CONTRACT NUMBER: W81XWH-16-D-0024

TITLE: Type O Whole blood and assessment of AGE during prehospital Resuscitation (TOWAR) 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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Type O Whole blood and assessment of AGE during prehospital Resuscitation (TOWAR) Trial

5a. CONTRACT NUMBER

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5c. PROGRAM ELEMENT NUMBER

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

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

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

TOWAR is a proposed 6-year (4-year enrollment) multicenter, open label, pre-hospital, randomized trial utilizing 10 level-1 trauma centers designed to determine the efficacy and safety of low titer whole blood resuscitation as compared to standard of care resuscitation in patients at risk of hemorrhagic shock and to appropriately characterize the hemostatic competency of whole blood relative to its age.

Specific aims are to determine whether prehospital low titer whole blood as compared to standard prehospital resuscitation results in lower 30-day mortality and results in lower early mortality, blood and blood component transfusion requirements, incidence of coagulopathy, improved hemostasis and platelet function and to determine whether prehospital whole blood (age > 14 days) as compared to young whole blood (age ≤ 14 days) is associated with equivalent clinical outcomes, hemostasis, prevention of coagulopathy, and platelet function in patients at risk of hemorrhagic shock.

15. SUBJECT TERMS
Trauma; Prehospital; Low-Titer Whole Blood; Whole Blood Age

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.

TOWAR is a proposed 6-year (4-year enrollment) multicenter, open label, pre-hospital, randomized trial designed to determine the efficacy and safety of low titer whole blood resuscitation as compared to standard of care resuscitation in patients at risk of hemorrhagic shock and to appropriately characterize the hemostatic competency of whole blood relative to its age. The principle secondary outcome will be the age of whole blood and its association with all primary and additional secondary outcomes including 3-hour mortality, 6-hour mortality, in hospital mortality, death from hemorrhage, death from brain injury, blood and blood component transfusion requirements in the initial 24 hours, incidence of Multiple Organ Failure (MOF), incidence of nosocomial infection, incidence of acute respiratory distress syndrome (ARDS), time to hemostasis, incidence of coagulopathy by TEG, incidence of allergic/transfusion reaction and measurements of platelet and overall patient hemostatic function. Trial will utilize prehospital agencies at ten LITES Network sites and will enroll a total of 1,020 subjects.

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

Trauma; Prehospital; Low-Titer Whole Blood; Whole Blood Age

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 0007 is to perform an open-label, multicenter prehospital randomized trial among trauma patients at risk of hemorrhagic shock requiring up to two units of whole blood initiated in prehospital phase of care, comparing prehospital low titer whole blood to standard prehospital resuscitation.

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.

- DCC continued regular database maintenance and responded to help tickets.
  - DCC added two new forms to MATRIX: Other Problem (PRB) and Other Problem Review (OPR).
  - QxQ Instructions were updated and posted to the LITES website.
- The IDSMB review was conducted on 31-OCT-2022 – final letter received 21-NOV-2022.
  - The Board voted for the study to continue without modification and to meet again in approximately 6 months (MAY-2023).

- Continuing review submitted Pitt IRB on 07-NOV-2022. The committee meeting was held on 15-NOV-2022 and approval was granted on 15-NOV-2022.
- OHRO continuing review documents were submitted on 05-DEC-2022.
  - Acknowledgment memo received on 11-JAN-2023.
- FDA/IND Annual report (incorporating protocol mod V8 allowing sites to transfuse either O+ or O- whole blood for the study) was submitted to the University of Pittsburgh's IND & IDE Support (IIS) office on 16-NOV-2022.
  - The 30–day review period was reached on 18-DEC-2022 – no comments or action items.
- Translated consents and notification letters were submitted to the sIRB on 01-DEC-2022 and approval was granted on 02-DEC-2022.
  - Translated versions of the Continuing & Prospective ICF have been distributed to site personnel and each consent folder in the document library has been updated.
- Notification letters were obtained in Spanish and Vietnamese for the following:
  - Notification for Deceased Letter, Discharged Subjects Letter, LAR Refusal, and Non-TOWAR Hospital
- 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.
- Minor modification submitted to the sIRB on 30-MAR-2023 – approval granted 04-APR-2023.
  - Revision to template prospective consent form and site-specific prospective consent forms to remove signature block for parental consent as minor subjects are excluded.
- Manual of Operations (MOP) was updated and distributed to sites on 24-FEB-2023.
- Per Patient payment structure was updated to include partial compensation for patients transported to a non-participating site.
- Modification submitted to the sIRB on 22-MAY-2023.
  - Modification included: Onboarding UAB (CC/PD results, consents & EMS addendum) and updated CC/PD results for Seattle with additional efforts to support opening to enrollment at additional EMS bases in Yakima.
  - Committee Review date: 30-MAY-2023 – approval was granted on 30-MAY-2023.
- The IDSMB review meeting was held on 02-JUN-2023 – Final letter received 18-JUL-2023.
  - Data lock occurred on 27-APR-2023 and the DCC created the tables.
  - The Board voted for the study to continue as is and to meet again in approximately 6 months (DEC-2023).

