

**DEFENSE HEALTH PROGRAM (DHP)**  
**16.1 Small Business Innovation Research (SBIR)**  
**Proposal Submission Instructions**

The DHP SBIR Program seeks small businesses with strong research and development capabilities to pursue and commercialize medical technologies.

Solicitation, topic, and general questions regarding the SBIR Program should be addressed according to the DoD Program Solicitation. For technical questions about the topic during the pre-release period, contact the Topic Authors listed for each topic in the Solicitation. To obtain answers to technical questions during the formal Solicitation period, visit <https://sbir.defensebusiness.org/sitis>.

**PHASE I PROPOSAL SUBMISSION**

Follow the instructions in the DoD Program Solicitation at <http://www.acq.osd.mil/osbp/sbir/solicitations/index.shtml> for program requirements and proposal submission.

SBIR Phase I Proposals have four Volumes: Proposal Cover Sheets, Technical Volume, Cost Volume and Company Commercialization Report. 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 include blank pages, duplicate the electronically generated cover pages or put information normally associated with the Technical Volume in other sections of the proposal as these will count toward the 20-page limit.

Only the electronically generated Cover Sheets, Cost Volume and Company Commercialization Report (CCR) are excluded from the 20-page limit. The CCR is generated by the proposal submission website, based on information provided by you through the Company Commercialization Report tool. Technical Volumes that exceed the 20-page limit will be reviewed only to the last word on the 20<sup>th</sup> page. Information beyond the 20<sup>th</sup> 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 solicitation must complete the Cost Volume using the on-line form, within a total cost of \$150,000 over a period of up to six months.

The DHP SBIR Program will evaluate and select Phase I proposals using the evaluation criteria in Section 6.0 of the DoD Program Solicitation. Due to limited funding, the DHP 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 solicitation, and unsolicited proposals, will not be considered. Awards are subject to the availability of funding and successful completion of contract negotiations.

**PHASE II PROPOSAL SUBMISSION**

Beginning with SBIR Phase II's resulting from a 13.1 Phase I award, invitations are no longer required.

All Phase I awardees from this Solicitation will be allowed to submit an initial Phase II proposal for evaluation and selection. The details on the due date, content, and submission requirements of the initial Phase II proposal will be provided by the DHP SBIR Program Office either in the Phase I award or by subsequent notification. All SBIR Phase II awards made on topics from solicitations prior to FY13 will be conducted in accordance with the procedures specified in those solicitations.

Small businesses submitting a Phase II Proposal must use the DoD SBIR electronic proposal submission system (<https://sbir.defensebusiness.org/>). 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 at (1-800-348-0787) or Help Desk email at [sbirhelp@bytecubed.com](mailto:sbirhelp@bytecubed.com) (9:00 am to 6:00 pm ET).

Section 4(b)(1)(ii) of the SBIR Policy Directive permits the Department of Defense and by extension the DHP SBIR Program, during fiscal years 2012 through 2017, to issue a Phase II award to a small business concern that did not receive a Phase I award for that Research/Research & Development. The DHP SBIR Program will NOT be exercising this authority for Phase II awards. In order for any small business firm to receive a Phase II award, the firm must be a recipient of a Phase I award under that topic.

The DHP SBIR Program will evaluate and select Phase II proposals using the evaluation criteria in Section 8.0 of the DoD Program Solicitation. Due to limited funding, the DHP 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 technology transition and commercialization plan describing feasible approaches for transitioning and/or commercializing the developed technology in their Phase II proposal. DHP SBIR Phase II Cost Volumes must contain a budget for the entire 24 month Phase II period not to exceed the maximum dollar amount of \$1,000,000. 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. The total proposed amount should be indicated on the Proposal Cover Sheet as the Proposed Cost.

DHP SBIR Phase II Proposals have four Volumes: Proposal Cover Sheets, Technical Volume, Cost Volume and Company Commercialization Report. 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 pages 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<sup>th</sup> page. Information beyond the 40<sup>th</sup> 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.

### **DISCRETIONARY TECHNICAL ASSISTANCE**

In accordance with section 9(q) of the Small Business Act (15 U.S.C. 638(q)), the DHP SBIR Program will provide technical assistance services to small businesses engaged in SBIR projects through a network of scientists and engineers engaged in a wide range of technologies. The objective of this effort is to increase DHP SBIR technology transition and commercialization success thereby accelerating the fielding

of capabilities to Soldiers and to benefit the nation through stimulated technological innovation, improved manufacturing capability, and increased competition, productivity, and economic growth.

The DHP SBIR Program has a Technical Assistance Advocate (TAA) available to provide technical assistance to small businesses that receive Phase I and Phase II contracts. As noted in Section 4.22 of this solicitation, firms may request technical assistance from sources other than those provided by the DHP SBIR Program. All such requests must be made in accordance with the instructions in Section 4.22.

PLEASE NOTE: If approved for discretionary technical assistance from an outside source, the firm will not be eligible for the DHP's Technical Assistance Advocate support.

## **PHASE II ENHANCEMENTS**

The DHP 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/non-STTR government program or Private sector investments. Phase II Enhancements allow for an existing Phase II DHP SBIR contract to be extended for up to one year per Phase II Enhancement application, to perform additional research and development. Phase II Enhancement matching funds will be provided on a one-for-one basis up to a maximum \$500,000 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.

## **RESEARCH INVOLVING ANIMAL OR HUMAN SUBJECTS**

The DHP SBIR Program discourages offerors from proposing to conduct Human or Animal Subject Research during Phase I due to the significant lead time required to prepare the documentation and obtain approval, which will delay the Phase I award.

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

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

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

## **FOREIGN NATIONALS**

If the offeror proposes to use a foreign national(s) [any person who is NOT a citizen or national of the United States, a lawful permanent resident, or a protected individual as defined by 8 U.S.C. 1324b (a)(3) – refer to Section 3.5 of this solicitation for definitions of “lawful permanent resident” and “protected individual”] as key personnel, they must be clearly identified. For foreign nationals, you must provide 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. Please ensure no Privacy Act information is included in this submittal.

## **DHP SBIR 16.1 Topic Index**

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DHP16-002	Severe Trauma Female Simulation Training System
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DHP16-008	Selective Brain Cooling for Traumatic Brain Injury
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## DHP SBIR 16.1 Topic Descriptions

DHP16-001 TITLE: Warrior Health Avatar

TECHNOLOGY AREA(S): Biomedical

**OBJECTIVE:** Develop and demonstrate a simulation framework and physiology based modeling tools of a warfighter body that could enable definite assessment of his/her health status, physical and physiological performance, and injury trajectory by both the user and medical personnel using mobile computing platforms.

**DESCRIPTION:** The experience of recent military conflicts indicates that highly trained medical personnel and combat casualty care physicians, at all levels in the theater, from the far-forward to field hospital to rehabilitation centers, are able to save lives of wounded soldiers at unprecedented rates. However, evolving asymmetric threats and smaller, more dispersed military operations may not have the advantage of the organized logistics and casualty care systems and will rely on self- and buddy-care. As the U.S. Military's medical training requirements continue to increase in scope and complexity the resources, including time, manpower, and funding, are becoming limited [CBO 2014]. Therefore, new medical technologies are needed to advance warfighter medical skills in primary and combat casualty care. In the last few years, remarkable progress has been achieved in personalized medicine, wearable physiological and activity sensors, mobile computing, bioinformatics and computational medicine. All of these technologies could be integrated in an advanced platform, a Warrior Health Avatar, to support growing demands for preventive and primary medical military health care as well as acute and combat trauma care.

In spite of spectacular progress in wearable, non-invasive biomedical sensor technology, which can collect large amount of physiological, physical activity and environmental data, there are no established methods to utilize that data in a predictive fashion [Friedl 2007]. Typical physiological sensor data processing algorithms involve data mining and stochastic correlations which have limited predictive capability. A fundamental, physiology based, "personalizable" mathematical model of a human body, calibrated on broad range of physiological and clinical data, could provide the predictive capability of human body responses to various stimuli and stressors such as physical exercise, surrounding environment or injury.

Personalized medicine is becoming the cornerstone of medical practice with prospects of the customization of healthcare - with medical decisions, practices, treatments tailored to the individual patient [Katsanis 2008, Snyderman 2012]. The use of genetic information and biomarkers has played a major role in personalized medicine in oncology and other chronic diseases such as asthma and diabetes [FDA 2013]. Effective deployment of personalized medicine is still limited by the diagnostic technology and limited capabilities of computational systems physiology and biology [Xie 2014, Reifman 2010]. The goal of this solicitation is to develop a simulation framework and physiology based modeling tools of a warfighter body that could enable definite assessment of his/her health status, physical and physiological performance as well as body responses to various injuries including blast wave, ballistic and blunt impact. For the model to be functional in military health care it should account for the subject specific body parameters such as gender, anthropometry, physical fitness, physiological vitals as well as other parameters used in contemporary personalized medicine. Because of its potential complexity the models and software tool could be first developed on conventional computers. However, the ultimate goal is to transition this technology to mobile computing platforms for the use by military medics and individual warfighters in the form of a Warrior Health Avatar. For this Avatar to be successful, it must be not only personal but also predictive, preventive, and participatory (P4) [Hood 2011]. Therefore, the simulation framework and the user interface in particular, should be designed to demonstrate the capability to address the above P4 requirements and provide military medicine functionality such as:

- Visual setup of the human body anthropometric parameters and basic physiological vitals,
- Simulate one selected human body physiological system (e.g., cardiovascular, respiratory) and its response to various stressors and activities,
- Simulate human body physiological responses to various injury patterns,
- Enable model calibration on patient specific parameters and vitals,
- Facilitate dynamic correlation between the physiological parameters collected from wearable sensors and the mathematical model parameters. Be portable to desktop and mobile computing systems,

- Provide user specific (medic, warrior, and scientist) graphical interface for model setup, execution, dynamic adjustment of parameters, interface to wearable sensors and analysis of results.

