## DEFENSE THREAT REDUCTION AGENCY BROAD AGENCY ANNOUNCEMENT HDTRA1-14-24-FRCWMD-BAA

Amendment 3
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Research and Development Directorate (J9)
Basic and Applied Sciences Department (J9-BA)

# Fundamental Research to Counter Weapons of Mass Destruction (C-WMD)

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#### **OVERVIEW INFORMATION**

#### **Agency Name:**

Defense Threat Reduction Agency (DTRA) Research and Development (J9) Directorate Basic and Applied Sciences (BA) Department 8725 John J. Kingman Road, MS 6201 Fort Belvoir, VA 22060-6201

**Funding Opportunity Title:** Fundamental Research to Counter Weapons of Mass Destruction (FRCWMD) Broad Agency Announcement (BAA)

**Announcement Type:** This is the initial announcement of this funding opportunity. This BAA is in effect from March 2015 through September 2024. It is anticipated that a majority of the actions funded from this announcement will be in the form of grants; however, other instruments such as contracts, cooperative agreements (CAs) or other transactions agreements (OTAs) may also be awarded from this announcement. Submissions for this BAA may occur in two ways: 1) in response to the published topics detailed in <a href="Attachment 1">Attachment 1</a> or 2) to a general thrust area as described in <a href="Section 1.5">Section 1.5</a>.

In general, all topic-specific and general thrust area submissions require pre-coordination in accordance with the guidelines in <u>Section 1.5</u> and <u>Section 4.2.1</u>. DTRA reserves the right to waive the pre-coordination requirement for topics on a case-by-case basis; and will state the waiver applies within the individual topic description. If a pre-application white paper is received without prior coordination, DTRA may not review it. From the date of the disposition email the applicant has 60 days to submit the pre-application white paper. If the submission is not feasible within this 60-day window, the abstract must be coordinated again to ensure the interest in the white paper remains.

The evaluation of all submissions will be conducted in two phases. Phase I is for receipt and evaluation of pre-application white papers in direct response to a published topic or by invitation based on the assessment of the idea by the Technical POC. Phase II is for receipt and evaluation of invited proposal applications. Invitation to the Phase II, invited proposal submission, will be based on the evaluation results of the Phase I pre-application white paper.

Funding Opportunity Number: HDTRA1-14-24-FRCWMD-BAA

Catalog of Federal Domestic Assistance (CFDA) Number: 12.351

**Dates:** This BAA is open continuously from March 2015 through September 2024. Published topics will include instructions on any topic-specific opening and closing dates. Submissions to a general thrust area may occur at any time this BAA is in effect. Applicants should take care to note requirements for pre-coordination of an abstract.

#### ADDITIONAL OVERVIEW CONTENT

Research, educational program, or other effort proposals are sought from accredited degree-granting colleges and universities. Research, educational program, or other effort proposals are also sought from industrial, commercial (including small businesses), and not-for-profit research entities. DTRA strongly encourages and may give preference to pre-application white papers and proposals that demonstrate a significant contribution (significant is defined as a minimum of 30% of total value) by one (1) or more universities.

All submissions (pre-application white papers and invited proposals) must be made in accordance with the submission instructions in this BAA through <a href="www.grants.gov">www.grants.gov</a> using the application packages provided with this BAA. Applicants are responsible for ensuring compliant and final submission of their pre-application white papers and proposal applications. Any submission that does not conform to the requirements outlined in the BAA and in the invitation for proposal may not be reviewed or considered further at the discretion of DTRA.

Pre-application white papers may be evaluated any time after receipt. Invitations for full proposal submission may occur any time after the pre-application white paper evaluation and will be limited to available program funds.

Efforts may be proposed for up to five (5) years. Awards may be for a base period of one (1) year with four (4) additional years as possible options, a base period of two (2) years with three (3) additional years as possible options, or a base period of three (3) years with two (2) additional years as possible options. Applicants should take care to propose the most logical mix of base and option years for the scope of work. Further, the base period should yield a logical completion point for the work. In cases where option years are proposed, decisions regarding exercising those options will be based on the evaluation of the work accomplished in the base period. Pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable; however, the Government reserves the right to invite option years for awards that originally only included a base period.

Grants may range from small dollar value (e.g., \$25K) up to \$1M annually (total, including both direct and indirect costs) depending on the nature and the scope of work. Payments on grants will be made in advance, subject to the conditions described in 2 CFR 200.305. Funding amounts for contracts, CAs, and other procurement instruments will be considered on a case-by-case basis. Fifteen (15)-30 individual awards are anticipated each year.

Any assistance instrument awarded under this announcement will be governed by the award terms and conditions, which conform to DoD's implementation of OMB circulars applicable to financial assistance. Terms and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in 2 CFR part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards."

#### 1. FUNDING OPPORTUNITY DESCRIPTION

1.1. DTRA safeguards America and its allies from weapons of mass destruction (WMD) and provides capabilities to reduce, eliminate, and counter the threat and effects from chemical, biological, radiological, nuclear, and high yield explosives. DTRA seeks to identify, adopt, and adapt emerging, existing and revolutionary sciences that may demonstrate high payoff potential to Counter-WMD (C-WMD) threats. This BAA is an extramural endeavor that combines the fundamental research, educational program, or other effort needs appropriate for basic or applied research funding of DTRA and other DoD interests.

This announcement solicits ideas and topic-based pre-application white papers for long-term challenges that offer a significant contribution: to the current body of knowledge, to the understanding of phenomena and observable facts, to significantly advance revolutionary technology, to new concepts for technology application, or that may have impact on future C-WMD threat reduction, expertise, or capabilities.

