh Education and Compliance Support for Human Subject Research (ECS-HSR) conducts interim monitoring visits, reviews consents/notifications, and regulatory documents for the Pittsburgh site (TBI cohort).	
Enrollment *(as of 30-SEP-2023)*		
CriSP-TBI	**Pittsburgh (goal: 100)**	**93**
Enrollment (goal reached on 07-SEP-2023):		
CriSP-HS	UCSF	52
	Baylor	19
	UT Houston	47
	Mississippi (UMMC)	82
	TOTAL (goal: 200)	**200**
	USC	N/A

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

CriSP
- Prepare In-Progress Review (IPR) presentation for NOV-2023 meeting.

CriSP-HS
- CCC/DCC will continue to hold monthly site coordinator calls.
- Conduct site monitoring visits/close-out visits at necessary sites.
- Conduct final remote consent monitoring.

CriSP-TBI
- Complete study enrollment.
- Continue to hold monthly meetings and collaborate with Neuro & MACRO teams on closing enrollment.

CriSP-HS Travel Reporting

Travel conducted:
- Mississippi's Interim Monitoring Visit (IMV-01) was conducted on 29-30-NOV-2022.
  - Two LITES personnel attended/conducted the IMV in-person as planned.
- UT Houston and Baylor's Interim Monitoring Visit (IMV-01) was conducted on 06-09-FEB-2023.
  - Four LITES personnel attended/conducted the IMV in-person as planned.
- Mississippi's Interim Monitoring Visit (IMV-02) was conducted on 16-19-MAY-2023.
  - Three LITES personnel attended/conducted the IMV in-person.
- One LITES personnel (Emily Kelly) attended the 2023 MHSRS conference in Kissimmee, FL – TO4 abstract accepted and poster presented on 15-AUG-2023.

Travel anticipated:
- Mississippi's third Interim Monitoring Visit (IMV) is in the process of being scheduled. We expect 1-3 LITES personnel to attend.

CriSP-TBI Travel Reporting: No travel funds are budgeted for this cohort.

Cumulative to Billing Period: **30-SEP-2023**	**Travel Funds Budgeted**	**Cumulative Actual Spent**	**Remaining Balance**

Upcoming Travel for Quarter: **OCT-2023 to DEC-2023**	**Traveler Name**	**Destination/ Purpose**	**Estimated Date of Travel**
	Elizabeth Gimbel	Jackson, MS IMV-03/Close-out Visit	NOV-2023 - TBD
	Renee Weinman	Jackson, MS IMV-03/Close-out Visit	NOV-2023 - TBD
	Meghan Buck	Jackson, MS IMV-03/Close-out Visit	NOV-2023 - TBD

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report.

What was the impact on other disciplines?

If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

5. **CHANGES/PROBLEMS:** The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

▪ CCC anticipates periods of CSP shortages throughout the year. - Enrollment for UCSF and Pittsburgh was put on pause a few times due to Vitalant not having product available. The longest pause was approx. 2.5 weeks for both sites in NOV-2022.	
Baylor Site	Reportable New Information (RNI2212001886) submitted to the Pitt sIRB on 23-DEC-2022. ▪ In DEC-2022, the Baylor research team was notified by their blood bank that a unit of CSP was administered to a non-study patient. It appears that someone from the clinical team removed the platelets from the fridge and administered it to the patient; there was no research team involvement. - The patient experienced no adverse reaction to the CSP. - The research team performed an investigation but was unable to determine exactly why the investigational product was used. - Additional signage has been added to the units and the physical location of the CSP to indicate that they are Investigational Use only. Additional training has also been provided to the clinical ED team. ▪ sIRB Committee meeting was held on 10-FEB-2023. The Committee decided to defer the RNI to obtain information from the study team on whether or not the patient who received the cold stored platelet unit would have been eligible for the study. Response submitted on 23-FEB-2023: - The research team was not involved in the screening of this patient. The patient was not eligible for the study due to having exposed brain matter (GSW to head). - Baylor risk management and patient LAR were notified of the incident. Due to the patient's injury, direct notification was not possible. ▪ 17-MAR-2023 sIRB Determination: Committee has determined this event to represent serious noncompliance for administration of a study product to a patient not enrolled in the study. ▪ The Pitt sIRB distributed the reporting letter from the Senior Vice Chancellor of Research Protections to OHRP, DoD, and the FDA as required by policy. Memo received 24-MAR-2023 that the IRB acknowledges the completion of the required actions and considers this RNI closed. ▪ OHRO indicated that an Executive Summary (EXSUM) would be filed – the file was sent to the Deputy Director in APR-2023. - Acceptance memo from OHRO was received on 09-MAY-2023. No further action required.
UT Houston Site	Reportable New Information (RNI2306002050) submitted to the Pitt sIRB on 20-JUN-2023. ▪ Patient came to the enrolling hospital for the UT Houston site as a transfer from another hospital for a fall with SDH and femur fracture on 10-JUN-2023. Patient was on platelet medications. Trauma was not consulted for the patient. Neurosurgery was consulted and the residents ordered platelets. The ED nurse obtained the platelet from the ED fridge which is where CSP is stored due to neuro telling her to transfuse platelets urgently. No technician was available to obtain room temp platelets from the blood bank and the nurse recalled having platelets in the ED fridge and transfused those despite signage and labeling indicating that CSP was for study use only. The blood bank stopped the nurse before the second infusion after receiving the blood requisition slip and noticing the error. Patient was made "comfort measures only" and passed on 11-JUN-2023. - No transfusion reaction or other event related to the transfusion of CSP was apparent before death. CMO designation was unrelated to CSP transfusion. ▪ UT Houston will label the basket in the blood fridge containing CSP denoting it for trauma research only. The RAs will also check the CSP at the beginning of each shift

