Defense Health Agency (DHA)
2023.C Small Business Technology Transfer (STTR)
Proposal Submission Instructions

INTRODUCTION

The Defense Health Agency (DHA) SBIR/STTR Program seeks small businesses with strong research and development capabilities to pursue and commercialize medical technologies.

The Defense SBIR/STTR Innovation Portal (DSIP) is the official portal for DoD SBIR/STTR proposal submission. Proposers are required to submit proposals via DSIP; proposals submitted by any other means will be disregarded. Detailed instructions regarding registration and proposal format submission via DSIP are provided in the DoD STTR Program Broad Agency Announcement (BAA). Proposals not conforming to the terms of this BAA will not be considered.

DHA requirements in addition to or deviating from the DoD Program BAA are provided in the instructions below. Only Government personnel will evaluate proposals and provide technical analysis in the evaluation of proposals submitted against DHA topics.

Specific questions pertaining to the administration of the DHA SBIR/STTR Program and these proposal preparation instructions shall be directed to:

DHA SBIR Program Management Office (PMO) Email: usarmy.detrick.medcom-usamrmc.mbx.dhpsbir@health.mil

For technical questions about a topic during the pre-release period, contact the Topic Author(s) listed for each topic in the BAA. To obtain answers to technical questions during the formal BAA period, visit the Topic Q&A: https://www.dodsbirsttr.mil/submissions/login.

Proposers are encouraged to thoroughly review the DoD Program BAA and register for the DSIP Listserv to remain apprised of important programmatic and contractual changes.

- The DoD Program BAA is located at: https://www.defensesbirsttr.mil/SBIR-STTR/Opportunities/#announcements. Be sure to select the tab for the appropriate BAA cycle.
- Register for the DSIP Listserv at: https://www.dodsbirsttr.mil/submissions/login.

PHASE I PROPOSAL GUIDELINES

Technical Volume (Volume 2)

The technical volume is not to exceed **20 pages** and must follow the formatting requirements provided in the DoD STTR Program BAA. Do not duplicate the electronically-generated Cover Sheet or put information normally associated with the Technical Volume in other sections of the proposal as these will count toward the 20-page limit.

Only the electronically-generated Cover Sheet and Cost Volume are excluded from the 20-page limit. Technical Volumes that exceed the 20-page limit will be deemed non-compliant and will not be evaluated.

Cost Volume (Volume 3)

The Phase I amount must not exceed $250,000 over a 6-month period of performance. Costs must be separated and clearly identified on the Proposal Cover Sheet (Volume 1) and in Volume 3.

Please review the updated Percentage of Work (POW) calculation details included in section 5.3 of the DoD Program BAA. Deviations from the POW requirements are not permitted.

Travel must be justified and relate to the project needs for direct Research Development Test & Evaluation (RDT&E) Technology Readiness Level (TRL) increasing costs. Travel costs must include the purpose of the trip(s), number of trips, origin and destination, length of trip(s), and number of personnel.

Company Commercialization Report (CCR) (Volume 4)

Completion of the CCR as Volume 4 of the proposal submission in DSIP is required. Please refer to the DoD STTR Program BAA for full details on this requirement. Information contained in the CCR will be considered by DHA during proposal evaluations.

Supporting Documents (Volume 5)

Volume 5 is provided for proposing small business concerns to submit additional documentation to support the submission. All proposing small business concerns are REQUIRED to submit the following documents to Volume 5:

1. Contractor Certification Regarding Provision of Prohibition on Contracting for Certain Telecommunications and Video Surveillance Services or Equipment (Attachment 1)
2. Disclosures of Foreign Affiliations or Relationships to Foreign Countries (Attachment 2)
3. Disclosure of Funding Sources (Attachment 4)

A completed proposal submission in DSIP does NOT indicate that the mandatory supporting documents have been uploaded. It is the responsibility of the proposing small business concern to ensure that the mandatory documents listed above have been uploaded and included with the proposal submission.

Fraud, Waste and Abuse Training Certification (Volume 6)

DoD requires Volume 6 for submission. Please refer to the Phase I Proposal section of the DoD STTR Program BAA for details.

