CHEMICAL AND BIOLOGICAL DEFENSE PROGRAM
FY21.2 Small Business Innovation Research (SBIR)
Proposal Submission Instructions

The approved FY21.2 topics included in the Chemical and Biological Defense (CBD) Small Business Innovation Research (SBIR) Program are listed below. Offerors responding to this Announcement must follow all general instructions provided in the Department of Defense (DoD) Program Announcement. Specific CBD SBIR requirements that add to or deviate from the DoD Program Announcement instructions are provided below.

Please read the entire DoD Announcement and these CBD SBIR instructions carefully prior to submitting your proposal. Also go to https://www.sbir.gov/about/about-sbir#sbir-policy-directive to read the SBIR/STTR Policy Directive issued by the U. S. Small Business Administration (SBA).

General Information

In response to Congressional interest in the readiness and effectiveness of U.S. Nuclear, Biological and Chemical (NBC) warfare defenses, Title XVII of the National Defense Authorization Act for Fiscal Year 1994 (Public Law 103-160) requires the Department of Defense (DoD) to consolidate management and oversight of the Chemical and Biological Defense (CBD) Program into a single office – Office of the Assistant Secretary of Defense for Nuclear, Chemical and Biological Defense Programs. The Joint Science and Technology Office for Chemical and Biological Defense (JSTO-CBD), located at the Defense Threat Reduction Agency (DTRA), provides the management for the Science and Technology component of the Chemical and Biological Defense Program. Technologies developed under the Small Business Innovation Research (SBIR) Program have the potential to transition to the Joint Program Executive Office for Chemical Biological Radiological and Nuclear Defense (JPEO-CBRND) if the appropriate level of technology maturity is demonstrated. The JSTO-CBD Science & Technology programs and initiatives improve defensive capabilities against Chemical and Biological Weapons of Mass Destruction. The SBIR portion of the CBD Program is managed by the JSTO-CBD.

The mission of the Chemical and Biological Defense Program is to ensure that the U.S. Military has the capability to operate effectively and decisively in the face of chemical or biological warfare threats at home or abroad. Numerous factors continually influence the program and its technology development priorities. Improved defensive capabilities are essential in order to mitigate the overall impact of chemical and biological threats. The U.S. military requires the finest state-of-the-art equipment and instrumentation available to permit our warfighters to 'detect to warn' and avoid contamination, if possible – and to be able to sustain operations in a potentially contaminated environment. Further information is available at the Office of the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs homepage at https://www.acq.osd.mil/ncbdp/cbd/

The overall objective of the CBD SBIR Program is to improve the transition or transfer of innovative Chem-Bio technologies to the end user – the warfighter – in addition to commercializing technologies within the private sector for mutual benefit. The CBD SBIR Program targets those technology efforts that maximize a strong defensive posture in a biological or chemical environment using passive and active means as deterrents. These technologies include chemical and biological detection for both point and stand-off capabilities; individual and collective protection; hazard mitigation (decontamination); medical pre-treatments (e.g., vaccine development and delivery); medical therapeutics (chemical countermeasures and biological countermeasures); medical diagnostics; Digital Battlespace Management (aka information systems technology) to include but not limited to modeling and simulation (e.g., meteorological dispersion), disease surveillance, data fusion, and health & human effects to include wearable technologies.

Proposals not conforming to the terms of this Announcement will not be considered. CBD SBIR reserves the right to limit awards under any topic, and only those proposals of superior scientific and technical quality as determined by CBD SBIR will be funded. CBD SBIR reserves the right to withdraw from negotiations at any time prior to contract award. The Government may withdraw from negotiations at any time for any reason to include matters of national security (foreign persons, foreign influence or ownership, or other related issues).

Use of Foreign Nationals (also known as Foreign Persons), Green Card Holders, and Dual Citizens

See the "Foreign Nationals" section of the DoD SBIR Program Announcement for the definition of a Foreign National (also known as Foreign Persons).

ALL offerors proposing to use foreign nationals, green-card holders, or dual citizens, MUST disclose this information regardless of whether the topic is subject to export control restrictions. Identify any foreign nationals or individuals holding dual citizenship expected to be involved on this project as a direct employee, subcontractor, or consultant. For these individuals, specify their country of origin, the type of visa or work permit under which they are performing and an explanation of their anticipated level of involvement on the project. You may be asked to provide additional information during contract negotiations in order to verify the foreign citizen's eligibility to participate on a SBIR contract. Supplemental information provided in response to this paragraph will be protected in accordance with the Privacy Act (5 U.S.C. 552a), if applicable, and the Freedom of Information Act (5 U.S.C. 552(b)(6)).

Submitting Your Phase I CBD SBIR Proposal

Your entire proposal submission must be submitted electronically through the Defense SBIR/STTR Innovation Portal (DSIP) located at: https://www.dodsbirsttr.mil

A hardcopy is NOT required and will not be accepted by the Chemical and Biological Defense SBIR Program. Hand or electronic signature on the proposal is NOT required.

Any questions pertaining to the DoD SBIR/STTR submission system should be directed to the DoD SBIR/STTR Help Desk at: DoDSBIRSupport@reisystems.com.

Questions pertaining to the CBD SBIR program and these proposal preparation instructions should be directed to: Mr. Larry Pollack, Chemical and Biological Defense (CBD) SBIR Program Manager, Joint Science and Technology Office for Chemical and Biological Defense (JSTO-CBD), e-mail: lawrence.p.pollack2.civ@mail.mil

The Proposal Technical Volume must be 20 pages or less in length. No other information included in the other proposal volumes counts against the 20-page Proposal Technical Volume page limit. Pages provided in excess of this length will not be evaluated or considered for review. The proposal must not contain any type smaller than 10-point font size (except as legend on reduced drawings, but not tables).

