

CONTRACT NUMBER: W81XWH-19-F-0539

TITLE: Prehospital Analgesia Intervention Trial (PAIN)

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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| 13. SUPPLEMENTARY NOTES | | | | | | |
| 14. ABSTRACT PAIN is a proposed 4 year (3-year enrollment) multicenter, prehospital, randomized, double-blind, clinical trial comparing fentanyl versus sub-dissociative ketamine for mortality outcome differences, safety and analgesia in trauma patients with compensated shock. Specific aims are to determine if, among prehospital trauma patients with compensated shock (Heart Rate (HR)>109 or Shock Index (SI)>0.9) and an indication for pain management, treatment with sub-dissociative IV ketamine as compared to IV fentanyl reduces mortality at 24 hours following admission, reduces the frequency of hemodynamic instability or respiratory depression associated with analgesia, decreases total prehospital exposure to opioids, 24-hour exposure to opioids, and anxiety/PTSD screen scores, improves the frequency of complications including opioid use / dependency, anxiety, and PTSD at 6 months, and improves arrival pain control as measured by numerical rating scale (NRS) and/or the critical care pain observation tool (CPOT). | | | | | | |
| 15. SUBJECT TERMS Trauma; Prehospital; Analgesia; Fentanyl; Sub-Dissociative Ketamine | | | | | | |
| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT Unclassified | 18. NUMBER 15 | 19a. NAME OF RESPONSIBLE PERSON USAMRDC | |
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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

PAIN is a proposed 4 year (3-year enrollment) multicenter, prehospital, randomized, double-blind, clinical trial comparing fentanyl versus sub-dissociative ketamine for mortality outcome differences, safety and analgesia in trauma patients with compensated shock.

The primary outcome for the trial will be 24-hour mortality among trauma patients with compensated shock following administration of the prehospital analgesia. Secondary outcomes will include incidence of adverse events (hypoxia, hypotension, and need for airway management) occurring in the prehospital environment, assessed after administration of the analgesic intervention. prehospital pain assessment (NRS, CPOT) following analgesia, trauma bay arrival pain score, number of analgesic doses necessary to reduce pain level to <5 or CPOT less than 2, total 24-hour opioid use, incidence of prehospital adverse events (allergic reactions, emergence, laryngospasm, dysphoria, pruritus, and nausea), anxiety/PTSD screening, hospital length of stay, survival to hospital discharge, ventilator free days, ICU free days and long-term opioid use (6-month). Trial will utilize prehospital agencies at six LITES Network sites and will enroll a total of 994 subjects.

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

Trauma; Prehospital; Analgesia; Fentanyl; Sub-Dissociative Ketamine

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 0006 is to perform a prospective, interventional, randomized trial among prehospital trauma patients with compensated shock (HR>109 or SI>0.9) and an indication for pain management, comparing patient centered outcomes following prehospital administration of ketamine hydrochloride versus fentanyl citrate.

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.

- Site coordinator calls started in FEB-2023 and the CCC/DCC continued to hold monthly calls throughout the year.
- 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.