PHASE II PROPOSAL GUIDELINES

Phase II proposals may only be submitted by Phase I awardees from this BAA. Phase II is the demonstration of the technology found feasible in Phase I. The details on the due date, content, and submission requirements of the Phase II proposal will be provided by the DHA STTR PMO typically in month five of the Phase I contract.

The DHA STTR Program will evaluate and select Phase II proposals using the evaluation criteria in the DoD STTR Program BAA. Due to limited funding, the DHA STTR Program reserves the right to limit awards under any topic and only proposals considered to be of superior quality will be funded.
Small businesses submitting a proposal are required to develop and submit a Commercialization Strategy describing feasible approaches for transitioning and/or commercializing the developed technology in their Phase II proposal. This plan shall be included in the Technical Volume.

The Cost Volume must contain a budget for the entire 24-month Phase II period not to exceed the maximum dollar amount of $1,300,000.

Budget costs must be submitted using the Cost Volume format (accessible electronically on the DoD submission site) and shall be presented side-by-side on a single Cost Volume Sheet.

DHA STTR Phase II Proposals have six Volumes: Proposal Cover Sheets, Technical Volume, Cost Volume, Company Commercialization Report, Supporting Documents, and Fraud, Waste, and Abuse. The Technical Volume has a 40-page limit including: table of contents, pages intentionally left blank, references, letters of support, appendices, technical portions of subcontract documents (e.g., statements of work and resumes) and any attachments.

Technical Volumes that exceed the 40-page limit will be deemed non-compliant and will not be evaluated.

DISCRETIONARY TECHNICAL AND BUSINESS ASSISTANCE (TABA)
The DHA STTR Program does not participate in the Technical and Business Assistance (formerly the Discretionary Technical Assistance Program). Contractors shall not submit proposals that include Technical and Business Assistance.

The DHA STTR Program has a Technical Assistance Advocate (TAA) who provides technical and commercialization assistance to small businesses that have Phase I and Phase II projects.

EVALUATION AND SELECTION
All proposals will be evaluated in accordance with the evaluation criteria listed in the DoD STTR Program BAA. Proposing firms will be notified via email to the Corporate Official of selection or non-selection status for a Phase I award within 90 days of the closing date of the BAA.

Non-selected companies may request feedback within 15 calendar days of the non-select notification. The Corporate Official identified in the firm's proposal shall submit the feedback request to the STTR Office at usarmy.detrick.medcom-usamrmc.mbx.dhpsbir@health.mil. Please note feedback is provided in an official PDF via email to the Corporate Official identified in the firm proposal within 60 days of receipt of the request. Requests for oral feedback will not be accommodated. If contact information for the Corporate Official has changed since proposal submission, a notice of the change on company letterhead signed by the Corporate Official must accompany the feedback request.

NOTE: Feedback is not the same as a FAR Part 15 debriefing. Acquisitions under this solicitation are awarded via "other competitive procedures". Therefore, offerors are neither entitled to nor will they be provided FAR Part 15 debriefs.

Refer to the DoD STTR Program BAA for procedures to protest the Announcement.
As further prescribed in FAR 33.106(b), FAR 52.233-3, Protests after Award shall be submitted to:

Ms. Samantha L. Connors SBIR/STTR Chief, Contracts Branch 8
Contracting Officer
U.S. Army Medical Research Acquisition Activity
Email: Samantha.l.connors.civ@health.mil

AWARD AND CONTRACT INFORMATION
Phase I awards will total up to $250,000 for a 6-month effort and will be awarded as Firm-Fixed-Price Purchase Orders.

Phase II awards will total up to $1,300,000 for a 24-month effort and will typically be Firm-Fixed-Price contracts. If a different contracting type is preferred, such as cost-plus, the rational as to why must be included in the proposal.

Phase I and II awardees will be informed of contracting and Technical Point of Contact upon award.

ADDITIONAL INFORMATION

RESEARCH INVOLVING HUMAN SUBJECTS, HUMAN SPECIMENS/DATA, OR ANIMAL RESEARCH

The DHA STTR Program highly discourages offerors from proposing to conduct Human Subjects, Human Specimens/Data, or Animal Research during Phase I due to the significant lead time required to prepare regulatory documentation and secure approval, which could substantially delay the performance of the Phase I award. While technical evaluations will not be negatively impacted, Phase I projects requiring Institutional Review Board approval may delay the start time of the Phase I award. If necessary regulatory approvals are not obtained within two months of notification of selection, the decision to award may be terminated.

