Defense Health Agency
2023.1 Small Business Innovation Research (SBIR)
Proposal Submission Instructions

INTRODUCTION

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

Proposers responding to a topic in this Broad Agency Announcement (BAA) must follow all general instructions provided in the Department of Defense (DoD) SBIR Program BAA. DHA requirements in addition to or deviating from the DoD Program BAA are provided in the instructions below.

The DHA Program participates in up to three DoD SBIR BAAs each year. Proposals not conforming to the terms of this BAA will not be considered. Only Government personnel will evaluate proposals with the exception of technical personnel from Goldbelt Frontier who will provide technical analysis in the evaluation of proposals submitted against DHA topic:

- Minimally or Non-invasive Systemic Oxygen Delivery and Carbon Dioxide Removal

Specific questions pertaining to the administration of the DHA SBIR 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
Phone - (301) 619-5146

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.

PHASE I PROPOSAL GUIDELINES

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 submission via DSIP are provided in the DoD SBIR Program BAA.

Technical Volume (Volume 2)

The technical volume is not to exceed **20 pages** and must follow the formatting requirements provided in the DoD SBIR 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 reviewed only to the last word on the 20th page. Information beyond the 20th page will not be reviewed or considered in evaluating the offeror's proposal. To the extent that mandatory technical content is not contained in the first 20 pages of the proposal, the evaluator may deem the proposal as non-compliant and score it accordingly.

Content of the Technical Volume
The Technical Volume has a 20-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 other attachments. Refer to the instructions provided in the DoD SBIR Program BAA for full details on content of the technical volume.

Cost Volume (Volume 3)
The Phase I amount must not exceed **$250,000**. 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. DHA will occasionally accept deviations from the POW requirements with written approval from the Funding Agreement Officer.

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 SBIR 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)
DHA SBIR will accept a Volume Five (Supporting Documents) as required under the DoD SBIR Program BAA.

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 SBIR/STTR Program BAA for details.

PHASE II PROPOSAL GUIDELINES
Phase II proposals may only be submitted by Phase I awardees. Phase II is the demonstration of the technology found feasible in Phase I. All DHA SBIR Phase I awardees from this BAA will be allowed to submit a Phase II proposal for evaluation and possible selection. The details on the due date, content, and submission requirements of the Phase II proposal will be provided by the DHA SBIR PMO. Submission instructions are typically sent in month five of the Phase I contract. The awardees will receive a Phase II window notification via email with details on when, how and where to submit their Phase II proposal.

Small businesses submitting a Phase II Proposal must use the DoD SBIR electronic proposal submission system (https://www.dodsbirsttr.mil/submissions/login). This site contains step-by-step instructions for the preparation and submission of the Proposal Cover Sheets, the Company Commercialization Report, the Cost Volume, the Technical Volume, Supporting Documents, and Fraud, Waste, and Abuse certificate.

The DHA SBIR Program will evaluate and select Phase II proposals using the evaluation criteria in the DoD SBIR Program BAA. Due to limited funding, the DHA SBIR 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 under topics DHA231-001, DHA231-002 and DHA231-003. Topic DHA231-004 is a candidate for a potential Jumbo award under the Phase II. Awardees under topic DHA231-004 may be awarded up to $3,000,000.

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 SBIR 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. Do not include blank pages, duplicate the electronically- generated Cover Sheets or put information normally associated with the Technical Volume in other sections of the proposal as these will count toward the 40-page limit.

Technical Volumes that exceed the 40-page limit will be reviewed only to the last word on the 40th page. Information beyond the 40th page will not be reviewed or considered in evaluating the offeror's proposal. To the extent that mandatory technical content is not contained in the first 40 pages of the proposal, the evaluator may deem the proposal as non-compliant and score it accordingly.

DISCRETIONARY TECHNICAL AND BUSINESS ASSISTANCE (TABA)
The DHA SBIR 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 SBIR 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 SBIR 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 SBIR Office at usarmy.detrick.medcom-usamrmc.mbx.dhpsbir@health.mil as specified in the non-select notification. 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 SBIR 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. Phase I awards will be awarded as Firm-Fixed-Price Purchase Orders indicating the Technical Point of Contact. Phase II awards will typically be Firm-Fixed-Price contracts with the Contracting Officer's Representative and other contracting staff identified.

