

CONTRACT NUMBER: W81XWH-16-D-0024

TITLE: Cold Stored Platelet Early Intervention (CriSP) trial

PRINCIPAL INVESTIGATOR: Jason Sperry

CONTRACTING ORGANIZATION: University of Pittsburgh

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Fort Detrick, Maryland 21702-5012

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				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Jason L. Sperry, Ashley Harner, Meghan Buck, Laurie Silfies, Natalie Rogers E-Mail: sperryjl@upmc.edu ; rymanam@upmc.edu ; buckml@upmc.edu ; silfiesl@edc.pitt.edu ; rogersnb@upmc.edu				5d. PROJECT NUMBER	
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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					
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- 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 17-DEC-2021!
- DSMB member selection and charter finalized in Q4 2021.
 - Initial meeting conducted 23-NOV-2021; received formal DSMB approval on 23-DEC-2021.

CriSP-HS

Data Coordinating Center

- DCC finalized forms and reports in the electronic data management system (MATRIX).
- CCC/DCC conducted MATRIX site testing and trainings. The QxQs were finalized for sites.
- CCC/DCC developed Manual of Procedures (MOP) for sites; this was disseminated during SIVs.
- DCC distributed Ops Memos:
 - Ops Memo 001 distributed 05-AUG-2022 - *MATRIX Consent Form (CON) update and New Comments Form (COM) added*
 - Ops Memo 002 distributed 22-AUG-2022 - *HSPLT Update*
 - Ops Memo 003 distributed 24-AUG-2022 - *HSSCR Update*

University of Pittsburgh Institutional Review Board (IRB)

- CCC submitted protocol modification on 18-FEB-2022. Pitt sIRB Committee review for protocol modification was held on 07-MAR; approval granted 16-MAR-2022
 - Site onboarding (CC/PD results, local consent language and translated consents).
 - Minor protocol/consent revisions requested in the iDSMB outcome letter.
 - Expand on “abdominal” from FAST criterion and include extended FAST (eFAST).
 - Script for mortality status follow-up.
- CCC submitted CR on 04-AUG-2022 and received approval from sIRB on 16-AUG-2022
- ICF changes for UT Houston requested by OHRO were approved by sIRB on 16-AUG-2022.

DoD OHRO (Formerly HRPO)

- Obtained initial study approval from HRPO on 01-DEC-2021.
- Continuing Review (CR) submitted to OHRO 19-AUG-2022.
 - OHRO CR acknowledgment was received on 22-SEP-2022.

FDA

- IND annual report and protocol v7 amendment submitted on 23-MAR-2022.
- CCC submitted CC/PD materials to FDA and public docket in MAY-2022; all items approved 26-MAY-2022.

CriSP-HS Enrolling Sites

- CCC continued conducting monthly Site Coordinator calls.
- CCC worked with participating sites in preparing for study commencement (see table below):
 - CCC requested remaining sites provide HRPO documents to expedite submission process (following necessary approvals).
 - Randomization materials are distributed to sites in advance of scheduled SIV.
 - PM is working with sites to collect study activation documents following their Site Initiation Visit (including training/DOA logs, site specific SOPs, etc.).

Items	USC	Houston	Baylor	UCSF	Mississippi
CC/PD results submitted	13-AUG-2021	16-NOV-2021	16-NOV-2021	16-NOV-2021	13-AUG-2021
CC/PD results approved	09-SEP-2021	16-MAR-2022	16-MAR-2022	02-DEC-2021	09-SEP-2021
MATRIX (eDCF) Training	15-NOV-2021	10-MAY-2022	09-MAY-2022	20-JAN-2022	10-MAR-2022
Site Initiation Visit (SIV)	22-NOV-2021	06-JUN-2022	10-JUN-2022	17-FEB-2022	25-APR-2022
Initial HRPO submission	08-OCT-2021	07-JUN-2022	02-JUN-2022	31-MAR-2022	07-FEB-2022
HRPO approval	02-DEC-2021	26-AUG-2022	07-JUL-2022	11-APR-2022	16-FEB-2022
Activation memo sent	<i>Pending</i>	27-SEP-2022	<i>Pending</i>	21-JUN-2022	15-SEP-2022
Open to enrollment		27-SEP-2022		23-JUN-2022	16-SEP-2022
First subject enrolled		<i>Pending</i>		23-JUN-2022	17-SEP-2022
IMV-01				01-AUG-2022	

CriSP-TBI

Data Coordinating Center

- CCC/DCC finalized electronic randomization logistics.
- CCC/DCC finalized data collection forms and processes and developed protocol specific reports.
- CCC/DCC conducted MATRIX trainings.
- DCC made modifications to eDCF as needed after study start.
- DCC distributed Ops Memos:
 - Ops Memo 001 sent 13-JUL-2022 – *TBI Data Form and Report Changes*
 - Ops Memo 002 sent 05-AUG-2022 – *MATRIX Consent Form (CON) update and New Comments form (COM) added*
 - Ops Memo 003 sent 22-AUG-2022 – *TBINH Update*
 - Ops Memo 004 sent 24-AUG-2022 – *TBSCR Update*