Offerors are expressly forbidden to use, or subcontract for the use of, laboratory animals in any manner without the express written approval of the U.S. Army Medical Research and Development Command (USAMRDC) Animal Care and Use Review Office (ACURO). Written authorization to begin research under the applicable protocol(s) proposed for this award will be issued in the form of an approval letter from the USAMRDC ACURO to the recipient. Modifications to previously approved protocols require re-approval by ACURO prior to implementation.

Research under this award involving the use of human subjects, to include the use of human anatomical substances or human data, shall not begin until the USAMRDC's Office of Human and Animal Research Oversight (OHARO) provides formal authorization. Written approval to begin a research protocol will be issued from the USAMRDC OHARO, under separate notification to the recipient. Written approval from the USAMRDC OHARO is required for any sub-recipient using funds from this award to conduct research involving human subjects. If the Offeror intends to submit research funded by this award to the U.S. Food and Drug Administration, Offerors shall propose a regulatory strategy for review.

Non-compliance with any provision may result in withholding of funds and or termination of the award.

WAIVERS

The DHA STTR Program highly discourages offerors from proposing a federal facility use waiver during Phase I due to the significant lead time required to prepare documentation and secure approval, which could substantially delay the performance of the Phase I award.

In rare situations, the DHA STTR Program allows for a waiver to be incorporated allowing federal facility usage for testing/evaluation. A waiver will only be permitted when it has been determined that no applicable U.S. facility has the ability or expertise to perform the specified work. The DHA STTR Program has the right of refusal. If approved, the DHA STTR Program will assist in establishing the waiver for approval. If approved, the proposer will subcontract directly with the federal facility and not a third-party representative.

Transfer of funds between a company and a Military Lab must meet the following APAN 15-01 requirements (the full text of this notice can be found at https://usamraa.health.mil/SiteAssets/APAN%2015-01%20Revised%20Feb%202018.pdf):

(1) The DoD Intramural Researcher must obtain a letter from his/her commanding officer or Military Facility director authorizing his/her participation in the Extramural Research project. This letter must be provided to the Extramural Organization for inclusion in the proposal or application.

(2) The DoD Intramural Researcher must also coordinate with his/her local Resource Manager Office (or equivalent) to prepare a sound budget and justification for the estimated costs. Where there are no DoD-established reimbursement rates [e.g., institution review board (IRB) fees, indirect cost rates, etc.], the Military Facility's RM office (or equivalent) must provide details of how the proposed rates were determined. The DoD Intramural Researcher must use the budget and justification form enclosed in APAN 15-01 when developing the estimated costs and provide it to the Extramural Organization for inclusion in the proposal or application.

(3) The Extramural Research proposal or application must include a proposed financial plan for how the Military Facility's Intramural Research costs will be supported [i.e., directly funded by DoD, resources (other than award funds) provided by the Awardee to the Military Facility, or award funds provided by the Awardee to the Military Facility (in accordance with the requirements below)].

(4) The DoD Intramural Researcher should also coordinate with his/her technology transfer office.

International Traffic in Arms Regulation (ITAR)
For topics indicating ITAR restrictions or the potential for classified work, limitations are generally placed on disclosure of information involving topics of a classified nature or those involving export control restrictions, which may curtail or preclude the involvement of universities and certain non-profit institutions beyond the basic research level. Small businesses must structure their proposals to clearly identify the work that will be performed that is of a basic research nature and how it can be segregated from work that falls under the classification and export control restrictions. As a result, information must also be provided on how efforts can be performed in later phases, such as Phase III, if the university/research institution is the source of critical knowledge, effort, or infrastructure (facilities and equipment).

