AWARD NUMBER: W81XWH-22-1-0601

TITLE: Prehospital Kcentra for Trauma Patients with Hemorrhagic Shock

PRINCIPAL INVESTIGATOR: Dr. Martin Schreiber, MD

CONTRACTING ORGANIZATION: Oregon Health & Science University

REPORT DATE: JULY 2023

TYPE OF REPORT: Annual

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

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4. TITLE AND SUBTITLE
Prehospital Kcentra for Trauma Patients with Hemorrhagic Shock

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W81XWH-22-1-0601

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Dr. Martin Schreiber, MD
John D. Peterson

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
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3181 SW Sam Jackson Park Rd
Portland, OR 97239-5024

8. PERFORMING ORGANIZATION REPORT NUMBER

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
Exsanguination remains the leading cause of preventable death after trauma and a large number of these death occur in the out of hospital setting. Field use of plasma has been shown to result in improved survival in civilian trauma patients compared to crystalloid but plasma (PAMPER Trial - Sperry et al) is frequently unavailable in out of hospital settings and it may have to be stored frozen and then thawed making it logistically prohibitive for routine use in the field. 4-Factor Prothrombin Complex Concentrates (4FPCCs) are readily available and provide many of the same beneficial proteins that are present in plasma and could serve as logistically feasible substitues in the out of hospital settings. Kcentra is a 4FPCC product. A single bolus of Kcentra carries logistic and therapeutic promise because the treatment may limit blood loss, can be carried on the battlefield, administered rapidly and easily used in the prolonged field care of wounded warfighters. Therefore, we hypothesize that Kcentra given in the field to patients with traumatic hemorrhagic shock will result in improved survival, decreased end organ failure and no increase in thromboembolic complications.

15. SUBJECT TERMS
Shock, Hemorrhagic, Trauma, Mortality, Wounds, Kcentra

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
U	U	U	UU	17	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.*

   Multi-center randomized, double-blinded study to evaluate the use of Kcentra (Prothrombin Complex Concentrate) versus a placebo to help to stop bleeding in trauma patients with hemorrhagic shock. The purpose of this study is to evaluate the mortality, feasibility and clinical outcomes of administering Kcentra in the field to trauma patients with severe hemorrhagic shock by EMS personnel. There are nine locations with eight Level 1 Trauma Centers in the United States to enroll 600 trial subjects.

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

   Shock, Hemorrhagic, Trauma, Mortality, Wounds, Kcentra

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.

Major Task 1: Planning Phase	**Timeline (Months)**	**Completion (%)**	**Date Complete**
1. Select enrollment sites.	1	100	Jul 2022
2. Initiate central IRB (cIRB) with Trial Innovation Network at OHSU.	1	N/A	N/A
3. Complete clinical protocol, informed consent/assent forms, and other documents.	1	100	Feb 2023
4. Hold initial Investigator Meeting.	2	100	Sep 2022
5. Submit protocol and corresponding documents to cIRB	2	0	Estimate Q3 2023
6. Submit IND modification	3	100	Feb 2023
7. Obtain cIRB approval to initiate community consultation.	3	0	Estimate Q3 2023
8. Conduct community consultation at each site.	4-5	0	Estimate Q3 2023
9. Submit community consultation results for final cIRB approval.	6	0	Estimate Q4 2023
10. Obtain final central IRB approval to start study.	7	0	Estimate Q1 2024
11. Submit protocol to HRPO.	8-9	100	Mar 2023

Major Task 2: Data Safety Monitoring Board	Timeline (Months)	Completion (%)	Date Complete
1. Constitute Data Safety Monitoring Board (DSMB) and develop charter.	2	95	Estimate Q3 2023
2. Hold initial DSMB meeting.	6	0	Estimate Q3 2023
3. Establish DSMB meeting schedule.	6	95	Estimate Q3 2023
4. DSMB charter finalized.	6	95	Estimate Q3 2023

Milestone 3: Reporting Procedures and Study Plan	Timeline (Months)	Completion (%)	Date Complete
1. Establish management and communication plan.	1-3	95	Estimate Q3 2023
2. Establish site performance plan.	1-3	95	Estimate Q3 2023
3. Establish data completeness and quality monitoring reporting plan.	7-9	100	Q3 2022
4. Establish overall Data Safety Monitoring Plan.	1-3	100	Q3 2022
5. Establish report formats for DSMB.	4-6	100	Q3 2022
6. Initiate monthly conference calls between CCC, DCC, and Clinical Sites.	2	100	Nov 2022

Milestone 4 not mentioned, as the number was skipped in the SOW in error.