A portion of this effort is expected to be devoted to awards for science, technology, engineering and mathematics education programs with a C-WMD focus; such as, but not limited to postdoctoral fellowships, stipends, degrees, visiting scientist programs, student exchange programs, and development of accredited C-WMD curricula.

1.2. Fundamental research means basic and applied research in science and engineering, the results of which ordinarily are published and shared broadly within the scientific community, as distinguished from proprietary research and from industrial development, design, production, and product utilization, the results of which ordinarily are restricted for proprietary or national security reasons.

Contracted Fundamental Research includes research performed under grants, contracts (awards), or OTAs that are (a) funded by budget Category 6.1 (Basic Research), whether performed by universities or industry or (b) funded by budget Category 6.2 (Applied Research) performed oncampus at a university. Fundamental research provides for science and technology (S&T) research and early applied development. It seeks to lower performance risk to a manageable level and facilitate transition and funding to capability end-state programs.

- 1.3. Technology Readiness Levels (TRLs) provide a systematic metric/measurement system that supports assessments of the maturity of a particular technology and the consistent comparison of maturity between different types of technology. Fundamental research may be defined within the first four (4) TRLs. For more information on TRLs, please consult the following link: <a href="https://acc.dau.mil/CommunityBrowser.aspx?id=23170&lang=en-US">https://acc.dau.mil/CommunityBrowser.aspx?id=23170&lang=en-US</a>.
- 1.4. This BAA seeks optimum approaches to meet DTRA fundamental research objectives. The Government encourages pre-application white papers and proposals that span a wide spectrum of research to expand fundamental scientific knowledge in response to specific topics and to the more general thrust areas. The Government reserves the right to award any combination of approaches which offer the best overall value to the Government and to oversee any and all processes and approaches once ongoing.
- 1.5. Thrust Areas 1-7 are described below. When a specific set of topics has been identified, these detailed needs will be described in <u>Attachment 1</u> along with any topic-specific submission instructions, deadlines, anticipated award structure, and funding requirements. Otherwise, preapplication white papers and proposals may be written against one of the general thrust area

descriptions.

DTRA may not review any pre-application white papers without prior coordination of the idea with the appropriate thrust area- e-mail address (Section 7). Applicants should note that there is extremely limited funding available for many of the thrust areas. Pre-application white papers will only be accepted from the coordinated abstracts under limited circumstances.

- 1.5.1. Thrust Area 1—Science of WMD Sensing and Recognition: The science of WMD sensing and recognition investigates the fundamental understanding of materials that demonstrate measurable changes when stimulated by radiation or particles from WMD in the environment. This involves the exploration and exploitation of interactions between materials and various electromagnetic phenomena, molecules, nuclear radiation, and particles. Furthermore, these interactions and the specific form of recognition they offer are used for the subsequent generation of information, providing knowledge of the presence, identity, and quantity of material or energy in the environment that may be significant. The goal of this thrust area's portfolio is to advance the following capabilities: location, identification and characterization of radiological-nuclear (RN) materials; detection of RN materials at significant stand-off distances; and the reduction of the technical nuclear forensics timeline. Thrust Area 1 is currently not interested in research focusing on the sensing of explosives or the detection of Improvised Explosive Devices (IEDs).
- 1.5.2. **Thrust Area 2**—*Network Sciences:* The fundamental science of network sciences includes advancing knowledge of complex disparate but interdependent networks critical to military operations where WMD-related robustness, resiliency, recovery of, and informational and operational utility is required. It includes response, resilience, and recovery of interdependent, multi-layered physical networks after exposure from electromagnetic pulse and other nuclear weapons effects, rapid discovery and analyzing low-observable WMD-related information from large, disparate WMD-related data sets from multiple types of networks, and to develop theories and representations for low observable WMD-related radical ideation from social networks.
- 1.5.3. **Thrust Area 3—Science for Protection:** Fundamental science for protection involves advancing knowledge in physical, biological, and engineering sciences to protect personnel, sensitive electronic systems, and structural infrastructure from the effects of weapons of mass destruction. Protection includes both passive and active defense against threats. Approaches include advanced highly-ordered materials and nanomaterials to hardening infrastructure and facilities against blast, nuclear events, or other CBRNE effects; exploring new methods to experimentally and computationally simulate the effects of a nuclear event; investigations of the interaction of radiation with sensitive electronics and systems as well as development of novel materials and methods that are robust against radiation effects; novel methods to protect personnel from the physical, radiological, and nuclear effects of WMDs; and the study of biological systems, including intact structures, metabolic products, or discrete components and pathways, as applied to protection of U.S. Forces during operations in areas actually or potentially contaminated by radiation. For protection of personnel the areas of interest include development of radiation countermeasures to prevent biological damage associated with exposure to ionizing radiation and development of novel biologically-based or -produced detection systems for wide area surveillance to determine the nature, extent, and distribution of contamination.