Participating Sites Progress

- The University of Pittsburgh IRB Representative continued working through the reliance process. As of OCT-2022, all nine sites have executed agreements.
- CCC/DCC continued to hold monthly site coordinator calls.
- PM distributed study materials (hangtags, posters) to necessary participating sites and associated EMS.
- Randomization sequences were assigned, and randomization calendars were distributed to necessary sites as they were onboarded.

- On 02-JUN-2023, CCC notified OHRO of the prisoner status of two enrolled subjects (one at Vanderbilt University Medical Center and one at University of Tennessee Health Science Center at Knoxville).
  - 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.

- 25% enrollment milestone reached on 04-AUG-2023!

- First interim (1/3 enrollment – 340 patients) reached on 26-SEP-2023.

Pittsburgh/ MACRO	Monitoring visit with the University of Pittsburgh's Education and Compliance Support personnel was conducted on 10-17-FEB-2023 and 09-16-JUN-2023.
Seattle	Site revised their CC/PD plan to include an additional EMS base (Yakima) for enrollment. ▪ sIRB modification was submitted on 13-JAN-2023. ▪ Committee review was held on 20-JAN and approval was granted on 02-FEB-2023.
	Addition of Yakima base (AirLift Northwest (ALNW 23 and 24)

	▪ The site worked through their additional CC/PD and held their final in-person activity on 20-APR-2023. - The Pitt sIRB approved the results of these efforts on 30-MAY-2023. ▪ EMS training was completed in APR-2023. ▪ sIRB approved documents were forwarded to OHRO on 01-JUN-2023. - CCC confirmed that Yakima base is owned and operated by ALNW and is part of UW medicine. The DoD previously approved AirLift Northwest (E02452.1c-1) in SEP-2022. - On 07-JUN-2023, OHRO confirmed that they had all necessary documents, noted this in their database and confirmed that they do not need to send an acknowledgment memo. ▪ The site is aiming to commence enrollment on 01-JUL-2023. - CCC provided an updated randomization scheme and base expansion activation memo on 23-JUN-2023.
	Yakima base (AirLift 23 and AirLift 24) – enrollment commenced on 01-JUL-2023. ▪ First patient was enrolled on 15-JUL-2023!
Vanderbilt	Site submitted to OHRO for initial review on 28-SEP-2022 ▪ Approval was granted on 21-OCT-2022
	Site activated on 07-NOV-2022 ▪ Enrollment commenced on 09-NOV and their first pt. was enrolled on 12-NOV-2022
Mississippi	Onboarding Mississippi (CC/PD results, consents & EMS addendum) ▪ sIRB Committee review was conducted and approval was granted on 09-DEC-2022
	Site & EMS submitted to OHRO for initial review on 20-DEC-2022. ▪ Approval granted on 10-JAN-2023.
	SIV was conducted on 25-JAN-2023.
	Site was activated on 17-MAR-2023 ▪ Enrollment commenced on 28-MAR and their first patient was enrolled on 30-MAR-2023!
MetroHealth	Local IRB has a new data transfer security procedure that required a contract modification to update the DUA. Fully executed amendment received on 01-MAR-2023!
	Local IRB acknowledgment of the study and reliance was obtained on 27-MAR-2023.
	Site & EMS submitted to OHRO for initial review on 29-MAR-2023. ▪ OHRO approval was granted on 20-APR-2023.
	The CCC conducted a study refresher on 25-APR-2023.
	EMS retraining was initiated and complete by 05-JUN-2023.
	The site was activated. Enrollment commenced on 12-JUN and their first patient was enrolled on 22-JUN-2023!
Cincinnati	Site submitted to OHRO for initial review on 21-SEP-2022. ▪ Approval was granted on 21-OCT-2022
	DCC conducted MATRIX (eDCF) training with this site on 05-DEC-2022 and monitored the completion of their test patient
	SIV was conducted on 13-JAN-2023.
	AirCare training was delayed due to the restructuring of their EMS (new care team model was established – MD/RNs replacing APPs). ▪ AirCare EMS training was reinitiated in JAN-2023 and was completed in early-MAR-2023!
	Hospital approval was obtained on 13-MAR-2023.
	Site was activated on 28-MAR-2023 ▪ Enrollment commenced on 03-APR and their first patient was enrolled on 05-APR-2023!
UT Houston	Revised local context form was submitted to HOU IRB on 09-DEC-2022 ▪ Executed copy was received on 20-DEC-2022
	Site & EMS was submitted to OHRO for initial review on 22-DEC-2022. ▪ Approval granted on 20-JAN-2023.