END

DHA STTR 23.C Topic Index

DHA23C-001	Multi-faceted mAb Development Program for Multi-Drug Resistant Wound Infections
DHA23C-002	Exosome Loaded Antibiotics for Bacterial Wound Infections
DHA23C-003	Development of an Exoskeleton Assistive Device that Augments Grip Strength for Seamless Mission Integration and Use in Military Casualty Transport Environment Scenarios

DHA23C-001 TITLE: Multi-faceted mAb Development Program for Multi-Drug Resistant Wound Infections

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): Military Infectious Disease

OBJECTIVE: The objective of this topic would be to develop human monoclonal antibodies (mAbs) that have demonstrated efficacy and safety in a screening infected wound animal model against multi-drug resistant bacteria.

DESCRIPTION: Multi-drug resistant (MDR) infections have caused significant morbidity and mortality for US Service Members with battlefield wounds.1 Among MDR bacteria, the ESKAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Entrobacter spp.) have been identified as particularly problematic pathogens that complicate wounds of U.S. military casualties.2 These species are commonly pan-resistant to most commercially available antibiotics. Monoclonal antibodies (mAbs) that specifically target and kill MDR are a promising alternative to antibiotics and vaccines. Passive immunotherapy with mAbs can provide protection against bacterial infection via multiple mechanisms, including neutralization, complement-mediated killing and opsonic phagocytosis. The use of biologics can also slow resistance development. Their long half-lives allow for minimal dosing which is optimal for prolonged field care. Typically mAbs storage conditions are minimal, (4oC) and have long shelf lives lasting 12 months or more allowing for reduced logistical challenges for deployed medical units. A targeted mAb would have utility at all roles of care within the military health spectrum. Utilizing the right techniques/methods, MDR specific mAbs can be generated significantly faster than small molecules or vaccines.

Thus far, development of therapeutic mAbs for use in bacterial infections have lagged behind other areas such as viral infections and cancer.3 Concentrated program efforts are needed instead of the typical use of a singular source through one development pathway. This program would require the combination of multiple sources and pathways with state of the art tools to maximize the efficiency and success rate.

This project would require a company to be able to draw from multiple sources of material for antibody generation: plasma cells from infected patients, Memory B cells from convalescent patients and plasma and Memory B cells from transgenic humanized animals. Each source of antibodies would undergo different screening and identification pathways using advanced methods such as single cell-based screening on Beacon instruments and the 10X Genomics Chromium system.

Combining multiple antibody sources from human and humanized animals with different pathways will enable high affinity antibodies that need no further modification to humanize them. The end product from this project will be at least 1 humanized antibody that has demonstrated in vitro and in vivo high affinity, safety and efficacy against one ESKAPE pathogen.

This approach to therapeutic antibody development will allow for a rapid, modifiable capability that should improve antibody therapeutic development timelines by months. This platform can be utilized for all the ESKAPE pathogens. In addition, it provides a mechanism for developing therapeutic antibodies for any emerging pathogen, greatly enhancing pandemic response capabilities.

PHASE I: This phase will be focused on antigen selection, synthesizing and purification. Based on available evidence, the most likely antigens to provide the most specific and robust immune response will be created and then purified. The company will need to demonstrate experience and capability in identifying ideal antigen candidates either through methods such as analysis of known surface protein sequences/structures or through antigen/phage library creation and down selection. Once candidates are selected, the synthesizing and purification of identified peptides will need to be demonstrated. The

company should have partners that they can collaborate with that has the ability to obtain human samples from infected patients. By the end of Phase 1 all necessary requirements to initiate human sample collection and animal immunization with target antigens will be performed.

PHASE II: This phase will focus on the development, purification, screening and testing of antibodies to generate at least 1 antibody specific for an ESKAPE pathogen. Antibodies that have undergone single cell screening and purification regardless of whether they came from human or transgenic animal sources will be further screened using rigorous in vitro tests. Any resulting antibody will be evaluated for efficacy and safety on a wound infection animal model validated for that ESKAPE pathogen. The resulting deliverable will be at least one antibody that has demonstrated in vitro and in vivo affinity, safety and efficacy in treating an ESKAPE pathogen. These antibodies will be ready for more advanced development. The multiple simultaneous approaches as part of this program allows for maximum opportunity for a successful antibody to be discovered and screened in a short time frame. A regulatory strategy that reflects a clinical Target Product Profile will need to be developed during this phase. It should include relevant in vitro/in vivo cross reactivity testing, immunogenicity, small and large animal toxicology studies and plans for pre-Investigational New Drug FDA meetings.