Milestone 5: Clinical Site Activation	Timeline (Months)	Completion (%)	Date Complete
1. Emergency Medical Services (EMS) Training.	7-8	0	Estimate Q4 2023
2. Conduct site initiation/training visits.	2-9	0	Estimate Q4 2023
3. Each site ensures all study personnel are trained.	8-9	0	Estimate Q1 2024
4. Begin and continue subject enrollment	9-40	0	Estimate Q1 2024

Milestone 6: Laboratory Assays	Timeline (Months)	Completion (%)	Date Complete
1. Receive subject samples at CCC.	13-43	0	Estimate Q1 2024
2. Complete proposed coagulation assays.	24-40	0	Unknown
3. Complete proposed assays for vascular endothelial function.	24-40	0	Unknown

Milestone 7: Data	Timeline (Months)	Completion (%)	Date Complete
1. Finalize Case Report Forms (CRFs) and data dictionary.	2-3	100	Q3 2022
2. Build database in Medrio.	3-6	95	Estimate Q3 2023
3. Test data transfers through (Clinical and Translational Science Awards Program) CTSAs and data entry by coordinators.	7-8	0	Estimate Q4 2023
4. Database goes live.	9	0	Estimate Q4 2023
5. Initiate data queries.	10	0	Estimate Q1 2024
6. Finalize data queries.	39	0	Unknown
7. Initiate data lock for analysis.	40	0	Unknown
8. Analyze data.	40-43	0	Unknown

Milestone 8: End of Study	Timeline (Months)	Completion (%)	Date Complete
1. Submit primary manuscript to peer-reviewed scientific journal(s); present data at scientific meeting	44-48	0	Unknown
2. Close out clinical sites	46-47	0	Unknown
3. Submit final report to DoD	48-49	0	Unknown

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.

- This Annual Technical Report will contain many corrected updates to the completion % to many of the tasks. Some of the calculations were done in error, as the author of the Quarterly Reports mistakenly combined the Pilot Study accomplishments with the DoD Study accomplishments – when in fact they are two specifically different studies. The two studies were originally set-up with the local OHSU IRB as one study – which added to the confusion. This Annual Report sets to correct these honest errors, a lesson learned and progress continues. Most of the modified completed calculations that have retreated from 100%, should be back to 100% in Q3 -2023.

Master Task 1: Planning Phase –

1. Eight Level 1 Trauma Centers involved and the ninth site is the Central Laboratory for coagulation results (updated from previous Quarterly Report - incorrectly stated as just eight sites).
2. It was discovered after the SOW creation and contract approval, that the cIRB did not have to initiate with the Trial Innovation Network as OHSU. Therefore, switched reporting in table to N/A as indicated.
3. All forms have been completed at this point and reported accordingly to the subtask – however, modifications will be made per OHRO and Advarra suggestions.
4. Nothing to report.
5. Originally the plan was to have OHSU as the first stop for the regulatory process. We are in the process of correcting this plan and have Advarra IRB (cIRB) to be involved after OHRO's review and prior to each local site IRB, if required. OHSU and/or the local site IRB would only be involved to ensure regulatory elements are met. Modified the completion % from 100% to 0% due to the previously noted incorrect process. An ID number was established with Advarra IRB in 04.2023 by OHSU personnel handling Regulatory at the time, now this will be completed by the author of this Annual Report in Q3 – 2023.
6. Initial FDA IND was approved 08.24.2018, with modifications filed with the FDA on 07.26.2021 and 02.06.2023 – and no FDA response within 30 days of filing.
7. As noted previously with the Advarra IRB (cIRB) and OHSU logistical plan, the Advarra IRB has not received the community consultation plan. Modified the completion % from 100% to 0%, we will plan progress with this subtask in Q3 – 2023.
8. Same circumstance as noted in subtask 7, will plan progress in Q4 – 2023, modified the completion % from 25% to 0%.
9. Same circumstance as noted in subtask 7, will plan progress in Q4 – 2023, modified the completion % from 25% to 0%.
10. Will obtain final Advarra IRB (cIRB) approval to start study in Q1 – 2024.
11. Protocol v1.3 was submitted to OHRO (referenced as HRPO in SOW) on 03.27.2023.

Master Task 2: Data Safety Monitoring Board –

1. The elements of a DSMB were originally established in March 2021 for a Prehospital Kcentra pilot study. No official business has been conducted with this specific DoD study. Again, the DSMB does exist, they will need to officially meet for this specific DoD study. Completion of this task was documented in error as 100% complete, it has been modified back to 95%. Will plan full completion in Q3 -2023.
2. Same circumstance as noted in subtask 1, will plan full completion in Q3 – 2023. This subtask was documented in error as 100% complete, and a meeting specifically for the DoD study has not taken place, therefore it is marked as 0%.
3. Same circumstance as noted in subtask 1, will plan full completion in Q3 – 2023. This subtask is determined by the DSMB Charter, which is 95% complete.
4. Same circumstance as noted in subtask 1, will plan full completion in Q3 – 2023. The DSMB Charter is about 95% complete, only specific language pertinent to the DoD study (i.e. study population, objectives, timeline, etc.) needs to be approved separate from the pilot study.