Development and deployment of such a framework will require collaboration between private, academia, and government teams and may have to accommodate both open source and commercial software components. There are several ongoing programs in the US, Europe, and worldwide developing open source tools for various aspects of personalized medicine including genomics, (e.g., OncoBlocks, <http://bcb.dfc.harvard.edu/~cerami/gsoc.html> for cancer genetics or BioGears for computational physiology <https://www.biogearsengine.com/>). Therefore it is envisioned that this project will establish a commercializable research engine that starts with the integration of open source/open access components but adds specific predictive algorithms and modules.

**PHASE I:** Formulate and design the Warrior Health Avatar simulation framework, its key functionalities, main components, communication with wearable sensors and the user interface. Select/develop software tools for modeling human body physiology, performance and injury in military related applications. Develop and demonstrate prototype tools on selected desktop and mobile computing platforms. Identify open source tools, framework, and models developed by academia and/or government that could be utilized in this effort. Prepare the Phase I final report describing details of the proposed simulation framework, preliminary results of relevant military applications, and rationale for further model development, validation and military deployment.

**PHASE II:** Develop and demonstrate a functional prototype of the Warrior Health Avatar. Develop interfaces to existing human anatomical, physiological and injury databases and models to enable model personalization and calibration. Validate model components on available experimental and clinical data. Develop direct interfaces to select at minimum one “off the shelf” sensor modality, such as physical activity, environmental, physiological, nutrition, etc. Demonstrate the capability of model calibration on static and dynamic wearable sensor data. Demonstrate the prototype Warrior Health Avatar to military medicine stakeholders.

**PHASE III DUAL USE APPLICATIONS:** The Warrior Health Avatar will have immense potential application in military, veteran and civilian medicine. Successful proposers should envision the transition of this technology into military health system supporting warfighters from enlistment, to service, to discharge to the veteran system. The target military users should include both military medics and individual warfighters. Interfaces to military physiological and injury wearable sensor and monitoring systems should be pursued. Ultimately the Warrior Health Avatar could become a ubiquitous through the US Military. The technology developed in this SBIR project could also support various civilian health systems in personalized health and medicine, in model-based management of chronic diseases, sports and performance medicine, drug discovery, clinical trials, geriatrics, rehabilitation, and many others.

#### REFERENCES:

1. CBO 2014, Approaches to Reducing Federal Spending on Military Health Care, Congress of the United States Congressional Budget Office, January 2014, <http://www.cbo.gov/sites/default/files/44993-MilitaryHealthcare.pdf>
2. Friedl, KE. (2007) Is it Possible to Monitor the Warfighter for Prediction of Performance Deterioration?. RTO Human Factors and Medicine Panel (HFM) Workshop held in Paris, France, 7-9 Feb 2007 Proc. RTO-MP-HFM-151 <https://www.cso.nato.int/pubs/rdp.asp?RDP=RTO-MP-HFM-151>
3. FDA 2013, Paving the Way for Personalized Medicine, FDA’s Role in a New Era of Medical Product Development, <http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/PersonalizedMedicine/UCM372421.pdf>
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Hood L, Friend SH. (2011) Predictive, personalized, preventive, participatory (P4) cancer medicine. *Nat. Rev. Clin. Oncol.* 8(3), 184–187

**KEYWORDS:** human body model, computational physiology, injury, wearable sensors, personalized medicine, combat casualty care, force protection, modeling and simulation.

DHP16-002            TITLE: Severe Trauma Female Simulation Training System

TECHNOLOGY AREA(S): Biomedical

**OBJECTIVE:** Develop a realistic simulation-based training system to support the development of psychomotor skills to treat severe trauma on female casualties at point of injury.

**DESCRIPTION:** Pre-hospital care plays a vital role in battlefield medicine. The primary mission of military medical personnel on the battlefield is to treat the wounded and save lives. The Army combat medic, also known as a 68W health care specialist, is responsible for providing the first line of medical care to casualties at the point of injury. We know that the majority of casualties who die in combat do so before they reach a definitive care facility. Army medics must assess a situation in a timely manner, and decide on an appropriate course of action in order to save lives under combat conditions. Tactical Combat Casualty Care has become the standard of care on the battlefield; establishing when and how much care can be provided based on the tactical situation. These care providers must act diligently, as the decisions that they make, and the treatments applied, directly impact the survivability of the casualty. First responders must be trained in a realistically accurate combat environment to ensure they have the necessary skills to treat the wounded effectively. Along with the increased understanding of wounding patterns, and how best to treat the acutely wounded in a tactical combat environment, the application of Tactical Combat Casualty Care (TC3) principles has proven highly effective. This is a major reason why the casualty fatality rate in recent US Overseas Contingency Operations (OCO) is lower than in any other conflict in the history of the United States. As of 2013, 14.9% of the United States' active-duty military force of 1.4 million was comprised of females. Although women have typically been excluded from combat arms roles in the past, they have been represented in significant numbers in front-line positions. Female Engagement Teams played a prominent role in the conflict in both theaters over the past ten years. Recent studies have shown that military female casualties are far more likely to die of their wounds than males, in contrast with civilian reports of females demonstrating higher survival rate than males with comparable injury. In fact, data from the Joint Theatre Trauma Registry showed that female casualties presented with a greater proportion of abdominal injuries, and tended to have more chest injuries than their male counterparts who survived. In a study of sucking chest wounds and other traumatic chest injuries, data showed that when assessed by gender, the Needle Chest Decompression (NCD) procedure was successful in less than a quarter of attempts in females compared to males where the procedure was successful in three quarters of attempts. Current human patient simulation models used to train first responders are decidedly masculine in appearance. Female simulation is unrealistic, and most of the time appears as a mere adjunct to the male-centric training device. This lack of a realistic female simulation model for first responders to practice lifesaving procedures on, in conjunction with ingrained societal taboos, both contribute to male medical personnel reacting differently to immediate medical needs of female patients in emergency situations. At point of injury, during which a male emergency care provider might be required to expose and/or touch a female Soldier's body parts, lack of proper training can induce hesitation, which could potentially compromise the chance of saving a critically injured female Soldier. Following Defense Secretary Leon Panetta's decision to lift the ban of women serving in combat arms in 2013, the number of females in combat roles is projected to increase drastically in the next few years. The female mortality rate is predicted to rise as well, in keeping with this increase. Based on the given data and the decision to make combat roles available to females, a change in how we train medics to provide battlefield care for females may prove necessary. Force health protection policies, training, and equipment must be better tailored to the characteristics of

the deployed force. Therefore, capabilities in the training environment should incorporate realistic female anatomy. In order to make male Soldiers more comfortable with providing care to women, and more capable of reacting without hesitation in life-threatening situations, male trainees should be given the opportunity to work with realistic female anatomy during training and be exposed to female severe trauma injury patterns observed at point of injury.

Research conducted under this effort should focus on the development and evaluation of a low cost female simulation-based model to support the training of medics in the development of psychomotor skills to treat severe trauma on female casualties at point of injury. The concept should address modularity and interoperability with a variety of existing human patient simulators. The proposed solution should consider retrofitting to currently commercialized systems as well as modular mannequins yet to be commercialized.

The system should:

- Support established TC3 training objectives.
- Provide a capability to judge proficiency performance.
- Support practice of both cognitive and psychomotor skills.
- Include palpable anatomical landmarks to support TC3 procedures.
- Include realistic female simulated anatomical features to augment physical exam and scenario training.

**PHASE I:** Develop a design for a simulation-based training model that would realistically simulate female anatomy to support the training of Battlefield Combat Casualty Care. The effort should clearly analyze and define the scientific and technical feasibility, as well as commercial merit, of using a low-cost simulation-based physical model for training first responders in Combat Casualty Care Training Programs. Proposed work should include research into feasibility of developing the capability to assess trainee performance without the need of an instructor and describing the overall concept. The effort should seek innovative and novel ideas for exploration of concepts to provide a rugged, low-cost, and realistic simulation solution that would allow for hands on training. Phase I deliverables should include a final report, a proof of principle prototype demonstration or a set of technical drawings in electronic format that would provide a 3-dimensional view of all components of the proposed system, Phase II design plans, and exploration of commercialization with potential medical development and manufacturing companies. Furthermore, a plan for partnerships with government and private industry for the transition and commercialization of the production version of the product developed should be included. The offeror shall identify innovative technologies being considered, technical risks of the approach, costs, benefits, plan for development, notional schedule associated with development, and a literature search to support feasibility.

**PHASE II:** From the Phase I design, develop a ruggedized prototype and demonstrate realistic and meaningful interaction for hands-on treatment. The prototype shall be rugged enough to be evaluated by combat medics at a military installation. The offeror shall conduct usability studies during development of the system. The offeror shall provide projection of costs to manufacture, maintain and resupply, as well as the equipment lifecycle. The offeror shall conduct a training effectiveness evaluation (TEE) of the final prototype with combat medics. The evaluation shall provide quantitative measures of the effectiveness of the system. Data from the usability studies and the TEE shall be provided, analyzed, and presented in a final report. The offeror shall continue commercialization planning and relationship development with military and civilian end users and begin to execute transition to Phase III transition and commercialization in accordance with the Phase I commercialization plan.

**PHASE III DUAL USE APPLICATIONS:** Refine and execute the commercialization plan included in the Phase II Proposal. The final production model of the severe trauma female simulation training system must be ruggedized for shock, dust, sand, and water resistance to enable reliable, uninterrupted operation in moving combat vehicles, as well as, lane training at combat medical training centers to include operation and storage at extreme temperatures. Size and weight are important factors. The ultimate goal of the system would be to enable the assessment of female patient medical stability and support practice of cognitive and psychomotor skills to perform procedures in order to save the life of the patient. Quantitative values for acceptable operational and storage temperatures and power requirements should be planned to comply with applicable MIL-SPECs (available online). In addition, follow-on activities are expected to be aggressively pursued by the offeror to demonstrate the application of this system to civilian hospitals, residency training programs, and other military medical personnel. The offeror shall demonstrate that this system could be used in a broad range of military and civilian medical training applications.