PHASE III DUAL USE APPLICATIONS: This phase would focus on in vivo and human research needed to obtain FDA approval. Starting with dose ranging and animal toxicology studies and progressing to the first in human Phase 1 study. Any company should have capabilities or partners with large scale Good Manufacturing Practices (GMP) manufacturing capabilities. Funding for further development efforts could be sought from such programs as the Joint Warfighter Medical Research Program, Biomedical Advanced Research and Development Authority or Medical Technology Enterprise Consortium. The end state would be an FDA approved therapeutic antibody to treat a multi-drug resistant ESKAPE pathogen. This would serve as a significant therapeutic tool to military and civilian caregivers. Once FDA approved, this product should have immediate interest from tertiary care civilian and military hospitals in treating highly resistant infections in intensive care or post-operative patients.

REFERENCES:

1. David R Tribble, MD, DrPH, Clinton K Murray, USA, MC, Bradley A Lloyd, USAF, MC, Anuradha Ganesan, MBBS, MPH, Katrin Mende, PhD, Dana M Blyth, USAF, MC, Joseph L Petfield, USA, MC, Jay McDonald, MD, After the Battlefield: Infectious Complications among Wounded Warriors in the Trauma Infectious Disease Outcomes Study, Military Medicine, Volume 184, Issue Supplement_2, November-December 2019, Pages 18–25, https://doi.org/10.1093/milmed/usz027
2. Katrin Mende, PhD, Kevin S Akers, MC, USA, Stuart D Tyner, MSC, USA, Jason W Bennett, MC, USA, Mark P Simons, USN, MSC, Dana M Blyth, USAF, MC, Ping Li, MS, Laveta Stewart, MSc, MPH, PhD, David R Tribble, MD, DrPH, Multidrug-Resistant and Virulent Organisms Trauma Infections: Trauma Infectious Disease Outcomes Study Initiative, Military Medicine, Volume 187, Issue Supplement_2, May-June 2022, Pages 42–51, https://doi.org/10.1093/milmed/usab131
3. Zurawski DV, McLendon MK. Monoclonal Antibodies as an Antibacterial Approach Against Bacterial Pathogens. Antibiotics (Basel). 2020 Apr 1;9(4):155. doi: 10.3390/antibiotics9040155. PMID: 32244733; PMCID: PMC7235762

KEYWORDS: Monoclonal antibodies, multi-drug resistant organisms, bacterial infections, monoclonal antibody development, wound infections, ESKAPE pathogens

DHA23C-002 TITLE: Exosome Loaded Antibiotics for Bacterial Wound Infections

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): Military Infectious Disease

OBJECTIVE: The objective of this topic would be to develop antibiotic loaded exosomes for topical application on wounds for prophylaxis or adjunct treatment indications.

DESCRIPTION: Multidrug-resistant bacterial infections increase mortality rates in wounded patients and are becoming a public health concern for both military and civilian patients worldwide.1 As current antimicrobial therapies continue to lose efficacy against these pathogens, new countermeasures must be identified to maintain sufficient control of these infections. Among MDR bacteria, the ESKAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Entrobacter spp.) have been identified as particularly problematic pathogens that complicate wounds of U.S. military casualties.2

Topical application of antibiotics have long been evaluated as a potential route of administration as an adjunct or to prevent wound infections. In addition to the logistical advantages and ease of use of a topically applied antibiotic therapeutic, this route of administration affords the opportunity to decrease systemic absorption minimizing potential systemic toxicity that is common among many antibiotics given intravenously or orally to treat ESKAPE organisms. While its use in the surgical arena has demonstrated benefit, the efficacy of topical antibiotics in the field has been met with challenges such as poor tissue penetrance and local contact dermatitis side effects. A topical antibiotic product that could overcome these issues while demonstrating efficacy would have significant utilization potential as a prolonged field care tool as well as in the hospital setting. Current Tactical Combat Casualty Care Guidelines recommend the use of intravenous ertapenem for wound infections in soldiers that cannot take oral medications.3 While ertapenem's broad spectrum of activity and bacteriocidal activity make it a highly effective antibiotic, its systemic use as a prophylactic therapeutic, especially in the prolonged field care setting, create an ideal situation for resistance development. A topical ertapenem with similar efficacy in preventing infections would offer improvements in stability, storage, ease of use, decrease risk of resistance and dosing error. It could be utilized by medics or physicians at any level of care in the deployed setting.