	EMS training was initiated on 29-MAR-2023.
	SIV was conducted on 07-APR-2023 and site was activated on 13-APR-2023.
	Enrollment commenced 17-APR & their first patient was enrolled on 20-APR-2023!
Knoxville	Contract with Memphis was executed on 13-OCT-2022
	Onboarding Knoxville (CC/PD results, consents & EMS addendum) – submitted to sIRB on 01-MAR-2023. ▪ sIRB Committee Review was conducted and approval was granted on 10-MAR-2023!
	Site & EMS submitted to OHRO for initial review on 16-MAR-2023. ▪ OHRO approval was granted on 05-APR-2023.
	SIV was conducted on 24-APR-2023 and site was activated on 03-MAY-2023.
	Enrollment commenced on 10-MAY & their first patient was enrolled on 13-MAY-2023!
Louisville	Reliance agreement was executed on 04-OCT-2022
	ULH Research (hospital) approval was obtained 14-FEB-2023.
	Local context form was fully executed in FEB-2023.
	Onboarding Louisville (CC/PD results, consents & EMS addendum) – submitted to sIRB on 13-JUL-2023. ▪ Committee Review date: 24-JUL-2023 – Modifications Required to Secure Approval (IRB requested additional language be added to both consent forms). ▪ Response submitted 26-JUL-2023. sIRB approval granted on 28-JUL-2023.
	Site submitted to OHRO for initial review on 18-AUG-2023. ▪ Approval was granted on 12-SEP-2023.
	SIV was completed on 15-SEP-2023 – report distributed 20-SEP-2023. ▪ The site was activated on 29-SEP-2023. Anticipated start date: 02-OCT-2023.
Alabama	Community consultation and public disclosure results were submitted to the CCC on 30-MAR-2023. ▪ The sIRB conducted a preliminary review and asked the site to complete in-person activities to supplement their online efforts. ▪ J. Sperry reached out to the site Investigators and research team to ensure they are meeting the Pitt IRB requirements for EFIC. ▪ The CCC provided the site Investigators and research team with sIRB correspondence RE: in-person activities. ▪ Additional in-person activities were completed, and the results were sent to the CCC for submission to the sIRB. ▪ The Pitt sIRB approved onboarding (CC/PD results, consents & EMS addendum) of the site on 30-MAY-2023.
	Updated local context form approved!
	Pending local IRB acknowledgement of sites change in PI and updated consents. ▪ PI change underway. The site is working to collect and update the necessary documents for the new PI.

DATA & CONSENT MONITORING

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.

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.

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.

SITE	IMV-01	IMV-02	IMV-03	IMV-04	IMV-05

Seattle	NOV-2022	MAY-2023	TBD	TBD	TBD
Vanderbilt	FEB/MAR-2023	AUG/SEP-2023	TBD	TBD	TBD
Mississippi	MAY-2023	TBD-NOV-2023	TBD	TBD	TBD
MetroHealth	SEP-2023	TBD	TBD	TBD	TBD
Cincinnati	JUL-2023	TBD-JAN-2024	TBD	TBD	TBD
UT-Houston	JUN-2023	TBD-DEC-2023	TBD	TBD	TBD
Knoxville	JUN-2023	TBD-DEC-2023	TBD	TBD	TBD
Louisville	TBD	TBD	TBD	TBD	TBD
Alabama	TBD	TBD	TBD	TBD	TBD

ENROLLMENT (as of 30-SEP-2023)	
University of Pittsburgh	82
University of Washington, Harborview Medical Center	62
Vanderbilt University Medical Center	33
University of Mississippi Medical Center	37
University of Cincinnati	19
Memorial Hermann - Texas Medical Center	85
University of Tennessee Medical Center	27
MetroHealth System	**5**
University of Louisville	*Not yet enrolling; anticipated start date 10/2/2023*
University of Alabama at Birmingham	*Not yet enrolling; anticipate starting in OCT/NOV-2023*
TOTAL (goal: 1,020)	**350**

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.