ADDITIONAL INFORMATION

RESEARCH INVOLVING HUMAN SUBJECTS, HUMAN SPECIMENS/DATA, OR ANIMAL RESEARCH
The DHA SBIR 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
In rare situations, the DHA SBIR 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 SBIR Program has the right of refusal. If approved, the DHA SBIR 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 APAN 15-01 requirements that will be included in the Phase II submission instructions.

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 SBIR 23.1 Phase I Topic Index

DHA231-001 TITLE: Wireless Core Temperature Measurement during Extreme Environmental Exposure

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): OPERATIONAL MEDICINE

OBJECTIVE: Develop a wireless technical solution and data logging system for measuring real-time core temperatures in humans during hot and cold exposure, to include water immersion, for up to 24 hours in resting and exercising individuals.

DESCRIPTION: Warfighters are exposed to austere environmental conditions during training and combat. They are at risk of suffering from hyperthermia and hypothermia, as well as peripheral cold injuries. For example, from 2017-2021, there were ~2,500 incidences of heat stroke and 9,700 heat exhaustion casualties across the Armed Forces and 2,466 cold injuries in active and reserve components across all the Services. Medical costs for heat injuries are greater than $6M per year and result in significant lost duty time. Methodologies are needed to measure core temperature during training in real-time so that the risk of an environmental injury is reduced. Identification of real-time temperatures could prevent these injuries. This technology needs to be robust so that specific individuals can be identified.

There have been technologies developed in the past, but the companies are no longer manufacturing these products. Although a robust and accurate core body real-time wireless thermometer system is the focus of this effort; solutions that offer the ability to measure additional sites/locations of temperature concurrently, inherently provide additional context and thus can lead to better assessments of environmental injury. Currently this capability does not exist in a commercial form, and hampers the ability of leadership to monitor their personnel. Furthermore, this technology is also very important for DOD researchers to collect this critical temperature information so that improved health-state algorithms can be developed that prevent injuries due to environmental stressors. There are technologies currently on the market to measure core body temperature, but they are unable to wirelessly measure core temperature and produce real-time continuously-updating temperature data during water immersion. No product exists that can measure temperatures to reduce the possibility of freezing cold injuries in extreme cold conditions. The envisioned system would employ technology using an innovative engineering approach that enables core body and other temperature locations to be measured, collected, and visualized in real-time with the data also logged to allow easy post-measurement evaluation and download. Accuracy of measurement will be a trade-off between this and simplicity of implementation. In the civilian community, this product can be used by firefighters, homeland security personnel (hazardous material cleanup), researchers in the exercise physiology community, and athletes. Military users for this product include all Warfighters exposed to extreme environmental conditions. If fielded, the technology may require secured communication methods.

PHASE I: The contractor will use novel/innovative concepts to design and develop a breadboard prototype to measure core body and any additional sites during environmental exposure during hot- and cold-weather operations, to include water immersion. Innovative technological designs are required as the specifications for this include high precision measurements, ability to operate in extreme and varied environments, such as the Arctic, desert, jungle, and underwater, need to be comfortable and transparent to the Warfighter so as not to encumber them, and the requirement for long battery life with infrequent recharging. The technology will be supported by documentation of proof-of-concept and data regarding scientific validity of the proposed solution.

PHASE II: The contractor will construct and demonstrate, in laboratory conditions, the operation of a core temperature measurement device/prototype and devices/prototypes that measure temperature at other locations s in real time and records data on a logger for later downloading. Demonstration of the prototypes will require laboratory experiments using human volunteers exposed to hot (> 90 °F air), cold

(< 40 °F air), and water immersion (between 50-80 °F) for 2 h. The prototype will also include any hardware/software interfaces that are required for system functionality. At the end of phase II, 20 prototypes suitable for phase III field evaluations will be manufactured. System requirements for Phase 2 include: (1) not interfere with other physiological functions; (2) digitally identify specific individuals; (3) waterproof; (4) transmit temperature signal from underwater environment to data logger (~3 meters); (5) data must be continuously logged to ensure minimal loss of data with sampling frequencies as low as 5 seconds and be time synchronized; and (6) core body temperature must have accuracy of +/- 0.01 °C and precision of +/- 0.02 °C; other temperature locations must have an accuracy and precision of 0.05 °C.