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| <ul style="list-style-type: none"> ▪ The IDSMB Board was assembled, and the initial review meeting was conducted 30-MAR-2023 – final letter received 24-APR-2023. <ul style="list-style-type: none"> - The Board voted for the study to begin without modification and to meet again approximately 6 months after enrollment starts. ▪ CCC finalized the Explendid video and Qualtrics survey, and they are available on the LITES website. ▪ DCC developed the electronic data capture system and finalized the Data Collection Forms (DCFs). <ul style="list-style-type: none"> - DCC is setting up study-specific reports. - The database was tested in MAY-2023 and the DCC made edits based on the first round of testing. ▪ CCC is investigating the addition of 2-4 more sites for a total of 11-13 – COR approval was obtained on 09-MAY-2023. ▪ DCC set up certification exams and posted associated documentation on the LITES website. ▪ Budget allocation request sent on 18-AUG-2023 – approval obtained 22-AUG-2023. <ul style="list-style-type: none"> - Request included: EMS Assistant Project Manager, Compensation for Medical Directors, EMS Educator(s), Adding Additional Sites, and Adding Additional EMS Agencies to Established Sites. ▪ EMS Onboarding/Training <ul style="list-style-type: none"> - Each site was given onboarding instructions for EMS services intended to participate. - Training materials were ordered and distributed to services currently onboarded (UPMC/AGH). - PAIN Educators are being onboarded to assist with on-site EMS training. ▪ Reallocation request submitted to DoD on 11-SEP-2023 – approval obtained 13-SEP-2023. <ul style="list-style-type: none"> - Request included: NAEMSP Investigator Meeting, Qualtrics for CC/PD, and Patient payments for survey completion. |
| <p>University of Pittsburgh sIRB</p> |
| <p>Modification to update the protocol sample size (from 1,544 to 1,136) was submitted to the IRB on 16-NOV-2022.</p> <ul style="list-style-type: none"> ▪ Mod also included revised consent forms, addition of notification letters, and revision to the Pitt sites CC/PD plan. ▪ Committee review was held on 09-DEC-2022. 13-DEC-2022 Committee Determination – Modifications Required to Secure Approval: <ul style="list-style-type: none"> - Minor edits requested to the Community Consultation and Public Disclosure Plan and discharge letter. - Response submitted on 19-DEC and approval was granted on 20-DEC-2022. |
| <p>Continuing review submitted to the IRB on 01-MAR-2023.</p> <ul style="list-style-type: none"> ▪ Committee Review meeting was conducted, and approval was granted on 14-MAR-2023. |
| <p>Protocol V6 (and ICFs) modification submitted to the IRB on 18-APR-2023.</p> <ul style="list-style-type: none"> ▪ Modification included: list of patient follow-up assessments and resource document, addition of UPMC Mercy, and administrative updates to notification letters. ▪ Committee Review date: 26-APR-2023 – Modifications Required to Secure Approval (memo received 01-MAY). <ul style="list-style-type: none"> - IRB requested the continued participation ICF be uploaded to the application. - Response submitted 11-MAY-2023 and approval was granted on 12-MAY. |
| <p>Modification submitted to the IRB on 24-MAY-2023.</p> <ul style="list-style-type: none"> ▪ Modification included: addition/removal of study team, Pittsburgh's community consultation and public disclosure results, Pitt sites Prospective and Continuing ICF, site plans (Cincinnati and UCSF). ▪ Committee Review date: 30-MAY-2023 – approval was granted on 06-JUN-2023. |
| <p>Modification submitted to the IRB on 27-JUN-2023.</p> <ul style="list-style-type: none"> ▪ Modification included: Spanish translations of the PAIN study survey and video script. ▪ Approval was granted on 28-JUN-2023. |
| <p>Modification submitted to the IRB on 17-JUL-2023.</p> <ul style="list-style-type: none"> ▪ Modification included: protocol v7, updated ICFs, corresponding updates to the IRB application for clarity, and sites plans (UCSD and Wisconsin). |