	to ensure that the CSP is in the basket, not on the shelf. Clinical nursing staff is also being re-educated regarding the CSP. ▪ In addition, the Coordinating Center will be requesting that all participating sites complete retraining of their ED staff on the study and restricted use of CSP. Although product accountability SOPs were collected prior to study start, and the monitoring team has been visually verifying appropriate signage and labeling on site during monitoring visits, the Coordinating Center will be reviewing current signage and labeling and providing suggestions for improvement. IRB determination received on 20-JUL-2023 – Modification Required to Secure Approval: ▪ The Committee requested that the corrective action plan be amended to include notification of Risk Management at the University of Houston of this event. ▪ The Committee also requested that the Coordinating Center consider the use of a sealed separate box inside the blood fridge for the investigational product. ▪ The Committee will consider this RNI closed once the requested actions are completed. Response Submitted to the sIRB on 25-JUL-2023. IRB reviewed response and closed the RNI with no further action required on 28-JUL. Correspondence was forwarded to N. Englar (OHRO) and UT Houston personnel on 28-JUL-2023. ▪ UTHealth Houston IO and risk management have been informed. UTHealth Houston also shared the information with their partner hospital Memorial Hermann-Texas Medical Center (MH-TMC), where the incident occurred. MH-TMC reviewed the case within the context of a Quality Committee. ▪ We appreciate the board's suggestions for increased security of product. Vitalant advised against the use of sealed/closed boxes for storage of CSP as they were concerned with adequate gas exchange with the units. Given this concern, we have not advised sites to implement a closed box system for storage. ▪ To date, notification of the use of CSP has not occurred. UTHealth Houston Risk Management and IO advised the study team against providing notification as they do not think it would be in the family's best interest to inform them about the event since CSP are approved for use in this indication. MH-TMC has not shared the results of their review. OHRO Reportable Event Acceptance Memorandum was received on 23-AUG-2023. No further action required.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report

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

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution

committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals

Not applicable to TO 0004

Significant changes in use of biohazards and/or select agents

Not applicable to TO 0004

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

  Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

- Study Design, Rational and Implementation for the Linking Investigators in Trauma and Emergency Services (LITES) Cold Stored Platelet (CriSP) for Hemorrhage and Brain Injury Trials
  - Abstract accepted and poster presented at MHSRS on 15-AUG-2023.

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

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report.

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

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Personnel Listing: see page 16

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

Nothing to report.

What other organizations were involved as partners?

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

Quad Chart: see page 16

9. APPENDICES:

Annual and final reports are submitted to: https://ers.amedd.army.mil/

AND
One Copy: Contract Specialist, Ronnie Sanford
Email: ronald.s.sanford2.civ@health.mil

One e-Copy: Contracting Officer's Representative (COR), Sandy Snyder
Email: sandy.j.snyder.civ@health.mil

Personnel Listing (as of 30-SEP-2023)

