Defense Health Agency (DHA)
2024.1 Small Business Innovation Research (SBIR)
Proposal Submission Instructions

INTRODUCTION

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

The Defense SBIR/STTR Innovation Portal (DSIP) is the official portal for DoD SBIR/STTR proposal submission. Proposers are required to submit proposals via DSIP; proposals submitted by any other means will be disregarded. Detailed instructions regarding registration and proposal submission via DSIP are provided in the DoD SBIR Program BAA.

Only Government personnel will evaluate proposal with the exception of the technical personnel from Cherokee LLC who will provide technical analysis in the evaluation of proposals submitted against DHA topic:

- Rapid Manufacturing of Personalized Braces and Splints for Musculoskeletal Injury

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

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

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

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

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

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

PHASE I PROPOSAL GUIDELINES

Technical Volume (Volume 2)

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

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

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

Please review the updated Percentage of Work (POW) calculation details included in the DoD Program BAA. DHA will occasionally accept deviations from the POW requirements with written approval from the Funding Agreement Officer.

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

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

Supporting Documents (Volume 5)
All proposing small business concerns are REQUIRED to submit the following documents to Volume 5:

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

Please refer to the DoD Program BAA for more information.

Fraud, Waste and Abuse Training (Volume 6)

DIRECT TO PHASE II PROPOSAL GUIDELINES

DHA Direct to Phase II Proposals are different than traditional DHA SBIR Phase I proposals. The chart below explains some of these differences.

	STANDARD DHA SBIR PROCESS	DHA D2P2 PROCESS
PHASE 1 TYPICAL FUNDING LEVEL	$250,000	None
PHASE 1 TECHNICAL *POP DURATION	6 months	None
PHASE 2 TYPICAL FUNDING LEVEL	$1,300,000	$1,300,000
PHASE 2 TECHNICAL *POP DURATION	24 months	24 months

*POP= Period of Performance

Direct to Phase II proposals must include all volumes, not to exceed maximum page limit, mentioned below, and must follow the formatting requirements provided in the DoD SBIR Program BAA.

A. DoD Proposal Cover Sheet (Volume 1)

B. Technical Volume (Volume 2):

   a. Part 1: Phase I Justification (20 Pages Maximum)

   b. Part 2: Phase II Technical Proposal (40 Pages Maximum)

C. Cost Volume (Volume 3)

D. Company Commercialization Report (Volume 4)

E. Supporting Documents (Volume 5)

F. Fraud, Waste, Abuse (Volume 6)

Technical Volume (Volume 2):

Phase I Justification: Offerors are **required** to provide evidence that the scientific and technical merit and feasibility have been established as described in the topic's description and Phase I.

Technical Proposal:

1. Results of current work – Discuss the objectives of your effort, the research conducted, findings or results, and estimates of technical feasibility.
2. Technical objectives and approach – List the specific technical objectives of the Direct to Phase II research and describe the technical approach in detail to be used to meet these objectives.
3. Work plan – The plan should indicate what is planned, how and where, a schedule of major events, and the final product to be developed.
4. Related work – Describe significant activities directly related to the proposed effort, including those conducted by the Principal Investigator, the proposing firm, consultants, or others. Report how the activities interface with the proposed project and discuss any planned coordination with outside sources. The proposers' awareness of the state-of-the art in the technology and associated science must be demonstrated.
5. Relationship with future research or Research and Development – State the anticipated results of the proposed approach if the project is successful. Discuss the significance of the effort in providing a foundation for a Phase III research or research and development effort.
6. Technology transition and commercialization strategy – Describe your company's strategy for converting the proposed SBIR research into a product or non-R&D service with widespread commercial use – including private sector and/or military markets. Note: The commercialization strategy is separate from the Commercialization Report. The strategy addresses how you propose to commercialize this research, while the Company Commercialization Report covers what you have done to commercialize the results of past awards.
7. Key personnel – Identify key personnel, including the Principal Investigator, who will be involved in the effort. List directly related education and experience and relevant publications (if any) of key personnel. A concise resume of the Principal Investigator(s) must be included.
8. Foreign Citizens – Identify any foreign citizens or individuals holding dual citizenship expected to be involved on this project as a direct employee, subcontractor, or consultant. For these

individuals, please specify their country of origin, the type of visa or work permit under which they are performing and an explanation of their anticipated level of involvement on this project. Proposing small business concerns frequently assume that individuals with dual citizenship or a work permit will be permitted to work on an SBIR project and do not report them. A proposal may be deemed nonresponsive if the requested information is not provided. Therefore, proposing small business concerns should report any and all individuals expected to be involved on this project that are considered a foreign national as defined in Section 3 of the BAA. You may be asked to provide additional information during negotiations to verify the foreign citizen's eligibility to participate on a SBIR contract. Supplemental information provided in response to this paragraph will be protected in accordance with the Privacy Act (5 U.S.C. 552a), if applicable, and the Freedom of Information Act (5 U.S.C. 552(b)(6)).

