CB BAA HDTRA122S0002 CALL 4

THE PROPOSAL SUBMISSION DEADLINE FOR THE FOLLOWING TOPICS IS MAY 29, 2024 AT 2:00PM EATERN DAYLIGHT TIME (EDT).

THE DEADLINE TO SUBMIT QUESTIONS RELATED TO THE FOLLOWING TOPICS IS APRIL 16, 2024.

CBA-01: Detection and Identification of Absorbed Chemical Agents within Porous Surfaces

Background: The successful detection and identification of surfaces and ground containing adsorbed/absorbed chemical warfare agents is critical in protecting the Warfighter during maneuver support and sensitive site exploitation mission sets as well as informing proper decontamination of materiel. Unfortunately, chemicals deposited onto porous and complex surfaces, such as soil and concrete, absorb within the pores of the material, effectively entraining the chemical within the surface. Given that the chemical interactions between these porous materials and chemical weapons are often reversible, this poses a potential secondary exposure risk for the Warfighter, even after successful decontamination of the external surface.

This topic seeks to identify new and innovative approaches to be able to detect and identify small quantities of chemical warfare agents trapped within the surface layers (up to 10 mm) of surfaces that include soil, concrete, and asphalt. The successful detection of entrained chemicals can help inform more robust decontamination measures on materiel, verify successful agent decontamination, inform Warfighter use of protective personal equipment to minimize secondary exposure risks, and inform maneuver operations. This information will allow the Warfighter to fight and succeed in a CB-contested environment.

A review of current literature suggests no current technology exists for the trace detection and identification of chemical warfare agents trapped within porous surfaces. However, several analytical approaches exist for understanding the chemical composition of porous materials.

The three main approaches identified are:

- Sample volatilization: The use of thermal radiation, low-temperature plasma, or laser-induced desorption of chemicals adsorbed/absorbed within a porous material to drive it out of the pores and be detectable in the vapor phase. Several limitations exist with this approach, including the secondary exposure of volatilized chemicals to the Warfighter and the successful volatilization of low vapor pressure chemicals or chemicals that strongly bind with the porous material for vapor analysis.
- Destructive surface analysis techniques: techniques using laser-ablation or other approaches to remove thin layers of the surface for analysis provide a direct means to providing depth-related chemical information, but in the case of chemically resistant coatings on military materiel, the destruction of that protective coating is not desired.
- Non-destructive optical analysis techniques: X-ray fluorescence and neutron activation have shown the ability to retrieve chemical composition information in samples up to several millimeters thick, but often have poor sensitivities, and rely on ionizing radiation that itself poses a risk to operators. Other promising approaches, which have been used to provide both chemical information and soil and concrete analysis, albeit not at the same time, include Fourier transform near-IR spectroscopy (FT-NIR), shifted excitation Raman difference spectroscopy (SERDS), spatially offset Raman spectroscopy (SORS) and terahertz imaging.

In addition to the aforementioned approaches, it's possible that other novel approaches or a combination of

approaches may be required to successfully address this problem set. Recent literature has demonstrated that spectral data fusion of mid-IR, near-IR, and X-ray fluorescence measurements were used to successfully characterize the concentration levels of seven key monitoring elements in the soil.

Objective: This topic seeks new and innovative detection prototypes that can be used to detect low concentrations of chemical warfare agents trapped within complex and porous surfaces to verify contaminated surface decontamination and prevent secondary chemical exposure risks.

Successful efforts will:

- Develop a sensor prototype capable of detecting chemical warfare agents absorbed into complex surfaces at threat-relevant concentrations; identification of individual chemical species is preferred, but class-based detection (i.e., H, G, V) is acceptable.
    - In the absence of a single, suitable detection technology, it is possible to propose orthogonal approaches, provided there is a detection algorithm developed to fuse the sensor data.
- Optical, non-destructive detection modalities are preferred, however solutions may include approaches that volatilize and desorb chemicals of interest from within the porous surface or destructively sample the surface, like laser ablation techniques.
    - Approaches may include, but are not limited to: spatially offset Raman spectroscopy (SORS), Fourier transform infrared spectroscopy (FTIR), SERDS, and terahertz imaging.
    - Optical approaches that are eye safe and do not produce ionizing radiation are preferred.
- Fabricate a final prototype system with low enough size, weight, and power to be man portable (<25 lbs.) or integrable onto unmanned ground vehicles.
- Ruggedize a final prototype to be operable under a wide range of operational environmental conditions (temperature, relative humidity, sun light/no light).
- Determine the sampling depth that the detection capability can probe based on surface media consistency.
- Evaluate breadboard prototypes against chemical warfare agent simulants entrained in representative complex surfaces.
    - As system matures, evaluate brassboard prototypes against live chemical agents in limited excursion testing.
- Develop a detection algorithm that can provide relevant threat indication based on sample concentration, chemical threat class, and sample depth.
- Allow for data output, reporting, and integration into the CBRN support for command and control (CSC2) or other relevant data frameworks to support Integrated Early Warning/Integrated Layer Defense.