University of Pittsburgh Institutional Review Board (IRB)

- Protocol modification approved by IRB on 27-JAN-2022
 - Revised v5 consent based on DSMB request.
 - Minor revisions to IRB application for congruence with FDA Protocol.
- FITBIR language added to consent and IRB application; approval was granted on 16-FEB-2022
- Pitt IRB protocol modification was reviewed on 29-MAR; approval granted 31-MAR-2022
 - Personnel added to perform the GOSE evaluation at the 6-month timepoint.
 - Expanded the description of data sharing with FITBIR.
 - Provided clarification to expand on the following exclusion criteria: Platelet transfusion contraindicated per care team (for example, recent vascular stent, embolic stroke, intracranial and/or vascular lesions).
- CCC/Neuro submitted protocol modification on 23-MAY-2022 & received IRB comments on 27-MAY. CCC responded to comments on 03-JUN-2022 and approval was granted on 08-JUN-2022.
 - Addition of GOAT assessment to assist with assessment of capacity to provide consent, particularly prospectively.
 - Addition of exclusion criterion "currently on therapeutic anticoagulants other than aspirin and/or clopidogrel." (Additional anticoagulants increase the risk of TBI progression, and their reversal agents will confound the laboratory results as we will be unable to discern whether the reversal agent or platelets are responsible for halting progression.)
 - Addition and removal of study staff to assist with trial execution.
- CCC/Neuro submitted protocol v11 on 20-JUL-2022 and received IRB approval on 21-JUL-2022.
 - Clarification that platelets may be ordered/directed by either neurosurgery or trauma surgery
 - Revision of the randomization section to describe the electronic randomization process
 - Added a description of the GOAT for potential subjects with a GCS of 15 into the Screening and enrollment section per FDA request
 - Consent forms updated to reflect new coordinator and correct third-person language

University of Pittsburgh Office of Education and Compliance

- CCC/Neuro submitted mod in response to comments received from RISE Review and received approval in OCT-2021.
- Pitt Education and Compliance conducted an audit of the Pittsburgh performance site 10-JUN-2022 through 16-JUN-2022.
- Pitt Education and Compliance conducted a monitoring visit of the Pittsburgh performance site 06-SEP-2022 through 09-SEP-2022.

FDA

- CCC submitted a protocol version 8 and CC/PD materials to FDA and public docket in APR-2022. Revisions to the protocol and public disclosure documents were accepted on 06-MAY-2022.
- CCC submitted a protocol version 9 to FDA in JUN-2022
 - FDA requested the language surrounding screening tests (GOAT and GCS) also be included in the

Screening and Enrollment section of the protocol.

- CCC submitted Annual Report and protocol v11 to FDA on 16-AUG-2022

DoD HRPO

- USAMRDC, CDMRP, and ORP HRPO conducted a successful site visit of the CriSP-TBI study at the University of Pittsburgh on 21-22-JUN-2022.
- Site Assessment Visit (SAV) – routine monitoring visit report received 28-JUL-2022.
 - No regulatory deficiencies or concerns
 - Commended us on monitoring, CC/PD toolkit, PMs w/ comprehensive knowledge to execute TOs, thorough process for reviewing AEs, external sites SOP review for onboarding, implementation of Florence.

CriSP-TBI Site (University of Pittsburgh)

- Pitt Site Initiation Visit (SIV) conducted 29-NOV-2021.
- Pitt performance site commenced enrollment on 21-MAR-2022; first TBI enrollment 04-APR.
- CCC/Neuro continued ongoing meetings to finalize details for study start-up.
- CCC conducted meetings with Multidisciplinary Acute Care Research Organization (MACRO) throughout this year to plan and finalize enrollment logistics and RA/lab training.
- CCC, Neuro, MACRO, and ED staff (in collaboration with Vitalant) developed a research fridge emergency plan to further secure investigational product and minimize possibility of CSP being inadvertently used off-study.
- CCC continued ongoing communication with Vitalant to continue working through study blood product logistics, blood ordering process, distribution, budget, and finalizing contract.
 - Vitalant contract was fully executed on 10-MAR-2022.
- CCC/MACRO began ordering lab supplies for start of enrollment.
 - Refrigerator for CSP storage in ED received in NOV-2021; initial validation by Vitalant in DEC-2021.
- CCC collaborated with Neuro/MACRO to provide training to study staff, ED staff, and residents.

