CONTRACT NUMBER: W81XWH-16-D-0024-0002

TITLE: Shock, Whole blood and Assessment of TBI (SWAT)

PRINCIPAL INVESTIGATOR: Jason Sperry

CONTRACTING ORGANIZATION: University of Pittsburgh
Pittsburgh, Pennsylvania 15213

REPORT DATE: OCT 2022

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

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5b. GRANT NUMBER
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5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

University of Pittsburgh
Pittsburgh, Pennsylvania 15213

8. PERFORMING ORGANIZATION REPORT

9. SPONSORING / MONITORING AGENCY NAMES) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Task Order 0002 is a multicenter, prospective, observational cohort study over a 4-year period to determine the impact of whole blood resuscitation in trauma patients with hemorrhagic shock at risk of large volume resuscitation with and without TBI. Specific Aim one is to evaluate patient centered outcomes associated with early whole blood resuscitation practice as compared to component resuscitation in poly-trauma patients with hemorrhagic shock and further characterize outcome benefits in those with traumatic brain injury. Specific Aim two is to characterize blood pressure and resuscitation endpoints during the acute resuscitation phase of care and the associated/attributable outcomes for traumatic brain injury in patients with hemorrhagic shock.

15. SUBJECT TERMS
Trauma; whole blood resuscitation; component therapy; traumatic brain injury; hemorrhagic shock

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRDC
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
U	U	U	UU	13	

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

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

Task Order 0002 is a multicenter, prospective, observational cohort study over a 4-year period to determine the impact of whole blood resuscitation in trauma patients with hemorrhagic shock at risk of large volume resuscitation with and without TBI. Specific Aim one is to evaluate patient centered outcomes associated with early whole blood resuscitation practice as compared to component resuscitation in poly-trauma patients with hemorrhagic shock and further characterize outcome benefits in those with traumatic brain injury. Specific Aim two is to characterize blood pressure and resuscitation endpoints during the acute resuscitation phase of care and the associated/attributable outcomes for traumatic brain injury in patients with hemorrhagic shock.

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

Trauma; whole blood resuscitation; component therapy; traumatic brain injury; hemorrhagic shock

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.

The purpose of Task Order 0002 to determine the impact of whole blood resuscitation in trauma patients with hemorrhagic shock at risk of large volume resuscitation with and without TBI. Early whole blood resuscitation will be compared to standard component resuscitation. The study will also further characterize blood pressure and resuscitation endpoints in poly-trauma 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.

- Successful virtual In Progress Review (IPR) meeting held on 17-DEC-2021!
- CCC/DCC held monthly site coordinator calls through AUG-2022.
  - The monthly coordinator call in MAR-2022 was replaced with individual site calls to discuss data completion & query resolution.
  - Transitioned from monthly calls to monthly email updates.
- Payment reports for invoicing were distributed quarterly.
- No Cost Extension (NCE) contracts were distributed and have been executed.
- CCC/DCC monitored the sites data entry progress & data completion forms.
  - Generated and distributed monthly Data Compliance Reports (DCR) to clinical sites.
  - Distributed edit error logs to individual clinical sites.
  - As of JUN-2022, all sites have complete data sets with no outstanding queries!
- DCC monitored status of new certifications completed.
- Study equipment was collected from each site (tablets, keyboards, & styli).
- Close-out visits were conducted between JUN-AUG2022.
  - Reports were distributed and fully executed reports were collected/filed.
- As of AUG-2022, all consent queries have been resolved!
- Final CTs were uploaded, and the remaining scans were read by the neuroradiologist on 29-SEP-2022!
- Final sample shipping was initiated in NOV-2021 & completed in FEB-2022.
- Alinity i-STAT training was conducted on 15-JUN-2022 and testing was initiated!
  - Testing complete on 11-AUG. Analysis on-going.
  - Testing some isolated, non-head injury patients. Anticipate doing this in early-OCT-2022.
- Fully executed copy of the contract to update the SOW (reallocation of funds for analysis of proteome, metabolome, and TBI biomarkers) was received on 26-MAY-2022.
  - Proteome and metabolome (anticipated completion OCT-2022) – pending results.
- Investigator meeting held on 09-SEP to discuss preliminary results and potential secondary analyses.
- MHSRS presentation on 13-SEP: Whole blood is associated with a lower independent risk of mortality and improved hemostasis: Results of a multi-center prospective observational study of patients in hemorrhagic shock

Enrollment goal reached in SEP-2021!

- Reportable New Information (RNI) for over-enrolling by one patient was submitted to the sIRB on 30-JUN-2022
  - sIRB acknowledged the RNI and no further action is required
  - OHRO & COR were notified, and no further action is required.

University of Pittsburgh	317
University of Pennsylvania	142
University of Texas Health Science Center at Houston	324
Denver Health & Hospital Authority	111
Oregon Health & Science University	112
University of Miami	34
University of Texas Southwestern (closed to enrollment)	11
TOTAL (goal: 1,050)	**1,051**

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.

- Draft manuscript
- Continue to send monthly updates to study personnel.
- CCC to address some final lab issues (ionized calcium).
- Additional lab testing on-going:
  - Alinity i-STAT analysis
  - Proteome and metabolome – anticipated completion OCT-2022

Travel Reporting: No travel conducted this quarter.
- No travel is anticipated for the next quarter.