- 1.5.4. **Thrust Area 4**—*Science to Defeat WMD:* Fundamental science for significantly improving energetic materials for use against WMD facilities and systems with minimal collateral effects from post-blast WMD release, for deeper penetration to deny the adversary sanctuary of WMD, and for predictable modeling of counter-WMD munitions and simulation of in-theater scenarios with accurate lethality calculations.
- 1.5.5. **Thrust Area 5**—*Science to Secure WMDs:* Fundamental science to support securing WMD includes: revolutionary means to safely handle, transport, control access, or eliminate WMD components and weapons; new physical or other methods to monitor compliance to support future agreements or treaties; and, exploring phenomena and means that facilitate reduction of nuclear or non-nuclear WMD proliferation pathways. This includes focus on: science principles to assist tagging, tracking, location to secure WMD; novel means to mark and read objects in order to secure inventories; remote or unattended monitoring to understand the nature of objects (e.g., is it nuclear, biological, chemical or conventional?); monitoring to detect intrusion, diversion or substitution, tampering, and other adverse activity; and, understanding of both physical and life science environmental signatures as witnesses of WMD-related activity. The ability to secure WMD may impact either verification of treaties, or control of WMD outside treaty regimes.
- 1.5.6. Thrust Area 6—Cooperative Counter WMD Research with Global Partners:

Cooperative fundamental research to reduce the global threat of WMD in collaboration with a broad range of global research partners. This thrust area involves exploratory basic and applied research that will address opportunities to reduce, eliminate, and counter WMD across the Chemical, Biological, Radiological, Nuclear, and High Explosive (CBRNE) spectrum. Efforts in this area will develop strong international relationships which will foster a smooth transition of program ownership to the partnering country. The goal is to improve international collaboration to detect, characterize, and report WMD, and to advance partner nation sustainment through a culture of long-term cooperation and scientific responsibility for such programs. Multi-disciplinary, multinational research in science, technology, engineering, and mathematics development will be conducted to promote transparency through quality research publications and continual dialogue between scientists/engineers and young researchers.

The Cooperative Biological Engagement Program (CBEP), a component of the DoD Cooperative Threat Reduction (CTR) Program, recognizes the danger to U.S. and global health security posed by the risk of outbreaks of dangerous infectious diseases, whether natural or manmade. Consistent with the national and departmental strategies, CBEP strives to address this risk by promoting best practices in biological safety and security, improving partner country capability to safely and rapidly detect and report dangerous diseases, and establish and enhance international research partnerships that focus on informing the disease surveillance network. The desired end state for CBEP engagements is the development of sustainable partner country capabilities to:

- Employ responsible bio-risk management best practices and principles,
- Conduct a modern and effective disease surveillance mission,
- Independently sustain engagement with, and effectively compete for funding within, the international scientific community,
- Comply with World Health Organization (WHO) International Health Regulations (IHR) and

World Organization for Animal Health (OIE)/U.N. Food and Agriculture Organization (FAO) reporting guidelines, and

• Promote the One Health Concept.

The goals and objectives of CBEP international research partnerships are to:

- Goal 1: Support Biosurveillance, Biosafety and Biosecurity (BS&S) Capability Building Efforts
  - Objective 1: Inform and enhance operational biosurveillance strategies and implementation through improved understanding of endemic disease burden and pathogen biology.
  - Objective 2: Institutionalize responsible biorisk management best practices with partner country scientists.
- Goal 2: Engage Partner Country Scientists in Hypothesis-Driven Research
  - Objective 1: Support local, national, and regional priorities for understanding and mitigating human and animal disease risk (e.g., small, focused projects within individual countries linked by broad, integrating projects that include regional partners).
  - Objective 2: Improve international collaborations to survey, detect, characterize, and report disease.
- Goal 3: Promote One Health Initiative
  - Objective 1: Emphasize the nexus of human health, animal health, and the environment, and seek to further understand the mechanisms and factors involved in disease transmission.
  - Objective 2: Advance partner country sustainment of global health security initiatives.
- Goal 4: Foster an International Culture of Responsible and Ethical Conduct in Biological Research
  - Objective 1: Transition to a culture of responsibility and ethical conduct in biological research through thoughtful experimental design and good laboratory practices that result in high-quality data, and active participation in professional societies and the peer-review process.
  - Objective 2: Train partner country researchers to think critically in the pursuit of ethical research and to be competitive in soliciting funding from the international scientific community.

Ultimately, the techniques, procedures, and approaches must be sustainable for the partner country and linked with appropriate training in order to promote global health security, reinforce norms of safe and responsible conduct, obtain timely and accurate insight on current and emerging infectious disease risks, and transform the international dialogue on biological threats.

CBEP research projects are not determined by or limited to specific biological agents, but must be plausibly linked to pathogens of security concern and aimed at measurably supporting threat reduction objectives that:

• Enhance partner country's/region's capability to identify, consolidate, and secure collections

- of pathogens and diseases of security concern in order to prevent the sale, theft, diversion, or accidental release of such pathogens and diseases.
- Enhance partner country's/region's capability to rapidly and accurately survey, detect, diagnose, and report biological terrorism and outbreaks of pathogens and diseases of security concern in accordance with international reporting requirements.

Region-specific areas of interest are described in CBEP Regional Science Plans. Examples of general CBEP research areas of interest include: Epidemiology (e.g. studies measuring disease prevalence and incidence), Pathogen Biology, Pathogen Characterization, Assay Adaptation and Optimization, Microbial Ecology within a Public Health Context, and Preventative Strategies and Countermeasures. For clarification, medical countermeasure development (i.e., development of diagnostic tools, vaccines, therapeutics) is supported by many other U.S. Government or international agencies and is generally not supported by CBEP; however, research projects may inform medical countermeasure development and support validation and verification testing (e.g., as part of proficiency testing, pilot studies/testing, or exercises, etc.). Additionally, CBEP does not generally support research with common disease agents such as HIV/AIDS, malaria, and tuberculosis where other U.S. agencies have dedicated missions to do so; however, the program may choose to capitalize on opportunities to leverage research on these diseases to further CBEP goals, for example by testing samples collected under the auspices of other programs. CBEP also will not support research which poses risks to the overall threat reduction mission of CBEP, Dual-Use Research of Concern, or related activities (i.e., in vivo pathogenicity studies, virulence studies, animal passaging, etc.).