9. Facilities/Equipment – Justify items of equipment to be purchased (as detailed in the cost proposal), including Government Furnished Equipment (GFE). All requirements for government furnished equipment or other assets, as well as associated costs, must be determined and agreed to during contract negotiations. State whether the facilities where the proposed work will be performed meet environmental laws and regulations of federal, state (name) and local governments for, but not limited to, the following groupings: airborne emissions, waterborne effluents, external radiation levels, outdoor noise, solid and bulk waste disposal practices, and handling and storage of toxic and hazardous materials.
10. Consultants – Involvement of university, academic institution, or other consultants in the project may be appropriate. If such involvement is intended, it should be described in detail and identified in the Cost Volume.

Cost Volume (Volume 3):

The Cost Volume must contain a budget that does not exceed $1,300,000 for the entire 24-month Direct to Phase II period. Costs must be separated and clearly identified on the Proposal Cover Sheet (Volume 1) and in the Cost Volume (Volume 3).

Please review the updated Percentage of Work (POW) calculation details included in section 5.3 of the DoD Program BAA. DHA will occasionally accept deviations from the POW requirements with written approval from the Funding Agreement Officer.

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

Company Commercialization Report (Volume 4):

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

Supporting Documents (Volume 5):

All proposing small business concerns are REQUIRED to submit the following documents to Volume 5:

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

Please refer to the DoD Program BAA for more information.

Fraud, Waste and Abuse Training (Volume 6)

PHASE II PROPOSAL GUIDELINES

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

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

The Cost Volume must contain a budget for the entire 24-month Phase II period not to exceed the maximum dollar amount of $1,300,000. Budget costs must be submitted using the Cost Volume format (accessible electronically on the DoD submission site) and shall be presented side-by-side on a single Cost Volume Sheet.

DHA SBIR Phase II proposals have six volumes: Proposal Cover Sheets, Technical Volume, Cost Volume, Company Commercialization Report, Supporting Documents, and Fraud, Waste, and Abuse.

The Technical Volume has a 40-page limit including: table of contents, pages intentionally left blank, references, letters of support, appendices, technical portions of subcontract documents (e.g., statements of work and resumes) and any attachments. Technical Volumes that exceed the 40-page limit will be deemed non-compliant and will not be evaluated.

DISCRETIONARY TECHNICAL AND BUSINESS ASSISTANCE (TABA)

The DHA SBIR Program does not participate in the Technical and Business Assistance (formerly the Discretionary Technical Assistance Program). Contractors shall not submit proposals that include Technical and Business Assistance.

The DHA SBIR Program has a Transition Lead who provides technical and commercialization assistance to small businesses that have Phase I and Phase II projects.

EVALUATION AND SELECTION

All proposals will be evaluated in accordance with the evaluation criteria listed in the DoD SBIR Program BAA.

Proposing firms will be notified of selection or non-selection status for a Phase I award within 90 days of the closing date of the BAA. Non-selected companies may request feedback within 15 calendar days of the non-select notification. The Corporate Official identified in the firm's proposal shall submit the feedback request to the SBIR Office at usarmy.detrick.medcom-usamrmc.mbx.dhpsbir@health.mil. Please note feedback is provided in an official PDF via email to the Corporate Official identified in the firm proposal within 60 days of receipt of the request. Requests for oral feedback will not be accommodated. If contact information for the Corporate Official has changed since proposal submission, a notice of the change on company letterhead signed by the Corporate Official must accompany the feedback request.

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

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

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

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

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

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

ADDITIONAL INFORMATION

RESEARCH INVOLVING HUMAN SUBJECTS, HUMAN SPECIMENS/DATA, OR ANIMAL RESEARCH
Prior to contract award when an IRB is indicated, proposers must demonstrate compliance with relevant regulatory approval requirements that pertain to proposals involving human subjects, human specimens, or research with animals. If necessary, approvals are not obtained within two months of notification of selection, the decision to award may be terminated.

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

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

*NOTE: Exempt animal or human research use shall also reflect 'yes' on the proposal coversheet for USAMRDC ACURO and OHARO records.

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

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

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

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

> (1) The DoD Intramural Researcher must obtain a letter from his/her commanding officer or Military Facility director authorizing his/her participation in the Extramural Research project. This letter must be provided to the Extramural Organization for inclusion in the proposal or application.
>
> (2) The DoD Intramural Researcher must also coordinate with his/her local Resource Manager Office (or equivalent) to prepare a sound budget and justification for the estimated costs. Where there are no DoD-established reimbursement rates [e.g., institution review board (IRB) fees, indirect cost rates, etc.], the Military Facility's RM office (or equivalent) must provide details of how the proposed rates were determined. The DoD Intramural Researcher must use the budget and justification form enclosed in APAN 15-01 when developing the estimated costs and provide it to the Extramural Organization for inclusion in the proposal or application.
>
> (3) The Extramural Research proposal or application must include a proposed financial plan for how the Military Facility's Intramural Research costs will be supported [i.e., directly funded by DoD, resources (other than award funds) provided by the Awardee to the Military Facility, or award funds provided by the Awardee to the Military Facility (in accordance with the requirements below)].
>
> (4) The DoD Intramural Researcher should also coordinate with his/her technology transfer office.