- Prepare In-Progress Review (IPR) presentation for NOV-2023.
- Commence enrollment at Louisville site (anticipated to begin on 02-OCT-2023).
- Continue working with UAB in preparation for commencing enrollment.
  - Submit site & EMS agency for initial OHRO approval.
  - Collect site-specific SOPs; initiate EMS training; conduct MATRIX training and Site Initiation Visit.
- Conduct site monitoring visits at necessary sites.
- Conduct quarterly remote consent monitoring.
- IDSMB interim analysis review to be conducted in DEC-2023/JAN-2024.

Travel conducted:

- University of Washington's first Interim Monitoring Visit (IMV) was conducted on 08-09-NOV-2022.
  - Three LITES personnel attended/conducted the IMV in-person as planned.
- Vanderbilt's first Interim Monitoring Visit (IMV) was conducted on 27-FEB to 02-MAR-2023.
  - Three LITES personnel attended/conducted the IMV in-person as planned.
- Mississippi's first Interim Monitoring Visit (IMV) was conducted on 16-19-MAY-2023.
  - One LITES personnel attended/conducted the IMV in-person.
- UT Houston's first Interim Monitoring Visit (IMV) was conducted on 06-09-JUN-2023.
  - Four LITES personnel attended/conducted the IMV in-person.
- TN Knoxville's first Interim Monitoring Visit (IMV) was conducted on 26-29-JUN-2023.
  - Three LITES personnel attended/conducted the IMV in-person.
- Cincinnati's first Interim Monitoring Visit (IMV) was conducted on 11-12-JUL-2023.
  - Three LITES personnel attended/conducted the IMV in-person.
- MetroHealth first Interim Monitoring Visit (IMV) was conducted on 20-21-SEP-2023.
  - Three LITES personnel attended/conducted the IMV in-person.

Travel anticipated:

- Mississippi's second Interim Monitoring Visit (IMV) is in the process of being scheduled. We expect 1-3 LITES personnel to attend.
- The following sites are expected to commence enrollment in the coming months and enroll at a rapid rate. Therefore, they may be ready for their first IMV.
  - University of Louisville and University of Alabama at Birmingham
  - If this is confirmed, we expect three LITES personnel to attend.

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 Renee Weinman Meghan Buck	Jackson, Mississippi IMV-02	NOV-2023 - TBD
	Elizabeth Gimbel Renee Weinman Meghan Buck	Louisville, KY IMV-01	Q4 2023 - TBD
	Elizabeth Gimbel Renee Weinman Meghan Buck	Birmingham, AL IMV-01	Q1 2024 - 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.

- Staff removal: Logan Owens (Data Entry – last day with LITES was on 02-JUN-2023).
  - Partial effort charged to TO7-TOWAR (50%).

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 whole blood shortages throughout the year. Typical shortage periods are Summer (JUN-AUG) and Holidays (NOV-mid-JAN).
  - The plan to have one unit WB during enrollment lag periods & two units WB during strong enrollment months we solidified and relayed to participating sites.

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 0007

Significant changes in use of biohazards and/or select agents

Not applicable to TO 0007

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) Type O Whole blood and assessment of Age during prehospital Resuscitation trial (TOWAR)
    - Abstract accepted for oral presentation at MHSRS and presented 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: 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 16

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: Science Officer Sandy Snyder
Email: sandy.j.snyder.civ@health.mil

Personnel Listing (as of 30-SEP-2023)