CBEP is interested in collaborative research engagements with foreign partners in any one of the following regions: Countries of the Former Soviet Union (FSU) (specifically, Armenia, Azerbaijan, Georgia, Kazakhstan, and Ukraine), Africa (including, but not limited to, Kenya, Tanzania Uganda, South Africa), Southeast Asia (including, but not limited to, Cambodia, Indonesia, Laos, Malaysia, Philippines, Thailand), and Middle Eastern /South Asian countries (including, but not limited to, Afghanistan, Iraq, India and Pakistan). CBEP encourages proposers to develop projects in conjunction with foreign institutions in CBEP-engaged countries.

Fundamental science for chemical and biological (CB) defense includes science and technology research that advances knowledge in physical and life sciences to defend and counter chemical and biological WMD that could be used against our Nation's warfighters. Fundamental research efforts enable capabilities such as development of improved detection devices for traditional and nontraditional chemical agents; development of diagnostics for existing and emerging infectious disease threats; increasing knowledge and improved capabilities for development of new or improved medical and material countermeasures to CB threats for both pre- and post-exposure scenarios; enhanced personal protection against, modeling of, prevention of, or decontamination

1.5.7. Thrust Area 7—Fundamental Science for Chemical and Biological Defense:

1.6. This BAA, in addition to any amendments issued in conjunction with this BAA, will be posted to the Grant Opportunities Website (<a href="www.grants.gov">www.grants.gov</a>), the Federal Business Opportunities Website (<a href="www.fbo.gov">www.fbo.gov</a>), and the DTRA website (<a href="www.dtra.mil">www.dtra.mil</a>). The DTRA website is not the official sites; applicants are responsible for monitoring both <a href="www.fbo.gov">www.grants.gov</a>.

of CB threats; and providing effective elimination strategies via non-kinetic approaches for

threat agent destruction, neutralization and/or sequestration.

Posted amendments supersede all previous versions of the BAA. Note that topics will be listed in Attachment 1 and will be added/closed with Amendments to this BAA.

1.7. All administrative coordination and communication between applicants and the Government will be conducted using the e-mail address associated with this BAA, specified in Section 7. DTRA will not release employee personal contact information.

#### 2. AWARD INFORMATION

2.1. Award Types. The full range of flexible procurement instruments available to DTRA are possible results from this announcement, including but not limited to contracts, grants, CAs, and OTAs; however, grants will likely be the predominant procurement instrument. Each of the applicable procurement instruments offer different advantages, liabilities and responsibilities for applicants and the Government.

Applicants must specify in their submittal their recommended approach (e.g. contract, grant, CA, or OTA); however, the Government reserves the right to negotiate and award the types of procurement instruments determined most appropriate under the circumstances. If warranted, portions of resulting awards may be segregated into pre-priced options.

Except for OTAs, the Government actions under this BAA shall adhere to the requirements of the Federal Acquisition Regulation (FAR), Defense Federal Acquisition Regulation Supplement (DFARS) and/or DoD Grant and Agreement Regulations (DoDGARS), as appropriate for the type of instrument. DoDGARs can be accessed online at <a href="http://www.ecfr.gov/cgi-bin/text-idx?SID=e5d686f6760f3274b3368f36723fbb7e&mc=true&tpl=/ecfrbrowse/Title32/32CIsubchapc.tpl">http://www.ecfr.gov/cgi-bin/text-idx?side=32dfbb7e&mc=true&tpl=/ecfrbrowse/Title32/32CIsubchapc.tpl</a>. See also 32 Code of Federal Regulations (CFR) 22, which can be accessed online at <a href="http://www.ecfr.gov/cgi-bin/text-idx?rgn=div5;node=32%3A1.1.3.16">http://www.ecfr.gov/cgi-bin/text-idx?rgn=div5;node=32%3A1.1.3.16</a>. Any assistance instrument awarded under this announcement will be governed by the award terms and conditions, which conform to DoD's implementation of OMB circulars applicable to financial assistance. The current version of the Terms and Conditions for grant awards may be found online at the DTRA website (www.dtra.mil).

On average, DTRA expects to award 15-30 individual awards each year. The predominance of awards will be grants. Payments on grants will be made in advance, subject to the conditions described in 2 CFR 200.305.

2.2. Scope of Awards. Awards may range from focused, exploratory projects with a high risk approach in innovative research in subjects with potential for high impact to C-WMD science to comprehensive programs of innovative research in an interdisciplinary area with potential for high impact.

Awards may have multiple Co-Principal Investigators (Co-PIs) and subawards. Authors of preapplication white papers and proposals should detail the contribution of all Co-PIs and any subawards to the C-WMD scientific impact.

Preference will be given to projects where undergraduate and/or graduate students, and/or postgraduate students are supported by the awards. Details regarding the participation of the students and the value of the research to the students as part of the pre-application white paper and full proposal are expected. Additional guidance regarding student and/or postgraduate student participation may be provided in the published topics or in communications with the

applicant to include the coordination of the abstract or in the debrief summary of the preapplication white paper. Any specific guidance provided in a topic or to an applicant supersedes the information provided herein.

2.3. Subawards. Subawards (subgrants and/or subcontracts) are permitted. Subawards may be used to carry out a portion of the research or efforts. Awards may have multiple subawards. Awards will be made by a single award, e.g., grant or contract, to the lead organization. Subawards, including all subgrants and subcontracts, are the responsibility of the award recipient; exceptions will not be made.

For submissions made to Thrust Area 6 and associated topics, there is no limitation on subawards. DTRA will review and consider the proposed subawards for all pre-application white papers and proposals on a case-by-case basis. The prime awardee will be responsible for transferring funds to the subawardee. Applicants are reminded that priority is given to projects with the main locus of activity in the region-of-interest, so budgets should be allocated accordingly. Preference will be given to proposals where the subaward component to the region-of-interest partner(s) represents more than half of the award value (as measured in U.S. dollars).