PHASE III DUAL USE APPLICATIONS: The prototypes will be extensively tested in field studies to demonstrate a reliable and robust solution for civilian and military application. In the civilian community, this product can be used by firefighters, homeland security personnel (hazardous material cleanup), researchers in the exercise physiology community, and athletes. Military users for this product include all Warfighters exposed to austere environmental conditions (e.g., infantrymen).

System requirements for Phase 3 include: (1) light-weight; (2) low-power requirements/long battery life; (3) non-flammable; (4) rugged enough to withstand routine use in military and civilian settings; (5) user friendly technology with the potential to be used in field operations; (6) The system must scale for use. Typically the system will need to be used in the field from a squad size (~10 Warfighters) all the way up to a company size (~100-200 Warfighters). Wireless technologies must be designed and managed to accommodate large numbers of personnel within a confined space. Additionally testing environments may not allow for research staff to be in close proximity (less than 3 meters) to volunteers; wireless technology must be scalable to accommodate long range communications without interfering with other military communication systems; and (7) Must meet MIL-STD-810G standard (https://www.atec.army.mil/publications/mil-std-810g/mil-std-810g.pdf). It will be used to measure, in real-time, core temperatures, as well as log data for up to 24 hours. The device should seek to generate data that could be submitted to the FDA for 510K equivalency for a temperature measurement system. The end-state of the Phase III effort will be a product suitable for use by civilian communities that have elevated risks of heat/cold injuries to include first responders and athletes. For the military community, this technology could be inserted into the Physiological Status Monitoring/Health Readiness and Performance program.

REFERENCES:

1. Buller MJ, Davey T, Fallowfield JL, Montain SJ, Hoyt RW, Delves SK. (2020). Estimated and measured core temperature responses to high-intensity warm weather military training: implications for exertional heat illness risk assessment. Physiol Meas., 41:065011. doi: 10.1088/1361-6579/ab934b;
2. Buller MJ, Delves SK, Fogarty AL, Veenstra BJ. (2021). On the real-time prevention and monitoring of exertional heat illness in military personnel. J Sci Med Sport. 24:975-981. doi: 10.1016/j.jsams.2021.04.008;
3. Buller MJ, Welles AP, Friedl KE. (2018). Wearable physiological monitoring for human thermal-work strain optimization. J Appl Physiol (1985). 2018 Feb 1;124(2):432-441. doi: 10.1152/japplphysiol.00353.2017;
4. O'Brien C, Hoyt RW, Buller MJ, Castellani JW, Young AJ. (1998) Telemetry pill measurement of core temperature in humans during active heating and cooling. Med Sci Sports Exerc., 30:468-72. doi: 10.1097/00005768-199803000-00020;
5. van Marken Lichtenbelt WD, Daanen HA, Wouters L, Fronczek R, Raymann RJ, Severens NM, Van Someren EJ (2006). Evaluation of wireless determination of skin temperature using iButtons. Physiol. Behav., 88:489-497

KEYWORDS: cardiovascular strain, core body temperature, heat illness, hyperthermia, hypothermia,

water immersion

TPOC-1: Dr. John Castellani
Phone: (508) 206-2195
Email: john.w.castellani.civ@health.mil

TPOC-2: Mark Buller
Phone: (508) 206-2187
Email: mark.j.buller.civ@health.mil

DHA231-002 TITLE: Portable Technology to Assess Ankle Instability

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): OPERATIONAL MEDICINE

OBJECTIVE: Improve service member readiness by objectively assessing ankle instability with technology that is portable and can be used by minimally trained personnel in the area of lower limb movement and ankle injuries.