The maximum dollar amount for a Phase I proof-of-concept/feasibility study is $167,500 for a period of performance of up to six (6) months. **The CBD SBIR Program will not accept Phase I proposals which exceed $167,500 for the Phase I effort**. The total SBIR funding amount available for Phase II activities from a resulting Phase II contract is not to exceed $1,100,000.

Selection of Phase I proposals will be based upon the three evaluation criteria discussed in this Program Announcement. The CBD SBIR Program reserves the right to limit awards under any topic, and only those proposals of superior scientific and technical quality in the judgment of the technical evaluation

team will be funded. All SBIR contract awards, both Phase I and Phase II, are subject to availability of funding.

Companies should plan carefully for any research involving animal or human subjects, chemical agents, biological agents, etc. The brief Period of Performance available for a Phase I project precludes plans that include these elements, as all DoD requirements and necessary approvals associated with animal and/or human use must be strictly adhered to, and require considerable coordination and significant time for final protocol approvals. See Section below for further information regarding all research that will include animal and/or human subjects.

Proposals not conforming to the terms of this Announcement, and any unsolicited proposals, will not be considered. All awards are subject to the availability of funding and successful completion of contract negotiations. The Chemical and Biological Defense Program is not responsible for any funds expended by the proposer prior to contract award.

CBD Program Phase II Proposal Guidelines

Phase II is the demonstration of the technology that was found feasible in Phase I. Phase I awardees may submit a Phase II proposal without invitation; however, it is strongly encouraged that a Phase II proposal not be submitted until sufficient Phase I progress can be evaluated and assessed based on results of the Phase I proof-of-concept/feasibility study. Therefore, it is suggested that a Phase II proposal be submitted no sooner than five months from date of Phase I contract award. **All Phase II proposal submissions must be submitted electronically through the Defense SBIR/STTR Innovation Portal system at: https://www.dodsbirsttr.mil**

At the proposal submission website, Phase II proposals MUST be submitted to '**CBD** SBIR' regardless of which DoD contracting office negotiated and awarded the Phase I contract. Additional instructions regarding the Phase II proposal submission process including submission key dates will be provided to Phase I awardees after the Phase I contract is awarded; additional information may also be found at http://www.cbdsbir.net.

The Phase II proposal must include a concise summary of the Phase I project including the specific technical problem or opportunity addressed and its importance, the objective of the Phase I project, the type of research conducted, findings or results of this research, and technical feasibility of the proposed technology. Due to limited funding, the CBD SBIR program reserves the right to limit awards under any topic and only proposals considered to be of superior quality will be funded.

All proposers are required to develop and submit a commercialization plan describing feasible approaches for marketing and manufacturing the developed technology. Proposers are required to submit a budget for the entire 24-month Phase II Period of Performance. During contract negotiation, the Contracting Officer may require a Cost Volume for a base year and an option year; thus, proposers are advised to be aware of this possibility. These costs must be submitted using the Cost Volume format (accessible electronically on the DoD SBIR/STTR submission site). The total proposed amount should be indicated on the Proposal Cover Sheet as the Proposed Cost. At the Contracting Officer's discretion, Phase II projects may be evaluated for technical progress prior to the end of the base year, prior to extending funding for the option (second) year.

The CBD SBIR Program is committed to minimizing the funding gap between Phase I and Phase II activities. The CBD SBIR Program typically funds a cost plus fixed fee Phase II award, but may award a firm fixed price contract at the discretion of the Contracting Officer.

It is recommended that Phase II awardees have a Defense Contract Audit Agency (DCAA) approved accounting system. If you do not have a DCAA approved accounting system, this could delay/prevent a Phase II contract award. Visit https://www.dcaa.mil/Customers/Small-Business for more information on DCAA approved accounting systems.

Technical Assistance

At this time, the CBD SBIR Program is not participating in the Technical and Business Assistance (TABA) Program.

Protest Procedures

Refer to the DoD SBIR Program Announcement for procedures to protest the Announcement.

As further prescribed in FAR 33.106(b), FAR 52.233-3, Protests after Award should be submitted to: Mr. Larry Pollack, Chemical and Biological Defense (CBD) SBIR Program Manager, Joint Science and Technology Office for Chemical and Biological Defense (JSTO-CBD), lawrence.p.pollack2.civ@mail.mil

CBD SBIR Projects Requiring Animal and Human Subjects

Companies should plan carefully for any research involving animal and/or human subjects in addition to the use of any chemical or biological warfare agents, and use of any agents associated with "Dual Use Research of Concern (DURC)". The brief Phase I Period of Performance precludes plans requiring the use of many of these materials as well as animal and/or human subjects prior to obtaining all necessary DoD approvals.

The offeror is expressly forbidden to use or subcontract for the use of laboratory animals in any manner without the express written approval of the U.S. Army Medical Research and Development Command's (USAMRDC), Animal Care and Use Review Office (ACURO). Written authorization to begin research under the applicable protocol(s) proposed as part of the CBD SBIR program will be issued after contract award in the form of an approval letter from the USAMRDC ACURO to the recipient. Furthermore, modifications to already approved protocols require approval by ACURO prior to implementation.