Extracellular vesicles (EVs) are nanoscale, lipid bilayer delimited vesicles that serve as the fundamental intercellular communication system. As such, these vesicles are optimized to transport biomolecular cargo (e.g., amino acids, nucleic acids, small molecules) throughout biological systems. A subset of EVs called exosomes feature specific receptors and proteins that decorate the lipid bilayer of the vesicle and enable rapid uptake into target cells and signal for efficient processing of the delivered cargo. By themselves, exosomes have exhibited wound healing properties demonstrating free radical scavenging to enhance cell survival, recruitment and support of local tissue progenitor cells to rebuild tissue and promotion of neoangiogenesis to restore blood supply.4 Exosomes loaded with an antibiotic would provide a safe, targeted topical approach to treating or preventing wound infections. Repurposing already approved antibiotics will allow for a quicker regulatory pathway.

PHASE I: This phase will focus on exosome formulation with a broad spectrum antibiotic that could be used for prophylaxis topically on wounds or a narrow spectrum antibiotic targeted as an adjunct treatment for a multi-drug resistant ESKAPE pathogen. The exosome should be a reproducible, sterile, easily re-constituted and scalable product. Exosome size should be relatively uniform ranging from 100-400nm. The product should be stable at room temperature. The company should have or be able to develop a process through which maximum drug loading efficiency can be achieved while maintaining the integrity of the exosomes. They should be able to scale this process to a degree in which sufficient doses could be provided for clinical use. Appropriate quality control checks The deliverables of this phase will be the

manufacturing and quality control reports as well as a finished Current Good Manufacturing Practice (cGMP) product available for future use.

PHASE II: This phase will focus on pre-clinical evaluation of the antibiotic loaded exosome. Initial in vitro or ex vivo screening assays can be performed to further screen and refine prototypes. An in vitro biofilm model should be included with these assays. The next stage would involve evaluation of the exosome loaded antibiotic on an animal wound model. The wound model should be validated against whatever pathogen is to be tested against or prevented. In addition to safety and efficacy endpoints it should include a pharmacokinetic analysis to determine systemic exposure levels. End points such as time to wound closure, weight change, bacterial burden and clinical observations should be included. The deliverable for this phase would be an antibiotic loaded exosome that demonstrated safety and efficacy in a validated wound animal model with limited systemic exposure.

A regulatory strategy that reflects a clinical Target Product Profile (TPP) will need to be developed during this phase. This TPP should include information related to desired formulation, excipients, stability, quality control measures and manufacturing considerations. The regulatory strategy should include relevant in vitro release test and in vitro permeation test recommendations, small and large animal toxicology and pharmacokinetic/pharmacodynamics studies and plans for pre-Investigational New Drug FDA meetings.

PHASE III DUAL USE APPLICATIONS: This phase would focus on in vivo and human research needed to obtain FDA approval. Starting with dose ranging and animal toxicology studies and progressing to the first in human Phase 1 study. Similar exosome products have already undergone Phase 1 studies and by using already FDA approved antibiotics with a known safety profile the regulatory pathway may be shorter than traditional new molecular entities. Funding for further development efforts could be sought from such programs as the Joint Warfighter Medical Research Program, Biomedical Advanced Research and Development Authority or Medical Technology Enterprise Consortium. Once FDA approved, the use of a topical antibiotic that can be used to treat ESKAPE pathogens would have immediate utility and interest from civilian surgical centers for post-operative care and tertiary care inpatient and intensive care units as an adjunct for skin/wound infections.