DESCRIPTION: The DoD seeks the capability to optimally and rapidly return to duty the high rates of Warfighters with destabilizing lower limb injuries. In the United States, approximately 25,000 ankle sprains occur daily (Bernstein, 2003). The rate of ankle sprains in military personnel is nearly five times greater than that reported in the civilian population (Cameron et al, 2010). Given the high prevalence of ankle sprains, there is a need for effective preventative and rehabilitative options in order to minimize the impact of ankle injuries on Warfighter readiness and lethality. Only 1 in 4 persons who incur an ankle injury receive rehabilitation. It is critical that these be diagnosed as soon as possible to get people to care early, when they are most likely to benefit. The probability of ankle sprain recurrence increases for each day that rehabilitation is not provided during the first week after injury (Rhon et al, 2021). In addition, up to 40% of persons who incur an ankle sprain do not fully heal and develop chronic ankle instability. Technology that can monitor for ankle sprains and evaluate ankle instability could help by assessing occurrence of injury, preventing further injury, and/or determine the success of therapy. The capability should objectively assess destabilizing ankle injuries that occur in both the operational and training environments. This capability would provide objective measurement of ankle instability and its progression/resolution over time. Currently, self-report questionnaires, magnetic resonance imaging (MRI) or radiographs, and/or subjective assessment by an experienced clinician are the current methods for identifying chronic ankle instability. Arthrometers that assess laxity are bulky and impractical in many clinical settings. Instrumented measures that can capture resolution of ankle-foot impairment are desired.

PHASE I: Design/develop a new concept that will objectively measure ankle instability. A solution is sought that is portable, can be used without an external power source, is easy to use by both clinicians and non-clinicians, is capable of measuring changes due to injury, healing and/or clinical intervention, and provides a visual display. The solution should demonstrate clear understanding of ankle and soft tissue mechanics and decrements due to injury. Solutions are intended to be used within the operational environment, training environment, and/or clinical care setting. It should require minimal setup, be easy to administer, and have understandable outcome metrics. Desirable solutions may be used in austere environments at or near the time of injury occurrence. The solution is intended to augment clinical expertise, laxity tests, patient-reported measures, and performance tests for rehabilitation progress or re-injury.

PHASE II: Design and develop the practical implementation of the product that implements the previously completed Phase I methodology towards a technology that is sufficiently sensitive to monitor and/or measure ankle injury and instability over time. Demonstrate that the developed solution is capable of accurately making these measurements and correlates with current subjective clinical assessments. Define field test objectives and conduct limited testing. Assess the validity of the technology and provide intra-rater and inter-rater reliability of the product. The testing and practical implementation of the product should be relevant to Warfighters who have experienced destabilizing ankle injuries (e.g. sprains) in training or operational settings. Solutions that rely solely on imaging of the underlying tissues do not meet the intent of the solicitation. Extended wear or use is not required. The expected Phase II end-product is a well-designed, portable product to be used in clinical, as well as research, settings. The investigator shall also describe in detail the transition plan for the Phase III effort. The offeror shall prepare the regulatory strategy and provide a clear plan on how FDA clearance will be obtained.

PHASE III DUAL USE APPLICATIONS: Investigators may work with commercial and military partners, and/or in the civilian marketplace to move towards a final commercial product that will be capable of accurately assessing ankle instability. For example, sports medicine. The system should be capable of generating an output report that meets the needs of the end user (or can be modified and customized to these needs). The investigator should ensure that the final product can be incorporated into clinical practice, including the considerations of ease of use, appropriate coding/billing, cost/benefit, and training, education, socialization, and outreach. Plans on the commercialization/technology transition and regulatory pathway should lead to eventual FDA clearance/approval.

REFERENCES:

1. Bernstein, J. ed., 2003. Musculoskeletal medicine (Vol. 1). Amer Academy of Orthopaedic;
2. Cameron, K.L., Owens, B.D. and DeBerardino, T.M., 2010. Incidence of ankle sprains among active-duty members of the United States Armed Services from 1998 through 2006. Journal of athletic training, 45(1), pp.29-38;
3. Rhon, D.I., Fraser, J.J., Sorensen, J., Greenlee, T.A., Jain, T. and Cook, C.E., 2021. Delayed Rehabilitation Is Associated With Recurrence and Higher Medical Care Use After Ankle Sprain Injuries in the United States Military Health System. Journal of Orthopaedic & Sports Physical Therapy, 51(12), pp.619-627;