## REFERENCES:

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**KEYWORDS:** Medical Modeling and Simulation, MM&S, Combat Trauma, Pre-Deployment Training, Tactical Combat Casualty Care, TCCC, TC3, Female Anatomy, Severe Trauma.

DHP16-003            TITLE: Value Based Monitoring of Cycles of Care

TECHNOLOGY AREA(S): Biomedical

**OBJECTIVE:** The objective is to develop software algorithms that reuse existing Military Health System data derived from healthcare operations to assess patient health and performance outcomes for condition-specific cycles of care, and their associated costs, for the purpose of measuring value.

**DESCRIPTION:** The United States Air Force Medical Service (AFMS) has a current need to measure the value of its healthcare delivery processes in a timely fashion to achieve higher reliability and guide continuous process improvement and innovation activities [1, 6]. Value (V) in healthcare is defined as outcome quality (Q) divided by cost (C):  $V = Q/C$  [3]. Shifting the focus from processes and resource utilization to value is the central challenge to improving healthcare delivery. Outcomes (the numerator) in the value equation are inherently condition-specific and multi-dimensional. Additionally, outcomes need to be defined from the customer's perspective and not the supplier's perspective, meaning they are outcomes that matter to patients (patient centeredness) as well as Service members and commanders (time until and degree of functional recovery). Cost (the denominator of the value equation) refers to the total cost of the full cycle of care for the patient's medical condition, which includes acute care, related complications, rehabilitation, and recurrences [3, 4, 5]. While many aspects of value-generating healthcare transactions become data, the use of that data is still embryonic. Going forth, the AFMS must learn how to reuse that data in interesting ways to ascertain value for cycles of care for specific conditions. Cycles of care involve all the healthcare activities associated with a condition and not just any one intervention or care episode [6, see 2 for an example]. While some aspects of defining cycles of care and related attributes can be directly derived from linkages between data elements, other aspects need to be inferred from the data, such as through pattern recognition. Human analysts are able to perform this task, but with attendant limitations in the volume of data that can be processed in an operationally timely manner. Consequently, software algorithms will be necessary to accomplish this task if the AFMS is going to compare the multitude of individual healthcare teams and treatment facilities comprising its healthcare delivery system.

**PHASE I:** As value is multidimensional, multiple outcomes are required to ascertain value for cycles of care for specific conditions. Five value-related measures are proposed to address the aim of better, faster, and more affordable (i.e., high value) care:

- Better care:
  - 1) Medical quality: whether or not patients received evidence-based care
  - 2) Patient satisfaction: proportion of patients satisfied with their health status
- Faster care:
  - 1) Same-day access to care: proportion of patients receiving care within one business day of their request
  - 2) Return to function: the number of days before patients could resume their normal work activities
- More affordable care:
  - 1) Total cost: the summation of costs from when the need for care arose until the problem was resolved
  - 2) Return to function: lost productivity cost based on the time to return to function metric.

The company will write algorithms to automate, to the maximal extent, measurement of these metrics for cycles of care associated with low back pain at three Military Treatment Facilities (MTFs). The foundational Phase I work will involve integrating diverse data sets to allow for data mining and the development of analytic approaches to define cycles of care and ascertain associated metrics. Anonymized data will be provided to support this work through a government-industry research partnership under the oversight of the 711th Human Performance Wing Institutional Review Board. Data will be accessed and maintained through the U.S. Army's Person-Event Data Environment (PDE). The Phase I product will be evaluated by using it on another dataset obtained from three different MTFs and comparing measures to that obtained by human analysts reviewing a random sample of the cases.

PHASE II: If the Phase I is successful, the company will expand upon the results to refine the analytic methodology and apply it to cycles of care associated with three other conditions (e.g., shoulder injuries, knee injuries, and ankle injuries) at three MTFs. The Phase II product will be evaluated by using it on another dataset obtained from three different MTFs and comparing measures to that obtained by human analysts reviewing a random sample of the cases.

PHASE III DUAL USE APPLICATIONS: The Air Force Medical Operations Agency requires this capability as a foundational element of the Air Force Medical Home Clinic Innovation, Test and Evaluation System [1]. However, the intent is that the capability be applicable throughout the Military Health System. If Phase II is successful, the company will be expected to support the AFMS in transitioning the algorithms for Air Force use should a Phase III award occur. Based on the Phase II results, the company will develop a scalable analytic methodology that uses existing AFMS data to generate value-related metrics within a management dashboard for cycles of care for pre-specified conditions. The solution needs to allow for comparisons between MTFs and provider teams to support process improvement and innovation initiatives.

PRIVATE SECTOR COMMERCIAL POTENTIAL/DUAL-USE APPLICATIONS: The analytic approach and algorithms developed under this topic is of direct relevance to the civilian healthcare sector [6].

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**KEYWORDS:** Business management, data management, health care management, models, organizational change and adaptation, statistical analysis, strategy, value.

DHP16-004            TITLE: Automated Vision Tester Technology Development for Aircrew Clinical Vision Screening

**TECHNOLOGY AREA(S):** Biomedical

**OBJECTIVE:** Develop, demonstrate, and deliver a computer-based, automated vision tester (AVT) capable of conducting a full range of clinical vision screening procedures for both near and far focus distances.

**DESCRIPTION:** Vision screening procedures for selection/retention of military aircrew have changed very little over the past several decades. Most currently used screening procedures for acuity; contrast, color, stereo-acuity, and ocular motility (hyper/hypo/eso/exo phoria/tropia) are based on paper charts and slides, and typically limited to pass/fail level of accuracy. Current procedures are time consuming, labor intensive, potentially subject to transcription errors, and to “test preparation” or coaching, which may compromise the integrity of the test. The Department of Defense is pursuing plans to modernize aircrew vision screening procedures, following the success of recent developments in color vision screening such as the Cone Contrast Test (CCT), Computer Assessment and Diagnosis (CAD) test, and Computerized Color Vision Test (CCVT). Automated vision testing would enable aeromedical personnel to more accurately track the health of patients through the use of threshold estimates, rather than pass/fail criteria for each aspect of vision. Additionally, labor involved in administering the tests could be greatly reduced since automated tests could be administered to multiple patients simultaneously with only minimal supervision. The purpose of this DHP SBIR technology development effort is to develop a computer-based vision screening device that takes advantage of recent developments in optics and electronic displays and that supports vision screening tests for a variety of aspects of vision for both near and far focus distances. At a minimum, threshold-based tests supporting vision screening relevant to most current Army, Air Force, and Navy aircrew standards should be demonstrated (e.g. acuity, color, ocular motility (hyper/hypo/eso/exo phoria/tropia) , and stereo). Inclusion of additional tests currently under research, such as motion perception, vergence range, etc., or novel testing procedures which minimize/eliminate self-reporting will also be considered. The contractor would be expected to work with US Army, Air Force, and Navy Aeromedical research laboratories to prioritize screening tests and identify clinical procedures that would affect the acceptance of the proposed AVT design. The design should support many different test procedures and different threshold-based pass/fail criteria, for different services or customers, or different career tracks with different vision standards. The purpose of this SBIR is to develop the optics, electronics, and hardware/software necessary to support administering computer-based clinical tests (test content may be developed separately). The resolution, luminance, contrast, field of view, color/cone stimulation, moving image quality, and any necessary tradeoffs should be thoroughly evaluated, including calibration methods. At a minimum, the device must characterize acuity thresholds at 0.5 arcminutes/line-pair, stereoacuity below 5 arcseconds, and provide cone contrasts of 0.25% or less at luminance greater than 100 cd/m<sup>2</sup> to support current DoD screening standards. It is highly desirable that the device also be able to support future tests (e.g. vergence range, contrast sensitivity, motion perception, etc.). The device must administer these tests at both near (14 inches) and far (6 meters) focal distances. Note: commercial marketing of this device for diagnostic applications may require medical device classification by the FDA (expected to be “Class 1, Ophthalmic, Visual Acuity Chart,” or similar). Pursuit of FDA classification is the sole responsibility of the contractor.

**PHASE I:** Design a concept for an AVT device. Work with DoD Aeromedical personnel to identify and prioritize clinical test procedures that could be implemented on the AVT, evaluate COTS optics, display devices, and electronics, and design an AVT concept device meeting the minimum requirements listed above (0.25 arcminute acuity, 5 arcsecond stereoacuity, less than 0.25% cone contrast, luminance greater than 100 cd/m<sup>2</sup>). Interactions

with DoD Aeromedical personnel will be facilitated by the Operational-Based Vision Assessment Laboratory (OBVA Lab) within the US Air Force School of Aerospace Medicine (USAFSAM/FHC), with equal access provided to all awardees at no cost. Contract deliverables include a final report which includes a recommended design approach for prototype development in Phase II. The Phase I research report should assess all aspects of the design, including color stability, luminance, contrast, field of view, resolution, and measurable threshold ranges. A method of color calibration should also be researched, to ensure the test stimuli are stable over time and different devices are able to administer identical tests. It is highly desirable, but not required, that a proof of concept device or demonstration (TRL 4) be delivered to USAFSAM/FHC at the conclusion of Phase I to enable identification of potential limitations and trade-offs. The device should be capable of supporting PC-based vision testing software (including moving imagery) for demonstration purposes. Such software may include commercially available software, custom software developed by the contractor, or government-owned software provided by the USAFSAM/FHC, OBVA Laboratory. Government-owned threshold-based experimental test data and software for acuity, stereo, color, contrast, motion perception, ocular motility, and vergence range can be provided equally to all contractors for this SBIR effort at no cost.