W81XWH-16-D-0024 / W81XWH-20-F-0383			
Department	**Personnel Name**	**UPitt Role**	**T0 % Effort**
Surgery	Brown, Joshua B	Co-PI	11%
Surgery	Brubaker, Donovan Paul	Clinical Research Coord.	10%
Surgery	Buck, Meghan L	Asst Proj Mgr.	28%
Surgery	Gimbel, Elizabeth	Assistant Project Manager	5%
Emergency Medicine	Guyette, Francis X III	Co-PI	15%
Surgery	Harner, Ashley Marie	Research Proj Mgr	22%
Surgery	Hayes, Hannah E	Clinical Researcher II	12%
Surgery	Kelly, Emily Theresa	Clinical Research Coord.	9%
Epidemiology (GSPH)	Luther, James Francis	Biostatistician IV	50%
Surgery	Neal, Matthew D	Co-PI	4%
Epidemiology (GSPH)	Panthalukaran-Bastin, Tina B	Data Management Assistant	100%
Surgery	Rayman, MaryAnne	Research II	23%
Epidemiology (GSPH)	Silfies, Laurie N	Systems Engineer IV	20%
Surgery	Sperry, Jason L	Co-Investigator	25%
Surgery	Stephenson, Joshua Paul	Data Entry Assistant	35%
Emergency Medicine	Weiss, Leonard S	Co-Investigator	15%
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 – TO7

17052001-TO7/W81XWH-16-D-0024, W81XWH20F0383

Type O Whole blood and assessment of AGE during prehospital Resuscitation (TOWAR) Trial - LITES Task Order 0007

PI: Jason Sperry MD MPH **Org:** University of Pittsburgh **Award Amount: $13,097,305**

STUDY AIMS

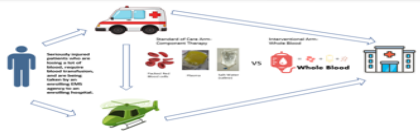
Determine the efficacy and safety of low titer whole blood resuscitation as compared to standard of care resuscitation in patients at risk of hemorrhagic shock and to appropriately characterize the hemostatic competency of whole blood relative to its age:

I. Whether prehospital low titer whole blood as compared to standard prehospital resuscitation results in lower 30-day mortality in patients at risk of hemorrhagic shock.

II. Whether old prehospital whole blood (age > 14 days) as compared to young whole blood (age ≤ 14 days) is associated with equivalent clinical outcomes, hemostasis, prevention of coagulopathy, and platelet function in patients at risk of hemorrhagic shock.

III. Whether prehospital low titer whole blood as compared to standard prehospital resuscitation results in lower early mortality, blood and blood component transfusion requirements, incidence of coagulopathy, improved hemostasis and platelet function in patients at risk of hemorrhagic shock.

Multi-center, open label, prehospital randomized trial



ACCOMPLISHMENTS

- ✓ Enrollment N (as of SEP-2023) = 350
- ✓ 8 of 10 sites opened to enrollment. We anticipate the remaining two to start in OCT/NOV-2023.
- ✓ First interim (1/3 enrollment – 340 patients) reached on 26-SEP-2023.

Timeline and Cost

Activities CY	SEP-20	21	22	23	24	25	26
Startup, Hiring, IRB approval, Contracts, Single IRB organization, Database creation, site selection							
6-year (4-year enrollment), 1020 patients							
1/3 enrollment; interim analysis							
2/3 enrollment; interim analysis							
Data analysis and publication							
Estimated Budget	91K	91K	2.6 M	2.6 M	2.6 M	2.6 M	2.6 M

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

Goals/Milestones

CY20 Goal – Study Development & Staffing
- ✓ Base Hiring & Budget negotiation

CY21 Goal – Study Startup & Site Selection Community consultation and public disclosure
- ✓ FDA IND approval
- ✓ Site selection
- ✓ Single IRB approval
- ✓ Army Surgeon General EFIC waiver approval (formally SecArmy)

CY22 Goal – Begin patient enrollment (N=1020)
- ✓ Data base creation and CRF completion, data dictionary
- ✓ OHRO approval – on-going | granted for study, Pitt, & UW
- ✓ Site Initiation Visits & eDCF training – on-going
- ✓ Begin Patient enrollment

CY23 – CY24 Goal – Patient enrollment
- ✓ Reach accrual goal for 1/3 interim analysis
- ❑ Continue study enrollment
- ❑ Reach accrual goal for 2/3 interim analysis

CY25 – CY26 Goal – Patient Enrollment
- ❑ Finish enrollment
- ❑ Data analysis and publication

Budget Expenditure compared to Actual thru 30-SEP-2023
- Actual Expenditure: $2,569,315.63
- Scheduled Expenditures: $6,735,757.03