Offerors are encouraged to develop R&D collaborations with other organizations in Government, academia, and the private sector to broaden and strengthen their knowledge, experience and capabilities. Additionally, offerors are encouraged to take advantage of specialized resources in the DoD and other Government agencies such as facilities/capabilities.

Impact: This topic will advance the science to ultimately develop capabilities for the Joint Force to be able to detect and identify chemicals trapped within surfaces to better inform materiel decontamination processes and provide better situational awareness and protective posture to the Warfighter after a chemical warfare agent release. This information will be critical for verifying successful decontamination of materiel to ensure that there is no secondary exposure risks to the Warfighter and that decontaminated materiel can return to the fight in a CB-contested environment.

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CBA-02: Automated Bioaerosol Collector/Analysis System

Background: DTRA RD CBA Detection's Operational Biological Sensing thrust area prioritizes developing the necessary expeditionary detection capabilities to inform and alert Warfighters for any biological hazards in an operational setting. Warfighters are often deployed to austere environments with potential exposure to either naturally occurring or adversary-produced biological pathogens. The ultimate goal of providing Integrated Layered Defense and Integrated Early Warning is to deploy autonomous sensors that can detect the presence of aerosolized biothreat and confirm if it is a hazard to personnel.

Objective: The goal is to develop a system with multiple components to address four basic tasks necessary to detect a bioaerosol and can therefore (1) **trigger** collection of samples, (2) **collect** (for example but not limited to filtration, impingement, cascade impactors, cyclone collectors, etc.) aerosol samples, (3) **analyze** data and results, and (4) **report** analyzed results in near real-time. All of these technologies currently exist individually in various commercial-off-the-shelf (COTS) products as partial solutions. This topic is focused on the innovative development of an autonomous, portable, low size weight, power, and cost (SWaP-C) system with multi-components to address these areas.

Impact: This topic seeks to support the Warfighter with an all-in-one fieldable biosensing capability that operates *autonomously* to (1) monitor for "anomalous" environmental activity, (2) collect sample(s), (3) analyzes the sample to identify aerosolized biothreats, and (4) reports analyzed results to the end user/command center. Emphasis will be placed on innovation of "trigger-to-collect" methodology. Such a system may utilize machine learning and artificial intelligence (ML/AI) to predict environmental conditions amenable to biological attack by tracking open-source wind direction, humidity, temperature, etc. The prototype system must be agile, man-portable, robust and rugged-designed, and low SWaP-C. The system should be able to perform multiple analysis of cycles between reagent replacement and human interaction.

In addition, this technology system should address the following. Preference will be given to proposals that can address all areas:

1. An indoor and outdoor surveillance of bioaerosols that can provide a triggering response to initiate an automated sample-to-answer read-out.
2. Trigger-to-collect and detect samples must be able to distinguish biotic particles within from common abiotic interferents (e.g. dust, dirt, diesel soot, etc.).
3. A capability/component adaptable to novel and emerging pathogen threats and/or biological warfare agents (BWAs).

Collaboration between institutions that have expertise in these areas, i.e. trigger, collection, detection, analysis, and reporting, is encouraged.

CBA-03: Strategic Multi-Omic Integration Solutions for Pathogen Agnostic Detection (SMOIS-PAD)

Background: In the event a biothreat agent is encountered, or a sample containing probable or potential biothreat material is recovered, it is critical to obtain as much valuable information about the sample as possible, including organism composition, pathogenicity, virulence, evidence of engineering, and related biological functions.