**PHASE II:** Based on the design approach recommended in Phase I, design, build, and demonstrate a full prototype AVT (expected TRL 6) capable of meeting the minimum standards described above. The demonstration should include a full characterization of the device (e.g. assess color gamut, color stability, luminance, contrast, field of view, resolution, near and far focus distance, etc.), and demonstrate calibration procedures to verify accuracy of test procedures (e.g. color, contrast, luminance, disparity, etc.). As in Phase I, interactions with DoD Aeromedical personnel will be facilitated by USAFSAM/FHC, with equal access provided to all awardees at no cost. USAFSAM/FHC personnel can provide a suitable test environment within the OBVA Laboratory to demonstrate achievement of the TRL 6 prototype AVT, as needed. The prototype device will be delivered to the Air Force at the conclusion of Phase II for further evaluation and validation.

**PHASE III DUAL USE APPLICATIONS:** The automated vision tester is intended to become an additional diagnostic tool to objectively characterize various aspects of ocular health. An automated vision tester would have both commercial and military aviation vision screening applications, such as aircrew ocular health screening performed by aeromedical ophthalmologists and researchers, as well as potential applications for screening operators of both military and commercial vehicles. Additionally, the automated vision tester would be widely applicable to both military and commercial clinical optometric/ophthalmological consultation and diagnosis, such as the prescription of eye glasses or diagnosis of color deficiency, as well as non-clinical screening applications (e.g. department of motor vehicle vision screenings). Note that commercial marketing of this device for diagnostic applications may require medical device classification by the FDA. The classification is expected to be “Class 1, Ophthalmic, Visual Acuity Chart,” or similar category based upon the functionality of the final design. Pursuit of FDA classification is the sole responsibility of the contractor, and contractors are advised to begin this process as early as practical (possibly in phase I or II), given the scope of the effort.

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**KEYWORDS:** Aircrew vision standards, Vision standards, Clinical vision screening, Color vision, Acuity, Contrast sensitivity, Stereoacuity, Phoria, Vision Test

DHP16-005            TITLE: Iron Status Determination Point-of-Care Device

TECHNOLOGY AREA(S): Biomedical

**OBJECTIVE:** Develop a point-of-care device that analyzes the serum iron indicators from a limited amount of blood to determine a diagnosis within minutes. The initial implementation plan for the device would be to screen military members for iron deficiency in a training setting where research has shown men and women will decrease or even deplete their iron stores due to the physiological demands of intense physical training. The device should provide rapid results with iron status analysis (normal iron, iron deficiency, or iron deficiency anemia) to guide health care personnel with information for a plan of care, yet least disruptive to training schedule.

**DESCRIPTION:** Much of what is known about iron status in training has been drawn from the research of iron status and its effect on performance in elite professional and non-professional female athletes. Iron Deficiency (ID) and Iron Deficiency Anemia (IDA) causes a host of adverse outcomes such as diminished work capacity and endurance (1, 2), diminished immune function (3), and neurocognitive impairment (4, 5), all of which directly affect successful completion of BMT and overall military readiness. Causal links between ID and IDA, decreased aerobic capacity and work performance have been reported for over a decade with far reaching economic and safety implications (1, 6). For women, menstruation is the likely contributor to decreased iron stores. Other possible causes for decreasing iron stores during intense physical training include inadequate iron-rich food intake; foot strike hemolysis; excretion through sweat, gastrointestinal blood loss, genitourinary blood loss, increased body temperature, and blood donation (7).

Although male military trainees are also predisposed, female trainees will exponentially be diagnosed with an iron deficient condition as compared to male trainees. Female military members present physiologic differences that directly impact performance and need to be targeted for specific interventions to promote safety and enhance force multiplying potential (8, 9). Yanovich et al found that despite increased dietary iron intake, iron status decreased during basic combat training (BCT) in men and women. However, women experienced greater iron losses over the nine weeks of BCT (10). Iron deficiency was found to be one of the predictors for stress fractures in female Israeli military recruits (11, 12). In one of the few longitudinal cohort studies of female soldiers before and after BCT, McClung et al (13) found compelling evidence of diminished iron status predictive of impaired aerobic performance. In the face of this persistent and increasing predicament, it is essential that primary healthcare

providers have clear, evidence-based guidelines for iron status screening and for providing countermeasures to treat and prevent iron decrements in military women.

Due to the high incidence of iron deficiency and anemia, this author developed a Clinical Practice Guideline (CPG) based on research evidence to test women at critical points within basic training. The evaluation of the CPG has just been funded by a Joint Program Committee (JPC) and will begin when funding is available. In 2013, JB-Lackland, TX population health personnel screened asymptomatic female trainees for anemia using hematocrit and hemoglobin only, which is not the ideal method for screening for iron deficiency, but was available and cost effective. The logistical issues with monitoring just hematocrit and hemoglobin put a burden on the clinic personnel, phlebotomists, laboratory personnel, and health care providers. Finally, trainees with abnormal results had to return to have their blood redrawn for iron panel, which caused disruption in the trainees' schedule.

**PHASE I:** Develop an innovative concept using a limited blood sample (preferably less than 3 cc) to analyze hemoglobin, hematocrit, mean corpuscle volume, red blood cell distribution width, iron, ferritin, total iron binding capacity, serum transferrin receptor, and transferrin saturation and provide a plausible medical diagnosis (normal iron status, iron deficiency, or iron deficiency anemia). It is not recommended to pursue PCR technology. This rapid diagnosis will aid in appropriately dispositioning the trainee back to training or to see the health care provider. It is preferred that the device is small, portable, and preferably handheld with rapid results turnaround. It is expected that there will be hundreds of trainees to screen in limited time and rapid response is key. The device will need to allow transfer of laboratory results into the Electronic Health Record (EHR) for appropriate medical follow-up in subsequent visits. Proposed work should include research into feasibility of developing the capability and describing the overall concept. The offeror shall identify innovative technologies being considered, technical risks of the approach selected, costs, benefits, and schedule associated with development and demonstration of the prototype. The FDA will need to be contacted at the end of the development of Phase 1.

**PHASE II:** Develop and demonstrate a prototype device from the recommended solution in Phase I that provides timely laboratory results for mass iron status screening. Deliver the pre-production prototype for DoD evaluation for use at an Air Education Training Command military installation with hands-on assessment in a laboratory setting (EHR/Device Integration and Device Quality Control Testing) by health care staff. Further, the offeror will deliver a report describing the design and operation of the pre-production prototype capability. The offeror shall consider projection of costs to manufacture, training of medical personnel, maintenance, and replenishment of disposable supplies (blood tubes/cassettes), as well as the equipment lifecycle. The evaluation of the proposed system by the user community as a military installation is required. The offeror shall conduct usability evaluations to assess the system in terms of ease of use and portability. At the end of Phase II, the offeror will provide instructions on the use of the device.

**PHASE III DUAL USE APPLICATIONS:** Refine and execute the commercialization plan included in the Phase II of the proposal. The devices should be compatible in military training and deployed settings where women and men are expected to maintain peak athletic performance. The first proposed location will be at an Air Education Training Command military installation. Other proposed locations include forward deployed settings with limited medical laboratory capabilities.

**Commercial Applications:** There are multiple health care settings where ID/IDA is a serious health concern and requires surveillance. Prospective commercial applications of this device include nutrition centers, athletic training centers, bariatric surgery centers, pediatric/adolescent medicine clinics, or nephrology clinics.

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**KEYWORDS:** Iron, anemias, military personnel, training, blood analysis, Iron Deficiency (ID), Iron Deficiency Anemia (IDA)

DHP16-006            TITLE: Diagnostic Device for Detecting Biomarkers of Early Multiorgan Injury in Saliva

TECHNOLOGY AREA(S): Biomedical

**OBJECTIVE:** Develop a salivary diagnostic system for existing, clinically qualified biomarkers of toxic (i.e., chemically-induced) organ injury normally detectable in plasma and/or urine in standard clinical practice.

**DESCRIPTION:** As modern warfare moves to urban environments and megacities, soldiers are at increased risk of exposure to chemical threats and the subsequent adverse health outcomes associated with such exposures (Harris, 2014). More than 84,000 toxic industrial chemicals are commercially available worldwide, and hundreds more are introduced for consumer use each year. Developing predictive assays for exposure and risk assessment to each individual chemical threat is logistically impractical. Assessing systemic toxicity with clinically validated biomarkers of adverse health effects is a viable alternative. Most diagnostic devices for these newly discovered and clinically validated biomarkers require blood or urine testing for diagnosis. Collecting blood in a field setting for predicting risk of chemically-induced organ injury is logistically impractical for the small, mobile units envisioned for Force 2025. Saliva represents an attractive alternative diagnostic fluid. Saliva is a readily accessible biofluid

easily transferrable to point of care, fieldable tests for emergent health concerns of soldiers exposed to toxic industrial chemicals in the field. Salivary diagnostics have evolved exponentially in recent years, becoming a focal point of biomedical basic and clinical assays (Malamud 2011). Saliva contains biomolecules of diverse chemistries which reflect physiological health. Saliva's diagnostic potential is fertile ground for development of militarily useful technologies to improve in-field diagnostic capability. The diagnostic potential of saliva has been exploited in cardiovascular disease, breast cancers and oral cancers (Pfaffe 2011). However, the following capability gaps and technological barriers must be addressed before current clinical practice in saliva diagnostics can be applied to diagnosing toxic organ injury in military field combat scenarios:

1. A panel of clinically used biomarkers of end organ injury has not been qualified for saliva
2. Analytes detected in saliva are often approximately 1000-fold less concentrated than in blood
3. Many of the commercially available techniques for salivary detection are not quantitative, or quantitative testing for blood does not apply to saliva.