Research under CBD SBIR awards involving the use of human subjects, to include the use of human anatomical substances or human data, shall not be proposed for any Phase I Period of Performance. If Human Subjects research is proposed during the Phase II Period of Performance, the studies may not begin until the DTRA Research Oversight Board (ROB) provides authorization that the research protocol may proceed. Written approval to begin research protocol will be issued from the ROB, under separate notification to the recipient. Written approval from the ROB is also required for any sub-recipient that will use funds obtained from any CBD SBIR awards to conduct research involving human subjects.

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

Notification of Selection or Non-selection

Proposing firms will be notified of Selection or Non-selection for a Phase I award within 90 days of the closing date of the BAA. For each proposal submitted, the individual named as the Corporate Official on the Proposal Cover Sheet will receive an email from *notification@dtrasubmission.net* with their official

notification of proposal Selection or Non-selection decision. Please check your Spam folder for the notification e-mail, should you not receive the notification to your inbox within the 90 day time period.

CBD 21.2 Phase I Topic Index

CBD212-001 TITLE: Multi-Modal Detection of Chemical Threats Using Deep Learning

KEY TECHNOLOGY AREA(S): Chemical/Biological Defense; Battlespace Environments; Sensors

OBJECTIVE: Develop a Deep Learning (DL) threat detection solution using a fusion of imaging sensors and chemical/biological sensors to detect and locate concealed chemical threats (with potential capabilities for both biological and explosives threats). The developed architecture must be deployable on edge computing platforms for use in real time (better than 60 second detection, 60 frames per second for video sensors) standoff threat detection platforms (50 m) such as Unmanned Aerial Vehicles (UAVs) and Unmanned Ground Vehicles (UGVs).

DESCRIPTION: Detection of concealed chemical threats through the development of sensor technology has improved over the last decade. Automated threat identification and location remains a challenge in operational environments. Multi-modal sensing promises to provide greater threat detection capability, as well as identification of threat location and type than individual sensing modalities can provide. Imaging solutions, such as infrared sensors, LIDAR, and RADAR, provide threat detection and location capabilities but cannot adequately differentiate chemical threat types. Chemical sensors provide remarkable capability of threat identification, and general vicinity detection but cannot adequately spatially locate chemical threats. A multi-modal approach to threat detection will provide improved situational awareness and inform appropriate threat response.

DL algorithms have significantly improved the ability to autonomously detect a wide range of threats. Recent developments of DL algorithms combine audio and visual representations of a state to increase the correlation of input data to a specific target. Extrapolating from visual and auditory inputs to other sensing modalities will drive automated detection algorithms for chemical/biological threats for environmental awareness of operational environments. Development of a DL architecture that jointly exploits the signature from a chemical sensor with a threat signature from an imaging sensor has multiple benefits over single mode detection modalities by increasing threat detection confidence, as well as threat identification/classification. Additionally, multi-modal DL architectures have shown promise of being less vulnerable to adversarial examples, inputs modified by introducing small perturbations to deliberately fool a target model into outputting incorrect results, bringing an additional layer of security to Department of Defense (DoD) threat detection technologies.

Phase I proposals should advance the state-of-the-art of automated chemical threat detection, location, and identification by incorporating multi-modal sensor inputs to a DL detection/identification process. To advance to a Phase II project, performers must demonstrate improved detection/identification rates higher than single mode detection techniques. It is expected that in Phase I and Phase II, performers will utilize Commercial-Off-the-Shelf (COTS) or novel sensor technologies.

PHASE I: Develop and test a DL architecture that jointly exploits multi-modal sensor inputs for chemical threat detection and identification. Demonstrate the improved detection performance of the multi-modal DL architecture over single mode DL automated detection algorithms. During the Phase I project, the proof-of-concept demonstration should focus on the discrimination of at least two or more chemical threats with a clear path forward on implementing the DL

architecture with low size, weight and power (SWaP) computing hardware for edge computing. Chemical warfare threats of all classes are of interested for threat detection and localization (better than 5 meter accuracy). Examples of chemical threats of interest include, but are not limited to, chlorine; tear gas/pepper spray; and nitrogen oxides.

The Phase I deliverable should explain the algorithms tested, software concepts, hardware requirements, results of single mode and multimodal detection tests, and potential use cases and limitations identified within the Chemical and Biological Defense program.

PHASE II: Phase II will focus on the development and testing of an embedded multi-modal DL algorithm on a field portable computational platform that can accept multiple sensor inputs. Design of the DL architecture will enable low SWaP requirements of the computation platform to enable ease of deployment to operational environments on small unmanned vehicles (UxV). Evaluation of the multi-modal DL chemical detection algorithms will be extended to multiple threat vectors and demonstrate improved threat detection and identification over single mode DL architectures. Laboratory based characterization and validation of the embedded DL algorithm will be required for a successful completion of Phase II. Technical demonstration and validation of the developed technology in operationally relevant environments will take place with government personnel.

PHASE III: The expected Phase II end-product is a well-designed, deployable edge computing device with an embedded DL algorithm trained for detection of chemical threats that can be used on ground and aerial vehicles. Follow-on government and civilian activities are expected to be pursued by the offeror. Transition of the developed technology will require refined algorithm training and testing to optimize the threat detection capability for the chemical threats of concern, as well as extending the number of trained threats and modalities that can be identified. Edge case testing will also be explored and defined.

PHASE III DUAL USE APPLICATIONS: Multi-modal target discrimination DL algorithms can support and enhance medical diagnostic applications for increased prognostic assurance. Additionally, leveraging multiple sensor inputs improves perception of a vehicle’s immediate environment.

