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**DEFENSE HEALTH AGENCY**
**21.3 Small Business Innovation Research (SBIR) Program**
**Proposal Submission Instructions**

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

Broad Agency Announcement (BAA), topic, and general questions regarding the SBIR Program should be addressed according to the DoD SBIR Program BAA. 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 https://www.dodsbirsttr.mil/submissions/login

Specific questions pertaining to the DHA SBIR Program should be submitted to the DHA SBIR Program Management Office (PMO) at:

Email - usarmy.detrick.medcom-usamrmc.mbx.dhpsbir@mail.mil
Phone - (301) 619-7296

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 Irving Burton Associates who will provide technical analysis in the evaluation of proposals submitted against DHA topic number:

- DHA213-008 Digital Human Model for Use in Simulation Environments for Tactile Human/Robot Interaction

## PHASE I PROPOSAL SUBMISSION

Follow the instructions in the DoD SBIR Program BAA for program requirements and online proposal submission instructions.

DHA SBIR Phase I Proposals have six Volumes: Proposal Cover Sheet, Technical Volume, Cost Volume, Company Commercialization Report (CCR), Supporting Documents, and Fraud, Waste, and Abuse training. Please refer to the DoD SBIR Program BAA for full details on the requirements of each proposal 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. Do not 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 20-page limit.

The electronically-generated Cover Sheets, Cost Volume, CCR, and Supporting Documents 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-responsive and score it accordingly.

Companies submitting a Phase I proposal under this BAA must complete the Cost Volume using the on-line form, within a total cost not to exceed $250,000 over a period of up to six months.

The Company Commercialization Report (CCR), Volume 4, allows companies to report funding outcomes resulting from prior SBIR and STTR awards. Information contained in the CCR will be considered during proposal evaluations. Please refer to the DoD SBIR Program BAA for full details.

The DHA SBIR Program will evaluate and select Phase I 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.

Proposals not conforming to the terms of this BAA, and unsolicited proposals, will not be considered. Awards are subject to the availability of funding and successful completion of contract negotiations.

## 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 will significantly delay the performance of the Phase I award.** For example, the ability to obtain Institutional Review Board (IRB) and Human Research Protection Official (HRPO) approval for proposals that involve human subjects can take 3-6 months, and that lengthy process can be at odds with the Phase I goal for time-to-award. Before DHA makes any award that involves an IRB or similar approval requirement, the proposer must demonstrate compliance with relevant regulatory approval requirements that pertain to proposals involving human subjects, human specimens/date or research with animals. It will not impact DHA's evaluation, but requiring IRB approval may delay the start time of the Phase I award and if approvals are not obtained within two months of notification of selection, the decision to award may be terminated.

The offeror is expressly forbidden to use or subcontract for the use of laboratory animals in any manner without the express written approval of the US Army Medical Research and Development Command's (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. Furthermore, modifications to already approved protocols require 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 Research Protections (ORP) provides authorization that the research protocol may proceed. Written approval to begin research protocol will be issued from the USAMRDC ORP, under separate notification to the recipient. Written approval from the USAMRDC ORP is also required for any sub-recipient that will use funds from this award to conduct research involving human subjects.

Research involving human subjects shall be conducted in accordance with the protocol submitted to and approved by the USAMRDC ORP. Non-compliance with any provision may result in withholding of funds and or termination of the award.

## CYBERSECURITY CONSIDERATIONS

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Appropriate cybersecurity considerations should be implemented at Phase III (or earlier if specified) for the potential transition of software and connected devices to be considered for future fielding. For initial information, please see the below reference to the *DoD Cybersecurity Reference and Resource Guide*.

*DoD Cybersecurity Reference and* Resource Guide
https://dodcio.defense.gov/Portals/0/Documents/Cyber/2019%20Cybersecurity%20Resource%20and%20Reference%20Guide_DoD-CIO_Final_2020FEB07.pdf

**PHASE II PROPOSAL SUBMISSION**

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 toward the end of 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, and how to upload the Technical Volume. For general inquiries or problems with proposal electronic submission, contact the DoD SBIR/STTR Help Desk email at DoDSBIRSupport@reisystems.com.

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 (please refer to the DoD SBIR Program BAA) describing feasible approaches for transitioning and/or commercializing the developed technology in their Phase II proposal. This plan should 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 $1,100,000. These costs must be submitted using the Cost Volume format (accessible electronically on the DoD submission site), and may 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 Company Commercialization Report may only be submitted if available at time of submission. 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 40$^{th}$ page. Information beyond the 40$^{th}$ 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-responsive and score it accordingly.

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The Company Commercialization Report (CCR), Volume 4, allows companies to report funding outcomes resulting from prior SBIR and STTR awards. Information contained in the CCR will be considered during proposal evaluations. Please refer to the DoD SBIR Program BAA for full details.

## PHASE II ENHANCEMENTS

The DHA SBIR Program has a Phase II Enhancement Program which provides matching SBIR funds to expand an existing Phase II contract that attracts investment funds from a DoD Acquisition Program, a non-SBIR government program or eligible private sector investments. Phase II Enhancements allow for an existing DHA SBIR Phase II contract to be extended for up to one year per Phase II Enhancement application, and perform additional research and development. Phase II Enhancement matching funds will be provided on a dollar-for-dollar basis up to a maximum $550,000 of SBIR funds. All Phase II Enhancement awards are subject to acceptance, review, and selection of candidate projects, are subject to availability of funding, and successful negotiation and award of a Phase II Enhancement contract modification.

## TECHNICAL AND BUSINESS ASSISTANCE (TABA)

The DHA SBIR Program does not participate in the Technical and Business Assistance (formally the Discretionary Technical Assistance Program). Contractors should 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.

## WAIVERS

In certain situations, the DHA SBIR Program allows for waivers to be incorporated per program regulations for cases of federal facility usage for testing/evaluation when it has been determined that another facility does not have the ability or expertise to complete the work. In those cases, the DHA SBIR Program has the right of refusal and will work to establish the waiver for Program Manager approval. The proposer will subcontract directly with the federal facility and not a third party representative.

## PROTEST PROCEDURES

Please refer to the DoD Program Announcement for procedures to protest an Announcement. As further prescribed in FAR 33.106(b), FAR 52.233-3, Protests after Award should be submitted to:

Ms. Micaela Bowers
SBIR/STTR Contracting Officer
U.S. Army Medical Research Acquisition Activity
Phone: (301)-619-2173
Email: micaela.l.bowers.civ@mail.mil

## NOTIFICATION OF SELECTION AND NON-SELECTION

Proposing firms will be notified of selection or non-selection status for a Phase I award within 90 days of the closing date of the BAA. The individual named as the Corporate Official on the Proposal Cover Sheet

will receive an email for each proposal submitted from the DHA SBIR Office with their official notification of proposal selection or non-selection.

# VERSION 4

DHA SBIR 21.3 Phase I Topic Index

# VERSION 4

DHA213-001 TITLE: Head and Neck Protection System for Acute and Chronic Injury Mitigation

OUSD (R&E) MODERNIZATION PRIORITY: General Warfighting Requirements (GWR)

TECHNOLOGY AREA(S): Bio Medical

OBJECTIVE: Develop prototype systems to mitigate acute head and neck injuries due to high G loading in the ejection environment and mitigate chronic neck fatigue and pain associated with prolonged low G use of Helmet Mounted Display Systems.

DESCRIPTION: Advancements in combat aircraft performance and flight equipment design, particularly the widespread use of helmet-mounted display systems (HMDS), have led to an increase in reported neck pain and injury due to G loading among aircrew across all services. While neck pain and injury has long been an established risk with fixed-wing and rotary-wing combat flight, increased use of head/helmet supported masses – from night vision goggles, to Joint Helmet Mounted Cueing System (JHMCS) and Helmet Mounted Inertial Tracker (HMIT) systems deployed in thousands of legacy aircraft, to advanced systems deployed in the HMDS of 4th and 5th Generation Fighter Aircraft – has exacerbated the issue. These helmet-supported masses shift the center of gravity (CG) more forward and superior to the normal CG of the current helmet system. Under rapid high G loading or over prolonged usage in the low G environment, this added weight and adverse CG location both increases the stresses placed the neck and spine at all times during flight operations and increases the risk of cervical spinal injury during ejection. Recent surveys show that over 80% of USAF pilots using such systems report neck fatigue associated chronic neck pain. These issues have the potential to jeopardize mission success and increase potential mishaps as pilots reportedly avoid flying to the aircraft's full potential in order to lessen their pain. Furthermore, these issues have reduced USAF force readiness, and in some instances, led to pilots seeking medical treatment from providers outside the Department of Defense.