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

DHA SBIR 24.1 Topic Index

DHA241-001 TITLE: Psoralen-UV-A Irradiation Based High-throughput Pathogen Inactivation Device

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

OBJECTIVE: Develop and validate a high-throughput psoralen/ultraviolet A(UV-A) based pathogen inactivation device capable of inactivating pathogens at a wide range of volumes (from 0.01 L to 50 L). The solution can facilitate rapid development of vaccines against any emerging infectious threats to protect civilian and military personnel against infectious diseases and reduce lost duty days.

DESCRIPTION: Emerging pathogens with epidemic and pandemic potential are a significant threat to US Forces that defend the homeland and US interests abroad. Historically, highly pathogenic novel viruses have impacted continuity of operations of US Forces with grave consequences. Recently, the COVID-19 pandemic has impacted operations, training, and military readiness across all services and has introduced quarantine and isolation challenges to the US Fleet carrying out freedom of navigation operations in the Pacific. It is imperative to develop, validate, and field an agile vaccine platform that can be rapidly adapted to produce a preventative countermeasure for the next emerging disease threat to US forces. To that end Naval Medical Research Command (NMRC) has developed a psoralen/UV-A based whole virus inactivation method in laboratory scale [1, 2]. NMRC has also developed and optimized a two-step chromatographic method to obtain highly purified psoralen inactivated whole virus vaccine candidates in large quantities to conduct preclinical immunogenicity and efficacy evaluations. We have prepared highly purified monovalent and tetravalent psoralen-inactivated dengue virus vaccines (DENV PsIVs) and a psoralen-inactivated SARS-CoV-2 (SARS-CoV-2 PsIV) vaccine candidate and evaluated their immunogenicity, efficacy and safety in animal models [3, 4]. Psoralen-UV-A based inactivation method can be easily adapted to develop whole cell inactivated vaccines against any pathogen including bacteria, viruses, and parasites, and has a great potential as an agile vaccine platform to rapidly develop vaccines against emerging infectious threats. Based on the preclinical immunogenicity data NMRC is currently working on establishing a contract with a commercial manufacturing organization to make SARS-CoV-2 PsIV under cGMP conditions to conduct a first in human Phase 1 clinical trial. However, our efforts to manufacture the GMP product is hampered by lack of a suitable psoralen/UV-A inactivation device for effectively inactivating pathogens at large enough volumes (10 mL – 50 L batches) under cGMP conditions. The prototype device developed in this SBIR topic should have the capability to inactivate pathogens in 10 mL to 50 L volume using psoralen and UV-A irradiation and the ability to adjust and optimize the parameters such as flow rate of the pathogen solution into and out of the UV-A irradiation chamber, time of UV-A irradiation and the total UV-A energy applied to the pathogen solution for achieving a complete pathogen inactivation without degrading the antigenic proteins. Availability of such a high-throughput psoralen-inactivation device for manufacturing the GMP product will significantly advance the psoralen-inactivated whole cell vaccine platform as an agile vaccine platform against emerging infectious diseases. This pathogen inactivation device can also be used for rapid inactivation of pathogens requiring high containment (BSL-3 and BSL-4 laboratories) without degrading their surface proteins and antigens before bringing them out of the BSL-3 or BSL-4 lab for antigen discovery and characterization.

PHASE I: The main goal of Phase I is a feasibility study towards developing a prototype high throughput UV-A irradiation device capable of handling 10 mL to 50 L volume of pathogens at high titers (greater than 1011 PFU or CFU per mL) while uniformly delivering the UV-A energy to the pathogen solution to achieve complete inactivation of the pathogen. NMRC Tech Transfer office and NMRC legal will work with the small business to license or otherwise distribute prior technology findings from NMRC to awardees at no cost. The proposed psoralen-UV-A irradiation should be a flow through inactivation device with inlets for pumping psoralen/pathogen mixtures into to the UV-A-irradiation chamber with a control the flow rate, and capable of uniformly delivering the UV-A energy to the entire

psoralen/pathogen mixture as it flows within the UV-A chamber, and an outlet from the UV-A irradiation chamber to collect the psoralen/UV-A processed inactivated pathogen into an appropriate bioprocessing container for downstream vaccine development processes. The prototype device should include the software and control switches necessary to regulate/adjust all the parameters including flow rate, stop and start flow, amount of UV-A energy applied (microjoules/second/cm2), and the time of application of UV-A energy. The design should include selection of tubing and materials that are low binding to ensure minimal loss of biological material during the inactivation process. Device design should allow for adjusting the total inactivation volumes of pathogens as required.

Phase I deliverables:

- Data demonstrating flow-through inactivation of 10 mL – 5 L of a virus, using psoralen-UV-A irradiation-based pathogen inactivation method/device.