REFERENCES:

1. Zhang, Shiqing, et al. "Multimodal deep convolutional neural network for audio-visual emotion recognition." Proceedings of the 2016 ACM on International Conference on Multimedia Retrieval. 2016.
2. Alshemali, Basemah, and Jugal Kalita. "Improving the reliability of deep neural networks in NLP: A review." Knowledge-Based Systems 191 (2020): 105210.
3. Ortega, Juan DS, et al. "Multimodal fusion with deep neural networks for audio-video emotion recognition." arXiv preprint arXiv:1907.03196 (2019).
4. Le, Minh Hung, et al. "Automated diagnosis of prostate cancer in multi-parametric MRI based on multimodal convolutional neural networks." Physics in Medicine & Biology 62.16 (2017): 6497.
5. Giering, Michael, Vivek Venugopalan, and Kishore Reddy. "Multi-modal sensor registration for vehicle perception via deep neural networks." 2015 IEEE High Performance Extreme Computing Conference (HPEC). IEEE, 2015.

KEYWORDS: Deep Learning, Chemical/Biological Threat Detection, Multi-Modal Sensing, Scene Perception, Algorithms

CBD212-002 TITLE: Augmented Reality CBRN Threat Display for Mounted Situational Awareness

KEY TECHNOLOGY AREA(S): Chemical/Biological Defense; Information Systems Technology; Human Systems

OBJECTIVE: To provide a real-time, geospatially accurate, augmented reality display of various CBRNE sensor data to mounted and dismounted warfighters.

DESCRIPTION: CBRN (Chemical, Biological, Radiological, Nuclear) sensors are present throughout the armed forces. The Stryker Nuclear Biological Chemical Reconnaissance Vehicle Sensor Suite Upgrade (NBCRV SSU) provides CBRN mounted reconnaissance capability for both manned and unmanned Stryker systems. Newer, smaller CBRN and EO/IR sensors are also increasingly being deployed to small Unmanned Ground Vehicles (UGV) or Unmanned Air Systems (UAS). Much of the effort is focused on collecting situational awareness at mission-speed. The increased amount and variety of data can be challenging to interpret, especially in a moving vehicle for a mounted reconnaissance mission. While strides have been made to populate CBRN sensor data into situational awareness tools such as the Android Team Awareness Kit (ATAK), additional real-time capabilities to present information at mission speed are desired. Augmented Reality (AR) capabilities such as the Integrated Visual Augmentation System (IVAS) are being developed to provide individual warfighters with real-time heads-up viewing capabilities for a variety of applications.

This development program seeks to join CBRN sensors and emerging Augmented Reality displays together to provide a detailed, unified real-time CBRN-centric view of the battlespace. Back-end integration with other existing C2 systems such as the Android Team Awareness Kit (ATAK), Inertial Navigation Systems (INS), and support for future higher-performance sensors utilizing AI/ML is desired. Support for open standards is also highly desired.

Of particular interest is the potential to integrate and display real-time sensor information coming from a downrange, vehicle-mounted, portable mass spectrometer device as well as a handheld radioisotope identification device (RIID) to show the capability to map chemical vapors and radiation fields in real-time by directly connecting the sensors to the Heads-up Display (HUD).

PHASE I: Phase I will consist of a proof-of-concept system utilizing existing CBRNE sensors, AR HUDs and other displays, user interface concepts, and accompanying system architecture showing the growth path to future sensors, phases, and capabilities. A key deliverable of Phase I will be a proof-of-concept showing direct communication of mature RIID and Mass Spectrometer data to a HUD device to generate an AR display of sensor data with localization of threats.

PHASE II: Phase II will consist of maturation of the concept and integration of the system onto a representative platform and show integration with geo-referenced, off-board sensor systems, greater fidelity on the display, and increased usability to include use while on-the-move. The key deliverable of Phase II will be the demonstration of the system in a relevant platform combining the sensors on a vehicle exterior with the real-time AR view on a HUD device from the interior of a vehicle to demonstrate real-time CBRNE situational awareness.

PHASE III: Phase III will transition the program to an operationally relevant environment, including testing and validation to certify the program for Department of Defense use (Joint Chemical and Biological Defense Program). The system has the potential to be installed on reconnaissance vehicles such as the Stryker or in other tactical vehicles and on unmanned reconnaissance platforms. The platform will be further extendable to other types of fielded sensors for situational awareness.

PHASE III DUAL USE APPLICATIONS: The same system could be installed on vehicles used by other agencies responsible for CBRN and EO/IR systems for surveillance missions such as the Department of Homeland Security (DHS).

REFERENCES:

1. Lazna, T (2018). The Visualization of Threats Using the Augmented Reality and a Remotely Controlled Robot. 15th IFAC Conference on Programmable Devices and Embedded Systems PDeS 2018. Volume 51, Issue 6, 444-449. (https://doi.org/10.1016/j.ifacol.2018.07.113.)
2. Nuclear Biological Chemical Reconnaissance Vehicle (NBCRV) — Stryker Sensor Suite. https://asc.army.mil/web/portfolio-item/cbd-nuclear-biological-chemical-reconnaissance-vehicle-nbcrv-stryker-sensor-suites/
3. Army conducts major milestone tests in development of next gen fighting system
4. https://www.army.mil/article/240584/army_conducts_major_milestone_tests_in_development_of_next_gen_fighting_system

KEYWORDS: CBRN, Augmented Reality, ATAK, UAV, radioisotope, Heads-Up Display

CBD212-003 TITLE: Field Portable Bioaerosol Identification via Mass Spectrometry

KEY TECHNOLOGY AREA(S): Chemical/Biological Defense, Biomedical

OBJECTIVE: Develop a field portable, mass spectrometry-based system that rapidly identifies aerosolized biological particulate, arising from the breath of a warfighter, or from their surrounding environment and the identification technology must be adaptable to the evolution of pathogens both natural and synthetic.