The development of an assistive technology to augment the pilot's ability to manage additional head-mounted mass and adverse CG during both normal maneuvers and ejection scenarios would greatly decrease pilot injury risk, improve force readiness, restore mission performance, and reduce medical treatment costs. Potential solutions should minimally impede a pilot's head motion and operational Range of Motion (ROM) while inside the aircraft and ideally would be virtually imperceptible to the user, yet provide assistive force when required. Failure to give attention to these concerns has caused previous attempts at a solution to be rejected by the user community. Potential solutions should also give consideration to size, weight, and power (SWaP) constraints present in fixed-wing and rotary-wing aircraft cockpits. The aircrew gender and size demographic is wide ranging, including the 5th percentile female (103 lbs) to 95th percentile male (245 lbs). Proposed solutions should accommodate this wide demographic and be interoperable with aircrew flight equipment (AFE) worn by all sizes of aircrew.

PHASE I: For the Phase I effort, contractors shall develop and execute a plan for establishing end user requirements and develop a proof of concept (TRL 2-3) for their proposed system to determine its technical feasibility. Establishing design requirements via engagement with end users is highly recommended for successful user integration. Early coordination with USAF Agile Combat Support Directorate Human Systems Division (AFLCMC/WNU) and other DoD PEOs interested in incorporating this technology into their systems is also recommended. Proofs of concept should demonstrate technical feasibility by delivering a report containing results of benchtop experiments, models and simulations, or calculations that show successful implementation of actuation schemes, control algorithms, developed hardware, and any other vital components of the system. Technical data, including AFE specifications, dangerous/safe neck loading conditions, aircraft information, etc. will be provided to Phase 1 awardees.

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PHASE II: Contractors awarded a Phase II shall mature their proof-of-concept into a prototype that simulates integration with aircrew flight equipment (AFE) or aircraft system integration (i.e., a reasonable surrogate of AFE or existing aircraft systems such as an ejection seat), and is testable in simulated flight environments with anthropometrically represented manikins (centrifuge, drop towers, and horizontal acceleration sleds). The system should demonstrate a capability for attenuating neck loads by at least 25% compared to an unaided helmet-supported mass in high +Gz testing on AFRL impact facilities with both 5th percentile female Lightest Occupant in Service (LOIS) and 95th percentile male Large Anthropomorphic Research Dummy (LARD) manikins. The system must demonstrate scalable attenuation up to a +12 Gz impulse (simulated ejection scenario) in order to ensure the system can provide adequate neck load protection, without introducing additional injury modes to the user. Prototype systems should also demonstrate they allow users to perform all necessary duty activities with minimal ROM loss and minimal additional effort of motion required. Finally, awardees shall deliver a detailed plan for integrating the system with existing aircraft systems and (AFE).

PHASE III DUAL USE APPLICATIONS: Phase III awardees shall build upon their Phase II prototype, such that it furthers the attenuation neck forces and head accelerations to safe levels under operationally relevant test conditions, without introducing additional modes of injury, reducing user ROM, or requiring additional effort of motion in order to complete duty tasks. The Phase III prototype must also demonstrate reasonable success at satisfying critical requirements for adoption, including those required to integrate with aircraft systems and AFE. The conclusion of the Phase III shall deliver a prototype system that demonstrates attenuation of a pilot's head and neck loads during routine High +Gz exposure, as well as ejection cases, to a Multi-axial Neck Injury Criteria (MANIC) rating of less than 5% injury risk in all three (X, Y, Z) axes (Parr, 2014). The prototype must be shown to be effective while also requiring little, if any, additional effort of motion on part of the user and not restrict user ROM in any way that would preclude them from accomplishing mission-critical tasks. This system would provide tremendous benefit to fixed-wing fighter squadrons that employ helmets equipped with HMDs or similar helmet-supported masses by reducing neck injury risks and will increase force readiness, while decreasing the need for medical rehabilitation. Potential transitions include the relevant fighter, attack and trainer aircraft program management offices of the USAF Life Cycle Management Center and NAVAIR. The system could also similarly benefit the Future Vertical Lift program (minus any components specifically needed for ejection) with similar helmet mounted systems. Additionally, this system could provide a therapeutic rehabilitation tool to medical professionals treating cervical spine injuries or neuromuscular conditions that affect the ability of a person to keep their head upright.

REFERENCES:


1. Harrison, M.F., Coffey, B., Albert, W.J., and Fischer, S.L. (2015). "Night vision goggleinduced neck pain in military helicopter aircrew: A literature review." Aerospace Medicine and Human Performance, 86(1), 46-55.
2. Philip S.E. Farrell et al. (2016) "Aircrew Neck Pain Prevention and Management". Human Factors & Medicine Panel NATO Research Task Group 252 STO Technical Report.
3. Turner, Anthony M. (2018) "Pilot Questionnaire to Characterize Neck Pain Related to Forward Helmet Center of Gravity (U.S. Air National Guard)". 711th Human Performance Wing USAF School of Aerospace Medicine.
4. LaFiandra, M. et. al. (July 2007) "The Effects of Personal Armor System for Ground Troops (PASGT) and the Advanced Combat Helmet (ACH) With and Without PVS-14 Night Vision Goggles (NVG) on Neck Biomechanics During Dismounted Soldier Movements". US Army Medical Research and Materiel Command report.
5. Parr, Jeffrey C., Michael E. Miller, Joseph a. Pellettiere, and Roger a. Erich. 2013. "Neck Injury Criteria Formulation and Injury Risk Curves for the Ejection Environment: A Pilot Study." Aviation Space and Environmental Medicine 84(12): 1240–48.

6. Parr, J. (2014). "A Method To Develop Neck Injury Criteria To Aid Design And Test Of Escape Systems Incorporating Helmet Mounted Displays." Doctoral Dissertation, Air Force Institute of Technology. Dayton, OH

KEYWORDS: neck pain, neck injury, chronic pain, helmet mounted display, aircraft ejection, head injury, head supported mass, ejection injury

# VERSION 4

DHA213-002 REMOVED

# VERSION 4

DHA213-003 TITLE: Advanced Nasopharyngeal Airway

OUSD (R&E) MODERNIZATION PRIORITY: General Warfighting Requirements (GWR)

TECHNOLOGY AREA(S): Bio Medical

OBJECTIVE: Design and produce an advanced nasopharyngeal airway (NPA) that provides more effective and reliable upper airway patency in unconscious patients than existing NPAs, which can be easily inserted and removed by medics/first responders such as combat life savers with varying skill levels.

DESCRIPTION: Airway compromise continues to account for approximately one in ten preventable battlefield deaths. Combat medics often provide care in no or low-light conditions, surrounded by the chaos of combat, and with the limited dexterity that accompanies bulky body armor, gloves, and heavy equipment. Therefore, a critical procedure such as airway management requires very simple tools that are highly effective. The purpose of this research and development effort is to revolutionize one of the most basic lifesaving airway management tools, the NPA. The NPA is a 140-year-old technology that was designed to open an obstructed airway in a patient who is unconscious or deeply sedated, and still factors prominently within Tactical Combat Casualty Care (TCCC) guidelines and civilian acute care. Although NPAs are easy to insert by medics, they are not universally effective in relieving airway obstruction, they are underutilized in the TCCC environment, and they are in need of an innovative overhaul.

A review of the Department of Defense Trauma Registry (DODTR) showed that only 2% of non-head and neck-injured in-theater trauma patients who had a prehospital airway intervention had a prehospital NPA placed by combat medics, yet 6% had a cricothyroidotomy (a hole cut in their neck to allow breathing). Similarly, the Prehospital Trauma Registry (PHTR) which is module of the DODTR capturing data during the Role 1 phase of care, found that only 19.5% of casualties requiring airway interventions had NPAs placed, which was closely followed by a 12% cricothyroidotomy rate, suggesting that NPAs are underutilized. This is further supported by observations that combat medics have been performing surgical airways on a number of occasions for casualties who were unconscious from hemorrhagic shock or traumatic brain injury (TBI) but who had no direct maxillofacial injuries or documented airway problems. This is troubling, because the failure rate for combat medic-performed cricothyroidotomy is as high as 33%. Recently, the TCCC Airway Working Group raised concerns about the effectiveness of current NPAs especially in battlefield applications. Despite the presence of a traditional NPA, airway obstruction can still occur in up to 42% of heavily sedated patients.

The pathophysiology of upper airway obstruction during depressed levels of consciousness is highly complex and is not fully addressed by the traditional NPA. Contemporary sleep apnea science has provided substantial insight regarding the locations, mechanisms, and forces associated with upper airway collapse. A novel NPA founded upon this new knowledge will potentially be more effective in relieving upper airway obstruction resulting in lives saved, greater operator confidence, and the avoidance of unnecessary and risky medic-performed surgical airways. A novel NPA technology should 1) be easy to insert and removed by low-skilled operators, 2) be no more traumatic than traditional NPAs, 3) demonstrate greater efficacy than traditional NPAs, and 4) have a relatively low cost of manufacturing to enhance dual-purpose utilization.