PHASE II: The main objective of Phase II is to develop and produce a fully functional prototype high throughput UV-A irradiation device that is capable of handling 10 mL to 50 L volume of pathogens at high titers (greater than 1011 PFU or CFU per mL) while uniformly delivering the UV-A energy to the pathogen solution to achieve complete inactivation of the pathogen. The major components of the device should include a) an inlet to add specific amount of psoralen derivative to the entire volume of the pathogen, b) an inlet to the UV-A-irradiation chamber and a pump to control the flow rate, c) the UV-A irradiation chamber capable of uniformly delivering the UV-A energy to the entire pathogen solution contained within the UV-A chamber, d) control switch to regulate/adjust the amount of UV-A energy applied to the pathogen solution, and an outlet from the UV-A irradiation chamber to collect the psoralen/UV-A processed inactivated pathogen into an appropriate bioprocessing container for downstream vaccine development processes. The prototype device should include the software and control switches necessary to regulate/adjust all the parameters including flow rate, stop and start flow, UV-A energy applied (microjoules/second/cm2), and the time of application of UV-A energy.

Phase II deliverables:

- One fully functional prototype psoralen-UV-A irradiation-based pathogen inactivation device with data demonstrating complete inactivation of 50 L of Dengue virus.

PHASE III DUAL USE APPLICATIONS: The main target of this high throughput psoralen/UV-A irradiation-based pathogen inactivation device is the GMP vaccine manufacturers who will be making the whole cell inactivated vaccines. Whole virus inactivated vaccines occupy a large proportion of the global viral vaccines market since they elicit a broad range of immune responses and have several advantages including safety and relatively low production cost. The global inactivated vaccines market is expected to increase by more than 10% from 2022 to 2027 (https://www.globalmarketestimates.com/market-report/inactivated-vaccine-market-3754). Formaldehyde and β-propiolactone, the chemicals currently used for making whole virus inactivated vaccines, are less than optimal since they alter the immunogenic proteins and are considered carcinogenic. Psoralen compounds on the other hand do not affect the immunogenic proteins and have been shown to be safe for use in biopharmaceutical applications. Therefore, after successfully delivering the prototype device and completing this SBIR phase II, the vision is for the small business to make a commercially viable psoralen/UV-A-based inactivation device by partnering with vaccine manufacturers. This device can be marketed for making psoralen-inactivated vaccines against a broad range of diseases caused by viruses including influenza, poliovirus, hantavirus and rabies virus. Availability of such a high-throughput psoralen-inactivation device for manufacturing the GMP product with a basic instrument manual with operating instructions to regulate/adjust the device parameters and anticipated troubleshooting guidelines (in accordance with FDA guidelines) will significantly advance the psoralen-inactivated whole vaccine platform as an agile vaccine platform against emerging infectious threats. This pathogen inactivation device can also be marketed for rapid inactivation of contaminants during biopharmaceuticals production such as recombinant proteins and

other therapeutic agents. It can also be marketed to academic and environmental scientists for inactivating high containment (BSL-3 and BSL-4 laboratories) pathogens without degrading their surface proteins and antigens before bringing them out of the BSL-3 or BSL-4 lab for antigen discovery and characterization. A basic instrument manual with operating instructions to regulate/adjust the device parameters and anticipated troubleshooting guidelines.

REFERENCES:

1. Raviprakash K, Sun P, Raviv Y, Luke T, Martin N, and Kochel T, Dengue virus photo-inactivated in presence of 1,5-iodonaphthylazide (INA) or AMT, a psoralen compound (4'-aminomethyl-trioxsalen) is highly immunogenic in mice. Hum Vaccin Immunother, 2013. 9(11): p. 2336-41. hvi-9-2336.pdf (nih.gov).
2. Maves RC, Ore RM, Porter KR, and Kochel TJ, Immunogenicity and protective efficacy of a psoralen-inactivated dengue-1 virus vaccine candidate in Aotus nancymaae monkeys. Vaccine, 2011. 29(15): p. 2691-6 https://doi.org/10.1016/j.vaccine.2011.01.077.
3. Sundaram AK, Ewing D, Blevins M, Liang Z, Sink S, Lassan J, Raviprakash K, Defang G, Williams M, Porter KR, and Sanders JW, Comparison of purified psoralen-inactivated and formalin-inactivated dengue vaccines in mice and nonhuman primates. Vaccine, 2020. 38(17): p. 3313-3320. https://doi.org/10.1016/j.vaccine.2020.03.008.
4. Sundaram AK, Ewing D, Liang Z, Jani V, Cheng Y, Sun P, Raviprakash K, Wu S-J, Petrovsky N, Defang G, Williams M, and Porter KR, Immunogenicity of Adjuvanted Psoralen-Inactivated SARS-CoV-2 Vaccines and SARS-CoV-2 Spike Protein DNA Vaccines in BALB/c Mice. Pathogens, 2021. 10(5): p. 626. • DOI: 10.3390/pathogens10050626.