DESCRIPTION: Aerosolized biological particles are a major vector causing the spread of disease from human to human and from animal to human [1]. This is particularly true for respiratory pathogens such as adenoviruses, influenza viruses, *Mycobacterium tuberculosis* and coronaviruses such as SARS-CoV-2. Currently, global healthcare systems and governments are in acute crisis because of the worldwide spread of SARS-CoV-2 and the COVID-19 pandemic disease caused by this virus - that arose from animal-to-human transmission. The ability to rapidly, accurately and affordably screen the environment for a wide range of aerosolized pathogens arising from agricultural sources (live animal markets) and human exhaled breath could revolutionize the discovery of emerging pathogens and the ability to identify spreaders of these diseases.

The ability to identify bioaerosols enables a system that could pinpoint persons who are actively shedding pathogen and spreading a disease. Identification of these spreaders, and superspreaders [2], is a vital tool aimed at shutting down the infectious cycle. The enormity and constancy of such a screening protocol argues for testing that is non-invasive, extremely low cost and requires little or no consumables.

In a patient care setting a bioaerosol identification system could be used to monitor the air surrounding the patients for the presence of infectious agent. Constant analysis of the levels of these agents in the air could be used to determine the efficacy of protective measures such as advanced filtration and ventilation on the patients and staff of the facility. Excursions of these measurements above an established baseline could alert personnel to dangerous situations, triggering responses such as donning of enhanced PPE or increasing technical measures such as the air exchange rate in the facility.

Finally, while a bioaerosol identification device has great utility against existing disease states, the tool could provide critical information on potential new organisms originating in agricultural or wildlife settings. Constant monitoring of the air in these environments could provide critical early stage biosurveillance as organisms mutate, potentially resulting in a future pandemic. This mode of operation could be used as a biosurveillance tool and could provide early warning of the rise of a new pandemic threat. If a potential new threat is detected, the signatures of that threat could be propagated through a distributed system of biosurveillance devices.'
This technology development focuses on mass spectrometry because it has the potential to meet the following requirements that would enable wide spread use of the technology:

- Direct, non-invasive sampling
- Rapid automated sample preparation (< 1 min)
- Very fast analysis (< 1 min)
- High sensitivity (10’s of organisms)

- High specificity using biomolecular signatures
- Rapid adaptability to new/unknown threats through electronic signature updates
- Very low cost of analysis (<$1 per test)

PHASE I: Phase I entails the design of a concept for a rapid identification system of aerosolized pathogens, identification of key system components and initial testing of those components. The drivers for a technically and commercially successful system will be adaptability, sensitivity, specificity, speed, and cost-per-test. The performer will perform a detailed literature search on the aerosol concentration of pathogens in and around sources of infectious particles to determine the operative sensitivity threshold within proposed use scenarios for their specific detection technology. For certain highly desirable use scenarios, particularly high-throughput screening using human breath samples, an analysis time that is in the 1 minute or less range is preferred. Such a rapid analysis drives a base detection/identification technology that is extremely sensitive, yet it must have sufficient specificity so as not to have unacceptable false alarm rates. Finally, given the massive screening use scenarios, the cost-per-test must be very low. The initial effort in Phase I will be the development of a concept that incorporates the speed, sensitivity, specificity, and cost elements described here. Critical elements or components of the design should be chosen and tested for applicability in the proposed overarching design. Finally, a refined preliminary design should be developed to lead to a proposed Phase II prototype.

PHASE II: In Phase II, the small business will develop, demonstrate and validate a system for aerosolized biopathogen identification using non-pathogenic simulants of bacterial and viral disease vectors.

Following a Preliminary Design Review (PDR), the performer will assemble and test a breadboard system that has the initial versions of the sampling, analysis, and data reporting subsystems interoperating. This system will be tested using aerosolized biopathogen simulants in relevant laboratory backgrounds. The system will be benchmarked against standard laboratory techniques of biopathogen identification. The key detection/identification parameters will be assessed, and necessary improvements identified. An initial analysis of the commercial applications of the system will be conducted focusing on the baseline cost of the system, the cost-per-test, and the market space addressed by the technology development.

Following the completion of the preliminary design system, the performer will upgrade the breadboard system with modifications that address deficiencies identified in testing and analysis, and leading to a Critical Design Review (CDR). Following this review, a complete prototype system will be fabricated and tested in a relevant environment. Depending on the ultimate use case for the technology, this could be a human disease sampling effort, or it could be an environmental testing scenario in a hospital unit or in an agricultural setting. The performer will provide a detailed test plan that must contain human usage approvals, if such testing is anticipated. A refined analysis of the commercial opportunities for the technology also will be completed.

PHASE III: Phase III work is typically oriented towards technology transition to Acquisition Programs of Record and/or commercialization of SBIR research or technology. In Phase III, the performer is expected to seek funding from non-SBIR government sources and/or the private sector to develop or transition the prototype into a viable product or service for sale in the

military or private sector markets. The Phase III description must include the "vision" or "end-state" of the research. It must describe one or more specific Phase III military applications and/or supported S&T or acquisition program as well as the most likely path for transition of the SBIR from research to operational capability. Additionally, the Phase III section must include (a) one or more potential commercial applications OR (b) one or more commercial technology that could be potentially inserted into defense systems as a result of this particular SBIR project.