PHASE I: The main goal of Phase I is to design an innovative concept for a novel NPA and to exhibit its feasibility by conducting a demonstration of a prototype to Department of Defense (DoD) end users. A first deliverable is a concept paper that describes how the new technology will function and why it will theoretically perform better than existing NPAs in relieving airway obstruction associated with depressed levels of consciousness. A physical description of the device along with its features should be included, as

well as a description of the proposed manufacturing process. Contractors are encouraged to develop innovate designs to address the stated problem. The technology should be able to be inserted through the nasopharynx with the no greater force or mucosal trauma than traditional NPAs. Once inserted into the airway, the NPA should provide relief of obstruction at multiple pharyngeal levels. Ideally, the technology should be a one-size-fits-all solution in order to minimize operator equipment burden. The device should allow for nasal as well as oral ventilation and should facilitate effective spontaneous breathing as well as positive pressure ventilation via face mask. The physical design must have an anthropometric form factor and material characteristics that will accommodate ease of insertion. Weight should be minimized. The device should be approximately the same size of the standard NPA and should be able to withstand the crushing forces within medic backpacks. The device should be designed to be entirely disposable. Innovation is strongly encouraged in each design aspect in order to prompt intuitive ease of use. A second deliverable is a computer-aided design (CAD) model of the concept NPA. A third and final deliverable is an in-person demonstration of a low fidelity prototype (e.g., 3D printed model) to end users in order to demonstrate the principle of operation. The exhibit should demonstrate that the conceptual design will be capable of achieving the long-term goals.

PHASE II: The overall objective of Phase II is to produce an operational advanced NPA that aligns with the specified goals, form factor, and functional characteristics outlined in Phase I. The first goal of Phase II is to produce an intermediate-fidelity prototype. The emphasis should be on form, function, and subcomponent interaction. Performers are encouraged to initiate a failure mode and effects analysis (FMEA) at this stage as a means to analyze the risk factors associated with a device. A first deliverable is a description of the prototype and a report detailing a small, interim formative user study of the intermediate-fidelity prototype performed by users in manikin and/or cadaver models. One example of a manikin model is the Advanced Modular Manikin (AMM) for healthcare simulation which is open source platform (see reference 6 below). Testing of improvements and changes is then encouraged in order to take advantage of data obtained from user feedback. The next goal is to produce a higher-fidelity prototype based upon usability study findings, additional user requirements, and other observations. Focus areas for this stage include material selections (e.g., biocompatibility, hardness and flexibility, frictional interactions), design for manufacturing, and minimizing cost of goods. The aim of this stage is to produce a second deliverable that is a modified form of the first prototype, except more closely functioning and performing as the final intended device. Design innovations resulting in an intuitive ease of use are strongly encouraged. A second deliverable is a description of the updated prototype and a report detailing modifications made based upon prior user testing and risk analysis. A third deliverable will be the report of another interim formative user study. This assessment should also evaluate labels and the comprehension of instructions for use (IFU). The last stage of development serves to finalize and validate component system design and interaction and to fabricate a final prototype. Here again, testing of improvements and changes are encouraged in order to take advantage of data obtained from usability studies and risk analysis. The presentation and demonstration of a fully functional device to DoD end-users will constitute the fourth and final deliverable, accompanied by a Food and Drug Administration (FDA) regulatory plan to illustrate the pathway to clearance, and any other relevant reports and designs.

PHASE III DUAL USE APPLICATIONS: A novel NPA should be designed with dual-use purpose. In addition to meeting DoD needs, the technology should also appeal to the broader civilian healthcare market including prehospital EMS, critical care transport, the hospital emergency department, intensive care units, and anesthesiology. The small business concern is encouraged to obtain funding from non-SBIR/STTR government sources and/or the private sector to develop or transition their device into viable product or service for sale to the DoD or private sector markets. Contractors are also encouraged to adapt aspects of their research or technology into other related technologies that could be potentially inserted into defense systems as a result of this particular SBIR project. Utility may be enhanced if the technology served the additional purpose of serving as an airway adjunct during procedural deep sedation. The contractor should refine and implement their regulatory strategy for obtaining FDA approval of their

technology for use as an airway device based on their initial FDA feedback. Phase III funding should also aim towards the development of training software and other training tools. This phase should culminate in a clear path to FDA approval. In conjunction with FDA submission, the contractor should develop scaled up manufacturing of the technology that follows FDA quality regulations. In addition, the work may result in technology transition to a DoD Acquisition Program likely through USAMMDA or a SOCOM/AFSOC unit with planned expansion to the military at large after initial entry into the government purchase pathways. The ability to provide a simple to use novel NPA that reliably prevents upper airway obstruction will result in lives saved and the avoidance of unnecessary emergency surgical airways.

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2. Otten EJ, Montgomery HR, Butler FK Jr. Extraglottic Airways in Tactical Combat Casualty Care: TCCC Guidelines Change 17-01 28 August 2017. J Spec Oper Med. 2017 Winter;17(4):19-28. PMID: 29256190.
3. Mabry RL. An analysis of battlefield cricothyrotomy in Iraq and Afghanistan. J Spec Oper Med. 2012;12(1):17-23.
4. Stoneham MD. The nasopharyngeal airway. Assessment of position by fibreoptic laryngoscopy. Anaesthesia. 1993 Jul;48(7):575-80.
5. David Hananel, BSEE, BACS, Dan Silverglate, BAFA, BSCS, Dan Burke, A.S, Benjamin Riggs, Jack Norfleet, PhD, Robert M Sweet, MD, FACS, The Advanced Modular Manikin Open Source Platform for Healthcare Simulation, Military Medicine, Volume 186, Issue Supplement_1, January-February 2021, Pages 49–57, https://doi.org/10.1093/milmed/usaa420

KEYWORDS: Nasopharyngeal, nasal, airway, obstruction, cricothyroidotomy

# VERSION 4

DHA213-004 TITLE: Bougie-Integrated Endotracheal Intubation Stylet

OUSD (R&E) MODERNIZATION PRIORITY: General Warfighting Requirements (GWR)

TECHNOLOGY AREA(S): Bio Medical

OBJECTIVE: Design and build a bougie-integrated endotracheal intubation (ETI) stylet that improves operator first pass success rates by resolving anatomic challenges associated with indirect and direct laryngoscopy. The technology should provide enhanced ETI performance and autonomy for providers of varying skill levels operating in austere and remote environments.

DESCRIPTION: Each year millions of patients will have a breathing tube, known as an endotracheal tube (ETT) inserted into their windpipe in order to assist with ventilation or to protect their airway. The procedure is called endotracheal intubation (ETI), and thousands who undergo ETI will experience serious complications as a result of operator difficulty during the process. ETI is a complex procedure that requires considerable skill. An improperly placed tube can deprive a patient of oxygen and can rapidly lead to death. Emergency circumstances, such as trauma and austere conditions make ETI riskier and more difficult. In the combat prehospital environment where airway loss and ventilatory compromise represents one of the leading causes of death, ETI encompasses over 80% of airway securement. It is also in this setting where airway interventions, specifically ETI, is one of the most common incorrectly performed life-saving interventions. A significant number of casualties arrive at Combat Support Hospitals in need of an immediate ETT, suggesting that many prehospital operators lack either the technology or skill to confidently provide definitive airway management.

Although anatomic, skill, and circumstantial issues all contribute this capability gap, there also exists an ETI technology gap. Rapid, first-pass ETI success is critical in order to save lives, decrease complications and minimize downstream casualty acuity. ETI needs to be more accessible to a broader range of operators, particularly those with lower skill and experience levels. This is particularly relevant in the context of future Multi Domain Operational (MDO) environments where small, widely dispersed units will require levels of self- sufficiency that are higher than what is currently demanded. In the MDO, endotracheal intubation will become more necessary due to evacuation constraints and prolonged transit times. The MDO environment is also where resource-consuming complications must be avoided. These challenges effectively widen the current ETI capability gap.

ETI is a three-step process that involves: 1) viewing the vocal cords with a device called a laryngoscope (visualization), 2) delivering the tip of the ETT to the vocal cords (insertion), and 3) advancing the tube into the trachea (cannulation). For over 120 years the visualization step with direct laryngoscopy (DL) has been the main procedural pain-point. With this in mind, video-assisted laryngoscopy (VL) was introduced into clinical practice relatively recently. Despite VL's ability to provide easier views, it has not resulted in a consistent improvement in airway management success. Therefore, a stylet technology that could resolve the anatomic and technical ETI challenges associated with both contemporary DL and traditional VL could be disruptive in terms of closing the deadly skill gap. Such a stylet technology would ideally incorporate 1) an intubating "bougie" that can be easily and atraumatically guided into the trachea, 2) a minimal gap between the bougie and the ETT, 3) a feature that allows advancement of the ETT into the airway to enhance operator autonomy, and 4) a feature that allows adjustments for ETT's of different lengths.