Genome data is typically the widely accepted standard information to initially detect and identify nucleic acid sequences encountered in the field. However, genome sequencing alone is not sufficient to predict the full effects of a potential biothreat. For that reason, coupling genome sequencing data with other sources of biological information, such as multi-omics (proteomics, transcriptomics, metabolomics, lipidomics) data, is critical for understanding the threat and protecting the warfighter. Multi-omics approaches are essential to determine the presence of, and to understand non-nucleic acid components, as well as to discover potential signatures/biomarkers associated with potential biothreats whether they are naturally occurring, accidental, or deliberate.

This topic is subjective on enhancement of multi-omic data science (MODS) based capabilities via integration and harmonization of data from multiple omics to extend and increase the in-depth understanding of biothreats, improve the accuracy and timeliness of detection and prediction, and shorten the threat analysis time.

SMOIS-PAD will focus on developing and incorporating cutting-edge data science methodologies for integration of data across multiple omics[1] . The SMOIS-PAD shall offer the advanced bioinformatic tools, algorithms, and relevant workflows specifically for curation, harmonization and integration of data and results from different types of omics which is already pre-processed using user-choice, no-hosted data processing software.

Objective: This topic is seeking innovative data science solutions for accomplishment of the SMOIS-PAD objectives below. This will be equipped with a modular "plug-in-play" capability that will allow the users to select tools/algorithms to customize a data processing workflow. The advanced tools should be developed and designated to support prediction, detection, and elucidation of emerging, engineered, and novel biological threats (virus, bacteria, toxins, etc.).

Successful multiple-year efforts, up to 5 years, should address the following, and preference will be given to proposals that address all areas, but not limit to:

1) The computing infrastructure of platform should be robust and scalable for running container workloads, and compatible with cloud based and on-premise environments without the need for adaption of code base, giving operational feasibility and flexibility.
    a. It also has workflows and storage capabilities to operate as a data repository.
    b. A Data Management, Sharing, and Transition Plan for all raw data and metadata generated from DTRA funded awards to a government owned software repository upon completion of the period of performance.
2) The tools and pipelines for integration of trans-omic data developed in SMOIS-PAD should be compatible with the commonly used file formats of input data which is preprocessed with the most popular industrial or open-source data pre-processing software for omics including, but not limited to genomics, transcriptomics, proteomics, metabolomics, lipidomics.
3) The data integration strategies applied for integrating data across multiple omic layers will support DoD laboratories as the end-user with capabilities of prediction, detection, recognition of virulent signatures, and elucidation of emerging and novel biothreats. Statistics and Artificial Intelligence

/Machine Learning/Deep Learning (AI/ML/DL) based data standardization, harmonization, and integration in multi-omic analyses are preferred.

   a. Conduct market research to determine advanced, state-of-the-art data processing software available for omics to build a workflow library.
   b. Define quantitative metrics to evaluate data as "trustworthy" and explainable.
   c. Tools and algorithms developed should be in accordance with FAIR Principles[2] based, modular and containerized to be compatible with cloud- and on-premise deployment.
   d. Provide standards for multi omics data generation, testing, validation, and evaluation.
   e. Discuss systematic determination of whether the choice of model affects performance across multiple omics data sets, and if so, which features of individual model types are determining this performance.
   f. Address the generalizability of the proposed solution to extract, harmonize, and correlate different multi-omic data sets across heterogeneous data types and reporting formats (e.g., Word documents, PDFs, PPTs, Hardware (hard drives), Instrument data files, etc.).
   g. Leverage the relevant pre-existing biological knowledge for exploring and discovering new biological mechanisms and pathways to best understand the biological activities of potential and novel threats.

4) Awardees, self or via collaboration, should have facility and capabilities, with DTRA consultation, to design plans, execute experiments, and generate adequate multi-omic raw data at an appropriate biosafety level to support the tool/algorithm developments and other relevant tasks.
5) Security measures must be employed for the platform to ensure security for sharing and integration of data across geographically dispersed sites and organizations.
   a. Address risks and provide risk mitigation solutions for technical issues pertaining to data security, provenance, governance, storage, and integrity (DevSecOps).
   b. Sustainable solutions that do not incur recurring licensing fees or restricted data rights are preferred.

Proposers are encouraged to develop research collaborations with other Government agencies, academic institutions, and private entities. In addition, utility of resources within the Department of Defense research laboratories is also recommended.

Impact: The SMOIS-PAD will provide an enhanced, high-performance capability of data science solutions through leveraging data integration across multiple omics supporting rapid, accurate detection and identification of future threats.