PHASE III DUAL USE APPLICATIONS: A rapid, sensitive, specific, low-cost approach to identification of bioaerosol components will have application beyond DoD needs. The ability to rapidly screen persons transmitting disease could revolutionize the control of infectious disease spread. For instance, Homeland Security components such as Transportation Security Agency (TSA) and Customs and Border Protection (CBP) could employ such a system to screen disease spreaders at transportation hubs and border crossings. In agricultural applications, such a system could signify the spread of a disease through a feedlot or even the emergence of a potential new vector for human disease.

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1. *Infection Prevention and Control of Epidemic- and Pandemic-Prone Acute Respiratory Infections in Health Care*. Geneva: World Health Organization; 2014. (https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions)
2. Frieden, T. R., & Lee, C. T. (2020). Identifying and Interrupting Superspreading Events—Implications for Control of Severe Acute Respiratory Syndrome Coronavirus 2. Emerging Infectious Diseases, 26(6), 1059-1066. (https://dx.doi.org/10.3201/eid2606.200495).
3. Yadana, S., Coleman, K. K., Nguyen, T. T., Hansen-Estruch, C., Kalimuddin, S., Thoon, K. C., Low, J., & Gray, G. C. (2019). Monitoring for airborne respiratory viruses in a general pediatric ward in Singapore. *Journal of public health research*, *8*(3), 1407. (https://doi.org/10.4081/jphr.2019.1407)

KEYWORDS: Aerosolized pathogens, breath sampling, environmental sampling, biosurveillance

CBD212-004 TITLE: Development and Testing of a Multi-dose Vial for Scopolamine Hydrobromide Trihydrate Formulation for Intramuscular Injection

KEY TECHNOLOGY AREAS: Chemical/Biological Defense, Biomedical

OBJECTIVE: To develop a multi-dose, scopolamine hydrobromide trihydrate vial containing a formulation that is stable, injectable, and suitable for GMP manufacture.

DESCRIPTION: The Joint Project Manager for Chemical, Biological, Radiological, and Nuclear Medical (JPM CBRN Medical) is developing scopolamine hydrobromide trihydrate (Scop-HBT) under the Improved Nerve Agent Treatment System - Centrally Acting (INATS CA) program. Scop-HBT is an anticholinergic medical countermeasure (MCM) that temporarily blocks severe or life-threatening muscarinic effects caused by organophosphorus nerve agent (OPNA) poisoning. The improved OPNA treatment regime will consists of the Scop-HBT intramuscular (IM) injection as an adjunct to the standard of care autoinjectors containing atropine and 2-PAM (2-pyridine aldoxime methyl chloride (Pralidoxime). The combined therapeutic action will help to decrease morbidity and mortality of military personnel and civilians exposed to OPNAs. Currently, the JPM CBRN Medical is developing Scop-HBT in an autoinjector format; the concentration is not yet final, but a concentration between 0.8 mg/ml and 2.0 mg/ml is anticipated. The autoinjector in development is suitable for use by an individual to deliver immediate treatment. However, the use of single dose devices and/or vials represents a significant logistical burden to military first responders that will need to deliver multiple injections during a mass casualty event. A multi-dose vial with Scop-HBT for IM injection, 20 ml total volume containing 10-20 doses, will significantly decrease logistical burden associated with having to use multiple single dose vials to treat during mass casualty OPNA exposure incidents, as well as for treating single OPNA exposure casualties over a prolonged period of time.

PHASE I: Establish preliminary specifications for a multi-dose formulation under International Conference on Harmonization (ICH) Pharmaceutical Development Guidelines**.** The active drug substance to be employed will be Scop-HBT (United States Pharmacopeia (USP) grade or Department of Defense (DoD) supplied). Initial test vials will contain a total of 20 ml of drug solution volume, containing a concentration range of 0.8 mg to 2.0 mg of Scop-HBT per ml in an appropriately sealed, pharmaceutical grade light-restricting glass vials, as designed for injectable drug formulations. Based on the single dose formulation ranging from 0.8 mg/ml to 2.0 mg/ml, the target pH of the formulation is approximately 3.00 ± 0.10 in pharmaceutical grade buffer, and tonicity adjusted to approximate isotonicity (270 to 310 mOsm (milliosmole). The test formulations will evaluate added U. S. Food and Drug Administration (FDA) approved, effective antimicrobial preservatives (e.g., 0.9% benzyl alcohol or 0.5% chlorobutanol) against analytical parameters established for the DoD single dose formulation (currently in development). Stability assessments could employ forced degradation and initial real time testing for the scopolamine drug substance, and development of degradants at targeted temperatures and relative humidity conditions: refrigerated (2-8°C), room temperature (25 ± 2°C / 60% ± 5% RH), and stressed (40 ± 2°C / 75% ± 5% RH).

PHASE II: Conduct further evaluation, improvements, and stability enhancements of selected candidate. Subsequent analytical testing is to be performed to determine the presence and

concentrations of extractables and leachables. Real-time stability is to be evaluated to achieve a targeted shelf-life of two years at 25 ± 2°C / 60% ± 5% RH. Subsequent studies may determine the effects of potential stability enhancement techniques as needed, such as utilization of head-space nitrogen purge, vacuum seal, or other to promote extended stability to two years. A syringe needle puncture study is to be performed to evaluate required 28 day drug stability (28 days at 2-8°C and 25°± 2°C / 60% ± 5% RH (relative humidity)). The performer may evaluate the use of lyophilization as a dry powder stability enhancer after reconstitution, with bacteriostatic saline or sterile water for injection. This may be accomplished with variable addition of the antimicrobial agent as needed. The performer may determine the shelf-life stability of the lyophilized powder as needed under vacuum seal or nitrogen purge. A 28 day stability study will be evaluated to determine shelflife after reconstitution. The last developmental step is analytical analysis to demonstrate equivalence to the single dose IM Scop-HBT formulation currently being developed by the DoD (final concentration and comparator to be provided at time of contract award).