PHASE I: The main goal of Phase I is to develop an innovative design for an advanced bougie-integrated ETI stylet and to exhibit its feasibility by conducting a demonstration of a prototype in a manikin model by end users. One example of a manikin model is the Advanced Modular Manikin (AMM) for healthcare simulation which is open source platform (see reference 6 below). The technology should provide a

leveraging advantage over existing devices in overcoming operator skill-level issues and the anatomic impediments that vex operators during DL and VL. A first deliverable should be a detailed description of the proposed trechnology for sponsoring end-users including its principle of operation.The technology should be able to deploy a flexible bougie into the trachea that will serve as guide for the ETT, thereby easing glottic insertion and preventing ETT hang-up on glottic and subglottic structures during ETT cannulation. The outer diameter of the bougie should be as close as possible to the inner diameter of the ETT, which may necessitate different size ranges in terms of length and diameter. The amount of collision between the tip of the bougie during advancement and the anterior trachea should be minimized. The tip of the bougie should be atraumatic. The bougie should be able to be retracted and redirected if necessary. The resting position of the ETT on the device should be adjustable. There should be a feature that allows the operator to advance the ETT off of the device and into the airway in order to provide more autonomous operation. The physical design must have an anthropometric form factor that will accommodate a wide range of hand sizes. The device should be designed to be entirely or partly disposable for space saving purposes. It should not require any electrical power. Innovation is encouraged in each design aspect to prompt intuitive ease of use. A second deliverable is a computer-aided design (CAD) model of the stylet. A third deliverable is the demonstration of low fidelity protype in a manikin model performed by sponsoring end-users at San Antonio Military Medical Center. The exhibit should validate that the conceptual design will be capable of achieving longer-term goals.

PHASE II: The overall objective of Phase II is to produce a fully operational bougie-integrated ETI stylet that aligns with the specified goals, form factor, and functional characteristics outlined in Phase I. The first goal of Phase II is to produce an intermediate-fidelity prototype. The emphasis should be on form, function, and component interaction. Contractors are encouraged to perform a failure mode and effects analysis (FMEA) at this stage as a means to analyze the risk factors associated with a device. A first deliverable is a description of the prototype and a report detailing an interim formative user study of the intermediate-fidelity prototype performed by ETI operators on manikin and/or cadaver models. Testing of improvements and changes is then encouraged in order to take advantage of data obtained from user feedback. The next goal is to produce a higher fidelity prototype based upon usability study findings, additional user requirements, and other observations. Focus areas for this stage include material selections for the final product (e.g., biocompatibility, frictional interactions, bougie characteristics), design for manufacturing, and minimizing cost of goods. The aim of this stage is to produce a second deliverable that is a modified form of the first prototype, except more closely functioning and performing as the final intended device. Design innovations resulting in an intuitive ease of use are strongly encouraged. A second deliverable is a description of the updated prototype and a report detailing modifications made based upon prior user testing and risk analysis. A third deliverable will be the report of another interim formative user study. This assessment should also evaluate labels and the comprehension of instructions for use (IFU). The final stage of development serves to finalize and validate component system design and interaction and to fabricate a completed device. Here again, testing of improvements and changes are encouraged in order to take advantage of data obtained from usability studies and risk analysis. The presentation and demonstration of a fully functional device to sponsoring end-users at San Antonio Military Medical Center will constitute the fourth and final deliverable, accompanied by a Food and Drug Administration (FDA) regulatory plan to illustrate the pathway to clearance, and any other relevant reports and designs.

PHASE III DUAL USE APPLICATIONS: A novel tracheal intubation stylet should be designed for dual-use purpose. In addition to meeting DoD needs, the technology should also appeal to the broader civilian healthcare market including prehospital EMS, critical care transport, the hospital emergency department, intensive care units, and anesthesiology. The small business concern is encouraged to obtain funding from non-SBIR/STTR government sources and/or the private sector to develop or transition their device into viable product or service for sale to the DoD or private sector markets. Phase III funding should aim towards the adaptation of a bougie-integrated stylet technology for DoD field use, which should include

formative usability testing by DoD end -users. Weight should be minimized and the device should be suitable for storage and transport in medical field packs. Contractors are also encouraged to adapt aspects of their research or technology into other related technologies that could be potentially inserted into defense systems as a result of this particular SBIR project. Utility may be enhanced if the technology incorporated optional visualization technology. The contractor should refine and implement their regulatory strategy for obtaining FDA approval of their technology for use as an airway device based on their initial FDA feedback. Phase III funding should also aim towards the development of training software and other training tools. This phase should culminate in a clear path to FDA approval. In conjunction with FDA submission, the contractor should develop scaled up manufacturing of the technology that follows FDA quality regulations. In addition, the work may result in technology transition to a DoD Acquisition Program likely through USAMMDA or a SOCOM/AFSOC unit with planned expansion to the military at large after initial entry into the government purchase pathways. The ability to provide a simple to use ETI stylet system that decreases required skill levels and improves ETI success rates will result in lives saved and enhanced casualty flow in MDO environments.

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KEYWORDS: Intubation, endotracheal, airway, stylet, bougie, laryngoscopy, video, direct

# VERSION 4

DHA213-005 TITLE: Chemical Sterilant for Far Forward, Austere Environments

OUSD (R&E) MODERNIZATION PRIORITY: General Warfighting Requirements (GWR)

TECHNOLOGY AREA(S): Bio Medical

OBJECTIVE: Develop and validate a chemical sterilant solution that can sterilize surgical instruments and other materiel through immersion. Product could be a powder or concentrated liquid that when mixed with potable water, creates the requisite solution capable of the desired sterilization.

DESCRIPTION: In the future, the Armed Forces will utilize multi-domain operations in order to fight and win against peer and near-peer adversaries. Armed conflict will likely occur via large-scale combat, resulting in high numbers of casualties over short time periods where degraded air superiority and ease of maneuver will make evacuation extremely difficult. These circumstances will force units to hold casualties at earlier roles of care for longer periods of time, where lifesaving surgical interventions will need to take place in order to preserve life. This creates significant challenges to safely operating on casualties with sterile equipment.

For example, the Army sterilizers that exist at the Role 3 Field Hospital, with smaller sterilizers present with the Forward Resuscitative Surgical Detachments at some Role 2s. However, heat/steam sterilization cycles can take close to an hour to complete and some items (e.g. retractors) can't fit into the sterilizers that are present at the Role 2. The inability to adequately sterilize some of these items is an issue in and of itself, but the mass casualty situations that will be prevalent during large-scale combat operations will compound this issue. In addition, medical units likely won't be able to sterilize surgical equipment quickly enough to meet surgical demand, and/or surgery will need to take place in settings without the space and infrastructure to support heat and steam sterilizers. As such, the desired chemical sterilant solution would not only address shortcomings at the Role 2, but it would also augment existing sterilization capabilities to help mitigate bottlenecks during mass casualty situations.

According to the Centers for Disease Control and Prevention (CDC) Guideline for Disinfection and Sterilization in Healthcare Facilities (2008), sterilization "destroys or eliminates all forms of microbial life" (page 9)1. This capability is looking for a chemical solution that is capable of sterilization according to these CDC guidelines. Because of the unique circumstances of performing surgery in austere conditions, the solution would need to have additional attributes beyond its ability to sufficiently sterilize surgical equipment. The solution would need to effectively sterilize instruments in 10 minutes or less (perhaps through immersion) at ambient temperatures (i.e. wouldn't require being warmed or cooled to be effective), and once activated (e.g. when a powder is mixed with water to create a sterilization liquid), should remain effective for at least 36 hours. The solution also needs to be safe enough to not require disposal as a hazardous chemical nor cause irritation if it comes into contact with bare skin. Additionally, because military logistics entail products being shipped in non-climate-controlled containers, the 1 https://www.cdc.gov/infectioncontrol/guidelines/disinfection/index.html product will need to be stable enough to withstand extreme temperatures (high and low) and a variety of humidity conditions without impacting its performance.

PHASE I: The Phase I effort should focus on designing and/or developing an innovative solution that could sterilize surgical equipment as described above. Testing of the solution should demonstrate its ability to sterilize per the CDC Guidelines. Additional testing/assessments should demonstrate the proposed solution's ability to adhere (or potential to adhere) to sterilization time and shelf stability once activated. Disposal considerations should also be assessed, as the product will need to eventually comply with Environmental Protection Agency (EPA) regulations as well as FDA regulations before being fielded. The product cannot be considered hazardous material, and should be safe enough to dispose of

down a drain and ideally, safe to dispose of on the ground. Additionally, the product should not cause irritation if it comes into contact with bare skin.

The concept of use in the field should also be developed, outlining the process to activate, use and dispose of the product. This should attempt to be as comprehensive as possible, e.g. how the product will be shipped and stored (e.g. environmental conditions, acceptable containers), including after activation, through to disposal. Safety precautions that personnel will have to take with the product (before, during, and after use) should also be addressed.