The military requires a single, multiplexed saliva diagnostic bioassay capable of detecting biomarkers of adverse health effects indicative of emergent organ injury. The device or platform must measure salivary concentrations of clinically proven biomarkers of emergent organ injury. Target organs include, but are not limited to, lung, heart, liver, kidney, reproductive organs (i.e., fertility assessment), and brain/CNS. Examples of relevant biomarkers include but are not limited to BUN or KIM-1 (kidney); alanine aminotransferase, micro-RNA-122 (liver); troponins (heart); and s100B, cholinesterase activity (CNS). The assay must detect salivary biomarkers with high sensitivity and specificity.

**PHASE I:** Phase I projects cover a 6-month, \$150K (max) effort. During Phase I, the contractor shall identify and define clinically verified blood-based biomarkers for toxic organ injury suitable for use in developing saliva-based diagnostic systems. Identify the technological barriers and demonstrate technical feasibility for adapting clinically used human urine and/or blood-based diagnostics to human saliva bioassays. Design, develop, and provide pilot data testing an innovative concept. Demonstrate proof-of-concept in specimens collected from individuals with an injury condition that the proposed salivary biomarkers are specific to detect emergent organ injury. Proof of concept could be measuring a deviation from normal salivary biomarkers (e.g., cortisol). Develop a detailed analysis, innovative technological strategy, and prototype which demonstrate the technology's potential to overcome the challenges of salivary biomarker detection in disease conditions, including analysis at high sensitivity and specificity, and identification of salivary biomarkers predicting end-organ injury. Phase I will develop a concept for a prototype assay and outline the success criteria for demonstrating adequate specificity and sensitivity in Phase II research and development with the prototype technology.

**PHASE II:** Phase II projects cover a 2-year, \$1M (max) effort. Develop the results from Phase I into a prototype bioassay with the following requirements:

1. Develop, test, and demonstrate a prototype for a rapid diagnostic assay with high sensitivity and specificity for chemically-induced multi-organ damage which can be adapted to a human saliva-based diagnostic. Challenges include detecting analytes at 1000-fold lower than concentrations found in blood (Pfaffe 2011). Provide a detailed plan for conducting life cycle and operational testing.
2. Based on the best approach identified in Phase I, design a fieldable assay for detecting and assessing biomarkers in saliva. Demonstrate that the technology performs algorithmic analysis of the biomarker quantities and is able to classify samples based on these quantities. Demonstrate proof-of-concept that clinically verified biomarkers of adverse health effects are detectable in saliva. Construct and demonstrate the operation of a prototype.

Based on Phase I modeling, fabricate and validate a prototype with the following key deliverables:

1. Total assay time, from collection to assay readout, is between 0.5-4 hours (threshold: 4 hours; objective: 0.5 hours).
2. The assay is an early predictor of toxic chemical injury and/or xenobiotic exposure.
3. The assay diagnoses specific organ injury with high sensitivity and specificity.
4. The assay analyzes saliva to detect biomarkers of end organ injury.
5. The assay analyzes biomarkers that are clinically verified in other biological fluids (e.g., urine, plasma, serum, bronchial lavage fluid, etc.).
6. The number of biomarker candidates included in the diagnostic assay should be no more than 100.
7. The assay can be used in-field without extensive medical training

8. The assay incorporates biomarkers which are verified clinical indicators of organ injury with known toxic chemical injury endpoints and/or biomarkers of metabolic changes indicative of xenobiotic exposure.
9. The assay has significant commercialization potential, both in military and civilian sector hospitals, clinics, and field applications.
10. The assay accurately diagnoses end organ injury based on saliva biomarkers in patients with a specific medical condition.
11. The Phase III should also include a plan for FDA clearance.

**PHASE III DUAL USE APPLICATIONS:** Potential military end users include combatant commanders, field medics, and designated soldiers assigned to small, mobile units in the strategy for Soldier 2025. Civilian end users include clinicians and triage nurses in emergency medicine and inpatient settings. Funding will be obtained from non-SBIR/STTR government sources and/or the private sector to develop the prototype into a viable product. The Phase III should (1) identify one or more potential commercial applications for the technology and/or (2) identify one or more commercially available technologies rendering the technology compatible with military defense systems. The Phase III should identify and define the applicability of the technology to toxic chemical injury exposure. Begin negotiations with FDA to validate the assay using a clinical trial paradigm.

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**KEYWORDS:** saliva diagnostics, multiplex, biomarker, toxic organ injury, chemical threats, megacities, sensor, detection device.

DHP16-007            TITLE: Creating Sterile Water for Injection (SWFI) at/near Point of Injury (POI)

**TECHNOLOGY AREA(S):** Biomedical

**OBJECTIVE:** Develop a hand-held, portable capability to generate small volumes of Sterile Water for Injection (SWFI) in austere locations to reconstitute dried plasma, dehydrated medications, and other freeze dried medicine at or near the point of injury. The system must be capable of maintaining the sterility of the SWFI when transferring sterile water to intravenous (IV) bags and not require any external power. To be viable, the system must be a force multiplier that is small, light, quickly deployable, and easy to use that allows medics to replace a liquid IV bag with capability to generate multiple IV bags. The source water for the system will be any potable drinking water available in theater.

**DESCRIPTION:** Hemorrhage continues to be a major mechanism of death in potentially survivable combat injuries, underscoring the necessity for initiatives to mitigate bleeding and provide immediate availability blood products, particularly in the prehospital environment<sup>1</sup>. As 24% of pre-medical treatment facility combat deaths were deemed potentially survivable<sup>2</sup>, and 91% of those were associated with hemorrhage, the need to develop faster, more effective capabilities to maintain hemostasis is critical to saving lives on the battlefield.

Currently deployed medics are required to transport, maintain, and be resupplied with liquid-based medications and materials that are heavy, expensive to transport, perishable, and may require refrigeration such as fresh frozen human plasma and other blood components. In addition, frozen blood components are subject to bag rupture with losses up to 15%. Also, frozen blood components require time and energy to thaw to body temperature before use. These limitations not only increase the logistical costs associated with deployment, but may result in certain

medications and materials not immediately available at forward deployed locations or point of injury that do not have refrigeration or rapid resupply.

United States Army Medical Research & Material Command and Office of Naval Research (USAMRMC & ONR) are developing dried plasma products that will be available in the near future that can be reconstituted on the battlefield. They will require sterile water for injection that must be transported with the dried plasma that requires logistical costs for transporting sterile water and limits the shelf life of the dried plasma to the expiration date of the prepackaged sterile water.

In addition to providing sterile water for injection to reconstitute dried plasma for immediate use, medics will be able to use sterile water for injection to rehydrate IV formularies such as Ringer's Lactate, saline, and other solution as needed. Also, will support reconstitution of other medications and materials that are or will be available in dehydrated formularies that require sterile water for injection to rehydrate for immediate use such as freeze-dried platelets. These medications and materials are often dehydrated in non-deployed (civilian) settings to extend the item's shelf life to years or indefinitely. Finally, this initiative supports a vision that Dr. John Holcomb shared at the 2013 MHSRS conference. During the plenary session on 12 Aug 13, he stated that for prehospital point of injury care at far-forward deployed locations, the military should dehydrate all medications and liquid supplies as much as possible and rehydrate with Sterile Water For Injection (SWFI) generated onsite.

Because United States Pharmacopeia (USP) sterile water for injection is readily produced and available in large quantities at stateside (civilian) settings, little research has been conducted to develop a small, portable capability to generate small amounts of SWFI in austere locations. NASA conducted research to rehydrate medications and IV fluids when needed aboard the International Space Station (ISS) to treat onboard personnel<sup>3</sup>. NASA conducted research into creating USP quality water to rehydrate IVs using reclaimed (drinking) water. NASA's demonstrated a capability to generate SWFI using novel resin filtration capabilities that are integrated into small portable system<sup>4</sup>. However, NASA lacked the ability to transition the medical technology to fielded capability due to the limited commercial applications. Advances over the last 20 with ionic adsorption micron filtration and resin-based polymers have proven effective in the removal of bacteria and virus to six logs (99.9999%)<sup>4</sup>. Nanofiltration is being developed to cleanse blood similar to kidney function using under low-pressure conditions but is not being researched for generating SWFI in a portable device<sup>4</sup>. Other research has shown that osmotic membranes can be incorporated in a small, portable device to generate SWFI using EPA potable water as a source<sup>5</sup>.

All three of the leading technologies for producing a portable SWFI generation system, membrane distillation, osmotic distillation (can only produce concentrated solutions), and nanofiltration are potential solutions that may be used separately or combined in series to provide the optimized solution. Each has advantages and disadvantages that would need to be assessed offer some potential advantages of weight and power, but are still in the development stage and would require more extensive work to produce WFI.

**PHASE I:** Phase I work will involve research to identify, assess, and select potential water filtration technologies to develop a concept and functional prototype. The offeror shall conduct a feasibility study that should determine and then demonstrate the innovative technologies being considered; limited testing that verifies key parameters can be achieved, especially meeting USP water quality standards; technical risks of the approach selected; costs, benefits, and schedule associated with development of the prototype. Phase I deliverables include a prototype demonstration, laboratory test results, a final project report, and a preliminary Phase II design plan. Offerer must include an exploration study of commercialization potential with civilian emergency medical service systems development and manufacturing companies and include a plan for partnering with government and private industry to transition a commercialized production version of this device with a market assessment.