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| <ul style="list-style-type: none"> Committee Review date: 24-JUL-2023 – Modifications Required to Secure Approval (IRB requested that UCSD revise the community consultation language from 'up to' to 'at least'). Response submitted to the IRB on 27-JUL-2023 and approval was granted on 07-AUG-2023. | |
| <p>Modification submitted to the IRB on 23-AUG-2023.</p> <ul style="list-style-type: none"> Modification included: protocol v8 (sample size from 1,136 to 994), updated ICFs, translated materials, follow-up assessments, Cooper CC/PD plan, revised CC/PD plans (UCSF & Wisconsin), onboarding AGH, LifeFlight OHRO EMS addendum for acknowledgement. Committee Review date: 30-AUG-2023 Determination received on 06-SEP: Modifications Required to Secure Approval (ICF formatting requested). Response submitted to the IRB on 08-SEP and approval granted on 11-SEP-2023. | |
| FDA | |
| <p>FDA/IND Annual report (incorporating protocol mod V5 to reduce the sample size) was submitted to the University of Pittsburgh's IND & IDE Support (IIS) office on 17-JAN-2023.</p> <ul style="list-style-type: none"> FDA confirmation of receipt was received on 18-JAN-2023. | |
| <p>FDA information request was received on 28-FEB-2023 RE: drug stability results.</p> <ul style="list-style-type: none"> CCC confirmed expiration date assigned to the fentanyl product – expiration is 120-days after it's manufactured. | |
| <p>Protocol amendment (V6) and copies of information publicly disclosed as part of the public disclosure plan for PAIN were submitted to the FDA on 12-JUN-2023.</p> <ul style="list-style-type: none"> FDA confirmation of receipt was received on 14-JUN-2023. | |
| <p>Protocol amendment (V7, V8, updated ICFs and AGH site) was submitted to the University of Pittsburgh's IND & IDE Support (IIS) office on 29-SEP-2023.</p> <ul style="list-style-type: none"> FDA confirmation of receipt was received on 02-OCT-2023. | |
| OHRO | |
| <p>Initial OHRO Submission, 26-MAY-2022</p> <ul style="list-style-type: none"> Army Surgeon General signature of EFIC waiver was obtained on 03-FEB-2023! OHRO approval for the Clinical & Data Coordinating Centers was granted on 06-FEB-2023! | |
| <p>OHRO continuing review documents were submitted on 10-APR-2023. Acknowledgment memo pending.</p> | |
| Pine Pharmaceuticals | |
| <p>CCC/DCC are meeting with Pine Pharmaceuticals (FDA-registered 503B outsourcing facility) on a monthly basis in preparation for product manufacturing and study start.</p> | |
| <p>DCC/Pine collaborated and finalized the process that will link the kit label to the patient and prehospital data. A unique number system embedded within a QR code will be utilized.</p> | |
| <p>CCC/DCC collaborated with UPMC IDS to develop an emergency unblinding plan.</p> | |
| <p>In JUL-2023, the first 222 form was completed and the CCC is working to have the remaining forms completed for an early-AUG. submission to Pine.</p> | |
| Participating Sites | |
| <ul style="list-style-type: none"> LITES finance team continued working with remaining sites to obtain fully executed contracts. The University of Pittsburgh IRB representative continued working through the reliance process with each participating site and EMS agency. | |
| Pittsburgh | <p>sIRB approval of Pitt's community consultation and public disclosure results and sites Prospective and Continuing ICF was granted on 06-JUN-2023.</p> <ul style="list-style-type: none"> Site demographics and catchment areas are the same for UPMC and AGH institutions. Consultation and public disclosure efforts were completed in tandem. |
| | <p>The Department of Health's Bureau of EMS reviewed and approved the participation of EMS agencies in the greater Pittsburgh area in the PAIN trial on 15-JUN-2023.</p> |
| | <p>CCC submitted Pittsburgh's EMS reliance documents to the sIRB on 26-JUN-2023.</p> <ul style="list-style-type: none"> Acknowledgement received on 28-JUN-2023 |
| | <p>Pittsburgh site and participating EMS agencies were submitted to OHRO for initial review on 30-JUN-2023. OHRO approval obtained on 24-JUL-2023.</p> |