Enrollment (as of 27-SEP-2022):

CriSP-TBI	Pittsburgh (goal: 100)	28
CriSP-HS	UCSF	15
	USC	<i>Enrollment anticipated to begin in Q4 2022</i>
	Baylor	<i>Enrollment anticipated to begin in Q4 2022</i>
	Houston	0
	Mississippi	2
	TOTAL (goal: 200)	17

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 <ul style="list-style-type: none"> ▪ Initiate quarterly remote consent monitoring. ▪ Conduct iDSMB meeting in OCT-2022. ▪ Prepare In-Progress Review (IPR) presentation for 14-NOV-2022. 			
CriSP-HS <ul style="list-style-type: none"> ▪ Continue monthly All Site Coordinator calls. ▪ Continue to work with sites to satisfy all prerequisites for site activation. ▪ Activate remaining enrolling sites. ▪ Continue study enrollment, IMVs, and consent monitoring. 			
CriSP-TBI <ul style="list-style-type: none"> ▪ Continue to meet with Neuro, MACRO, and lab personnel weekly. ▪ Continue study enrollment. 			
CriSP-HS Travel Reporting: No travel conducted this quarter. <ul style="list-style-type: none"> ▪ Mississippi’s first Interim Monitoring Visit (IMV) is anticipated to be scheduled in the upcoming quarter. ▪ Plans have not yet been solidified but we expect a minimum of 3 LITES personnel to attend/conduct the IMV in-person. 			
CriSP-TBI Travel Reporting: No travel funds are budgeted for this cohort.			
Cumulative to Billing Period: 30-SEP-2022	Travel Funds Budgeted	Cumulative Actual Spent	Remaining Balance
Upcoming Travel for Quarter: OCT-2022 to DEC-2022	Traveler Name	Destination/ Purpose	Estimated Date of Travel
	TBN	Jackson, Mississippi IMV-01	NOV/DEC-2022
	TBN	Jackson, Mississippi IMV-01	NOV/DEC-2022
	TBN	Jackson, Mississippi IMV-01	NOV/DEC-2022

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.

- COVID-19 pandemic may impact regional blood center engagement for study planning as institutional priorities shift toward pandemic response nationwide. CCC worked with sites to resolve issues with blood centers.

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.

- Several sites have expressed difficulty with staffing and bandwidth. The CCC worked with these sites to continue completing startup tasks but must be sensitive to conditions at each institution.

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.*

Nothing to report.

- **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?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change”.

Example:

*Name: Mary Smith
Project Role: Graduate Student
Researcher Identifier (e.g. ORCID ID): 1234567
Nearest person month worked: 5*

*Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.
Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Personnel Listing: see page 15

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

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

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report.

What other organizations were involved as partners?

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

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *Collaboration (e.g., partner’s staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner’s staff use each other’s facilities, work at each other’s site); and*
- *Other.*

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.

Quad Chart: see page 15

9. **APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

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-2022)

W81XWH-16-D-0024 / W81XWH-19-F-0494			
Department	Personnel Name	UPitt Role	TO % Effort
Neurosurgery	Borrasso, Allison Jean Hricik	Health Professional II	7%
Epidemiology (GSPH)	Gillis, Jenna	Research III	51%
Emergency Medicine	Guyette, Francis X III	Co-PI	8%
Surgery	Harner, Ashley Marie	Health Professional II	105%
Surgery	Hayes, Hannah E	Clinical Researcher II	23%
Epidemiology (GSPH)	Macey-Kalcevic, Melody	Research IV	50%
Surgery	Neal, Matthew D	Faculty Researcher	8%
Neurosurgery	Okonkwo, David O	Co-Investigator	5%
Epidemiology (GSPH)	Over, Lisa Ann	Research Specialist IV	33%
Epidemiology (GSPH)	Pattison, Angela Dawn	Research Specialist IV	50%
Surgery	Peet-Michelessi, Chelsea Ann	Asst Project Mgr.	45%
Neurosurgery	Puccio, Ava M	Co-Investigator	5%
Surgery	Rogers, Natalie	Research Coordinator (CRC)	42%
Epidemiology (GSPH)	Silfies, Laurie N	Systems Engineer IV	18%
Surgery	Sperry, Jason L	PI	25%
Epidemiology (GSPH)	Wisniewski, Stephen R	Co-PI	2%
Pathology	Yazer, Mark Harris	Co-Investigator	5%

YEAR 3 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.

ACCOMPLISHMENTS

- ✓ Enrollment N (as of SEP-2022): TBI = 28 and HS = 17
 - First Crisp-TBI cohort enrollment was on 04-APR-2022
 - First Crisp-HS cohort enrollment was on 23-JUN-2022
- ✓ All Crisp-HS performance sites have obtained initial OHRO approval
- ✓ USAMRDC, CDMRP, and OHRO conducted a successful site visit of the Crisp-TBI study in JUN-2022.

Timeline and Cost

Activities	CY	SEP-19	20	21	22	23
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

Updated: (University of Pittsburgh 14-OCT-2022)

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
- ✓ Data base creation and CRF completion, data dictionary
- ✓ SecArmy EFIC waiver approval
- ✓ Site Initiation Visits and Site training (*initiated*)
- ✓ HRPO approval (HS/TBI CCC/DCC & TBI performance site)

CY22 Goal

- HRPO approval (HS performance sites) – partially complete; 2 of 5 sites pending
- ✓ Begin Patient enrollment (150) - TBI Cohort only
- ✓ 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-2022

- Actual Expenditures: \$1,866,999.14
- Scheduled Expenditures: \$4,011,837.81