**PHASE II:** Phase II work will refine, optimize, and validate the technical concepts and prototype developed in the phase I effort into a ruggedized prototype system. The developer shall conduct quality testing to statistically verify and validate that the system will consistently deliver sterile water for injection that meets the USP quality standards and rule making (USP37–NF32) using source water that meets EPA potable water standards. The performer is to deliver a well-defined prototype (i.e., a technology, product or service) that meets the topic requirements and which can be made commercially viable. The developer must demonstrate that the system can maintain sterility of the water during transfer to the receiving container (intravenous (IV) bags or equivalent). In addition, the design must

minimize the size and weight of the system, and optimize the design to ensure rapid and ease-of-use for rapid deployment and use. A focus group of medics with deployed medical treatment experiences will be used to evaluate prototype designs and provide feedback to improve/enhance design parameters. The system being developed must also be compatible with standard, commercially available IV bags. The developer may be required to demonstrate and validate the component and overall system fabrication and integration processes for regulatory and quality control considerations. A tradeoff evaluation will be conducted to assess the feasibility of a medic to carry this system (size and weight) to generate multiple IV bags in lieu of carrying one or more liquid IV bags (each 1000ml bag weighs approximately 2.5 lbs). The required deliverables include up to ten (10) developed pre-production prototypes for joint military utility assessments that meet the requirements of the original solicitation; independent lab verification of sterile water quality that meets USP standards; a final project report, and a plan for partnering with private industry to transition and commercialize a production version of this device. The results of the military utility assessment will be shared with the developer for final design changes. The developer shall consider projection of costs to manufacture, maintain and resupply, as well as the equipment lifecycle, sustainment considerations, user training development, and failure mode analysis in the transition and commercialization plan. Ideally, the final system shall be capable of producing one (1) liter of SWFI in ten (10) minutes [threshold] and one (1) liter in six (6) minutes [objective]. It shall weigh less than four (4) pounds (lbs) [threshold] and one (1) lb [objective] empty and not require power. It will be reusable for 5 [threshold] to 10 [objective] cycles before disposing, depending on water quality. The system shall be no larger than zero point one five (0.15) cubic foot (cf3) [threshold] and zero point zero eight (0.08) cf3 [objective]. Based on successful development of a viable system, the vendor(s) will provide an updated market assessment of the commercial viability for this device that includes assessment of interest by foundations such as Gates Foundation for providing enhanced humanitarian support (reduces logistics required for supplying IVs to disease stricken nations).

**PHASE III DUAL USE APPLICATIONS:** The Phase III work will culminate in the development of a commercial capability to manufacture the portable sterile water generation system, and a quality assurance and control plan that ensures consistency for device production. The final production model and packaging must be ruggedized for shock, dust, sand, and water resistance to enable reliable and rapid set up and use. The phase II work may result in technology transition to an Acquisition Programs of Record and/or commercialization of this technology capability. The developer shall seek additional funding from other government sources and/or the private sector investors to develop or transition the prototype into a viable product for sale to the military and private sector markets. The culmination of the Phase III will result in a system that enables DoD medics to generate sterile water for injection as needed and at any location to save the lives of US military members, coalition forces, and indigenous populations being supported by the military. In addition, the commercial applications of this system will enable sterile water for injection to be produced upon demand by emergency medical technicians in austere locations from Alaska to Antarctica, and possibly in orbit or deep space<sup>4</sup>. While the commercial market for developing a portable SWFI generation system will be developed in Phase I and enhanced in Phase II (with possible funding/collaboration with humanitarian focused foundations), the final manufacturing plan will include a commercialization strategy to ensure this capability is available for purchase off-the-shelf.

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KEYWORDS: Water For Injection (WFI), Sterile Water For Injection (SWFI), Intravenous (IV), Dried Plasma, Reconstitution, Hemostasis, U.S. Pharmacopeia (USP)

DHP16-008            TITLE: Selective Brain Cooling for Traumatic Brain Injury

TECHNOLOGY AREA(S): Biomedical

OBJECTIVE: Develop a selective brain cooling (SBC) device that provides measurable neuroprotective effects after a moderate or severe traumatic brain injury by cooling the brain during the acute and sub-acute post-injury phase.

DESCRIPTION: Traumatic brain injury (TBI) remains the leading cause of mortality and disability in the United States [1]. Approximately 1.5 million Americans are affected annually and 5.3 million Americans require assisted living as a result of TBI. TBI is the signature injury of Iraq and Afghanistan conflicts, accounting for approximately 20-25% of the Joint Theater Trauma Registry (JTTR) reviewed combat casualties [2]. Between 2000 and Q1FY15 36,559 Service members sustained a moderate/severe/penetrating brain injury (Defense & Veterans Brain Injury Center, <http://www.dvbic.org/dod-worldwide-numbers-tbi>). The worldwide numbers represent TBI incidence in both the deployed and non-deployed setting and while more TBIs occur in the non-deployed setting, the economic costs of work days lost and long term care for those who have sustained more severe injuries are significant. Current DoD initiatives include provider training and detailed CPGs; however, remaining gaps are treatment of casualties with moderate to severe TBI at the point of injury and during transport when they are most at risk for secondary brain injury.

Induced hypothermia as a therapeutic treatment for severe TBI has been studied intensively in the last 20 years [5]. Pre-clinical research has consistently demonstrated that therapeutic hypothermia is a promising neuroprotective strategy for treating traumatic brain injury (TBI) by effectively reducing injury-induced increases in intracranial pressure and cellular damage and improving neurological outcomes. Uncontrolled hypothermia is considered a threat in treating soldiers with TBI engaged in military operations as it causes increased platelet dysfunction and inhibits the coagulation cascade promoting coagulopathy and contributing to the lethal triad. Thus, hypothermia induced by whole-body cooling techniques is contraindicated for combat TBI victims who suffer from multiple wounds. In keeping with this, the DoD is seeking innovative materiel solutions to provide a deployable device that can effectively reduce brain temperature to 33 – 35 °C within 30 minutes of induction without causing detectable pathology and vulnerability from polytrauma.

PHASE I: Design/develop an innovative concept for using selective hypothermia to reduce the brain temperature. The effort should clearly analyze the scientific, technical, and commercial merit, as well as feasibility of using a low-cost medical device for use by advanced medical providers of all levels in Army Combat Medical Programs. Proposed work should include research into feasibility of developing the capability and describing the overall concept. The effort should seek innovative and novel ideas to provide a hands-on, low-cost, and realistic solution. The offeror shall identify innovative technologies being considered; technical risks of the approach selected; costs, benefits, and schedule associated with development and demonstration of the prototype. The final report shall include design of a medical device for reducing brain temperature, including, performance goals, associated metrics, conceptual validation through simulation or other means.

PHASE II: Based on the Phase I design and development feasibility report, the performer shall produce a prototype demonstrating potential medical utility in accordance with the success criteria developed in Phase I. The performer

will then deliver the prototype for DoD evaluation. The performer shall deliver a report describing the design and operation of the prototype. The intent of this phase is for the developer to deliver a well-defined prototype (i.e., a technology, product or service) meeting the requirements of the original solicitation topic and which can be made commercially viable. The prototype shall effectively reduce brain temperature to 33 – 35 °C within 30 minutes of induction, while maintaining body temperature between 36.5 and 37.5 °C. The device should have physiological alarms that monitor the temperature if a deviation occurs outside the prescribed temperature range. Prior to conducting human studies, animal studies must assess the benefit of hypothermia versus normothermia continued for 48 to 96 hours while minimizing side effects often associated with whole body cooling to include: decreased platelet count, increased dependence on vasopressors, increased prothrombin times, and need for plasma and/or platelet transfusions. The pathologies of a TBI model including physiological (ICP, cerebral blood flow etc), electrophysiological, histological, cellular/molecular, and functional (motor and cognitive) profiles exist in the literature; demonstrate evidence that SBC provides a measurable neuroprotective effect. The developer shall demonstrate a clear benefit regarding re-warming rates (spontaneously 30 min re-warming vs prolonged 60 min re-warming). The offeror shall initiate contact with FDA representatives and provide a clear plan on how FDA clearance will be obtained.

**PHASE III DUAL USE APPLICATIONS:** Follow-on activities shall include a demonstration of the application of this system to the Military Health System in deployed and non-deployed environments, civilian hospitals, residency training programs, and other military medical personnel. The performers shall demonstrate effectiveness and generate a safety profile of induced hypothermia versus normothermia for neuroprotection in patients. The study will provide the pre-clinical evidence for our SBC method to treat the polytrauma casualties, which is critically important for combat casualty care. Effectiveness shall be measured in terms of short and long term mortality and functional neurological outcomes. Safety can be assessed in terms of the rate of the adverse events infection, myocardial infarction, ischemic stroke, congestive cardiac failure and any other adverse events. The offeror shall focus on transitioning the technology from research to operational capability and shall demonstrate that this system could be used in a broad range of military and civilian medical facilities by physicians and physician assistants in austere medical environments.

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**KEYWORDS:** Selective brain cooling, neuroprotection, traumatic brain injury, hypothermia

DHP16-009            **TITLE:** Selective Aortic Arch Perfusion Technologies for Hemorrhage-induced Cardiac Arrest

**TECHNOLOGY AREA(S):** Biomedical

**OBJECTIVE:** Develop and refine active selective aortic occlusion and perfusion technology (SAAP) that addresses non-compressible torso hemorrhage, hemorrhage-induced traumatic cardiac arrest (HiTCA) that is compatible with

currently existing extra-corporeal life support systems (ECLS).

**DESCRIPTION:** The most common cause of potentially survivable (PS) death in both the military and civilian setting is hemorrhage. Published reports of combat death during OIF/OEF attribute between 58% and 90% of PS deaths to hemorrhage. A major improvement in the survivability of extremity hemorrhage was made in 2007 with the introduction of combat application tourniquets; reducing the mortality of this type of hemorrhage by 85%. There has been no such improvement in the management of hemorrhage within the chest, abdomen, and pelvis: non-compressible torso hemorrhage (NCTH). Data from OIF/OEF demonstrates that up to 75% of PS hemorrhage deaths are due to NCTH.1-3 In civilian data approximately two-thirds of PS hemorrhage deaths are due to NCTH.5 Published reports that specifically examine the combat fatality rate (CFR) of NCTH demonstrate the lethality of this type of injury (with the medical treatments available during OIF/OEF) – a CFR up to 85.5%. Furthermore, up to 90% of these combat deaths occur before arrival to a medical treatment facility.