KEYWORDS: Ankle instability, Balance, Sprain, Musculoskeletal injury, Lower extremity, Rehabilitation, Soft tissue injury

TPOC-1: Dr. Elizabeth Russell Esposito
Phone: (732) 778-9319
Email: Elizabeth.m.russell34.civ@health.mil

TPOC-2: Pinata Sessoms
Phone: (619) 767-4474
Email: pinata.h.sessoms.civ@health.mil

DHA231-003 TITLE: Development and Testing of Dual-lumen Femoral Cannula with Echogenic Material for Faster, Safer, and More Reliable Delivery of Extracorporeal Life Support during Prolonged Field Care

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): COMBAT CASUALTY CARE

OBJECTIVE: Design, build, and demonstrate a femoral dual-lumen cannula that will allow for the initiation of lifesaving extracorporeal life support (ECLS) treatment in a prolonged-field-care environment. The end goal is to save the lives of warfighters with severe lung failure. This will be accomplished by (1) limiting the risks associated with two separate cannula placements; (2) enabling confirmation of cannula placement by means of handheld ultrasound in the field; and (3) making cannulation easy to perform by non-subspecialist providers.

DESCRIPTION: Over the past two decades, industry advancements in material science and engineering for ECLS have led to exponential growth in the use of this technology worldwide, for the treatment of patients with lung failure caused by, e.g., trauma, burns, or COVID-19.
ECLS is the most advanced form of life support in existence for combat casualties and other patients experiencing acute cardiac and/or pulmonary failure [1]. ECLS provides support for these patients using an artificial membrane lung and blood pump. It provides gas exchange and systemic perfusion for patients when their own heart and/or lungs are unable to function adequately, and it has been shown to improve survival rates and outcomes in patients with severe acute respiratory distress syndrome (ARDS). A retrospective series by Bein et al of U.S. casualties placed on ECLS both in theater and at Landstuhl Regional Medical Center from 2005 to 2011 showed a 1-year survival rate of 90% [2]. However, there are major limitations for the use of ECLS in both far-forward and en route environments. These include the difficulty of cannulation, the need for advanced imaging to avoid damage to the heart and great vessels during cannulation, and difficulty in confirming correct cannula placement both during cannulation and en route.

ECLS requires placement of either two separate cannulas (e.g., internal jugular vein in the neck, and femoral vein in the groin), or a single dual-lumen cannula (internal jugular vein in the neck). Cannula placement in the internal jugular (IJ) vein is currently performed in advanced clinical settings by skilled users. This type of placement can be technically challenging, requiring a high degree of precision in addition to large and expensive adjunctive imaging such as fluoroscopy or transesophageal echocardiogram to ensure proper placement. This ease-of-cannulation problem is the single greatest obstacle to wider use of ECLS on the battlefield or in the civilian community. This topic calls for the development of a dual-lumen cannula for femoral vein placement, which would overcome the problems of complex imaging requirements and limited experience. This would enable ECLS initiation on the battlefield.

The goal is a faster, safer, and more reliable delivery of ECLS to the combat casualty on the battlefield. A dual-lumen cannula for femoral vein placement could be safely used in a Role 2 or 3 facility. The femoral location is easier and safer in the hands of a less-experienced operator than placement in the neck or chest. A femoral catheter will remain in place until the patient arrives at a Role 4 facility; there, the patient would be evaluated for a long-term cannulation strategy, such as two-site cannulation or upper body dual lumen cannulation—if necessary. It would allow for evacuation of patients off the battlefield who have high ventilator settings, that would otherwise preclude them from movement. Additionally, the design would decrease the overall risks of placing two cannulas compared to one cannula. Finally, the design would allow for the cannula to be converted into a drainage cannula if conversion to a definitive two-site cannulation strategy is needed for higher or more efficient blood flow at the higher level of care. Maintaining correct cannula position is paramount. Low cannula positions may result in high negative access pressures and altered flow dynamics, and high cannula positions may result in trauma to blood

vessels and the heart. Furthermore, upper body dual-lumen cannulation is simply not feasible for enhanced combat casualty care, given the technical challenges of placement and the risk of vascular perforation. In order to mitigate potential wire misplacement, this technology must be designed with echogenic materials to enable determination of cannula location with hand-held ultrasounds, in lieu of x-ray or fluoroscopy. This type of material will ensure that the cannula is placed correctly. Between a dual-lumen cannula for femoral placement and the echogenic material, this catheter would be ideal for civilian uses in rural hospitals; providers could place the catheter in the less-specialized hospital until transport to a tertiary referral hospital.