Required Phase I deliverables will include the results of all testing and assessments done on the product to support its ability to meet the parameters outlined in the Details section, along with a demonstration of how the product is used (can be a video). Additional key information about the product should be summarized in a report. The report should also address the solutions' ability or potential to meet all of the parameters.

PHASE II: Using the results from Phase I, further develop, demonstrate and validate the solution identified and tested in Phase I. The performer should produce enough material to fully validate whether the solution can meet the CDC Guidelines for sterilization of surgical equipment, as well as begin to validate the solution's ability to meet the other parameters. Through this testing and validation process, the performer should make iterative refinements to the proposed solution to enable it to meet all of the parameters. The Phase II effort should also include verification of how well the solution can be integrated into the intended field environment.

The Phase II effort could include finalizing the proposed solution, as well as conducting environmental studies and preclinical or clinical studies to support regulatory submissions to the Environmental Protection Agency and Food and Drug Administration (respectively). Stability and shelf life studies could also be included during Phase II. Additional testing on the product to evaluate its compatibility with the intended fielding environment could also be included. This may entail demonstrating how the product can be utilized in different scenarios given the materials available at the Role 2 aid station and Role 3 field hospital. These demonstrations could also include user testing.

Required Phase II deliverables will include results that demonstrate all the parameters that the solution can meet, along with any data/information that support its potential to meet any parameters that aren't already met. Demonstrations of how the proposed solution can be integrated into the Role 2 and 3 environment (video submission is acceptable) and/or results of user testing could also be a Phase II deliverable. Additional required deliverables would be any regulatory submissions and communications with the EPA and FDA. The status of the effort and all deliverables should be captured in a report that captures the detailed outcomes of the work completed during Phase II, the status of regulatory submissions, and the degree to which the proposed solution(s) meets the additional performance parameters.

PHASE III DUAL USE APPLICATIONS: Using the results and progress made during Phase II, a Phase III effort would complete any remaining work necessary to have the proposed solution meet the performance parameters described in this topic, obtain regulatory clearance from both the EPA and FDA, establish appropriate stability and shelf life of the product, demonstrate its performance in a military-relevant environment, become production ready, and become commercially available. Based on the progress made in Phase II, the product would be considered as the solution to be fielded under the Chemical Sterilant program managed by the Warfighter Expeditionary Medicine and Treatment Project Management Office (WEMT PMO). Phase III would include any remaining product development to progress it towards being ready for commercialization and fielding, such as packaging, manufacturing, regulatory clearances, and military testing. Beyond this, the U.S. Army would procure the finalized

product in quantities sufficient to satisfy its fielding requirements. Other services would also be able to procure the finalized product for their capability needs as well. Units would then purchase resupply of this product to maintain this specific sterilization capability.

In the civilian market, this solution may provide a new, innovative option for rural clinics to sterilize critical tools and instruments (e.g. forceps, scalpels, scalpel handles) where they don't have the capacity for large sterilization equipment, but would also work well for emergency response situations where field hospitals are set up by the American Red Cross, the Federal Emergency Management Agency, or other non-profits. Additionally, international development and non-profit organizations focused on improving healthcare in resource-poor settings outside of the U.S. may also find this product a useful way to push a sterilization capability into areas where surgery is difficult or dangerous, such as isolated village clinics in under-developed countries.

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KEYWORDS: chemical sterilant, sterilant, sterilization, surgery, surgical instruments, austere environment, mass casualty event, field surgery, secondary infection, infection prevention

# VERSION 4

DHA213-006 TITLE: Sterilizer, Field, Special Materiel for Far Forward, Austere Environments

OUSD (R&E) MODERNIZATION PRIORITY: General Warfighting Requirements (GWR)

TECHNOLOGY AREA(S): Bio Medical

OBJECTIVE: Develop and validate a sterilization cabinet that can sterilize heat-sensitive surgical instruments and other materiel.

DESCRIPTION: In the future, the Army will utilize multi-domain operations in order to fight and win against peer and near-peer adversaries. Armed conflict will likely occur via large-scale combat, resulting in high numbers of casualties in short periods of time where degraded air superiority and ease of maneuver will make evacuation extremely difficult. These circumstances will force units to hold casualties at earlier roles of care for longer periods of time, where lifesaving surgical interventions will need to take place in order to preserve life. This creates significant challenges to safely operating on casualties with sterile equipment.

Sterilizers that utilize heat and steam exist at the Role 3 Field Hospital, with smaller sterilizers present at the Role 2-level Forward Resuscitative Surgical Detachment (FRSD). However, some specialized equipment (e.g. surgical scopes) cannot undergo heat/steam sterilization. High-level disinfection of these scopes is often not sufficient to mitigate the risk of infection in surgical patients due to crevices and hard-to-reach areas on the instrument. Even when traditional sterilization is possible, these methods often result in retained moisture that allows for bacterial growth. Unfortunately, many of these instruments include highly sensitive components that cannot be exposed to the high pressure, temperature, and moisture of heat/steam sterilization. Therefore, a sterilization method that sterilize the unique form factor of surgical scopes is needed.

According to the Centers for Disease Control and Prevention (CDC) Guideline for Disinfection and Sterilization in Healthcare Facilities (2008), sterilization “destroys or eliminates all forms of microbial life, including bacterial spores” (page 9).1 The desired solution would provide a solution capable of sterilizing sensitive surgical scopes according to these CDC guidelines. While there may be some solutions in the marketplace, manufacturers of commercially-available products have not built to their systems for frequent transport and lack the rugged structure required for field use.

PHASE I: The main goal of Phase I is to design a concept for a rugged benchtop sterilization cabinet. The physical design of the cabinet should put the centerline of the cabinet door no less than 48 inches from the floor and weigh no more than 182 pounds, with preference towards a lighter build. The internal compartment should be capable of holding two or more midsize sterilization baskets (17” x 11” x 4”) and large enough to house one or more standard-sized surgical scopes. The sterilization cabinet should operate by 110/20 VAC, 50/60 Hz power supply, and run times for optical equipment (i.e. surgical scopes) should last no longer than 75 1 https://www.cdc.gov/infectioncontrol/guidelines/disinfection/index.html minutes. The system display should be simple to navigate, allow for manual interruption of cycles, and the system should follow industry standards for data logging and recall of cycle data. Innovation is encouraged in each design aspect to create a lighter and more rugged cabinet.

Required Phase I deliverables include a mock-up or early prototype of the desired sterilization cabinet. A report should also describe the cabinet design and features, the proposed sterilization process, progress made towards meeting the various parameters, and the results of any preliminary testing.

PHASE II: The overall objective of Phase II is to produce a fully operational prototype sterilization cabinet that can sterilize sensitive surgical scopes based on the Phase I design. Phase II work can include

building and testing of the prototype, iterative design improvements, manufacturing assessments, generating data necessary for regulatory submissions, building out multiple/additional sterilization cycles and testing them, and other related work. At the conclusion of Phase II, the performer should have achieved design lock of the system, developed a finalized prototype and be ready to move into more manufacturing-focused development.

Required Phase II deliverables include a report describing the work accomplished under Phase II, with the latest design of the sterilization cabinet including specifications, a description of the final sterilization process for any/all cycles and options, a description of the user interface, and identification of all intellectual property and proprietary information. The ruggedization of the sterilization cabinet must also be addressed in the system design and performance documentation. Other deliverables include all regulatory submissions for the sterilization cabinet and subsequent communications with the Food and Drug Administration (FDA). Additional deliverables could include any manufacturing development that has been done.

PHASE III DUAL USE APPLICATIONS: Building on the work completed under Phase II, a Phase III effort would complete any remaining work to test and validate performance of the sterilization cabinet, including its ability to withstand military rugged conditions. Phase III could also include completing work to successfully obtain regulatory clearance from the FDA, begin production prototyping and/or early manufacturing runs, and to bring the product to the commercial market.

Based on the progress made in Phase II, the product would be considered as the solution to be fielded under the Sterilizer, Field, Special Materiel program managed by the Warfighter Expeditionary Medicine and Treatment Project Management Office. Phase III would include any remaining product development to progress the cabinet towards being ready for commercialization and fielding, such as packaging, manufacturing, regulatory clearances, and military testing. Beyond this, the U.S. Army would procure the finalized product in quantities sufficient to satisfy its fielding requirements. Other services would also be able to procure the finalized product for their capability needs as well. Units would then purchase resupply of this product to maintain this specific sterilization capability.

In the civilian market, this solution is applicable to an ongoing problem in civilian healthcare facilities, as evidenced by the 2015 CDC “Call to Action” and the 2015 Joint Commission on high-level disinfection (see references). Despite the dates of these documents, this problem still persistents. If a sterilization cabinet that can fully and adequately sterilize these sensitive, hard-to-clean instruments becomes commercially available, it would greatly reduce the current burden
on hospitals and outpatient clinics to sufficiently clean these instruments. As such, the commercial market for a technology of this nature would provide ample demand for the product.