Unsuccessful treatment of NCTH results in hemorrhage-induced traumatic cardiac arrest (HiTCA) and death. Current management of NCTH includes closed chest compressions (CCComp) and, where the capability exists, resuscitative thoracotomy (RT). The evidence of efficacy of CCComp in hypovolemia and HiTCA is almost non-existent – a single study of three baboons in 1989 demonstrated its ineffectiveness. Despite this, the use of CCComp in HiTCA is advised in both US and UK, civilian and military guidelines to date. Survival from RT in traumatic arrest in multiple clinical series was historically as low as 2.6%. More modern trauma systems have reported survival between 5.3 and 8%. However, the majority of the survivors had a penetrating thoracic injury, causing cardiac tamponade, and had an arrest within a medical facility that was capable of RT; survival for HiTCA specifically, is extremely rare. The most comprehensive (2006-2011) military evaluation of HiTCA demonstrated that survival from pre-hospital HiTCA was 0%. Globally, a few pre-hospital services deliver RT – this is impractical in the combat environment, and currently no military pre-hospital service undertakes RT.

Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) has been shown in large animal models to increase survival in NCTH, increase blood pressure, increase brain oxygenation, increase carotid flow, with less physiological derangement than RT. There are two small published case series of the clinical use of REBOA in hemorrhagic shock with assumed lethal injuries (total n=19). The survival rates were between 46% and 67%. REBOA certainly provides part of the solution in management of NCTH in the military environment, and can be used pre-hospital. However, it probably cannot be used to manage HiTCA. Selective aortic arch perfusion (SAAP) is a natural progression of REBOA that has a large central lumen, through which oxygenated fluids can be delivered to the brain, heart, and lungs while also preventing ongoing NCTH. SAAP has the potential to rescue a patient with a HiTCA who has cardiac standstill and an agonal or bradycardic arrhythmia.

**PHASE I:** Determine the technical feasibility of integrating SAAP technology with limited, partial or full ECLS or extra-corporeal membrane oxygenation (ECMO) technologies. Demonstrate perfusion catheter feasibility to provide high-flow perfusion of heart and brain in addition to aortic occlusion and afterload support. Successful demonstration would allow for Phase II animal efficacy testing of SAAP-ECMO technology.

**PHASE II:** Develop, test and demonstrate the efficacy of a SAAP catheter integrated with limited ECLS or ECMO in large animal translational model of NCTH with HiTCA. Anesthetized large animals with surgically created NCTHs will be treated with the new device which will demonstrate the ability to achieve the following: 1) provide complete occlusion of the aorta and thereby arterial inflow control, 2) demonstrate ability of system to perfuse vital organ systems above the level of occlusion in a clinically and physiologically relevant manner. The FDA approval pathway will be outlined and considered at each developmental stage. Parameters such as organ survival rate and avoidance of HiTCA after NCTHs will be used to assess efficacy and suitability of the device. Potential commercial and clinical partners for Phase III and beyond should be identified, and a detailed explanation should be provided for how the small business will obtain a monetary return on investment after completion of Phase II.

**PHASE III DUAL USE APPLICATIONS:** In a manner relevant to military pre-hospital care providers (trauma surgery, emergency medicine) and civilian in-hospital providers of acute and trauma care demonstrate efficacy of SAAP-ECLS/ECMO technology to address NCTH and HiTCA in target civilian and/or military population with FDA approval of interventional devices. Demonstrate efficacy of SAAP-ECLS/ECMO technology to address medical cardiac arrest in target civilian and/or military population with FDA approval of interventional devices.

Specifically, device would be applicable to use in the following: 1) fixed wing critical care air transport, 2) rotary wing MEDEVAC and civilian life-flight and 3) Role three hospitals in a combat theater of operation and/or civilian Level I and II trauma centers.

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**KEYWORDS:** selective aortic arch occlusion and perfusion; hemorrhage induced cardiac arrest; non-compressible torso hemorrhage; extra-corporeal life support

DHP16-010            TITLE: Filtration Technologies for Bridge Dialysis in Austere Medicine

TECHNOLOGY AREA(S): Biomedical

**OBJECTIVE:** Develop and refine filtration technologies that bind serum potassium in the context of hyperkalemia induced by traumatic injury and acute kidney injury.

**DESCRIPTION:** Hyperkalemia has been a recognized complication of combat injury since World War II, when severe renal dysfunction was associated with a mortality rate of 90%.<sup>1</sup> In the Korean War, hyperkalemia was a leading cause of death in patients with post-traumatic acute kidney injury (AKI), until the use of renal replacement therapy (RRT) improved mortality to 53%.<sup>2,3</sup>

Renal replacement therapy remains the standard of care for the treatment of hyperkalemia that does not respond to medical management. Rapid evacuation out of Iraq and Afghanistan ensured that most hyperkalemia occurred further up the evacuation chain (Role IV to Role V). However, the occasional need for RRT in theater led to the deployment of the NxStage System One (NxStage Medical, Lawrence, MA) to Craig Joint Theater Hospital, Bagram Airfield, Afghanistan.<sup>4</sup>

In future theaters of operation, the military research community should prepare for prolonged field care and extended evacuation times.<sup>5</sup> One implication of this delay is that complications of combat injury, including hyperkalemia, will be more common in the forward deployed setting. During the Korean War, approximately one-

third of combat casualties with oliguric renal dysfunction had a potassium greater than 7mEq/L within four days of injury.<sup>3</sup> Rapid evacuation times less than four days from Iraq and Afghanistan as well as fixed facilities with RRT capability negated the need for field care of hyperkalemia, however the future battlefield may not have these robust capabilities.

Hyperkalemia will continue to be a concern in the treatment of combat casualties. Future armed conflict and humanitarian crisis interventions may involve large numbers of patients with AKI or with prolonged extraction times. Similar to other stabilizing interventions such as damage control resuscitation, the development of “Bridge Dialysis” for damage control of hyperkalemia may impact the survival of patients with post-traumatic AKI. This technology would require a minimal resource footprint, portability, and simplicity of use.

While this is intended for use in the forward deployed setting, it could also be used in large scale humanitarian disasters. For example earthquakes, which result in building collapses with resultant crush injury that can be complicated by AKI and hyperkalemia. Another example would be for the treatment of hyperkalemia in hemodialysis patient after large scale floods or storms, such as Hurricane Katrina. Under normal circumstances traditional renal replacement therapies are more than adequate for the treatment of hyperkalemia. However, in these rare settings, the need can outstrip capacity. Because this occurs in less than 200,000 patients per year, the FDA Orphan Products Program can be utilized. Using this mechanism will greatly simplify the approvals process for the end product of this SBIR.

Preliminary requirements for filtration media and delivery system:

- Long duration: Be able to decrease potassium to a safe range (i.e. <6meq/L) and maintain it at that level for up to 6 hours
- Pump systems: If a pump system is used, it should be light-weight (<5 pounds), have a minimal footprint (<1 square foot) and be able to operate with battery power (for at least 6 hours)
- Filtration media should be minimally bioactive (i.e. not cause inflammation or be likely to clot)
- Filtration media should have multiple methods of delivery (e.g. extracorporeal blood purification and intra-peritoneal dialysis methods)

**PHASE I:** Identify ideal filtration or binding compound for efficacious K<sup>+</sup> removal over 6 hours without adverse reactions with whole blood (in vitro or ex vivo, ex. Platelet aggregation, filtration of calcium etc.). Product should be compatible with intra-peritoneal dialysis technology including but not limited to the following form factors: 1) intra-abdominal mesh packing, 2) extracorporeal filtration canister, 3) wound vacuum systems for temporary closure of the abdomen. Phase I should result in prototype products appropriate for testing in large animal translational models of hyperkalemia.

**PHASE II:** Demonstrate efficacy of filtration or binding media in animal models of trauma or ischemia-reperfusion induced hyperkalemia. Identify, design and test delivery mechanism for application of filtration or binding media ideal for use in austere environments (logistically limited/remote). Product should meet requirements of Phase I funding. Product(s) will be small in cube and weight while remaining efficacious for primary indication and shelf stable at extremes of temperature (ex. desert or arctic tundra). End-users for product would include but not be limited to the following: 1) United States Department of Defense Acute Care Providers, 2) Special Operations Forces Acute Care Providers, 3) Multi-disciplinary providers of Austere Medicine or Prolonged Field care that are not necessarily trained or certified in the provision of acute care. The end state of Phase II is a prototype that can enter the FDA approval process.

**PHASE III DUAL USE APPLICATIONS:** The filtration technology can be applied in an austere environment with minimal clinical footprint and support (ex. Role II/II+ facilities in a combat theater, Role III facilities) or in a civilian treatment facility for the treatment of hyperkalemia in end stage renal disease patients. The technology can be applied by two methods of delivery in a manner approved for use by the Food and Drug Administration. Phase III should include the generation of an IDE filing for each technological application as well as appropriate clinical trials to garner FDA approval for the technology. As noted above, the Orphan Products Program can be utilized for approvals. Phase III endpoints will serve customers described in Phase II. The end state of Phase III is an approved,

deployable product for the treatment of hyperkalemia in the austere combat environment.

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KEYWORDS: hyperkalemia, trauma, acute kidney injury, dialysis

DHP16-011 TITLE: Device to Prevent Retained Hemothorax

TECHNOLOGY AREA(S): Biomedical

OBJECTIVE: Develop a device that can replace or work with existing large bore (>28 French) chest tubes to help evacuate or prevent accumulation of blood in the chest space after chest trauma or chest surgery. The device should be a replacement for invasive surgical procedures such as video assisted thorascopic surgery (VATS) or thoracotomy. It should be able to evacuate blood without the need for sedation or single lung ventilation.