PHASE I: Given its short duration, Phase I should focus on system design and development of proof-of-concept prototypes for a dual lumen cannula for femoral vein placement with echogenic material. At the end of this phase, fabricated prototypes should demonstrate feasibility using relevant testing platforms for the proposed technology, including reasonable detection of the cannula by ultrasound. Evaluation of the product's durability should include data for the first 6, 24, 48, and 72 hours at a minimum.
No animal or human subjects should be utilized in Phase I. Testing and evaluation of the prototype will demonstrate operational effectiveness in simulated environments (i.e., integrity of bonded connectors and joints, kinking of cannula, incidence of stress fractures, etc.). Simulations should utilize a high-fidelity cannulation simulator.

PHASE II: During this phase, the integrated device should be further refined from proof-of- concept into a viable prototype. Further optimization of the technology as a single-use, echogenic dual-lumen catheter that provides both venous drainage and reinfusion of blood via the femoral vein should demonstrated during this phase. Qualitative and quantitative outcomes of product include cannula size availability (26 and 28 Fr.), the inclusion of an introducer to facilitate wire-guided placement into the vasculature by normal access techniques, wire reinforcement of the catheter for flexibility and kink-resistance, and the inclusion of depth marks and tantalum markers for ultrasound confirmation. A vessel dilator for percutaneous catheterization may be included to assist in vessel cannulation.

The cannula and guidewire with echogenic material should undergo bench testing under rigorous conditions. Verification and validation testing should be used to establish the performance characteristics of the dilators, including biocompatibility, packaging integrity, transportation integrity, sterilization validation, and functional testing. Product optimization should achieve desirable duration, security, and the ability to be deployed.

Testing and evaluation of the prototype will demonstrate operational effectiveness in simulated environments (i.e., cannulation success rate, time from initiation of cannulation to confirmation of correct placement, etc.). Simulations should utilize a high-fidelity cannulation simulator.
Simulated use of the device should be tested by a diverse clinical team to include providers with varying degrees of cannulation expertise.

The offeror will articulate the regulatory strategy and provide a clear plan on how FDA clearance will be obtained.

PHASE III DUAL USE APPLICATIONS: The ultimate goal of this phase is to achieve FDA submission with the proper regulatory clearance or authorization for human or Department of Defense (DOD) use exemption. Phase III funding strategies could include CDMRP funding announcements and/or other DOD opportunities. Accompanying application instructions, simplified procedures, and training materials will be drafted in a multimedia format for both civilian and military use and integration of the product into market. Once developed and demonstrated, the technology must be adaptable for both civilian and military settings to save lives.

RESEARCH INVOLVING ANIMAL OR HUMAN SUBJECTS

The SBIR/STTR Programs discourage offerors from proposing to conduct Human or Animal Subject Research during Phase 1 due to the significant lead time required to prepare the documentation and obtain approval, which will delay the Phase 1 award.

All research involving human subjects (to include use of human biological specimens and human data) and animals, shall comply with the applicable federal and state laws and agency policy/guidelines for human subject and animal protection.

Research involving the use of human subjects may not begin until the U.S. Army Medical Research and Materiel Command's Office of Research Protections, Human Research Protections Office (HRPO) approves the protocol. Written approval to begin research or subcontract for the use of human subjects under the applicable protocol proposed for an award will be issued from the U.S. Army Medical Research and Materiel Command, HRPO, under separate letter to the Contractor.