- 2.4. Award Values. Grants resulting from submissions to Thrust Areas 1-7, including topics associated with these thrust areas, may range from small dollar value (e.g., \$25K) up to \$1M annually (total, including both direct and indirect costs) depending on the nature and the scope of work. Contracts, CAs, and OTAs will be considered on a case-by-case basis. All awards are subject to the availability of funds. Funding for participation in this program is highly competitive and the cost of proposed research should strictly be maintained as detailed herein or as indicated in the invitation instructions.
- 2.5. Period of Performance and Award Structure. Efforts for Thrust Areas 1-7, including topics associated with these thrust areas, may be proposed for up to five (5) years. Awards may be for a base period of one (1) year with four (4) additional years as possible options, a base period of two (2) years with three (3) additional years as possible options, or a base period of three (3) years with two (2) additional years as possible options.

Applicants should take care to propose the most logical mix of base and option years for the scope of work. Further, the base period should yield a logical completion point for the work. In cases where option years are proposed, decisions regarding exercising those options will be based on the evaluation of the work accomplished in the base period.

DTRA is flexible on the award structure unless otherwise specified in the published topics or in communications with the applicant to include the coordination of the abstract or in the debrief summary of the pre-application white paper. Applicants should take care to clearly label the tasks and anticipated outcomes for the base and option years in the pre-application white papers and the proposals. Pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable; however, the Government reserves the right to invite option years for awards that were originally awarded with only a base period.

2.6. The Government does not anticipate the need to provide any hardware or software to execute the proposed research. However, DTRA will review and consider any hardware/software requests for all pre-application white papers and proposals on a case-by-case basis.

- 2.7. The Government reserves the right to fund all, some, or none of the proposals submitted; may elect to fund only part of any or all proposals; and may incrementally fund any or all awards under this BAA. The Government also reserves the right to request applicants make any changes necessary to submitted full proposals to increase the feasibility of making the proposal fundable. Applicants may decline to participate in any revisions to application packages requested by DTRA.
- 2.8. The Government may offer funding for any full proposals or portions of proposals at any time during the lifetime of this BAA.

#### 3. ELIGIBILITY INFORMATION

- 3.1. Pre-application white papers and proposals submitted for this BAA will be considered from the following U.S. and Foreign Institutions as follows:
- Accredited degree-granting colleges, universities, and academic institutions.
- Industrial and commercial entities, including small businesses.
- Not-for-profit entities with a portfolio predominantly in research and foreign government laboratories. Proof of 501(c)(3) status from the Internal Revenue Service may be required. For foreign-based establishments entirely based outside the U.S. and/or its territories, proof of not-for-profit status may be required. Foreign based government laboratory equivalents include those residing in the Ministry of Defense, Ministry of Health, Ministry of Agriculture, Ministry of Education and Science and Food Safety Agencies.

DTRA strongly encourages and may give preference to pre-application white papers and proposals that demonstrate a significant contribution (significant is defined as a minimum of 30% of total value) by one (1) or more universities.

The following entities <u>may not</u> participate as prime awardees nor furnish Principal Investigators (PIs) in awards made under this BAA but <u>may</u> act as collaborators, including as Co-PIs, and/or subawardees:

- Federal Academic organizations (e.g., Naval Postgraduate School).
- Federal laboratories (including DoD and Department of Energy (DOE)).
- U.S. Government agencies.
- DoD-sponsored Federally Funded Research and Development Centers (FFRDCs) specified in the Defense Federal Acquisition Regulation Supplement (DFARS) 235.017-1 (http://farsite.hill.af.mil/VFDFARA.HTM) and click on 'DFARS Part 35'.
- DOE-sponsored FFRDCs.

Note: Federal laboratories (including DoD and DOE) and FFRDCs are eligible to submit abstracts (when required), pre-application white papers, and proposals in response to the Government Call issued by the DTRA Basic Research and Applied Sciences Department. However, a FFRDC (other than the DoD FFRDCs specified in DFARS 235.017-1) must have authorization from its sponsoring agency in accordance with FAR 35.017-1. Eligibility requirements under the Call are subject to change. See <a href="http://www.dtrasubmission.net">http://www.dtrasubmission.net</a> and after

logging in, follow the link to the 'FY16-24 Fundamental Research to Counter Weapons of Mass Destruction (C-WMD) Government Call'.

- 3.2. Cost Sharing or Matching. In general, cost sharing or matching is not required for applications to this announcement. However, DTRA reserves the right to require cost sharing or matching on a case-by-case basis. Such instances will be specifically detailed in the published topics or in communications with the applicant to include the coordination of the abstract or in the debrief summary of the pre-application white paper.
- 3.3. Other. DTRA uses the System for Award Management (SAM) to exclude recipients ineligible to receive Federal awards. SAM can be accessed online at <a href="http://sam.gov">http://sam.gov</a> (Reference 2 CFR 1125).

#### 4. APPLICATION AND SUBMISSION INFORMATION

- 4.1. Address to Request Application Package. This announcement contains all information required to submit a pre-application white paper and invited proposal. For convenience, Microsoft (MS) Word and MS PowerPoint templates for Phase II proposal submissions are provided on the DTRA website (<a href="www.dtra.mil">www.dtra.mil</a>) for applicant use. Applicants are encouraged to use the templates for preparing submissions; however, use of the templates is not required. Note: there is not a template available for the pre-application white paper.
- 4.1.1. The required application packages for the pre-application white papers and for the invited proposals are posted with this announcement. Note that each thrust area (as outlined in <u>Section 1.6</u>) and each topic (as outlined in <u>Attachment 1</u>) has a unique application package posted with this BAA. The application package corresponding to both: a.) the thrust area or topic of interest and b.) the phase, should be used for submission of pre-application white papers and invited full proposals.
- 4.1.2. The application packages posted to <a href="www.grants.gov">www.grants.gov</a> consist of the forms as detailed in Table 2.