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**
	N/A	N/A	N/A

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.

Unbalanced comparison groups because the last remaining component site transitioned to using whole blood as part of their resuscitative strategy.

- The final split of whole blood patients to component patients is estimated to be 60/40 respectively.
- Differences in baseline characteristics were observed between those classified in the whole blood group to those not in whole blood group. To account for these differences, and allow for comparison, statistical modeling techniques will be used. In particular, propensity scores which estimate the likelihood of being classified in the whole blood group. These propensity scores will then be used in the statistical analyses as an inverse probably weight to control for the confounding effects of the imbalanced characteristics.

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 0002

Significant changes in use of biohazards and/or select agents

Not applicable to TO 0002

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.*

  - Abstract accepted for oral presentation at MHSRS and presented on 13-SEP-2022. Whole blood is associated with a lower independent risk of mortality and improved hemostasis: Results of a multi-center prospective observational study of patients in hemorrhagic shock

- **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 13

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.

Year 5 Quad Chart: see page 13

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-0024-0002			
Department	**Personnel Name**	**UPitt Role**	**T0 % Effort**
Neurosurgery	Battistella, Cara	Health Professional I	37%
Surgery	Gimbel, Elizabeth	Assistant Project Manager	28%
Surgery	Hayes, Hannah E	Clinical Researcher II	20%
Surgery	Kar, Upendra Kumar	Faculty Researcher	17%
Epidemiology (GSPH)	Luther, James Francis	Biostatistician IV	3%
Epidemiology (GSPH)	Odonnell, Jeffrey H	Systems Programmer IV	17%
Neurosurgery	Okonkwo, David O	Co-Investigator	1%
Epidemiology (GSPH)	Over, Lisa Ann	Research Specialist IV	33%
Surgery	Owens, Logan	Data Mgmt. Coord.	67%
Surgery	Rayman, MaryAnne	Research II	67%
Epidemiology (GSPH)	Silfies, Laurie N	Systems Engineer IV	23%
Surgery	Sperry, Jason L	PI	5%
Surgery	Stephenson, Joshua Paul	Data Entry Assoc	67%
Surgery	Vincent, Laura Everett	Program Administrator	22%
Epidemiology (GSPH)	Wisniewski, Stephen R	Co-PI	1%

YEAR 5 QUAD CHART

Linking Investigations in Trauma and Emergency Services – TO2

17052001-TO2/W81XWH-16-D-0024-0002 LITES Task Order 0002
Shock, Whole blood and Assessment of TBI (SWAT)

PI: Jason Sperry MD MPH **Org:** University of Pittsburgh **Award Amount:** $7,452,420

STUDY AIMS

Determine if whole blood resuscitation is associated with improved mortality and morbidity outcomes following hemorrhagic shock with and without TBI.

I. Evaluate patient centered outcomes associated with early whole blood resuscitation practice as compared to component resuscitation in poly-trauma patients with hemorrhagic shock and further characterize outcome benefits in those with traumatic brain injury. Whole blood Clinical Practice Guidelines will be prepared, including staff training resources, and provided for use by the Government.

II. Characterize blood pressure and resuscitation endpoints during the acute resuscitation phase of care and the associated/attributable outcomes for traumatic brain injury in patients with hemorrhagic shock.

Task Order 0002 is a multicenter, prospective, observational cohort study over a 4-year period to determine the impact of whole blood resuscitation in trauma patients with hemorrhagic shock at risk of large volume resuscitation with and without TBI.

Enrollment goal (1051) reached in SEP-2021!

ACCOMPLISHMENTS

- ✓ Abstract accepted for oral presentation at MHSRS; presented on 13-SEP-2022! *Whole blood is associated with a lower independent risk of mortality and improved hemostasis: results of a multi-center prospective observational study of patients in hemorrhagic shock*
- ✓ Close-out visits were conducted at all sites! All data and consent queries have been resolved!
- ✓ Final CTs were uploaded, and the remaining scans were read by the neuroradiologist .

Timeline and Cost

Activities CY	SEP-17	18	19	20	21	22	23
Startup, Hiring, IRB approval, Contracts, Single IRB organization, Database creation, site selection							
1 year thru 4-year enrollment							
Interim analysis at 50 % enrolled							
Reach Enrollment Goal (1050 pts.)							
Data analysis and publication							
Estimated Budget	933K	933K	933K	933K	933K	1.4 M	1.4 M

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

Goals/Milestones

CY18 Goal – Network Startup and Data procurement/extraction
- ✓ Base Hiring; IRB approval; Central IRB organization, Sub-Contract organization
- ✓ Data base creation and CRF completion, data dictionary
- ✓ Begin Patient enrollment 200-30

CY19 Goal
- ✓ Begin Characterization of variation of patient centered outcomes related to whole blood vs. component therapy

FY20 Goal
- ✓ Interim analysis reached

CY21 Goal
- ✓ Interim Data Tables and Exec Summary
- ✓ Reach enrollment goal

CY22 | CY23 Goal
- ❑ Data analysis and publication
- ❑ Begin Characterization of blood pressure and resuscitation endpoints for TBI subjects in hemorrhagic shock
- ❑ Prepare whole blood administration clinical guidelines

Budget Expenditure compared to Actual thru 30-SEP-2022
- Actual Expenditures: $3,863,752.93
- Scheduled Expenditures: $6,713,404.10