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KEYWORDS: sterilization, surgical scopes, austere environment, surgery, field surgery, high-level disinfection, sensitive surgical equipment, secondary infection, infection prevention

# VERSION 4

DHA213-007 TITLE: Anionic Nanoparticle Carriers for Neuron-targeting of Synthetic and Protein Drugs

OUSD (R&E) MODERNIZATION PRIORITY: General Warfighting Requirements (GWR)

TECHNOLOGY AREA(S): Bio Medical

OBJECTIVE: Construct a population of uniformly sized anionic nanoparticles (NPs) with consistent size, composition, and charge that can be loaded with traditional water-soluble synthetic drugs and, alternatively, protein therapeutics in the lumen and on the surface of the vesicles.

DESCRIPTION: Current medical treatments for casualties are heavily reliant upon diffusion of water-soluble synthetic drugs to reach their site of action to protect critical cells and tissues. Typically, synthetic drugs need to be administered at levels such that non-target sites can saturate prior to reaching physiologically relevant concentrations. To minimize drug dosage and maximize the time to effective dose, nanoparticle carriers can be tailored to focus drug delivery to those critical cells and tissues and shift the time tables towards better protection and, ultimately, faster recovery for patients.

NPs are increasingly used in applications for drug delivery and other biomedical technologies. Their small size range (1-100 nm diameter) affords them unique properties that can be significantly leveraged to improve systemic delivery and cell-mediated absorption. Their high surface-to-volume ratios enable them to carry significant quantities of synthetic small molecule drugs, as well as protein drugs. The intrinsic properties of the NP's constituents can also be exploited to intricately specify which cells are targeted by the NPs and their payload.

Most somatic cells in the human body have an anionic (negative) membrane potential, including neurons. The membrane potential is consistently maintained by gated ion channels, assisting the separation of cytoplasm from extracellular fluids. Neurons have the unique characteristic of switching their membrane potential from negative to positive, albeit transiently, during action potentials. It has been shown that negatively charged NPs are attracted to electrically active neurons, regardless of their size, shape, or composition (Dante et al., 2017).This complimentary charge-charge attraction between NPs and neurons is the cornerstone for this SBIR initiative.

PHASE I: The main goal of Phase I is to formulate and construct non-toxic NP constituents which will consistently produce uniformly sized NPs with a negative surface charge. The NPs must have the capacity to be easily loaded with water-soluble synthetic drugs. The NPs must also have the capacity to lumen load protein drugs with encapsulation efficiencies greater than 25% with no decrement to enzyme activity. Developing an efficient NP loading strategy will be paramount to completing Phase I. As a separate milestone, protein drugs must also be functionalized to adhere to the surface of the NPs by any means, as long as there is no interference with enzyme catalytic efficiency.

The NPs must be capable of retaining these drugs in a closed vesicle of any shape. NPs can take various shapes during production, including spherical vesicles or rod-shaped hexasomes (Angelova et al., 2017; Eygeris et al., 2020). NP size distributions will be measured using quasi-electric light scattering (QELS) or a similar method. Diffusion coefficients are used to develop population characteristics in terms of hydrodynamic radius (Rh) by quantifying dynamic fluctuations in scattered light. After extrusion, NPs should have a narrow Rh histogram. Some variation in NP sizes will exist within any singular population, which should be captured using QELS and monitored across three (3) distinct production batches. Stability of the nanoparticles can be evaluated by incubating NP samples at elevated temperatures (e.g., 37 °C) in buffer and measuring population shifts in Rh.

# VERSION 4

PHASE II: The main goal of Phase II is to evaluate cytotoxicity of the primary NP product from Phase I. A colorimetric thiazolyl blue tetrazolium bromide (MTT) assay for assessing cell metabolic activity or a similar assay measuring cytotoxicity effects may be used. Cytotoxicity can also be assessed in cultured neurons using fluorescent dyes (SYTO 13 and Hoechst 33342) to monitor membrane fluidity and neuron viability (Hubbard et al., 2012). Attraction to neurons in vitro may also assist in developing confidence in the NP net charge (e.g., anionic). Primary neuronal cell cultures can potentially be used to assist in determining cytotoxicity and neuronal attraction simultaneously.

A stability study of loaded NPs spiked into animal plasma will need to be completed at room temperature and at 37 °C. This will help evaluate the stability of the NP in an ex vivo milieu. NP size and size distribution changes can be monitored using QELS to determine if osmotic shifts will impact loading buffer ionic strength or command the use of loading adjuvants.

PHASE III DUAL USE APPLICATIONS: The main goal of Phase III is to show stability and efficacy of the engineered NP with full payloads of both synthetic small molecule drugs and protein drugs in either the lumen or adorned to the surface in a small animal study comparing safety and efficacy results to a non-NP approach using the same drugs. Stability will be measure by injecting loaded NPs into an animal and evaluating their ability to be cleared from the bloodstream by following protein drug pharmacokinetics. This will be a “follow on” experiment to the study in Phase II where loaded NPs are spiked into animal plasma to evaluate stability ex vivo. Ultimately, this phase of the SBIR will involve direct contact between key DoD laboratories involved in neurological and surgical research, allowing for collaborative assessment using advanced injury models.

To evaluate the ability of the NPs to confer neuroprotective capabilities, animals shall be challenged with paraoxon, an organophosphorous compound that is known to inhibit acetylcholinesterase, a key enzyme involved in the transmission of nerve signals at the neuromuscular junction. The proposed animal study will incorporate two therapeutic approaches by examining protective efficacies against 2 x LD50 challenges of paraoxon using conventional chemotherapeutics (atropine and 2-PAM) compared to anionic NPs loaded with these drugs or with a protein-based drug designed to hydrolyze organophosphorus threat agents or loaded with a combination of small molecule and protein drugs. Mice would be an ideal choice because they maintain a body temperature similar to humans at 37° C, putting the experimental NPs under conditions that they will encounter when transitioned to clinical trials. These animals also have a small blood volume which will minimize the use of the experimental NP drugs.

As an advanced application of the NPs, they may be transitioned to the administration of pain relieving drugs for both kinetic and thermal traumatic wounds. The neurons responsible for transmitting pain from the source undergo excessive depolarization to send the pain signal back to the central nervous system. Time is the most critical factor in treating any traumatic wound of any kind. In drug development, drug onset of action is critical to success of the product. The short-term effect of these new therapeutic vesicles is that they will provide an improvement in targeting neurons and delivering drugs faster once administered. These NPs will also help extend limited supplies of pharmacological drugs needed in a crisis by using a smaller drug quantity per person, thereby helping more people.

Additionally, as a transition product that could also have additional use in the Chemical-Biological Defense Program, a future direction that would be beneficial is in the area of kinetic or thermal traumatic wounds that are exacerbated by the presence of chemical agents. This area is lacking because, currently, a patient’s skin can be decontaminated, but there is not a decontamination product appropriate for use in wounds. Without proper decontamination of wounds, the chemical warfare agent continues to be absorbed into the patient’s bloodstream. As an adjunct to conventional wound treatment, the anionic nanoparticles could be applied, potentially in the form of a bandage-based treatment solution, to detoxify chemical agents sustainably, immediately, and locally, while traditional administration of therapeutics

would attempt to treat the whole body. Ultimately, this new drug design will open the possibility to reformulate the way we present therapeutic drugs to patients, with an emphasis on treating combined injuries involving traumatic wounds contaminated with chemical warfare agents.

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KEYWORDS: neurons, nanoparticles, anionic, drug delivery, pain management, and chemical agents

# VERSION 4

DHA213-008 TITLE: Digital Human Model for Use in Simulation Environments for Tactile Human/Robot Interaction

OUSD (R&E) MODERNIZATION PRIORITY: General Warfighting Requirements (GWR); Autonomy

TECHNOLOGY AREA(S): Bio Medical

OBJECTIVE: The objective for this topic is to develop a biomechanically correct human parametric model to be used in digital simulation environments, capable of interacting with robotic manipulators in computer simulation and express stress metrics in the form of contact forces on the body and force-torques at the body joints.

DESCRIPTION: The use of Robotic and Autonomous Systems (RAS) at the tactical edge will increase as technology matures, providing multi-functional utility while minimizing risks to Soldiers during future operations[1]. The Army's RAS Strategy, approved in 2017, describes the use of RAS to penetrate high-risk areas and to provide support in future contested environments to increase reach, capacity, and protection. Faced with the operational challenges emphasized by the Multi-Domain Operations (MDO) concept, medical forces would benefit by using forward-deployed RAS as force multipliers. Medics could employ RAS in ways that augment their capacity to provide care or reduce their exposure to particularly dangerous tasks. One such high-risk task that Soldiers are faced with is the need to locate the wounded and extract them to a place of relative safety so that Medics are able to perform life-saving Tactical Combat Casualty Care. As illustrated in the Army RAS Strategy, many of the required technologies and programs to enable this application of RAS are well underway by the larger RAS research and development community.