Form Name	Phase I Pre-Application White Paper	Phase II Invited Proposal
SF-424 (R&R) Application for Federal Assistance Form	Required	Required
RR Budget Form	N/A	Required
R&R Subaward Budget Attachment(s) Form(s)	N/A	If Applicable
Research & Related Senior/Key Person Profile Form	N/A	Required
Research & Related Other Project Information	N/A	Required
Disclosure of Lobbying Activities (SF-LLL)	N/A	If Applicable
Attachments Form	N/A	Required

Table 2: Forms. The instructions for completing each of these forms may be found online at the following web

link: http://www.grants.gov/web/grants/form-instructions.html.

- 4.2. Content and Form of Application Submission. Submissions for this BAA will be conducted in two phases. Phase I is for receipt of pre-application white papers. Phase II is for receipt of invited proposal applications. Invitation to the Phase II proposal submission will be based on the evaluation results of the Phase I pre-application white paper.
- 4.2.1. The predominance of efforts, including all submissions to the thrust areas and most submissions to topics posted in <a href="Attachment 1">Attachment 1</a>, <a href="must be">must be</a> coordinated with the relevant technical point of contact (POC) for the appropriate thrust area prior to submission of a pre-application white paper; an e-mail for the DTRA technical POCs for Thrust Areas 1-7 are provided in <a href="Section 7">Section 7</a>. Coordination of research ideas and efforts must be accomplished via these email addresses, except in cases where a topic specifically states that pre-coordination is not required, and includes submission of an abstract (recommend less than 250 words) of the proposed project/effort or a paragraph description of the proposed project/effort to the email address in <a href="Section 7">Section 7</a> and a reply email from the relevant email address in <a href="Section 7">Section 7</a> with the disposition to the applicant. Pre-coordination may not be accomplished with email addresses other than those listed in <a href="Section 7">Section 7</a>. DTRA may not review white papers without prior coordination. Please note that attachments to e-mails may not be reviewed.

Applicants should note that there is extremely limited funding available for the general thrust areas. Pre-application white papers will only be accepted from the coordinated abstracts under very limited circumstances.

Under limited circumstances, topics will be posted in <u>Attachment 1</u> of this announcement that may not require pre-coordination of an abstract. Please review the topics carefully.

4.2.2. Pre-application white papers and invited proposals **must be** submitted electronically using <a href="www.grants.gov">www.grants.gov</a> and the corresponding application packages provided with this BAA on <a href="www.grants.gov">www.grants.gov</a>. All applications, including all supporting documents, must be submitted in the English language.

Applicants are responsible for ensuring compliant and final submission of their Phase I preapplication white paper and Phase II invited proposal application. Note that this also applies to applicants using third party systems to submit application packages and attachments. Any submission that does not conform to the requirements outlined in the BAA and in the invitation for proposal may not be reviewed or considered further at the discretion of DTRA.

- 4.2.3. DTRA will not review any of the following:
- Pre-application white papers and proposals that are not submitted in the English language.
- Pre-application white papers that are submitted to topics that have been previously closed via an amendment to the BAA.
- Application packages and proposals for Phase II submissions that were not invited.

Exceptions WILL NOT be made under any circumstances.

4.2.4. Phase I Pre-Application White Paper Submission and Content.

Each pre-application white paper must address only one thrust area or topic. Each pre-application white paper must use the corresponding thrust area or topic application package.

#### Each Phase I application package contains the following form:

Form	Attachment	Action
SF-424 (R&R) Application for Federal Assistance Form	Up to four (4) page white paper	Enter the appropriate information in data fields

Table 3: Phase I Pre-Application White Paper Package Chart.

Each Phase I application package contains the SF 424 (R&R) Application for Federal Assistance. To be considered a complete package, an up to four (4) page white paper is required to be uploaded as an attachment to the SF 424 (R&R). DTRA-specific instructions for completing the SF 424 (R&R) Application for Federal Assistance are below, general application instructions can be found on www.grants.gov:

- Block 1 Type of Submission. Applicants should indicate the Phase I submission is a "Pre-Application."
- Block 2.1 Applicant Identifier. Not applicable.
- Block 3 Date Received by State. Not applicable.
- Block 3.1 State Application Identifier. Not applicable.
- Block 5 Applicant Information. You must provide a Business Office Point of Contact (BPOC) with an e-mail address.
- Block 19 Authorized Representative. The "signature of AOR" is not an actual signature and is automatically completed upon submission of the electronic application package. Hard copies or email attachments of applications will not be accepted.
- Block 20 Pre-application. Must be used to attach an up to four (4) page white paper. The
  white paper itself should provide sufficient information on the research being proposed (e.g.,
  the hypothesis, theories, concepts, approaches, data measurements and analysis, etc.) to allow
  for an assessment by a technical expert.

Any pages submitted for the white paper that exceed the limit of four pages will not be read or evaluated. A page is defined as 8 ½ x 11 inches, single-spaced, with one-inch margins in type not smaller than 12 point Times New Roman font. The white paper must be provided in portrait layout.