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

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KEYWORDS: extracorporeal life support (ECLS), cannula, echogenic

TPOC-1: Dr. Leopoldo Cancio
Phone: (210) 916-0990
Email: leopoldo.c.cancio.civ@health.mil

TPOC-2: Garrett Britton
Phone: (814) 564-0157
Email: garrett.w.britton.mil@health.mil

DHA231-004 TITLE: Minimally or Non-invasive Systemic Oxygen Delivery and Carbon Dioxide Removal

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): COMBAT CASUALTY CARE

OBJECTIVE: Develop a drug, biologic, or device that is capable of facilitating transport of oxygen (O2) into the body and carbon dioxide (CO2) out of the body in a minimally-invasive or non-invasive manner without the need for oxygen generating systems. The proposed product must be usable in an austere environment with minimal clinical staff operation requirements. The ideal product will be usable by medical first responders such as combat medics (or equivalent). The final product will be low size, low weight, low power, stable at temperature extremes, with a prolonged shelf life.

DESCRIPTION: Acute Respiratory Distress Syndrome (ARDS) is a life-threatening condition characterized by failure of O2 and CO2 movement (gas exchange) across the alveolar-capillary membrane. ARDS secondary to trauma or severe illness such as viral and/or bacterial infection or due to direct lung injury such as chemical or smoke inhalation is a major contributor to mortality among critical care patients, resulting in death in 30-50% of those with the condition1. Among survivors, ARDS carries a high degree of morbidity and frequently leads to long-lasting health complications. The respiratory complications of traumatic injury, direct exposure to chemical and/or biological warfare agents, or pandemic respiratory viral illnesses pose a serious threat to operational success, particularly in resource-limited settings. A lack of definitive treatment for ARDS threatens the health of military Service Members and civilians alike.2 Pharmacotherapeutics aimed at treating ARDS have shown promise in preclinical studies but fail to demonstrate success in clinical trials likely owing to the inability of drugs to reach the damaged alveolar surface either directly or systemically. Clinical management of ARDS is supportive and involves the use of adjunctive measures to correct critical hypoxemia such as mechanical ventilation for respiratory failure, systemic corticosteroids to reduce inflammation and, if available, extracorporeal life support (ECLS) to deliver O2 and remove CO2 directly from the blood. Despite the availability of these adjuncts, mechanical ventilation may result in cellular-level trauma as the alveoli are stretched and deformed under positive pressure, thus contributing to additional lung damage; corticosteroids reduce inflammation but the underlying inflammatory processes leading to ARDS remain; and ECLS is not available in most hospitals, and when available carries a high complication rate and requires much logistical support and manpower at a time when healthcare providers are already stretched thin. Consequently, there is a strong need for new or refined treatment options for ARDS-associated refractory hypoxemia and hypercapnia, particularly at the point when the lungs are no longer able to effectively facilitate normal O2 and CO2 transport.

The Department of Defense operates worldwide, including in remote and austere environments without access to modern medical facilities. The task of caring for traumatically injured and/or critically ill soldiers on the battlefield, especially in isolated regions, remains a challenge and warrants the need to develop effective treatment capabilities for ARDS. This topic seeks the identification and development of a minimally-invasive or non-invasive method of O2 delivery and removal of CO2 for ARDS-induced respiratory failure. Ideally, the candidate product will utilize unique treatment approaches, for example, nanotherapeutics capable of facilitating gas transport through fluid-filled, inflamed alveoli or intravenous O2 delivery coupled with miniaturized extracorporeal CO2 removal/scavenging. An ideal product will operate without the need for O2 generating systems, although proposals presenting a simplified means of generating O2 for use with a unique product will be considered. The successful candidate product could be incorporated 1) into an existing device, 2) into an inhalable formulation, or 3) into a systemic delivery system. The proposed product and delivery system (if applicable) is expected to have no, or minimal, toxicity and should be easily administered by a minimal number of health care personnel in resource limited settings.