KEYWORDS: Psoralen inactivation of pathogens, UV-A irradiation, Psoralen-inactivated pathogen, Whole virus inactivated vaccine, Emerging infectious diseases, Agile vaccine platform

DHA241-002 TITLE: Development of a Junctional Tourniquet

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

OBJECTIVE: To rethink the form factor and engineering approach of existing junctional tourniquets, providing reliable control of junctional hemorrhage. Such a solution must be readily accessible at the point of injury and designed to be user-friendly and intuitive, enabling use by non-medical personnel for self-aid and buddy care scenarios.

DESCRIPTION: Exsanguination from massive blood loss accounts for more than 80% of potentially survivable battlefield deaths [1]. A junctional tourniquet solution would address the 32% of these fatalities that arise from uncontrollable extremity and junctional bleeding [2]. Junctional tourniquets apply external compression to stop blood flow in the groin and axilla, i.e., at the junction of the trunk and the appendages. Junctional indication demands precise placement and, ideally, single-point pressure. The tourniquet design must ensure user accuracy in high-stress situations. Currently, four designs meet FDA approval and have shown effectiveness in occlusion under controlled conditions [3]. This topic seeks a form factor that allows for fast and easy application by non-medical personnel with minimal training.

When proposing a technology, consider the following factors:

- The device should be able to control a junctional bleed within about one minute as operated by a trained user.
- Ideally, a well-designed junctional tourniquet can replace the use of an extremity tourniquet.
- The total weight of the device should be under 1.5 lbs. The stored volume should be no more than 500 cubic inches to remain minimal for transport and individual warfighter use.
- The design should be amenable to one handed use.
- Engineer the device to efficiently manage both upper and lower junctional hemorrhage through compression of axillary and femoral arteries, respectively.
- Ensure the device's availability at the point of injury, i.e., it must be able to be commonly carried.
- Use of the device shall be simple with minimal steps. Anatomical knowledge should not be required for operation of the device. Device shall not require more than 2 hours of standardized training.
- The tourniquet design should address stability over time, including factors such as physiological response to hemorrhage, type of uniform, surface conditions (blood or rain) and transport.
- The materials should have the ability to withstand dirt/dust/sand, UV exposure, fresh and salt water, hot and cold temperatures, requiring minimal special storage conditions.
- Engineering solutions should require minimum logistical/technical support.

PHASE I: Phase I feasibility will be demonstrated through evidence of: a completed proof of concept/principal or basic prototype system; definition and characterization of framework properties/technology capabilities desirable for both Department of Defense/Government and civilian/commercial use; and capability/performance comparisons with existing state-of-the-art technologies/methodologies (competing approaches).

Phase I-type effort: conduct a study to determine the technical feasibility (as demonstrated through clinical data, benchtop testing, etc.), end-user human factors testing and an initial design of a junctional tourniquet.

PHASE II: During this phase, the offeror will advance the system towards TRL 4, refining it from a proof-of-concept. The design should be optimized for efficacy and qualitative and quantitative hemorrhage control outcomes should be demonstrated to include metrics such as the time to apply to occlusion and percentage of successful occlusion attempts (i.e., how does the tourniquet fit different

anthropomorphic types). Testing and evaluation of the prototype to demonstrate operational effectiveness in simulated stressful environments should be demonstrated. Stability of the product over time (to include considerations for physiological response to hemorrhage, type of uniform, surface conditions (bloody or wet) and transport) and survivability of the materials under extreme conditions (heat, cold, wet, UV and dirt/dust) should be demonstrated. Draft application instructions, procedures, technical specifications, and training materials should be provided for technical and end-user evaluation. A major criteria for acceptance by the end-user will be a favorable form factor in order for the device to be carried at all times. The offeror should plan to deliver fifteen example prototypes at the end of the Phase II effort for Government evaluation. The offeror shall articulate the regulatory strategy and provide a clear plan on how FDA clearance will be obtained.

PHASE III DUAL USE APPLICATIONS: The goal of this phase is to secure an FDA approved device and demonstrate effectiveness and usability for the military and civilian end-user. Funding from either a non-SBIR Government source (e.g., Navy Advanced Medical Development, U.S. Army Medical Materiel Development Activity's Warfighter Expeditionary Medicine and Treatment Project Management Office, Marine Corps System Command, Joint Warfighter Medical Research Program), the private sector, or both should be investigated to develop the prototype into a viable product for sale in military and/or private sector markets. Civilian end-users can include police, fire and medical first responders, hospitals, air ambulance and evacuation, recreational medical services such as lifeguards and ski patrol, and emergency management agencies. Scenarios requiring junctional tourniquets can include automobile and motorcycle accidents, industrial accidents, mass shootings, terrorist incidents and natural disasters.