PHASE III: Develop scale-up processes and technology transfer protocol for the pilot lot and good manufacturing practice (GMP) production. Develop regulatory strategy, and initiate interactions with the FDA.

PHASE III DUAL USE APPLICATIONS: The Department of Health and Human Services (HHS) has a similar need for improved anticholinergic therapeutics, including multi-use vialed Scop-HBT for use in civilian casualty situations. Successful completion of all three phases under this solicitation will support small business valuation by confirming technical merit that invites further investment. This award mechanism will bridge the gap between laboratory-scale innovation and entry into a recognized FDA regulatory pathway leading to commercialization.

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2. Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products. Guidance for Industry. *Division of Drug Information, Center for Drug Evaluation and Research, FDA.* June 2015 Pharmaceutical Quality/CMC. 2015.
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KEYWORDS: atropine, scopolamine, chemical nerve agent, medical countermeasure, drug formulation

CBD212-005 TITLE: Improved Technologies for Protection and Treatment of Dermal Injuries Caused by Sulfur Mustard

KEY TECHNOLOGY AREAS: Chemical/Biological Defense, Biomedical

OBJECTIVE: To develop capabilities and obtain FDA approval for dermal dressing technologies that provide multiple advantages over current wound dressings for treating dermal injuries caused by sulfur mustard.

DESCRIPTION: Sulfur mustard (military designation HD or H) is a chemical warfare agent that affects multiple tissues, and causes blistering of the skin and mucous membranes on contact. The dermal lesions caused by HD resemble burn lesions, and can cover large portions of exposed skin surfaces. Like burn injuries, HD dermal lesions are extremely painful, can lead to fluid loss, and are highly susceptible to infection. Battlefield management of these wounds by military first responders can be especially challenging due to the high potential for mass casualties, the necessity to treat during ongoing operations in austere environments, and delays in medical evacuation.

The Joint Project Manager for Chemical, Biological, Radiological, and Nuclear Medical (JPM CBRN Medical) is interested in developing technologies (dressings, treatments, etc.) to treat HD dermal injuries in a battlefield environment. Candidate technologies for this application need to provide physical protection to burn-like injuries, be stable in a large range of conditions (temperature and humidity), be easy to apply, be suitable for application to various surface areas, allow inspection of injuries without removal, provide antimicrobial protection, and pain relief. The ultimate goal is to demonstrate efficacy in treating HD dermal injury in appropriate animal models of HD injury (see Phase II). In addition to being efficacious in protecting and treating HD dermal injuries to allow faster healing, top candidates for consideration will also possess additional desirable properties mentioned above. Among these are ease of application to facilitate use in a mass casualty event, and low logistical footprint (not cumbersome to carry, minimal cold chain storage requirements, sufficient shelf life, etc.). Other desirable properties sought are selective permeability to prevent fluid loss through the wound(s), antimicrobial properties to protect against infections, providing pain relief, and relative ease of removal for performing required treatments after application. These technologies have a broad potential application beyond just HD injuries; hence, they are expected to reduce logistical burden to the military first responder.

PHASE I: If the proposed technologies have been previously tested for other injury types, provide *in vivo* data demonstrating the efficacy of the product when used to treat similar injuries such as burns, severe abrasions, and/or other comparable injuries. Quantitative data that provides clear metrics that allow the comparison of the candidate to other products or standard medical care (wound size reduction over time, time to restoration of dermal layers, etc.) is preferred. Generate and provide a regulatory plan to obtain an FDA approval or an HD dermal injury indication. The plan should align with the timing and funding levels expected for SBIR Phase I and II, with the balance of funding and studies conducted in Phase III of the project. Obtain confirmation from the FDA, via pre-IND, Q-submission or pre-submission, that the regulatory plan is acceptable to obtain the HD dermal injury approval or indication for the

candidate technology. A research partner should be identified that can perform the needed pre-clinical animal studies using sulfur mustard. No animal studies are permitted during the Phase I period of performance.

PHASE II: Perform an efficacy study in a small animal model. Provide a report of the small animal study to determine if the product should proceed to testing in a large animal model. Plan the large animal study, and submit an estimate of cost for conducting Phase III objectives. If feasible, perform packaging/container designs to allow treatment of larger surface areas and for multiple casualties. At this stage, accelerated stability studies to obtain estimates on storage shelf life and operational conditions should be performed.

PHASE III: Perform the efficacy study in a large animal model. Prepare regulatory strategy and submit FDA documentation to add HD injury indication to the product. Submit final reports that include the results of the animal studies, and any relevant FDA information/documents to the JPM CBRN Medical.

PHASE III DUAL USE APPLICATIONS: The technologies proposed for development are also applicable to a broad range of battlefield injuries. This significantly increases the value of the technologies and reduces the burden on military first responders since it eliminates the need to carry equipment solely dedicated to chemical agent injuries. Furthermore, the Department of Health and Human Services (HHS) has a similar need for technologies that allow treatment of HD and burn injuries in a mass casualty event. Successful completion of all three phases under this solicitation will support small business valuation by confirming technical merit that invites further investment. This award mechanism will bridge the gap between laboratory-scale innovation and entry into a recognized FDA regulatory pathway leading to commercialization.