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| | <p>CCC/DCC finalized Site Initiation Visit (SIV) protocol training PPT in preparation for the Pitt/MACRO SIV on 29-SEP-2023.</p> <ul style="list-style-type: none"> ▪ EMS training is underway! ▪ MACRO RA training is scheduled for 04-OCT-2023. ▪ The product is anticipated to arrive at UPMC EMS agencies in mid-OCT-2023. ▪ Anticipated start date at the Pittsburgh sites (Presby and Mercy): 30-OCT-2023. |
| AGH | Fully executed contract obtained. |
| | <p>CCC submitted EMS reliance documents to the sIRB on 26-JUN-2023.</p> <ul style="list-style-type: none"> ▪ Acknowledgement received on 28-JUN-2023 |
| Wisconsin | Fully executed contract obtained. |
| | CC/PD Plan approved in AUG-2023 – activities efforts underway. |
| Utah | Fully executed contract obtained. |
| | Site drafting CC/PD Plan. |
| Cincinnati | Fully executed contract obtained. |
| | CC/PD Plan approved in JUN-2023 – activities efforts underway. |
| San Diego | Fully executed contract obtained. |
| | CC/PD Plan approved in AUG-2023 – activities efforts underway. |
| Cooper | Fully executed contract obtained. |
| | CC/PD Plan approved in SEP-2023 – activities efforts underway. |
| | <p>State waiver to administer ketamine in the prehospital setting:</p> <ul style="list-style-type: none"> ▪ MAC meeting approval obtained on 12-DEC-2022. ▪ OEMS and State Commissioner approval pending. |
| UCSF | Fully executed contract obtained. |
| | CC/PD Plan approved in JUN-2023 – activities efforts underway. |
| Arkansas | Fully executed contract pending. |
| | Site drafting CC/PD Plan. |
| Wash U | Fully executed contract pending. |
| | Site drafting CC/PD Plan. |
| Guthrie | Fully executed contract pending. |
| | Site drafting CC/PD Plan. |
| Vermont | Participation and EFIC considerations are an on-going discussion. |
| Enrollment: Not yet recruiting | |

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 meeting.
- Continue monthly calls with Pine Pharmaceuticals.
- Continue monthly site coordinator/EMS calls.
- Collect remaining site budgets & executed contracts from outstanding sites.
- Collect remaining reliance agreements from outstanding sites.
- Continue collecting CC/PD plans and regulatory documents from sites.
- Submit site CC/PD plans and/or results to the sIRB for approval.
- Submit necessary sites to OHRO for initial review/approval.
- Onboard and train PAIN Educators to conduct EMS trainings.
- Begin enrollment at the Pittsburgh sites (Presby, Mercy and possibly AGH) in Q4 2023.

Travel Reporting

Travel conducted:

- One LITES personnel (Larry Ivanco) attended the 2023 MHSRS conference in Kissimmee, FL – TO4 abstract accepted and poster presented on 15-AUG-2023.
 - Note: funds for this travel have not yet hit the account; updated expenses will be reflected in next reporting period.

No travel is anticipated for the next quarter.

| 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 |
| | 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.

- Staff removal: Denise McCarthy (Project Manager – left LITES in mid-APR-2023).
 - Partial effort charged to TO6-PAIN (50%).
- Staff addition: Rachel Molinaro (Project Manager – transitioned in AUG-2023).
 - Partial effort charged to TO6-PAIN (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.

- Nothing to report.

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 0006

Significant changes in use of biohazards and/or select agents

Not applicable to TO 0006

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) Prehospital Analgesia INtervention trial (PAIN)
- Abstract accepted and poster presented at MHSRS on 15-AUG-2023.

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

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

Nothing to report.

- **Technologies or techniques**

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

Nothing to report.

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

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

Nothing to report.

- **Other Products**

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

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

| |
|--------------------|
| Nothing to report. |
|--------------------|

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

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: Science Officer René Smith

Email: rene.k.smith.civ@health.mil

Personnel Listing (as of 30-SEP-2023)