However, there are specific technical challenges that are unique to medical applications of RAS as described in the U.S. Army Medical Department's Position for the Employment of Robotic and Autonomous Systems. Medical applications, such as autonomous extraction of casualties and RAS-assisted diagnostics/interventions, will require robots to safely and precisely make physical contact, grasp, and/or apply forces to humans. Developing methods and technologies for safe physical interaction between emerging robot platforms and humans is a key technical challenge that is yet to be addressed. This topic calls for the development of a biomechanically correct human parametric model to express relevant body stress metrics in order to design, develop, and test methods of safe physical human-robot interaction in a simulation environment. This human parametric model will fill a key technology gap by providing information such as joint torques at the limbs or contact forces on the skin. This data will in turn ensure safe operation and motion planning throughout the research and development process of many medical RAS technologies.

For all of the advancements in robotic technology driven by new techniques in computer vision, precise path planning and acute control systems, little development has been made for refining safe and effective grasping and manipulation of the human body by a robotic manipulator. In order for RAS to be used for casualty extraction, the actual moments of robotic grasping on the casualty need to be accurately modelled during Research and Development (R&D) in simulation environments to allow for safe and rapid iterations to be made to refine controls and develop motion planning algorithms. A major feature missing from existing robotic simulation environments is anatomically correct and physically accurate digital human models. Existing human models for open-source robotic simulation environments are rudimentary[2], lacking both accurate collision physics as well as force metrics on the model. Some open source models, however are very advanced, such as those focused on musculoskeletal modeling for mapping out both the dynamics of the body but also the forces acting upon the joints during motion[3]. Those musculoskeletal models do not however focus on outside forces acting on the body such as a robotic manipulator. The goal of this topic will be to develop a biometrically accurate human parametric

model able to be inserted into simulation environments allowing for the advancement of robotic grasping and manipulating techniques. In order for the digital manikin model to further robotic grasping development, the model must provide stress and strain metrics to quantify the safety and efficacy of a grasping technique. Metrics include, but are not limited to, contact force at the spot of the robotic grasp, and force metrics of strain on the muscles, and stress at the joints. As a robotic end effector grasps a human limb and begins to manipulate it into a new position, the digital model will need to supply the forces generated at each joint. The model must be able to calculate real-time and accurate reaction force during manipulation. The model must represent accurate musculoskeletal dynamics as manipulation is taking place. In order to achieve this, it must represent accurate density and mass along the entire anatomy. The model developed needs to be able to be imported into commonly used simulation environments for robotic motion planning development. The intended use case is to simulate an unconscious soldier, therefore the model is only required to be reactionary in nature.

PHASE I: Develop a proof of concept demonstration capability to conduct a feasibility study describing approaches to meet the technical challenges in developing a digital biometric human model as described above. The feasibility study should take into account all of the different forces that can be applied on the body from contact with a robotic system, both from grasping of a limb and manipulation to non-prehensile manipulation. Design a proof of concept digital model that outputs preliminary stress metrics during interaction with a robotic manipulator in simulation. The proof of concept design should include a human model with accurate biometric form and the required architecture for measuring reaction forces at the joints, contact forces, and distributed loads on the surface of the body. Design should take into account maximizing the ability for the digital model to be integrated into common robotic simulation environments. Work done in Phase I should focus on demonstrating feasibility of the elements of the overall technical solution that present the highest technical risk and will inform the design and development plan for Phase II.

PHASE II: From Phase I work, develop and demonstrate the functionality of the human model capable of quantifying stress and strain metrics as it is manipulated by a robotic system in a simulation environment. The technical solution shall be based on research conducted into the accurate application of biomechanics and musculoskeletal dynamics inside simulation environments. Similarly, research must be conducted to accurately translate collision of objects (manipulator, human limb) into point and distributed force metrics at the point of the joints and the surface contact of the skin in a simulation environment. The model should be biometrically correct demonstrating accurate musculoskeletal dynamics in all of its movements. All motions of the body should represent anatomically realistic limitations of the range of motion of joints. This also means accurate forces applied to a part of the body reflect down the kinematic chain. The Phase II development work will target an application consisting of a robotic system grasping and lifting different limbs of the human model and manipulating them to new positions, using both prehensile and non-prehensile manipulation. The interactions between a 7 degree of freedom (DoF) robot and the human digital model in a simulation environment should include:

1) A robot gripping a wrist and lifting the arm.
2) A robot gripping the ankle and lifting the leg
3) A robot rolling the body from prone to supine pose
4) A robot dragging the body from a grasping point on the arm
5) A robot dragging the body from a grasping points on the leg
6) A series of palpations from the robot across the surface of the body.

These interactions will be pre-determined and online planning is not required. Net forces at key anatomical joints such as the shoulder, elbow, wrist, neck, hip knee and ankle must be calculated and expressed. Contact forces along the surface of the body where interaction occurs from the robot must also be measured. The distributed forces applied to the human model at the contact locations and at the joints as the limbs are manipulated must be able to be logged and saved (to eventually be used to refine robotic

motion planning algorithms). To demonstrate grasping and manipulation it is recommended that readily available grippers be used for simulation, as the development of new types of robotic grippers are outside the scope of this topic. The goal of the Phase II demonstration is to verify the performance of the human model when interacting with any surrogate/notional robotic system in simulation.

PHASE III DUAL USE APPLICATIONS: In Phase III, the technical solution will be matured to TRL 7 or 8 and dual-use applications will be explored. A refined Phase III end state would focus on interoperability, as the model should be in a plug and play state for commonly used simulation environments. Phase III provides an opportunity to apply the Phase II development work to specific needs identified by laboratories and program offices across the DoD. For example, the Telemedicine and Advance Technology Research Laboratory, a subordinate USAMRDC science and technology laboratory, is currently engaged in a variety of research initiatives related to the medical applications of RAS. Phase III efforts should focus on technology transition to product development/program management offices within USAMRDC, and DoD mission programs. For example, the U.S. Army Medical Materiel Development Activity's (USAMMDA) Warfighter Health, Performance and Evacuation (WHPE) Project Management Office, could benefit from technology solutions under this topic in their mission to develop, rapidly prototype and procure medical support products, combat casualty care support systems, and ground and aeromedical evacuation vehicles. Phase III efforts have the ability to expand the functionality of the digital model, for example, including internal injury modeling in additional to external force mapping. These advancements could provide injury mitigation solutions, as well as enhance Soldier lethality in multi-domain battlefield environments, which would be of benefit to DoD operational medicine research programs.

While the primary intended use for this digital model is to support the development and testing of medical RAS technologies that require physical interaction between robots and humans, alternate use cases should be explored in Phase III such as emergency response robotics, human collaborative industrial robotics, and injury prevention health hazard assessment tools. Companies that produce robotic systems requiring close human-robot interaction should be targeted for potential dual-use commercialization opportunities. Phase III works includes the refinement and execution of the commercialization plan included in the Phase II proposal, potentially through collaborative relationships with partners identified in Phase II. The resulting technical solution, which provides an advanced biometric human model designed for simulation and development environments, has the potentially to accelerate progress in the field of human-robot interaction.

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KEYWORDS: Robot, Simulation, Manikin, Manipulation, Biometric, Human-Robot Interaction, Simulation Environments, Robotics, Casualty Extraction, Autonomous Systems, Combat Casualty Care, Medical Robotics, Musculoskeletal Dynamics, Digital Human Model

# VERSION 4

DHA213-009 TITLE: Prolonged Care: To Demonstrate a Wearable Wound Infection Treatment Delivery Device

OUSD (R&E) MODERNIZATION PRIORITY: General Warfighting Requirements (GWR)

TECHNOLOGY AREA(S): Bio Medical

OBJECTIVE: To reimagine the combat wound medication packet (CWMP) in a wearable format capable of delivering treatment for the prevention of infection in a prolonged care (PC) setting. The technology shall be in an easy-to-use format, durable instrumentation, lightweight, and compatible with PC. The approach should enable treatment administration for 72 hours near the wound bed. The end goal for this effort is to assemble a system of systems to prevent the development of infection in an austere environment when the provision of surgical intervention is delayed.