PHASE I: This Phase will demonstrate the feasibility of producing a candidate drug, biologic, or device, and will demonstrate criteria required for success. During this phase the researcher will define and characterize a candidate drug, biologic, or device that is capable of directly or indirectly delivering systemic

O2 and removal of CO2 as stated in the Objective and Description. Proposals should describe the rationale for the appropriateness of the proposed product. Other supportive data may also be provided during this 6-month Phase I, $250,000.00 (max) effort. Proposals should contain preliminary data (published or unpublished) supporting the rationale for the development of candidate product(s) and data related to the mechanism of action of the proposed drug(s)/biologic(s) (if applicable), if known. Describe how the product will be usable in a resource-limited setting. The Phase I effort will include prototype plans to be developed under Phase II. Provide a plan for practical deployment of the proposed O2 delivery/CO2 removal product. Animal/human testing is discouraged during the Phase I (6 month) period. Deliverables of this phase include: 1) strong proof-of-concept and rationale for further development of the candidate product, 2) a prototype candidate drug, biologic, device, or system, and 3) a detailed Phase I final report that includes concepts and plans to develop and test the prototype product, including future FDA regulatory considerations.

PHASE II: The investigator shall design, develop, test, and validate the prototype developed during Phase I. The testing and practical implementation of the prototype product should be relevant to ARDS-associated respiratory failure. During this 2-year, $3M (max) effort the performer may consider early communication with the FDA for guidance and to ensure that regulatory clearance can be pursued during Phase III.

Required Phase II deliverables will include: 1) Successful refinement of a working prototype, 2) further evaluation of the efficacy of the product(s) in a relevant in vivo model(s) of ARDS-associated respiratory failure (pre-clinical studies), 3) detailed annual and final reports about the overall project including all data that demonstrate the ability to address the problem as stated in the Objective and Description and 4) regulatory strategy with a clear FDA clearance plan.

RESEARCH INVOLVING ANIMAL OR HUMAN SUBJECTS: All research involving animals and humans (to include use of human biological specimens and human data) shall comply with the applicable federal and state laws and agency policy/guidelines for protection of animals and/or humans used for research purposes.

Research involving the use of animals or humans may not begin until the U.S. Army Medical Research and Development Command's Office of Human Research Oversight (OHRO) approves the protocol. Written approval to begin research or subcontract for the use of human subjects under the applicable protocol proposed for an award will be issued from the U.S. Army Medical Research and Development Command, OHRO, under separate letter to the Contractor.
Non-compliance with any provision may result in withholding of funds and or the termination of the award.

PHASE III DUAL USE APPLICATIONS: If successful, Phase II work will result in a product that directly or indirectly treats hypoxemia and hypercapnia and is commercially applicable to both civilian and military applications. Civilian and/or military healthcare professionals could utilize the newly developed product to treat respiratory failure in medical facilities worldwide, reducing morbidity, mortality and global healthcare costs. The product would be particularly useful during global pandemics that threaten to overwhelm emergency departments with respiratory failure patients. The developed product may transition to an Acquisition Program managed by the Service Product Developers for inclusion into the fielded medical system, or be available to Service Medical Treatment Facilities, for the treatment of those who suffer from hypoxemia and/or hypercapnia resulting from respiratory failure after combat- and noncombat-related trauma or critical illness.

During Phase III, further assessment of effective dose ranges (if applicable) and/or application frequencies (if applicable) may be conducted. In addition, applicants are expected to conduct a pre-IND (drugs/biologics) or pre-submission (devices) meeting with the FDA prior to the completion of Phase III. A plan for protection of intellectual property should be created and executed. The small business should have plans to secure funding from non-SBIR government sources and/or the private sector to develop or transition the prototypes into a viable product for sale to the military and/or commercial markets. The end-

state of the research will be the full development of one or more innovative products that minimally- or non-invasively corrects hypoxemia and hypercapnia and that can be administered to or used on military and civilian patients in a clinically relevant manner.

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KEYWORDS: respiratory failure, ARDS, ALI, hypoxia, hypoxemia, hypercapnia, ECMO, oxygenation, CO2, O2, ventilation, scavenging, mechanical ventilation, respiratory, pulmonary, lung, artificial respiration

TPOC-1: Ms. Sandy Snyder
Phone: (301) 619-7047
Email: sandy.j.snyder.civ@health.mil

TPOC-2: Christie Vu
Phone: (301) 619-4227
Email: bao-han.c.vu.civ@health.mil