W81XWH-16-D-0024 / W81XWH-19-F-0494			
Department	**Personnel Name**	**UPitt Role**	**T0 % Effort**
Neurosurgery	Agnone, Allison	Staff Nurse	40%
Surgery	Alsaadi, Nijmeh Nasser	Post doc research fellow	100%
Neurosurgery	Borrasso, Allison Jean Hricik	Health Professional II	75%
Surgery	Brubaker, Donovan Paul	Clinical Research Coord.	40%
Emergency Medicine	Dias, Ethen	Medical Student Worker	0%
Epidemiology (GSPH)	Gillis, Jenna	Research III	50%
Surgery	Gimbel, Elizabeth	Assistant Project Manager	20%
Emergency Medicine	Guyette, Francis X III	Co-PI	25%
Surgery	Harner, Ashley Marie	Health Professional II	78%
Surgery	Hayes, Hannah E	Clinical Researcher II	16%
Surgery	Kelly, Emily Theresa	Clinical Research Coord.	43%
Surgery	Neal, Matthew D	Faculty Researcher	5%
Neurosurgery	Okonkwo, David O	Co-Investigator	5%
Epidemiology (GSPH)	Over, Lisa Ann	Research IV	50%
Surgery	Peet-Michelessi, Chelsea Ann	Asst Proj Mgr.	29%
Neurosurgery	Puccio, Ava M	Co-Investigator	4%
Surgery	Rayman, MaryAnne	Research II	23%
Epidemiology (GSPH)	Silfies, Laurie N	Systems Engineer IV	20%
Surgery	Sperry, Jason L	PI	25%
Surgery	Stephenson, Joshua Paul	Data Entry Assistant	15%
Epidemiology (GSPH)	Wisniewski, Stephen R	Co-PI	2%
Pathology	Yazer, Mark Harris	Co-Investigator	5%

YEAR 4 QUAD CHART

Linking Investigations in Trauma and Emergency Services – TO4

17052001-TO4/W81XWH-16-D-0024, W81XWH19F0494

Cold Stored Platelet Early Intervention (CriSP) Trial - LITES Task Order 0004

PI: Jason Sperry MD MPH **Org:** University of Pittsburgh **Award Amount: $5,529,830**

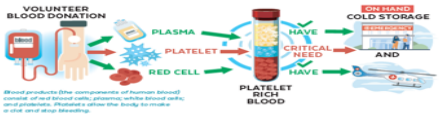
STUDY AIMS

Determine the feasibility, efficacy and safety of urgent release cold stored platelets as compared to standard care in injured patients in hemorrhagic shock

I. Determine the feasibility, most appropriate study population and primary outcome that will lead to a large multicenter clinical trial designed to evaluate the effectiveness of cold stored platelet early intervention in patients with injury and hemorrhagic shock.
II. Determine whether early cold stored platelet infusion compared to standard care results in improved clinical outcomes and hemostatic function in injured patients with hemorrhagic shock.
III. Determine if early cold stored platelet hemostatic function is similar at 1 through 7 days as compared to 8 through 14 days in patients with hemorrhagic shock.

Open label, multi-center, randomized trial designed to determine the feasibility, efficacy and safety of urgent release cold stored platelets in patients in hemorrhagic shock.

COLD STORED PLATELET EARLY INTERVENTION TRIAL (CriSP)



ACCOMPLISHMENTS

CriSP TBI:
- ✓ Enrollment N (as of SEP-2023) = 93
- ✓ Enrollment hit 90% complete on 04-SEPT-2023.

CriSP-HS:
- ✓ Enrollment goal (200) reached on 07-SEP-2023! Enrollment was projected to take 2 years and the goal was reached in 14 months!

Timeline and Cost

Activities CY	SEP-19	20	21	22	23	24
Startup, Hiring, Single IRB approval, Contracts, Central IRB organization, Database creation, site selection						
3-year (2-year enrollment), 300 patients						
Site training; 1 year enrollment, 1/2 enrolled - interim analysis – 150 patients						
Enrollment 2 year – 150 patients						
Data analysis and publications						
Estimated Budget	320K	320K	320K	2.3M	2.3M	NCE

Updated: (University of Pittsburgh 13-OCT-2023)

Goals/Milestones

CY19 Goal – Study Startup
- ✓ Finalize study protocol
- ✓ IND application submission to FDA

CY20 Goal – Study Startup & Patient enrollment
- ✓ IND approval
- ✓ TBI cohort modification
- ✓ IRB submission

CY21 Goal – Patient enrollment (N=300)
- ✓ IRB approval; SecArmy EFIC waiver approval
- ✓ Data base creation and CRF completion, data dictionary
- ✓ Site Initiation Visits and Site training *(initiated)*
- ✓ HRPO approval (HS/TBI CCC/DCC & TBI performance site)

CY22 Goal
- ✓ HRPO approval (HS performance sites)
- ✓ Begin Patient enrollment (150)
- ✓ Interim analysis – 50% enrollment

CY23 Goal – Request No Cost Extension (NCE)
- ❑ Finish enrollment (150)
- ❑ Data analysis and publication

Budget Expenditure compared to Actual thru 30-SEP-2023
- Actual Expenditures: $3,548,231.63
- Scheduled Expenditures: $4,592,571.08