| W81XWH-16-D-0024 / W81XWH-19-F-0539 | | | |
|--|------------------------------|--|--------------------|
| Department | Personnel Name | UPitt Role | T0 % Effort |
| Surgery | Brown, Joshua B | Co-PI | 67% |
| Surgery | Gimbel, Elizabeth | Assistant Project Manager | 29% |
| Emergency Medicine | Guyette, Francis X III | Co-PI | 18% |
| Surgery | Hayes, Hannah E | Clinical Researcher II | 8% |
| Surgery | Ivanco, Larry S | Assistant Director - Clinical Research | 27% |
| Epidemiology (GSPH) | Kania, Michael A | Systems Developer III | 40% |
| Surgery | Merti, Alexandra K | Regulatory Coordinator | 53% |
| Surgery | Molinaro, Rachel | Project Manager | 36% |
| Emergency Medicine | Pacella, Maria Lynn | Co-Investigator | 5% |
| Surgery | Peet-Michelessi, Chelsea Ann | Asst Proj Mgr | 40% |
| Emergency Medicine | Reddy, Keshav | Research Coordinator | 22% |
| Surgery | Rogers, Natalie | Research Coordinator (CRC) | 12% |
| Surgery | Rush, James | EMS Assistant Project Manager | 12% |
| Epidemiology (GSPH) | Silfies, Laurie N | Systems Engineer IV | 20% |
| Surgery | Sperry, Jason L | CO-Investigator | 25% |
| Epidemiology (GSPH) | Wisniewski, Stephen R | Co-PI | 3% |

YEAR 4 QUAD CHART

Linking Investigations in Trauma and Emergency Services – TO6

17052001-TO6/W81XWH-16-D-0024, W81XWH19F0539
Prehospital Analgesia Interventional (PAIN) Trial - LITES Task Order 0006

PI: Jason Sperry MD MPH

Org: University of Pittsburgh


Award Amount: \$8,798,845

STUDY AIMS

Determine if prehospital management of moderate to severe pain with sub-dissociative IV ketamine as compared to IV fentanyl in patients at risk of hemorrhage or compensated shock:

- Reduces 24-hour mortality
- Improves the incidence of hemodynamic instability or respiratory depression (hypotension, hypoxia or need for airway management) following analgesia for traumatic injury
- Decreases total prehospital exposure to opioids, 24-hour exposure to opioids, and Anxiety/PTSD screen scores
- Improves the frequency complications including opioid use/ dependency, anxiety, and PTSD at 6 months
- Improves pain control as measured by NRS or CPOT scores in patients at risk of hemorrhage or compensated shock

Multicenter, prehospital, randomized, double-blind, clinical trial



ACCOMPLISHMENTS

(Not yet enrolling)

- ✓ Army Surgeon General signature of EFIC waiver was obtained on 03-FEB-2023!
- ✓ OHRO approval for the Clinical & Data Coordinating Centers was granted on 06-FEB-2023!
- ✓ DCC developed the electronic data capture system and finalized the Data Collection Forms (DCFs).
- ✓ The IDSMB Board was assembled, and the initial review meeting was conducted 30-MAR-2023. The Board voted for the study to begin without modification.

Timeline and Cost

| Activities | CY | SEP-19 | 20 | 21 | 22 | 23 | 24 |
|---|----|--------|------|------|------|------|------|
| Startup, Hiring, IRB approval, Contracts, Single IRB, Database creation, site selection | | | | | | | |
| 4-year (3-year enrollment), 994 patients (497 per group) | | | | | | | |
| 1/3 enrollment; interim analysis | | | | | | | |
| 2/3 enrollment; interim analysis | | | | | | | |
| Data analysis and publication | | | | | | | |
| Estimated Budget | | 147K | 147K | 147K | 2.7M | 2.7M | 2.7M |

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

Goals/Milestones

CY19 | CY20 | CY21 Goal – Study Development & Staffing

- ✓ Base Hiring & Budget negotiation

CY22 Goal – Study Startup, Site Selection

- ✓ FDA approval
- ✓ IND, single IRB approval

CY23 Goal – Patient Enrollment

- ✓ Data base creation and CRF completion, data dictionary
- ✓ Army Surgeon General EFIC waiver approval; OHRO approval
- Community Consultation/Public Disclosure – on-going at Pittsburgh site
- Site Initiation Visits
- Begin Patient enrollment

CY24 Goal – Patient Enrollment

- Reach accrual goal for 1/3 interim analysis
- Request No Cost Extension (NCE)
- Reach accrual goal for 2/3 interim analysis
- Finish enrollment
- Data analysis and publication

Budget Expenditure compared to Actual thru 30-SEP-2023

- Actual Expenditure: \$2,208,944.66
- Scheduled Expenditures: \$7,281,802.76