DESCRIPTION: Chest injuries occur in ~60% of polytrauma cases; a rough estimate of the occurrence of hemothorax related to trauma in the United States approaches 300,000 cases per year (1). Tube thoracostomy is a diagnostic and therapeutic treatment for many of these trauma patients (2, 3). Unless indications for chest surgery are found, the chest tube is the only treatment for chest trauma in a majority of patients. Of trauma patients that require a chest tube, approximately 4-20% have a measureable amount of blood that remains in the chest (4). Blood that remains in the chest after placement of a chest tube is called post-traumatic retained hemothorax (PTRH). Complications of not evacuating a hemothorax include infection (empyema) and/or trapped lung (the lung cannot expand to its full potential). The volume of hemothorax that remains in the chest makes a difference. In general, the greater the size of the PTRH increases the risk of empyema. Empyema is a life threatening condition that requires swift treatment and can require days of intensive care. Likewise, the greater the size of PTRH increases the amount of trapped lung, which causes diminished lung function. The precise volume at which a hemothorax or PTRH starts to cause problems is unknown, however the Eastern Association for the Surgery of Trauma (EAST) has a series of recommendations for treatment of hemothorax. These recommendations are as follows:

1. All hemothoraces, regardless of size, should be considered for drainage.
2. Attempt of initial drainage of hemothorax should be with a tube thoracostomy.
3. Persistent retained hemothorax, seen on plain films, after placement of a thoracostomy tube should be treated with early VATS, not a second chest tube.
4. VATS should be done in the first 3 days to 7 days of hospitalization to decrease the risk of infection and conversion to thoracotomy.
5. Intrapleural thrombolytic may be used to improve drainage of subacute (6-day to 13-day duration) loculated or exudative collections, particularly patients where risks of thoracotomy are significant.

The gap in capability is between a chest tube (cheap, easy-to-do, can-do-it in anybody) and VATS (expensive,

requires general anesthesia with a specialized breathing tube, contra-indicated in patients with spinal injuries or marginal lung function). In addition to trauma patients, blood or fluid can accumulate in the chest after surgical procedures such as lung or heart procedures (4). This device could be applicable to that patient population as well. Retained hemothorax is a very common problem, which costs millions of dollars in health care spending each year (4). The problem intuitively seems quite simple but a good solution does not exist.

Research conducted under this effort should focus on the development and evaluation of a device that fills the gap in treatment between tube thoracostomy and VATS procedure.

The proposed device should:

- work with existing large bore (>28 French) chest tubes
- provide mechanical agitation to break-up the hemothorax
- be able to be deployed early in the hospital stay

The proposed device should not:

- require general anesthesia or single lung ventilation
- be a permanent implantable device

It can be an automated or manually operated device. It can be image guided or work in conjunction with other imaging modalities. Ideally it would be deployed somewhat routinely in patients who are suspected of or at high risk of retained hemothorax. It can be utilized with thrombolytic agents as deemed appropriate and safe.

**PHASE I:** Design a device that can work with existing large bore (>28 French) chest tubes to help evacuate or prevent accumulation of blood in the chest space after chest trauma or chest surgery. The effort should clearly analyze the scientific, technical, and commercial merit, as well as feasibility of using a mechanical device to improve the drainage of existing chest tubes. The proposal must provide an explanation for the proposed design. The proposal must provide a mechanism for how the device will work. It must adequately address the requirements stated above or provide an explanation for how they may be circumvented. It must be clear from the proposal that the participants understand the clinical problem. For example, the proposal should not be a surgical device to be used in the operating room. Participants should provide a plan for practical deployment of the proposed device. Chest wall and lung models can consist of artificial constructs or real tissue but not live animals. The offeror shall identify innovative technologies being considered; technical risks of the approach selected; costs, benefits, and schedule associated with development and demonstration of the prototype. Initiate commercialization planning.

**PHASE II:** Develop and demonstrate a prototype system from the recommended solution in Phase I that provides for experimentation in animals. During this process, participants should decide on the necessary materials and an outline for the fabrication of such materials. The offeror shall consider projection of costs to manufacture the proposed device. A trauma surgeon should evaluate the prototype and provide written feedback. Vendors will escalate the fidelity of the experiments during this phase ie. progression from artificial “chest wall” constructs to large animal experiments. Moreover, a critical component regarding the practical application of this device depends on the properties of the fluid or blood that accumulates in the chest. Therefore experiments should utilize real blood. The experiments should define how well the device works once the blood has coagulated. For example, what amount of force or agitation is required to disrupt coagulated blood. Additionally, results should quantitate the effectiveness of blood evacuation. Head to head comparison to existing alternatives should be performed. During these experiments, safety and potential pitfalls must be described. Absolute or relative contraindications need to be described. A loose set of “operating instructions” need to be developed. As needed, the device may undergo iterative changes to enhance performance. Continue commercialization planning and relationship development with military and civilian end users to conduct proof-of-concept evaluations. Data from these studies shall be provided, analyzed, and presented in a final report. Participants should have a plan for approval by the Food and Drug Administration.

**PHASE III DUAL USE APPLICATIONS:** Refine and execute the commercialization plan included in the Phase II Proposal. Execute proof-of-concept experiments in live animals. Invite trauma surgeons to these experiments to use the device. Present the prototype to trauma surgeons at surgical meetings. Begin the FDA approval process. Execute further commercialization and manufacturing through collaborative relationships with partners identified in

Phase II.

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KEYWORDS: Trauma, retained hemothorax, evacuation, chest, blunt, penetrating, empyema, surgery, video-assisted thoracoscopy (VATS).

DHP16-012            TITLE: Genitourinary Tissue Repair, Restoration and Protection: Preserving Fertility and Function in Wounded Warriors

TECHNOLOGY AREA(S): Biomedical

OBJECTIVE: Development of methods that enable protection, repair and restoration that preserve continence, sexual function, fertility and hormonal balance in male and female service members

DESCRIPTION: Methods are sought to conserve, salvage, revive and/or repair genitourinary tissues and tissue systems (e.g. vagina, cervix and uterus, fallopian tubes, ovaries, penis and penile tissue, testes, anus, anal sphincter, pelvic floor muscle, urethra, bladder, ureter, and other systems related to the kidney) or to substitute with relevant engineered tissues.

In 2006 DoD leadership acknowledged the need to find critical capabilities for combat injuries and identified a need to support tissue engineering and regenerative medicine to overcome the most challenging clinical problems facing military surgeons. In 2008, the DoD established the Armed Forces Institute of Regenerative Medicine (AFIRM) to partner with a consortium of academic institutions and industry to translate such products into the clinic as rapidly as possible. The DoD's Tissue Injury and Regenerative Medicine (TIRM) program office identified genitourinary (GU) protection and repair as a key focus area for AFIRM II. This solicitation seeks industry participation within this priority area, with a focus on enabling protection, repair and restoration that preserves continence, sexual function, fertility and hormonal balance in male and female service members.

The number as well as severity of genitourinary injuries increased in Iraq and Afghanistan relative to other conflicts (primarily driven by ground-based explosive injuries) [1], while risks of radiation or chemical agent injury in future conflicts also mandate the need for good medical options to deal with injuries from these kinds of threats. There are currently very few therapeutic strategies to restore form and function to our Wounded Warriors as it pertains to the catastrophic and often permanent physical impairment from genitourinary injuries. The nature of these injuries extends well beyond the physical to critical reproductive, hormonal, behavioral health and psychological effects on these casualties and their families [2].

However, while genitourinary protection and repair is a more recent focus for DoD health programs, important breakthroughs and advances have occurred in surgery [3], civilian and regenerative medicine in general and the recently established field of oncofertility/endocrine preservation. Efforts that address the often enormous civilian need in addition to those of military medicine and tap into large commercial markets are of interest.

**PHASE I:** The performer will carry out foundational work to develop methods that will allow salvage of testes, penile tissue, and other genitourinary tissues on or near a battlefield setting, maintenance, regeneration/repair, and banking of those tissues to achieve tissue quality that allows re-transplantation. The performer will propose or adapt existing model systems that are suitable to evaluate and clearly demonstrate efficacy outcomes. This model will be used in Phase II. The focus of this phase is on developing methods that will allow for salvage of testes, penile tissue, and other genitourinary tissues to enable maintenance, regeneration/repair and banking of those tissues to achieve tissue quality that allows re-transplantation, and select biological model systems that are suitable for use in Phase II. Computational modeling and simulation of system performance during Phase I is expected. Preliminary evaluation and testing of novel protocols in the selected biological model system is encouraged. The biological model system may be engineered tissue or tissue derived from an animal or human source as long as new Institutional Review Board approval is not required or initiated as part of Phase I

**PHASE II:** The performer will build on the foundational work performed during Phase I to develop and evaluate novel methods that will allow salvage of testes, penile tissue and other genitourinary tissues on or near a battlefield, followed by maintenance, regeneration/repair, and banking of those tissues to achieve tissue quality that allows re-transplantation and test protocols to demonstrate their effectiveness using the biological model system identified in Phase I. This phase will require demonstration of protocols in human or animal explants, with preference given to larger, more complex model systems. The performer will develop a regulatory strategy for FDA approval of the proposed approach as deliverable in Phase II.

**PHASE III DUAL USE APPLICATIONS:** Progress in methods to allow salvage of testes, penile tissue and other genitourinary tissues would impact fertility, form, and function for thousands living with trauma injuries and create new treatments. Large potential markets exist for technologies that can extend the preservation, maintenance, repair, or storage of genitourinary tissues for periods spanning days to years. It is envisioned that the performer will pursue development of the approach to permit the salvage, repair, and preservation of GU tissues.

#### REFERENCES:

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**KEYWORDS:** genitourinary, combat injury, function, fertility, reproduction, regeneration, tissue preservation