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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, PA 15213

REPORT DATE: OCT-2018

TYPE OF REPORT: Annual Task 0002

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

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6. AUTHOR(S)

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University of Pittsburgh
Pittsburgh, Pennsylvania 15213

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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
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified		USAMRMC

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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.

- The DCC distributed the LITES Quarterly Update newsletters to study personnel on: 2017 Q4 - 19-OCT-2017 | 2018 Q1 - 18-JAN-2018 | 2018 Q2 - 18-APR-2018 | 2018 Q3 - 25-JUL-2018.
- Network sites selected to participate in TO 0002 were notified on 25-SEP-2017.
- Initial site teleconference was held on 08-NOV-2017. CCC/DCC discussed the Study Synopsis, SMART IRB, Contracts, and Software.

- All sites have ceded review rights to the University of Pittsburgh IRB.
- All 6 participating Network sites received initial IRB approval on or before 20-SEP-2018.
- 3 of the 6 participating Network sites received initial HRPO approval on or before 21-AUG-2018.
- 3 of the 6 participating Network sites were activated between 29-APR-2018 and 12-SEP-2018.
- University of Pittsburgh participating site commenced enrollment on 30-APR-2018.
- Oregon Health & Science University's standard of care switched to Whole Blood on 09-JUL-2018.
- Conducted the Site Initiation Visit at 5 of the 6 participated sites through 15-AUG-2018.
- The CCC/DCC set up certification tests (clinical/data/GOAT)
- University of Pennsylvania participating site commenced enrollment on 23-AUG-2018.
- The University of Texas Health Science Center at Houston participating site commenced enrollment on 17-SEP-2018.
- All 6 participating Network sites had fully executed contracts by 08-AUG-2018.
- The DCC developed:
  - TO2 Manual of Operations
  - Data Management Manual
  - Data Dictionary.
  - Q-by-Q instructions for completion of data collection forms.
  - Issues Log from Pitt site experiences was created into a FAQ for external sites.
  - CT transfer process.
  - Sample collection and transfer protocol.

- Enrollment

SITE	ENROLLMENT THROUGH 30-SEP-2018
University of Pittsburgh	43
University of Pennsylvania	5
University of Texas Health Science Center at Houston	4

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.

- Initiate monthly coordinator calls.
- Initial HRPO approval for all remaining participating sites.
- Activate remaining sites.
- Commence enrollment at remaining participating sites.

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.

- Some component sites may transition to whole blood if their standard of care changes.
  - Add more sites if enrollment goals are not on target.
- Many sites had not worked with a central IRB previously so, the process took longer than anticipated.
  - Continue providing guidance as needed.

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.

The contractual process was more efficient than TO 0001 however delays in IRB processes subsequently deferred expenditures.

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.

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.)*

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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.

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, Mr. Paul Martha
Email: paul.m.martha.civ@mail.mil

One e-Copy: Contracting Officer's Representative (COR), Wilbur Malloy
Email: wilbur.w.malloy.civ@mail.mil

LITES Project Personnel - Task Order 0002 (as of September 2018)

	Department	Last Name	First Name	Middle Initial	Role	Account #413531	Other Department Subaccounts
1	Epidemiology (GSPH)	Fabio	Anthony		CO-Investigator		5.0%
2	Emergency Medicine	Guyette	Francis	X	PI		7.5%
3	Epidemiology (GSPH)	Luther	James	F	Biostatistican IV		10.0%
4	Neurosurgery	Borrasso	Allison	J.H.	Health Professional II		50.0%
5	Neurosurgery	Okonkwo	David	O	CO-Investigator		5.0%
6	Epidemiology (GSPH)	Rosario-Rivera	Bedda	L	CO-Investigator		5.0%
7	Epidemiology (GSPH)	Silfies	Laurie	N	Systems Engineer IV		40.0%
8	Surgery	Sperry	Jason	L	PI	7.5%	
9	Epidemiology (GSPH)	Wisniewski	Stephen	R	PI		2.5%
10	Surgery	Neal	Matthew		PI	2.0%	
11	Epidemiology (GSPH)	O'Donnell	Jefferey		Systems/Programmer IV		100.0%
12	Epidemiology (GSPH)	Macy-Kalcevic	Melody		Research IV		100.0%
13	Epidemiology (GSPH)	Pattison	Angela		Research IV		25.0%

Running Personnel Updates:

IRB received. Efforts updated for January 2018 business

Project Manager postion not hired as of Sept2018

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: $**$7,452,420.12

Study Aims

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.**

Approach

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.

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

YR 1 ACCOMPLISHMENTS

- ✓ All participating sites have ceded review rights to the University of Pittsburgh IRB.
- ✓ Conducted Site Initiation Visit at 5 of the 6 participated sites.
- ✓ Commenced enrollment at 3 of the 6 participating sites.

Timeline and Cost

Activities / CY	18	19	20	21
Startup, Hiring, IRB approval, Contracts, Central IRB organization, Database creation				
1 year thru 4 year enrollment, 1050 patients; interim analysis at 50 % enrolled				
Characterize for variation of patient centered outcomes related to whole blood vs component therapy				
Characterization of bp and resusc endpoints for TBI in hemorrhagic shock ; prepare WB clinical practice guidelines				
Estimated Budget ($K)	**$1M**	**$2.5M**	**$2.5M**	**$1.5M**

Updated: (23-OCT-2018)

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 – Patient enrollment 300-400
- ❑ Begin Characterization of variation of patient centered outcomes related to whole blood vs. component therapy

CY20Goal – Patient enrollment 300-400
- ❑ Begin Characterization of blood pressure and resuscitation endpoints for TBI subjects in hemorrhagic shock
- ❑ Prepare whole blood administration clinical guidelines

Comments/Challenges/Issues/Concerns
- Differences in local resuscitation protocols across sites

Budget Expenditure to Date
- Actual Expenditure To-Date: $391,038.70 (*paid to-date 10-OCT-2018*)
- Project Expenditures: $72,527.88 (*reflects invoice for the month of SEP-2018 business*).