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KEYWORDS: Hemorrhage Control, Tourniquet, Combat Casualty Care, En Route Care, Mass Casualty, Prolonged Field Care, Trauma, Junctional, Extremity, Care Under Fire, Buddy Care

DHA241-D001 TITLE: Rapid Manufacturing of Personalized Braces and Splints for Musculoskeletal Injury

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): Military Operational Medicine

OBJECTIVE: This topic is intended for technology proven ready to move directly into Phase II and is accepting Direct to Phase II proposals only. To develop a manufacturing framework to rapidly produce personalized, human-usable braces and splints with no-to-minimal manual intervention. The solution can accelerate musculoskeletal injury recovery, reduce the need for medical evacuation, and facilitate Warfighter readiness, while mitigating the impact on logistics and storage limitations in military environments and medical treatment facilities.

DESCRIPTION: The DoD lacks the capability to rapidly manufacture rehabilitation devices and equipment in areas where space and/or storage requirements are minimal. Musculoskeletal injuries (MSKIs) are the largest burden of injury for the U.S. military [1]; with 85% of service members medically evacuated following an MSKI not returning to theater [2]. Rehabilitative braces and splints are commonly used to manage and rehabilitate MSKIs. Braces and splints provide partial rigidity to protect and stabilize an injury, while still allowing some movement where needed. Current off-the-shelf braces and splints come in various sizes and designs for different body parts, sides, and injuries. The quantity potentially needed presents a significant challenge for adequately stocking these items where, when, and for whom they are needed. Currently, specific braces are manufactured, selected, transported, and stored, based on anticipation of how many of each type of brace will be required. This is of particular concern in military environments, particularly deployed and maritime care settings, where space may be limited, and the need exists to improve the medical readiness of someone with minor injuries. There is currently no role of care requirements; however, this technology is envisioned in a Role of Care 2/en route care setting.

Additive manufacturing can reduce the logistical burden of transporting and storing an array of medical supplies. Currently, applications of 3D printed technology are growing in popularity within medicine [3], with applications in orthopedics being used for personalized implants and customized prostheses [4]. As 3D printing advances, it may provide innovative solutions, such as becoming a more personalized and accessible option than off the shelf bracing/splinting [4]. The desired end stage product/system will be able to rapidly manufacture personalized braces and splints onsite and on-demand for MSKI to accelerate recovery, reduce the need for medical evacuation, and facilitate Warfighter readiness. Desired products contain both flexible and semi-rigid elements, depending on the nature of the injury. Moreover, the ideal solution should have the potential to provide an array of bracing/splinting products across various MSKIs to promote Warfighter return to duty.

PHASE I: This topic is intended for technology proven ready to move directly into Phase II. Therefore, the offeror must be able to demonstrate and provide documentation to substantiate that the scientific and technical merit and feasibility described in Phase I has been met and describes the potential commercial applications. Documentation should include all relevant information including, but not limited to technical reports, test data, prototype designs/models, and performance goals/results.
Completed Phase I efforts should demonstrate research and development towards a rapid fabrication solution for personalized bracing or splinting technology that requires minimal manual intervention. Feasible and practical solutions have the potential to combine the rigidity of personalized 3D-printed elements with flexible textiles, garments, or similar materials. Completed efforts should additionally demonstrate research and development towards a solution that can be customized based on user anthropometrics for braces/splints to be worn for lower and/or upper extremity musculoskeletal injuries. The fabrication framework is expected to minimize the logistical footprint and be used within a setting with access to power.

PHASE II: Design and develop the practical implementation of the system that incorporates the previously completed Phase I methodology toward a technology that can rapidly, and optimally generate personalized braces or splints with minimal manual intervention. Product development can be an innovation of existing technologies. Semi-rigid elements combined with textiles or soft materials and fastening or securing materials make up the key design elements. Designs should be capable of personalization to user size and anthropometrics, injury location, right/left side. They should also be capable of personalization based on requirements for mobility (e.g. semi-flexible to semi-rigid). Input requirements (manual measurements, scans, etc.) are not pre-defined. Testing and implementation should be relevant to Warfighters who have sustained an upper and/or lower extremity MSKI. The framework/system begins with a scan or computer-based inputs and the output is the final brace/splint. The user inputting the data or scans may be a clinician. The end recipient is the injured patient. The test-case for the output of this Phase II will be a single ankle brace/splint and hand/wrist brace/splint as a proof of concept, with a request for a physical prototype. The Phase II development should focus on a clinician interface for personalization inputs and the rapid-manufactured, personalized bracing/splinting solution outputs for human-usable production. Technical specifications should focus on a framework that can fit (dimension and weight-wise) on a table/desk and are expected to produce a product in an operational environment. Material selection considerations for environmental exposure during hot and cold weather operations should be considered. Frameworks that have the potential to interface with additive manufacturing systems that are multi-purpose are desirable. Systems can expect to be supplied by a standard 120V/60Hz outlet. The offeror shall articulate the regulatory strategy and provide a clear plan on how FDA clearance will be obtained.