DESCRIPTION: Multi-domain operations (MDO) of the future anticipate division-on-division combat operations with casualty volumes and medical intervention times that mirror what was observed in World War I and II. In MDO, the deployment of anti-access and area denial (A2AD) technologies will not only limit evacuation to degrade the Golden Hour timeline for medical support but also constrain medical resupply, which will leave wounded Warfighters and first line medical support providers stranded in PC scenarios for unknown duration. Furthermore, repeated events of mass casualty and greater dependency on PC (i.e. limited resources) will increase the number of deaths from wounds as the infection rate will rise in these wounds within 72 hours and beyond as was observed in previous conflicts. Here, the amount of wound dressings and antibiotics needed to prevent infection from polytraumatic wounds based on current US military medical doctrine designed for “Golden Hour” doctrine are untenable in PC scenarios. As a result, the need for innovative solutions that are massively scalable and distributive (i.e. affordable and for all combatants) focused on amplifying self/buddy care (i.e. fire and forget solutions that enable less supply to be carried for longer duration or the ability of one medical provider to provide care for a high number of wounded casualties) is urgent. Furthermore, adding materials to the improved first aid kit (IFAK) or combat lifesaver (CLS) bag presents significant challenges. The critical need for wound infections and sepsis mitigation at point-of-care and Role1 is to design alternative and/or adjunctive solutions that prevent infection for the first 72 hours following injury. One approach is to reimagine components of IFAK as a system of systems to prevent the development of infection in polytraumatic wounds by extending treatment over 72 hours and buying time for surgical intervention. This topic explores the current CWMP (Combat pill pack, NSN 6505-01-548-5129) as a drug delivery device to specifically meet the need for fire and forget treatment of infection for at least 72 hours in prolonged care settings without the need to carry more pill packs and track of treatment administration.

In MDO (TRADOC PAM 525-3-1), especially those involving large scale combat operations, the deployment of Golden Hour medical doctrine from OEF and OIF is not tenable and new weapon systems by near-peer adversaries to deprive superiority on land, sea, and air anticipates accumulation of large volumes of casualties with complex wounds of wide variety without medical evacuation for surgical intervention for unknown duration. In this scenario, the ability to treat penetrating combat wounds for longer duration becomes paramount to limit mortality and morbidity. Operationally, the ability to treat even minor breaks in the skin and prevent infection underpins the instruments of maintaining combat power. Here, numerous studies have demonstrated that the timing of antibiotic treatment significantly correlated with the infection development process. Animal studies of open fractures revealed that early antibiotic treatment and surgical debridement within 2 hours prevented infection, but delayed administration of antibiotics and surgery after 2 hours significantly increased the development of infections. These observations were further validated in retrospective clinical studies in civilian trauma involving open fractures and further studies have revealed that administering antibiotics immediately after traumatic injury reduced infection rates significantly (i.e. 7% of infection if treated within one hour to

28% if treated after 1.5 hours). According to the Tactical Combat Casualty Care (TCCC) guidelines (available online), the initial response to injury recommends administration of moxifloxacin (400 mg, PO once a day) from the CWMP. The current CWMP also contains two slow-release bilayer Tylenol caplets (650 mg, PO every 8 hours) and meloxicam (15 mg, PO once a day). Unfortunately, adherence to CWMP intervention for injury patterns meeting indications set by TCCC guidelines is very low for a variety of reasons including hierarchy of life-saving interventions and lack of oral administration tolerance by casualties. The conceivable lack of a reasonable timeframe for medical evacuation in large scale combat operations and issues of compliance with CWMP intervention for the prevention of infections requires the adaption of PC to the new operational environment to meet the balanced need for ease-of-use, scalability, longevity treatment, and efficiency of treatment delivery focused on point-of-injury and Role 1 care.
The ultimate goal of the technology in this request is, but not limited to, to automate treatment delivery in a wearable format as a convergent technology to increase treatment delivery at the earliest time possible after injury for an extended duration without additional attention from a medical provider with respect to treatment administration for relevant injuries. In doing so, this convergent technology should prevent infection development, enable dose adjustment based on weight of warfighter, customize treatment, overcome compliance with the combat wound medication packet (CWMP) usage, and extend treatment duration all in one single step at point-of-injury and Role 1. The aim of this SBIR/STTR is to develop and commercialize a technology that addresses the unmet need of delayed definitive care and to accelerate the next generation of medical innovations that increase, but not limited to, the efficiency treatment delivery at point-of-injury and Role 1 care. Offerors are encouraged to familiarize themselves with the TCCC handbook, TCCC pharmacology, and field medicine literature.

When proposing a wearable technology, it is paramount, but not limited to, to consider the factors below:
1) The starting technology must plan to have or already has Food and Drug Administration (FDA) or equivalent clearance as a wearable device
2) The packing dimensions should not exceed CWMP generations (i.e. LxWxH- 2x2x0.5 in)
3) The system design should accommodate suitable formulations for the TCCC pharmacology and the route of administration for multiple days of application
4) Modular designs with a library of medications incorporating exchangeable cartridges, microneedles, micropumps, catheters, gels… etc. are welcomed, but should describe a ruggedization plan and durability of design
5) Designs must have a manual fail-safe backup option for motorized or automated designs. Use of adhesives must consider human skin safe products.
6) Treatment for prevention of infection shall start with TCCC pharmacology, but not limited to, other small molecule-based antibiotics, metal ions, lantibiotics, natural products, bacteriophages, antibodies, polymers, nano-fibers/sponges, antimicrobial peptides, and or any pathogen agnostic treatment. Stable formulations with long shelf-life should be considered.
7) Other treatments such as analgesics for pain management are optional but preferred
8) Dose customization features are optional
9) Built in sensors are optional
10) Ease of application, ability to withstand water, high positive and negative pressures, hot and cold temperatures and minimal storage conditions will be factored in the nomination process

PHASE I: Given the short duration of Phase I and the high order of technology integration required for Phase II, Phase I should focus on system design and development of proof-of-concept prototypes that address the treatment delivery requirement. Starting material may include off the shelf commercially available wearable technologies with proper agreements. Proposals may include different formulations of treatments. Prototypes may combine “classes” of applications into different “sets” of designs. At the end of this phase, fabricated prototypes should demonstrate feasibility, ease-of-use, proof-of-concept and establish “release profile”, using relevant test beds for the proposed technology. This phase should down-select designs as well as identify a pre-clinical animal model, such as, but not limited to, open fracture or

soft tissue wounds with and without infection for use in Phase II.

PHASE II: During this phase, the lead integrated system should be further refined from proof-of-concept into a viable product. Further optimization of technology for deep penetration of treatments and prevention of infection should be demonstrated during this phase. Evaluation of the product's efficacy both antimicrobial activity must include data for the first 6, 24, 48, and 72 hours at a minimum, if not longer. Qualitative and quantitative outcomes of product with regards to prevention of infection, and/or decolonization by invading organisms must be demonstrated as specific performance characteristics of the product. This testing should be controlled, and rigorous.. Testing and evaluation of the prototype to demonstrate operational effectiveness in simulated environments shall be demonstrated. Here, the selected offeror/contractor may choose but not required to coordinate or consult with WRAIR/NMRC for control of infection as testing site and models if needed. Contract research organizations (CROs) and Universities are suitable partners at the phase. Stability of product in an austere environment should be evaluated to include extreme conditions (i.e. extreme heat, cold, wet environment). This phase should also demonstrate evidence of commercial viability of the product. Accompanying application instructions, simplified procedures and training materials should be drafted in a multimedia format for use and integration of the product into market. The offeror may define and document the regulatory strategy and provide a clear plan on how FDA clearance will be obtained at the end of this phase. Offeror should also consider a pre-pre-submission communication with the FDA.

PHASE III DUAL USE APPLICATIONS: This phase should encompass both large animal models and randomized clinical trials that would require formal IRB approval as well as shelf-life optimization of at least 120 days to 2 years in austere environments. The ultimate goal of this phase is work closely with USAMMDA and the Warfighter Expeditionary Medicine and Treatment (WEMT) office to secure funds to develop and demonstrate a technology enabling the prevention of infection in wounded service members from infected traumatic combat wounds under PC with proper regulatory (FDA) clearance or authorization for human or Department of Defense use exemption. If funded, this effort will focus on coordinated activities to seamlessly integrate product into the TCCC paradigm of initial response to trauma. Once developed and demonstrated, the technology can be used both commercially in civilian or military settings to increase efficiency of treatment delivery. For instance, wound infections are projected to account for 27 billion dollars of the market size by 2026 and the post-surgical treatment care over 10 billion dollars. Performer should formulate a plan to penetrate this market. The selected contractor shall make this product available to potential military applications beyond prevention of infection to include analgesic, medical countermeasures for Chemical, Biological, Radiological, and Nuclear (CBRN) Injury, human performance augmentation solutions, and anti-sepsis treatment. Price estimate and comparison analysis for new design relative current fielded equipment shall be provided. The contractor should coordinate with Medical Research and Development Command (MRDC) to establish a National Stock Number (NSN) as the first step towards the potential inclusion into appropriate "Sets, Kits and Outfits" that are used by deployed medical forces in the Defense Acquisition System. If the product is transitioned into Acquisition Programs of Record, the Government may work with performer to harmonize design with other relevant products.

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# VERSION 4

KEYWORDS: MDO, drug delivery, wearable, trauma, prolonged care