REFERENCES:

1. Calhoun JH, Murray CK, Manring MM. Multidrug-resistant organisms in military wounds from Iraq and Afghanistan. Clin Orthop Relat Res. 2008 Jun;466(6):1356-62. doi: 10.1007/s11999-008-0212-9. Epub 2008 Mar 18. PMID: 18347888; PMCID: PMC2384049.
2. Katrin Mende, PhD, Kevin S Akers, MC, USA, Stuart D Tyner, MSC, USA, Jason W Bennett, MC, USA, Mark P Simons, USN, MSC, Dana M Blyth, USAF, MC, Ping Li, MS, Laveta Stewart, MSc, MPH, PhD, David R Tribble, MD, DrPH, Multidrug-Resistant and Virulent Organisms Trauma Infections: Trauma Infectious Disease Outcomes Study Initiative, Military Medicine, Volume 187, Issue Supplement_2, May-June 2022, Pages 42□51, https://doi.org/10.1093/milmed/
3. Committee on Tacticle Combat Casualty Care. Tactical Combat Acsualty Care Guidelines for Medical Personnel. 15 December 2021. https://books.allogy.com/web/tenant/8/books/b729b76a-1a34-4bf7-b76b-66bb2072b2a7/. Accessed 17 May 2023.
4. Shi A, Li J, Qiu X, Sabbah M, Boroumand S, Huang TC, Zhao C, Terzic A, Behfar A, Moran SL. TGF-β loaded exosome enhances ischemic wound healing in vitro and in vivo. Theranostics. 2021 Apr 30;11(13):6616-6631. doi: 10.7150/thno.57701. PMID: 33995680; PMCID: PMC8120220

KEYWORDS: Exosomes, topical antibiotics, multi-drug resistant organisms, bacterial infections, wound infections, ESKAPE pathogens

DHA23C-003 TITLE: Development of an Exoskeleton Assistive Device that Augments Grip Strength for Seamless Mission Integration and Use in Military Casualty Transport Environment Scenarios

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): Combat Casualty Care

OBJECTIVE: Develop, demonstrate, and deliver an exoskeleton device that augments grip strength while using a litter in a military medical casualty transport environment without interfering in other mission requirements or medical transport device/equipment design and operation.

DESCRIPTION: Litter transport is a standard on-foot procedure for initial casualty evacuation from the point of injury to the tactical evacuation zone and at times the only mode of transportation to move the injured person. Using a litter is physically demanding for Service Members (SMs). During the evacuation, the litter team may be required to provide critical medical care while actively engaging in combat to protect themselves and the patient. A straightforward approach to the dilemma of litter bearer fatigue and injury is to develop a medical assistive device that lessens the physical demands on the litter bearer. Using an assistive device (e.g., exoskeleton) during litter transport could decrease fatigue and increase the litter bearer's ability to carry the litter, provide critical medical care, and sustain SM tasks.

Recently published recommendations by Madison (2022) are essential considerations for the development of a successful exoskeleton devices to maintain grip strength and dexterity of the SMs during dismounted litter load carriage tasks. Currently there are other available exoskeleton devices available for use however they do not meet the field medicine design requirements to specifically address grip strength augmentation while simultaneously allowing for dynamic movement over long distances. Designers should consider a possible solution to develop a quasi-passive, multi-joint, upper extremity exoskeleton for the medical user. The presence of a lower extremity exoskeleton would be beneficial to a litter bearer; however, grip strength is the first component to fatigue to exhaustion. This exhaustive state is why upper extremity exoskeletons take priority, but both can be beneficial to the SM. Thus, if lower extremity is included at any time during the design process, upper extremities must also be incorporated to assist with grip strength augmentation. Designers should consider using a combination of lighter actuators, such as pneumatic actuators or series elastic actuators, and passive actuators, such as springs or dampers. Combining these types of actuators may allow the exoskeleton to be lighter and consume less energy than if electric or hydraulic actuators were used. The use of passive actuators could also serve as a backup augmentation component if the exoskeleton runs on a limited power supply. The materials should be selected for durability in any terrain. The exoskeleton is required to withstand any environment in which they are employed and extreme temperatures (Crowell et al., 2019). Care must be taken to ensure the exoskeleton is adjustable to accommodate vast anthropometric variances among SMs. Exoskeletons should also easily be donned and doffed by the user to alleviate or reduce the possibility of improper fit (Gordon et al., 2014). The exoskeleton cannot require the litter team to surrender their weapons or remove body armor. The exoskeleton must not interfere with other current military medical equipment or weaponry (Crowell et al., 2019). The exoskeleton needs be easily integrated into the medical mission at hand and Army medics must also continue their care of the patient, which requires them to perform dexterity skills. For that reason, future exoskeletons must not interfere with patient evaluations, typical medical procedures, or any extra duties required of the SM (Blackbourne et al., 2012).