PHASE III DUAL USE APPLICATIONS: The goal of this phase is to secure an FDA approved device and demonstrate effectiveness and usability for the military and civilian end-user. Finalization and validation of the prototype and terminal system involves producing comfortable, durable, and easily applied braces/splints that adhere to similar biomechanical outcomes as off-the-shelf models. The target market should be the commercial market for sustainability. The final commercialized product will likely integrate into a clinical practice setting, account for coding/billing requirements, complete cost/benefit analyses, identify training/education requirements (if needed), and account for socialization/broader outreach. Expected dual use of the end-product may extend to the needs of civilians and individuals post-military, such as orthopedic and VA rehabilitation facilities, urgent care centers with limited overhead, remote care settings, mobile care units, sports medicine, and other physical medicine situations. Thus, procurement by the government is likely post-commercialization by industry.

MSKIs are an immense burden in global healthcare and present a significant challenge to military readiness; therefore, innovative technology that has the potential to provide a rapid, personalized brace/splint to accelerate recovery and shorten the period in which a Warfighter can return to duty is desirable.

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KEYWORDS: Rehabilitation, Brace, Injury, Musculoskeletal, Individualized Medicine; Additive manufacturing

DHA241-D002 TITLE: Wireless, Wearable Personal Metabolic Sensor

OUSD (R&E) CRITICAL TECHNOLOGY AREA(S): Military Operational Medicine

OBJECTIVE: This topic is intended for technology proven ready to move directly into Phase II and is accepting Direct to Phase II proposals only. A low-cost sensor that accurately measures oxygen consumption (VO2) and carbon dioxide production (VCO2) and provides immediate feedback that Service Members can use to improve fitness, refueling practices, body composition and readiness. If fielded, may require additional security measures. Designs that limit connectivity to Bluetooth (BT) are discouraged.

DESCRIPTION: The wide prevalence of metabolic dysfunction, emanating from low physical fitness, low physical activity, and obesity, is a public health concern and a national security issue across all service branches and phases of a military career, including recruitment, retention, training, deployment, and retirement from service [1,2]. The military needs new ways to optimize metabolic health of the nondeployed force and ensure sufficient and consistent warfighter fitness levels.
Athletes tailor their daily diet and physical activity routines to optimize metabolic health, body composition and physical performance [3]. Service members could do likewise, guided by actionable information provided by a personal non-invasive metabolic measurement and tracking device. Such a device would use a classic technique known as indirect calorimetry where volumetric rates of oxygen consumption (VO2) and carbon dioxide production (VCO2) are measured, and metabolic energy expenditure and metabolic fuel selection (fats versus carbohydrates) determined.

Providing service members with and easy-to-use device, capable of on-demand measurements of respiratory gas exchange and determination of energy expenditure and metabolic fuel mix, would enable individuals, small military units, and the groups that support them, to design and implement personalized diet and exercise regimens. This individualized metabolic feedback would directly support at-risk military personnel who need to meet professional standards for body composition and physical fitness and avoid the consequences of failure which can extend to separation from service.

Existing wearable systems capable of respiratory gas exchange measurements outside of a laboratory are (a) too large, heavy (~1kg), and challenging to operate, and too expensive for routine day-to-day use by large groups of minimally trained individuals, or (b) are small and simple to use but inaccurate and/or have limited capabilities (e.g., only measure VO2, only make resting measurements). However, new research and improvements in O2 and CO2 sensor technology suggest a compact, accurate, simple-to-use, cost-effective and scalable metabolic measurement device for use by individuals is achievable.

PHASE I: This topic is accepting Direct to Phase II (DPII) proposals ONLY. Therefore, the offeror must provide documentation to substantiate that the scientific and technical merit and feasibility described above and in Phase I has been met and describes the potential commercial applications.
Proof of feasibility includes a wireless, wearable, low-cost personal metabolic device prototype is sought to enable hands-free on-demand VO2 and VCO2 measurements, data recording, and wireless streaming to a platform-agnostic hand-held device of data to include derived metrics (e.g., metabolic energy expenditure (EE), fuel substrate mix, respiration rate). The body-worn device should be light-weight (<300g), compact, simple to use, tolerant of rain and ambient temperatures above freezing, and capable of confirming system device gas sensor calibration by referencing ambient air O2 and CO2 concentrations. Battery life should support at least 14 h of on-demand measurements. Errors of <10% in measurement of VO2 and VCO2 from rest to high intensity exercise is desired. A rigorous case and supporting data for technical and commercial viability must be presented. Evidence that the proposed solution will be viable, with adequate risk-mitigation. A proof-of-concept breadboard or early prototype with key components identified and accuracy quantified by means of a metabolic simulator (e.g., mechanical breath simulator

with injectable gas mixtures) is desirable. This Phase shall include a detailed discussion of the approach and feasibility of producing a prototype sensor for follow-on lab and human testing.