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KEYWORDS: sulfur mustard, blister agent, vesicant, dermal, topical, wound healing, dressing

CBD212-006 TITLE: Development of Small Molecule Therapeutics Specifically Targeting Members of the Bunyavirales Order

KEY TECHNOLOGY AREA(S): Chemical/Biological Defense, Biomedical

OBJECTIVE: Develop an antiviral drug to be used as a therapeutic in the event of disease or as a prophylactic medical countermeasure (MCM) following exposure or threat of exposure to viruses of the Bunyavirales order.

DESCRIPTION: The *Bunyaviridae* are a very large family of single-strand, enveloped RNA viruses (more than 300 viruses) and consists of five genera of viruses: *Orthobunyavirus, Phlebovirus, Nairovirus, Hantavirus,* and *Tospovirus* (Tospoviruses infect only plants). They are found in and transmitted by arthropods (e.g. mosquitoes, ticks, sand flies) and rodents, and can occasionally infect humans. Several viruses of the *Bunyaviridae* virus family can produce mild to severe disease in human, in animals, and sometimes in both.[1]

Hantaviruses were first observed in the early 1950's among troops deployed in the Korean conflict. Eventually named Hantaan virus after the nearby Hantaan River where the human cases occurred, the field mouse (Apodemus agrarius) was discovered to be the specific rodent host for the virus. The disease is actually known as Hemorrhagic fever with renal syndrome (HFRS) and described in the Old World. Following a cluster of cases of severe illness, called Hantavirus Pulmonary Syndrome (HPS), in the American southwest in 1993, a newly identified virus, called the Sin Nombre virus, was isolated. Related viruses, but responsible for the same clinical disease, are described in the New World (North, Central and South America).[1]

Emerging Viruses posing a threat to the warfighter include members of the Bunyavirales order (e.g. Rift Valley Fever virus [RVFV], Severe Fever with Thrombocytopenia Syndrome virus [SFTSV], Crimean-Congo Hemorrhagic Fever virus [CCHFV]; Sin Nombre virus [SNV]). Outbreaks of several of these viruses have occurred during 2018 in global areas of U.S. military presence.

The presence of vectors in new areas where these viruses are not currently endemic could lead to expansion of endemic areas or pose sporadic outbreak risks. For example, SFTSV is a new emerging Phlebovirus in China, Japan, and South Korea that causes hemorrhagic fever with mortality rates of up to 30%, and the tick vector for SFTSV recently has been isolated in the United States. Autochthonous infection has been demonstrated for CCHFV, a Nairovirus whose global distribution in over 30 countries is second to Dengue virus. For some viruses, animal models have not been fully developed; thus, use of transgenic mouse or hamster lines or immunosuppression may be required for initial, in vivo assessments. [2, 3, 4]

This topic seeks to identify small molecule inhibitors of any phase of virus replication. The preferred therapeutic is a small molecule that exhibits broad activity across virus families. Ideally the therapeutic can be self-administered orally or at least by administration within a reasonably short time frame in clinical settings.

PHASE I: Identify small molecule inhibitors of Bunyavirus replication. A) Identification and development of working stocks of appropriate strains of virus(es) for testing. Alternatively,

surrogate assays (e.g. pseudotyped particles, replicase assays) in lower safety containment laboratories are sufficient for early screening. Modeling data for potential broad-spectrum inhibition of Bunyavirus replication can be used to support intermediate development at the Phase II stage. B) Using high throughput screening of existing or novel libraries, identify small molecule inhibitors to virus replication of one or more of the members of the Bunyavirales order. The screening should assess antiviral activity and cytotoxicity. Studies that include any animal use will not be permitted during Phase I; obtaining all necessary DoD Animal Care and Use Review Office (AUCRO) approvals before any animal use may commence requires significant time and will preclude completing the Phase I project beyond the allowed six-month Phase I Period of Performance.

PHASE II: The objective of this phase is to assess the antiviral properties of a target small molecule for eventual IND filing. This will be accomplished by: A) Using compounds identified through high throughput screening, or for compounds in more advanced development stages, confirm the mechanism of action of optimized candidates; B) Develop clinical material for determining the PK/PD and ADME (absorption, distribution, metabolism, and excretion) of the compound and half maximal effective concentration(s) (EC50); C) In a single or series of pilot experiments, determine appropriate dose (using PK/PD modeling informed by successive experimental approaches) in an applicable animal model and assess toxicity and efficacy against one or more viruses. This stage will require development of working stocks of appropriate strains of virus(es) for testing (if not developed in Phase I), and performance within high containment laboratories.

PHASE III: Preclinical development of down-selected candidates to support submission of an application for an Investigational New Drug (IND). Construction of a Development Plan through consultation with a sponsor and the Food and Drug Administration (FDA). Discussions and preparations would include identification of appropriate virus strains, animal models, and if applicable, clinical trial location and development.

PHASE III DUAL USE APPLICATIONS: The viral agents listed in this SBIR topic lack treatment options, and any therapeutic derived from this research will be of significant use for both civilian and military populations at risk.

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KEYWORDS: antiviral, small molecule, medical countermeasure (MCM); therapeutic; Bunyavirus, Bunyavirales, Rift Valley Fever virus [RVFV], Severe Fever with Thrombocytopenia Syndrome virus [SFTSV], Crimean-Congo Hemorrhagic Fever virus [CCHFV], Sin Nombre virus [SNV], Hantavirus (HV)