Milestone 3: Reporting Procedures and Study Plans -

1. – 5. The DCC has completed work on a majority of subtasks, with minor details to finish as we move closer to enrolling patients.

6. Monthly meetings between CCC/DCC and Clinical Sites started 11.2022 and continue actively each month.

Milestone 5: Clinical Site Activation –

1. Training specifically for the EMS has not started with the DoD study. There was training that had started with the Pilot study in 2022 with the specific technique of dosing Prehospital Kcentra. Due to this confusion in reporting with the completion %, we dial it back to 0%. Again, we plan to ramp this up quickly in Q4 – 2023, if training materials are made available from CSL Behring in a timely manner.
2. Once the regulatory process begins completion of items in Q3 -2023, we will be able to conduct the SIV and ramp up training. Due to this confusion in reporting with the completion %, we dial it back to 0%.
3. Once the regulatory process begins completion of items in Q3 -2023, we will be able to ramp up training of the study personnel at each site.
4. We do plan to begin enrollment in Q1 – 2024.

Milestone 6: Laboratory Assay -

1. – 3. Nothing to Report at this time, until subject enrollment begins.

Milestone 7: Data –

1. Case Report Forms have been completed
2. DCC will finalize the activation of the Medrio database with the agreement on the contract of service.
3. DCC will be moving forward with testing the database with transfers and data entry in Q4 - 2023, with the final goal in this Q4 to have the database live.
4. DCC will begin data queries as the patients begin to be enrolled in Q1 – 2024.

5. – 8. Nothing to Report at this time, until subject enrollment begins.

Milestone 8: End of Study –

1. – 3. Nothing to Report at this time, until subject enrollment begins.

Other Accomplishments Not Associated with the SOW –

- On 04.06.2023 - No Cost Extension was granted by the DoD to extend Performance End Date to 09.30.2023.
- A plastic hard case has been created to help with the packaging and ultimately the administration of Kcentra in the field.

Describe the Regulatory Protocol and Activity Status (as applicable).

TOTAL PROTOCOLS: Two human subject regulatory entities and each site's local IRB will be required to complete the Statement of Work – OHRO and the Advarra IRB (cIRB). As previously reported, the protocol was first submitted to the OHSU IRB and approved – this was in error. Current plan is that we have submitted protocol to OHRO on 03.27.2023, and then will submit to Advarra (cIRB) Q2 2023 and subsequently to each local IRB what Advarra has approved, if required.

Protocol (1 of 1 total):
Protocol [Advarra IRB ID]: Pro00070537
Title: Prehospital Kcentra for Hemorrhagic Shock
Target required for clinical significance: 600
Target approved for clinical significance: 600
Submitted to and Approved by:

- Submitted Protocol v1.3 to OHRO on 03.27.2023

Status:

- OHRO received Protocol v1.3 on 03.27.2023

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 not 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.

Most updates & plans to accomplishing goals are found earlier in this Section 3, however this is presented in chronological order per Quarter with notes expanded.

Q3 2023:

- All regulatory work with the Advarra IRB (cIRB) will be completed such as – submission of protocol, other corresponding documents and community consultation start at each site.
- Obtain final study approval from OHRO. Currently working on the initial review of materials and questions on the study. Protocol was submitted to OHRO in March 2023, with initial response in later April 2023.
- DSMB will convene under specific DoD study business and DoD specific DSMB Charter.
- DCC will finalize the management, communication, and site performance plans.
- DCC will finalize the activation of the Medrio database with new contract of service.
- A DoD "No-Cost-Extension" will be submitted in order to allow extra time for the EFIC approval process to be completed and approved by the Army Surgeon General.

Q4 2023:

- After conducting community consultations at each site, we will plan to submit the results to Advarra IRB.
- Training of the EMS crews will be in full swing at this time – if training materials (i.e. placebo IV vials, Mix2Vial devices, sterile water IV vials) are made available from CSL Behring in a timely manner.
- As study materials are approved by OHRO, Advarra IRB – we will be able to conduct site initiations, along with training for each site.
- DCC will be moving forward with testing the database with transfers and data entry, with the final goal in this Quarter to have the database live.

Q1 2024:

- With all regulatory institution approvals complete - we will be able to start the study.
- As we continue to complete items in the stated SOW, by this time - each of the sites will ensure all study personnel are trained and enrollment will begin.
- With study enrollment beginning, the Central Laboratory at UCSF will begin to receive samples as patients are enrolled.
- DCC will begin the process of initiating data queries in the database as patients are enrolled.