At minimum, the white paper should address the following:

- A project abstract, which should be concise (less than 250 words), provide a summary of the
  proposed work, and demonstrate relevance to the topic being addressed. The abstract should
  not contain any proprietary data or markings.
- Potential scientific impact to provide greater knowledge or understanding of the fundamental
  aspects of phenomena and of observable facts, including how the research contributes to the
  C-WMD science needs outlined in the thrust area or topic.
- The impact of the research on C-WMD science must be clearly delineated.
- Cost estimate by year and total dollars required to accomplish the research as presented in the white paper (no details or breakout of costs is required).

- Potential team and management plan, including details on student involvement.
- Multidisciplinary white papers should carefully detail each of the institutions/departments involved and the contribution that will be made by each of the investigators.
- Do NOT include corporate or personnel qualifications, past experience, or any supplemental information with the white paper. References may be included within the 4-page limit at the discretion of the applicant; however, extensive references are not required.
- Thrust Area 6 pre-application white papers must also include a description of the extent and duration of the relationship/collaboration between the universities/institutes/entities and/or scientists.
- The thrust area or the topic should be included as a header on the white paper attachment and referenced in the text of the white paper.

#### 4.2.5. Phase I Pre-Application White Paper Re-Submission and Content.

On a limited basis a second pre-application white paper may be submitted without pre-coordination of an abstract. These re-submissions will be based on the review of the original pre-application white paper and will be allowed when changes to the project scope, technical approach, and/or cost are envisioned for any potential full proposals. Revised pre-application white papers must conform to the standards for the pre-application white papers detailed in Section 4.2.4.

All submissions should be made with the appropriate Phase I application package which contains the following form:

Form	Attachment	Action
SF-424 (R&R) Application for Federal Assistance Form	Up to four (4) page white paper	Enter the appropriate information in data fields

Table 4: Phase I Pre-Application White Paper Package Chart.

Each Phase I application package contains the SF 424 (R&R) Application for Federal Assistance. To be considered a complete package, an up to four (4) page white paper is required to be uploaded as an attachment to the SF 424 (R&R). The DTRA-specific instructions for completing the SF 424 (R&R) Application for Federal Assistance are the same as for the original pre-application white paper submission except for the following:

- Block 1 Type of Submission. Applicants should indicate the Phase I re-submission is a "Changed/Corrected Application."
- Block 4c Previous Grants.gov Tracking ID. Enter the Phase I Grant ID for the original submission.

At minimum, the revised white paper should address the issues and questions detailed in the debrief summary.

#### 4.2.6. Phase II - Invited Proposal Submission and Content.

Each proposal must address only the thrust area or topic for which it was invited. The application package corresponding to the thrust area or topic of interest should be used for submission of invited full proposals.

Each Phase II application package contains the following forms and attachments:

Form	Attachment	Action
SF-424 (R&R) Application for Federal Assistance Form	N/A	Enter the appropriate information in data fields
RR Budget Form	Budget Justification for entire performance period	Attach to Section K in budget period one
RR Subaward Budget Attachment(s) Form (if applicable)	Individual subaward budgets	Attach a separate budget with justification for each subaward
Research & Related Senior/Key Person Profile Form	PI Biographical Sketch	Attach to Biographical Sketch field
	PI Current/Pending Support	Attach to Current & Pending Support field
	Key Personnel Biographical Sketches	Attach to Biographical Sketch field for each senior/key person
	Key Personnel Current/Pending Support	Attach to Current & Pending Support field for each senior/key person
Research & Related Other Project Information Form	Publically Releasable Proposal Summary/ Abstract	Attach to Block 7 Project Summary/ Abstract
	Project Narrative/Technical Proposal	Attach to Block 8 Project Narrative
Disclosure of Lobbying Activities (SF-LLL) (if applicable)	N/A	N/A
Attachments Form	Attachment 1 – SOW	Upload as Attachment 1
	Attachment 2 – Quad Chart	Upload as Attachment 2
	Attachment 3 – Supporting Documentation (Thrust Area 6 submissions only)	Upload as Attachment 3

Table 5: Phase II Proposal Package Forms and Attachments.

DTRA reserves the right to consider incomplete application packages and required attachments and to request any missing information via email. Should the applicant fail to provide all the requested information either as part of the <a href="www.grants.gov">www.grants.gov</a> submission or in response to email requests from DTRA, at their discretion, DTRA may not consider the proposal further.

<u>SF 424 (R&R) Application for Federal Assistance</u>: DTRA-specific instructions for completing the SF 424 (R&R) are below. General application instructions can be found on www.grants.gov:

Block 1 – Type of Submission. Applicants should indicate the Phase II submission is an "Application."

- Block 2.1 Applicant Identifier. Not applicable.
- Block 3 Date Received by State. Not applicable.
- Block 3.1 State Application Identifier. Not applicable.
- Block 4b Agency Routing Identifier. Enter the corresponding Phase I Grant ID. If resubmissions were involved, enter the Grant ID for the last submission.
- Block 5 Applicant Information. You must provide a Business Office Point of Contact (BPOC)

with an e-mail address.

Block 19 – Authorized Representative. The "signature of AOR" is not an actual signature and is automatically completed upon submission of the electronic application package.

**RR Budget Form:** The Research and Related Budget Form provided as part of the application package for the Phase II submission should be filled out in its entirety for each project year proposed. Applicants are responsible for ensuring appropriate, approved rates are used in their budget forms. When notified of selection applicants will be requested to provide their current rate agreement and the rate agreement of their subcontractor(s), if applicable. Applicants should note that in accordance with 32 CFR 22.205(b), grants shall not provide for the payment of fee or profit to the recipient.