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CBA-04: Microbiome Microphysiological Systems (MPS)

Background: The microbiome consists of a complex community of micro-organisms and their genes which plays an important part in human health and disease (1). The expansion of next-generation sequencing (NGS) has provided insight into the composition, dynamics, and function of the human microbiota. The role of the microbiome has expanded to healthcare and is most readily evident in the cases of intestinal and fecal microbiota which has utilized NGS to identify important microbial genomic elements in infectious disease diagnostics (2), cancer screening (3), and others (4). While the gut flora has been extensively studied and characterized, little headway has been made to utilize the oral and skin microbiomes in a similar fashion. Oral and skin microbiomes are desirable sites for minimally invasive sampling and hence are appealing areas for potential diagnostic development. Indeed, meta-analysis revealed large differences in genetic diversity between the oral and gut microbiome (5), and most research has focused on dental disease (6) and oral cancer diagnostics (7). While diversity exists in the microbiome between individuals, there is a shared core microbiome that can be exploited for diagnostic purposes (8). There is limited research exploring the use of microbiota dysbiosis as a predictive diagnostic (9). This presents an opportunity to use the oral cavity and/or skin as regions of minimally invasive diagnostic potential for exposure to biological agents.

Microphysiological Systems (MPS), also called "Organs-on-a-chip", are a novel technology that combines *in vitro* cell culture with a microfluidics platform to replicate human tissues in their physiological environment (10). MPSs are gaining traction as a valuable tool that can replace animals as a model system for many types of experiments. MPS models of disease pathology have also provided insight into disease progression and cellular responses, with the most recent examples focusing on SARS-CoV-2 infection and relating data to human clinical samples (11). While animal studies persist as a necessary step before drug testing can occur in human trials, MPSs present a new option with the potential to provide a more accurate picture of the human physiological response and the ability for high throughput screening.

There is limited research incorporating elements of the microbiota into a microphysiological system and interrogating the resultant interdependent dynamics. DTRA-JSTO RD CBA Medical Diagnostics is presently funding initiatives for minimally, or non-invasive diagnostic tools, which we are seeking to expand. Buccal swabs and skin swabs represent attractive sample collection methods for future minimally invasive diagnostics. Furthermore, there is a need to examine and characterize the microbiome's potential to provide prospective information about pre-symptomatic indicators and serve as a novel diagnostic prognosticator capable of utilizing these minimally invasive sampling techniques.

Objective: CBA Medical Diagnostics seeks to fund the development of an MPS that can accurately replicate the microbiome of the skin and/or oral cavity. This MPS should mimic its human tissue counterpart as well as incorporate a representative microbial community, and where possible have comparative multi-omic biomarker analysis, including transcriptomics, metabolomics, and proteomics. Subsequently, the MPS should be utilized to examine the biomarker profile both pre- and post-exposure with biological agents relevant to the RD-CB portfolio. It is expected that model systems will be used to perform analysis and identify changes in biomarkers and alterations of the microbiota landscape that can be used as a diagnostic indicator on the type of agent used.

Successful efforts should address any or all of the following (preference will be given to proposals that address more areas):

- Establish a standardized microbiome representative of the core microbial community in the human oral and skin niches.
- Develop a microphysiological system that recapitulates the oral cavity and/or the skin and incorporates an appropriate and representative microbiome.

- Perform a comparative study of the MPS to equivalent human tissue/microbiome.
- Utilizing MPS, characterize the microbial landscape pre- and post-exposure to biological agents and determine its applicability to pre-symptomatic indications.
- Perform multi-omic biomarker analysis of the MPS pre- and post-exposure to biological agents.
- Integrate data into a machine learning platform to develop software for microbiome analysis from future clinical samples.

Applicants are encouraged to develop research collaborations with other Government agencies, academic institutions, and private entities. In addition, applicants can leverage resources within the Department of Defense research laboratories.

Impact: This topic will advance the science to ultimately enable the development of capabilities for pre-symptomatic diagnostics of exposure to biological agents to support the Joint Force. The use of the MPS will provide more relevant biomarker and microbiome data than a typical animal model, and is a necessary first step to the understanding of how the microbiome responds to threat agents. The maturation of this technology will be critical to ensuring the Warfighter has the necessary tools to respond quickly and efficiently to hazards which may arise in contested environments.

References:

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