Q2 2024:

- Study enrollment, training for new employees, data entry and safety monitoring will continue.
- Monthly all site meeting collaborations will continue.
- Quarterly Technical Progress Reports will continue for each Quarter up to this point.

4. **IMPACT:** D*escribe 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.

- **Finalizing a contract with CSL Behring to obtain study drug.**
  - Dr. Schreiber and designated research staff continue engagement with CSL Behring representatives with frequent video Team meetings for updates on the contract.
- **Re-packaging of drug for EMS staff use has been noted as difficult to conduct the administration of Kcentra.**
  - A plastic hard case has been created to help with the packaging and ultimately the administration of Kcentra in the field.
  - Will continue to obtain feedback from the EMS crews, MDs, Pharmacists, and other Clinical Research professionals to modify packaging.

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

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

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".

Name	Project Role	Researcher ID	Effort	Contribution
Martin Schreiber, MD	PI	0000-0002-4430-6779	1.0	Oversight of project execution
Sam Underwood	Research Admin.	N/A	1.0	Study coordination, no longer involved at same level since Feb'23.
John D. Peterson, PharmD, RPh	Project Coordinator	N/A	1.0	Study coordination since Feb'23.
Julie Mitchell	Operations Leader (DCC)	N/A	1.0	Create and manage database, eCRF, EDC
Jill Metz	Project Manager (DCC)	N/A	1.0	Create and manage database, eCRF, EDC
Cynthia Morris, PhD	PI (DCC)	0000-0001-7300-0456	1.0	Oversight of DCC

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 (ver. 20 April 2023) Attached.*

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.*

- *Nothing to Report.*

Prehospital Kcentra for Trauma Patients with Hemorrhagic Shock

PR210463
W81XWH-22-1-0601

PI: Martin Schreiber, MD **Org:** Oregon Health & Science University **Award Amount:** $15,828,835

Full Study Title

- A Prospective Randomized Prehospital Trial Comparing Kcentra Plus Standard of Care to Standard of Care Alone in Trauma Patient with Hemorrhagic Shock

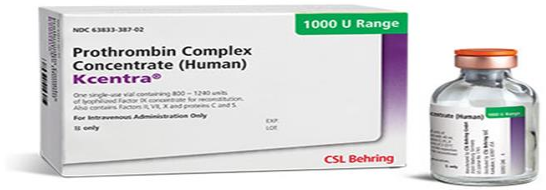
Objectives

- Primary objective is to evaluate survival at 3-hours, 24-hours, and 30 days.
- Secondary objective is to evaluate the incidence of acute respiratory distress syndrome, multiple organ failure, acute renal failure. Ventilator free days, ICU free days, hospital free days will be evaluated. The amount of fibrinogen concentrate, tranexamic acid, units of whole blood RBCs, plasma, cryoprecipitate, and platelets transfused in the first 24 hours will be recorded.

Hypothesis

- We hypothesize that Kcentra administered in the field to trauma patients with severe hemorrhagic shock plus standard of care will improve survival compared to current standard of care alone.

Kcentra® by CSL Behring



All subjects will receive resuscitation with

- **Treatment A:** Single dose of Kcentra based on estimated body weight
  OR
- **Treatment B:** Single infusion of volume matched placebo solution

Accomplishments: An IND was obtained from the FDA for the entire study trial. This study has IRB approval. The study has been submitted to OHRO for further approval.

Approach

- Placebo-Controlled, Double-Blinded Trial
- 7 locations with 8 Level I Trauma Centers
- 600 trial subjects to be enrolled, study duration is 48 months

Summation

- The use of Kcentra to mitigate the effects of hemorrhagic shock and coagulopathy suffered in the field directly addresses the FY21 PRMRP topic area of hemorrhage control.
- A single bolus of Kcentra carries logistic and therapeutic promise because the treatment may limit blood loss, can be carried on the battlefield, administered rapidly, and easily used in the prolonged field care of wounded warfighters.

Updated: (20 April 2023)

Goals/Milestones

CY23 Goal – Planning Phase/Study Start-Up

- ❑ Regulatory approvals, Training Staff/Sites, Drug Delivery, Contract

CY24-CY26 Goals – Clinical Trial Enrollment

- ❑ Begin to enroll patients in clinical study
- ❑ Continuous monitoring of patient safety and data results

CY27 Goals – Study Close-Out

- ❑ Finish patient enrollment
- ❑ Begin to close study and report results

Comments/Challenges/Issues/Concerns

- ❑ Concern – finalizing contract with CSL Behring to obtain study drug

Budget Expenditure to Date

Projected Expenditure: $15,828,835
Actual Expenditure: $0.00