PHASE I: Develop device concepts and designs that address the desired capabilities and identified design requirements for an augmented grip strength exoskeleton to assist with casualty litter transport (Madison et al., 2022). Perform a technical trade assessment of the conceptual designs, to include improved combat performance following litter carry, a decrease in evacuation times, and decreasing the necessary four-person carry down to a two-person team. Work in Phase I should demonstrate the ability to integrate an exoskeleton device that augments grip strength during use in a military environment and during military

litter transport without interfering in other mission capabilities. Additionally, work in Phase I should demonstrate the field compatibility of the design by delivering documentation on the two most promising concept designs, anticipated developmental testing requirements, proposed test procedures and preliminary data to demonstrate functionality and compatibility of major design elements, working principles, and use. The performer will establish a work plan for subsequent development and prototyping. Along with the concept designs, the performer shall deliver breadboard mock-ups to the sponsor.

PHASE II: Government representatives will evaluate the proposed mock-up exoskeleton for use in simulated and real-world litter transport scenarios and provide feedback to the performer for development of a refined design for use in further testing. Performers will improve upon the selected design and refine the prototype design for wear by SM by additional testing and design improvements. The performer will deliver 6 functional prototypes (or 3 pairs if prototypes are developed as a singular side or separated into a left and right side) for use in testing and evaluation. The exoskeleton needs to be adjustable to work cohesively with the vast anthropometric variances among SMs as well as current and future field medical transport equipment and devices (e.g., litter systems, etc.). The prototype will also include any hardware/software interfaces that are required for system functionality (e.g., external power, charging capabilities, data download and processing, etc.). The Government representatives will evaluate the exoskeleton against the identified design requirements and engage subject matter experts for feedback on device design and use. Device feedback will be delivered to the performer, who will use the provided feedback in conjunction with the performer's identified deficiencies to refine the final design of the exoskeleton. After completion of the final design, 6 exoskeletons (or 3 pairs if design is developed as a singular side or separated into a left and right side) will be delivered along with design and validation testing documentation. The exoskeleton will be adjustable to work cohesively with the vast anthropometric variances among SMs. The final 6 prototypes (or 3 pairs as outlined above) will be evaluated in human volunteer research efforts to demonstrate their effectiveness in litter transport scenarios. The effects of the device on measures such as carry distance, grip strength, hand steadiness, marksmanship, and subjective user ratings will be evaluated.

PHASE III DUAL USE APPLICATIONS: A successful device will allow for litter bearers to transport casualties over greater distances with less fatigue, resulting in greater survivability for the Warfighter. Future and possible customers for a medical use exoskeleton intended to augment grip-strength are organizations with Search and Rescue responsibilities. Additionally, the device will be capable of integration with current and future-fielded civilian and military medical equipment/devices. Such organizations include local and State level first responders and the Department of Homeland Security Federal Emergency Management Agency during structural collapse in urban environments, the United States Department of Interior and National Park Services for inland-wilderness incidences and the Air Force Rescue Coordination Center, Air Education and Training Command, the Civil Air Patrol, the United States Navy, and United States Marine Corps helicopter squadrons during aeronautical search and rescues.

In several occupational fields, manual material handling tasks are still prevalent. Engineering an assistive device is one way to deal with these physically demanding jobs. The most common physically demanding activities performed by U.S. Army soldiers were found to be carrying and lifting. Conducting these tasks can cause injury, according to qualitatively analyzed evidence. Injuries to the musculoskeletal system are thought to cost the US economy at least $7 billion and $50 billion annually, respectively. Thus the exoskeleton could also find use in a number of industrial and commercial applications such as load carriage, tool handling, and manufacturing.

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