PHASE II: Expected military users of the technology are both individuals desiring to track impact of diet and exercise on metabolic health and performance as well as small-to-medium military units engaged in training or mission-planning activities. Ease of use in field environments is an important characteristic of the desired technological solution. The developed technology should be durable and readily applicable in resource-limited field conditions, be designed for at least 14 hours of use before recharging of battery. Gas sensor calibration accuracy must be able to be confirmed using ambient air reference. The offeror should consider final procurement cost as well as system operation and maintenance costs, creation of instruction manuals, definition of replacement/warranty policies, and training requirements for users. A user manual is desirable.Offeror will design, fabricate, integrate and test at least two prototype wireless, body-worn personal- use metabolic devices, and demonstrate accuracy of measured (e.g., O2, CO2, respiration) and derived parameters (e.g., Respiratory Exchange Ratio (RER), EE) using a mechanical lung simulator and injection of certified dry gas mixtures. The device must be suitable for use in field training environments where user(s) can stream data from the device, and record meta data (e.g., events) on the device, via Bluetooth Low Energy (BLE). The device shall be: 300g or less; attachable to standard Army MOLLE webbing; capable of sampling breath without headgear removal; capable of making measurements from rest (peak flow < 15 L/min) to intense exercise (peak flow > 350 L/min) with a respiratory burden <2" H2O; capable of simple field gas calibration check and recalibration; capable of detecting onset of breathing and storing all raw data measured; and capable of accurately measuring VO2 and VCO2 with average EE and RER errors of <10% and <15%, respectively, over a RER (VCO2:VO2) range of 0.7-to-1.2. Documentation should include, but is not limited to, technical reports, test data, prototype designs/models, and performance goals/results.

If experimentation with human test volunteers is planned, the offeror must provide a detailed plan for compliance with all applicable rules and regulations regarding the use of human subjects, to include Institutional Review Board approval(s). Specifically, the proposed experimentation with human test volunteers must be reviewed for compliance with Federal, Department of Defense (DoD), and Army human subjects protection requirements and receive approval by the Office of Human and Animal Research Oversight (OHARO) Office of Human Research Oversight (OHRO) prior to implementation; this requirement derives from DoDI 3216.02 and the Defense Federal Acquisition Regulation Supplement requirement for Human Research Protection Official (HRPO) review of DoD-supported human subjects research.

Prototype Requirements: Offeror will provide two physical prototypes that include the following features and specifications: body-worn; accurate O2 and CO2 measurement of expired air; accurate volumetric measurement of inspired and expired air; calculation of accurate parameters (Respiratory Exchange Ratio and Energy Expenditure); demonstration of successful Bluetooth connectivity; demonstration of adequate device storage for up to 14 hours of minute-by-minute metabolic data collection; demonstration of adequate battery life for up to 14 hours of operation; weight of less than 300 grams; demonstration of accurate measurements ranging from rest to vigorous exercise; demonstration of ease of use; demonstration of simple calibration techniques. Error rates for measurements must be < 10% for energy expenditure (EE) and < 15% for respiratory exchange ratio (RER).

PHASE III DUAL USE APPLICATIONS: Phase III will include manufacturing planning. Markets envisioned include commercial and recreational entities responsible for performance and metabolic health with a particular emphasis on the impact of diet on metabolic fuel substrate, body glycogen (carbohydrate) stores and body composition. For both military and civilian applications the device will provide individuals with guidance regarding body weight management. optimized nutrition, and training

for endurance and strength events. If the derived metrics include any diagnostic capabilities, all applicable Federal Drug Administration review and certification requirements must be met.

Commercial applications would target the clear gap between very expensive research-grade metabolic sensor systems, and inexpensive but less-capable systems with a low-cost easy-to-use metabolic sensor that provides immediate feedback to individuals seeking to improve their health and quality of life through improved physical fitness, dietary practices, and body muscle and fat mass management. The metabolic sensor would be a key new lightweight user-friendly resource for use in fitness facilities by personal trainers designing and monitoring specialized training and weight reduction programs. Additionally, the metabolic sensor would be used by athletes and sports teams across a wide range of sporting disciplines and age. It is expected that athletes from high school to professional would benefit from a device that provides individualized feedback to maximize training and performance. The individuals that could benefit range from athletes [3] to the large group of Americans who are either prediabetic (96 million) or diabetic (37.3 million) [2].

Military physical training programs across the Joint services are potential beneficiaries of this product. Likely end users of the metabolic sensor are the Armed Forces Wellness Centers (AFWC), which provide programs and services that improve and sustain health, performance, and readiness of military personnel. The AFWC staff are active users of sophisticated wearable metabolic monitoring systems, but have a clear need for more cost-effective, accurate, and easy-to-use indirect calorimeter systems. Another example of where metabolic sensor systems could be used by the DoD is in support of the US Army's Holistic Health and Fitness (H2F) program.

Armed Forces Wellness Centers:
https://phc.amedd.army.mil/topics/healthyliving/al/Pages/ArmyWellnessCenters.aspx
US Army's Holistic Health and Fitness (H2F) program:
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KEYWORDS: Metabolic energy expenditure, indirect calorimetry, personal metabolic sensor, metabolic health, diet, exercise, aerobic fitness, body fat management.