Applicants should plan and budget for travel to accommodate the two meetings outlined below:

- National Conferences/Workshops/Symposia: Applicants are strongly encouraged to attend a
  nationally recognized conference, workshop, or symposium in the field of research each
  calendar year (1 at minimum). Research should be presented as soon as adequate data are
  available to support posters and presentations. Conferences/workshops/symposia should be
  attended by the PI and students supporting the research, as appropriate.
- Annual Technical Review: Applicants should plan to attend an annual technical program review meeting. For planning purposes the review will be for five days and will be held in Northern Virginia.

**<u>Budget Justification:</u>** Applicants are required to submit a budget justification. The budget justification should be prepared as outlined in the instructions for the Research and Related Budget and uploaded as an attachment to Section K "Budget Justification" of the Research and Related Budget Form. The budget justification does not have a page limit, but should include sufficiently detailed information for meaningful evaluation. In addition, the budget justification must specifically address subaward costs and type to include the portion of work to be subawarded with a supporting rationale. The budget justification should include a discussion of how the subawardee(s) cost was determined to be fair and reasonable.

**RR** Subaward Budget Attachment(s) Form (if applicable): Detailed cost estimates are required for each proposed subaward. The cost estimate for the subawards should include sufficiently detailed information for meaningful evaluation, including labor rates and indirect cost rates.

**Research and Related Senior/Key Person Profile Form:** The Research and Related Senior/Key Person Profile Form should be completed in its entirety for each of the PIs and Co-PIs on the project. The inclusion of additional personnel is at the discretion of the PI. For Thrust Area 6 submissions, the PI (and Co-PIs) in the region-of-interest should be included as key personnel.

A biographical sketch is required for each PI and Co-PI on the project. DTRA does not have a preference for the format of the biographical sketch; however, it should be limited to 1 page per person. The biographical sketch should be uploaded as an attachment to the corresponding field on the Research and Related Senior/Key Person Profile Form.

Additionally, a statement of current and pending support must be provided for each PI and Co-PI on the project. This statement should include a summary of the current and pending support of related work and requires disclosure of all grants and contracts through which each PI and Co-PI is currently receiving or may potentially receive financial support.

#### Research and Related Other Project Information Form:

Block 7 – Project Summary/Abstract. To fulfill the requirements of Section 8123 of the Defense Appropriations Act, which states: "The Secretary of Defense shall post grant awards on a public Web site in a searchable format," DTRA will collect and post via the Defense Technical Information Center (DTIC) basic information about all awards made under this BAA. The information posted will include the abstract submitted to Block 7 of this form.

The uploaded project abstract should be less than one page and provide a summary of the proposed work and demonstrate relevance to the topic being addressed. Most importantly, the abstract **must be** written such that the general public may easily understand the potential scientific contribution and the impact of the research. The header of this uploaded document must contain the following statement:

"This publically releasable abstract is provided to DTRA for use in fulfillment of Section 8123 of the Defense Appropriations Act and future versions of the same."

The abstract absolutely must not contain any proprietary data or markings.

Block 8 – Project Narrative (Technical Proposal). The uploaded technical proposal must not exceed 20 pages (including references). If the proposal exceeds 20 pages, only the first 20 pages will be reviewed. A page is defined as 8 ½ x 11 inches, single-spaced, with one-inch margins in type not smaller than 12 point Times New Roman font. The technical proposal must be provided in portrait layout. A template for the technical proposal format may be found online at the DTRA website (www.dtra.mil) (MS Word format).

The project narrative (technical proposal) must include the following components:

- *Abstract*. Should be a technical project abstract that is distinct from the Project Summary/Abstract that is attached to Block 7.
- Scope.
- *Objective.* A clear and concise objective of the proposed project.
- *Background*. Provide the necessary technical and scientific background to support the scientific and/or technical merit of the proposed project.
- **Programmatics.** Describe your organization's management plan for the proposed project; list supporting and collaborating centers, and the roles/responsibilities of each identified academic and/or industrial subcontractor supporting the project. Authors of multidisciplinary proposals must take great care to clearly outline the impact to C-WMD science that is to be gained from the investment and justify the scientific contribution from each investigator.
  - Thrust Area 6 narratives must also describe of the extent and duration of the relationship/collaboration between the universities/institutes/entities and/or scientists. Teams with pre-existing collaborative research relationships and those which propose to establish new collaborations will be considered, provided teams can supply documentation to demonstrate that an operational framework exists to support the proposed work. Please see Attachment 3 below for information on the submission of this documentation.
- *Relevance*. Describe the relevance of the proposed project in terms of advancing the state of the science and the anticipated scientific impact on capabilities to potentially reduce,

- eliminate, counter, provide greater knowledge or understanding of the threat, and mitigate the effects of WMD fundamental aspects of phenomena and of observable facts.
- *Credentials.* Describe the PI's qualifications and the organization's qualifications to perform the proposed work. Summarize the credentials of the primary performing center, and supporting academic and industrial partners to perform the work. Describe specific examples of equipment and/or facilities available to perform the proposed work. Focus on information directly relevant to the proposed work.
- Work to be Performed. Provide details of the work to be performed by task and subtask. Tasks must be grouped by project year; base and option years should be clearly labeled. Additional details that are required include the following:
  - *Sample Repository.* Thrust Area 6 narratives must also clearly identify how the applicant plans to maintain samples collected during the proposed research effort, along with relevant metadata, for at least 12 months after the project end date. The format for the Sample Repository is at the discretion of the applicant.
  - **Protection of Human Subjects.** For full discussion, see Section 6.2.2. If the proposed research does involve human subjects or materials, applicants are asked to: a) justify the use of human subjects, b) outline the human use, and c) include the source of the human subjects or materials involved in the research. Applicants shall submit written evidence, to include a provisional protocol number and Institutional Review Board (IRB) point of contact information, that a human use protocol has been submitted to, and is pending approval by, a qualified IRB. Further information may be required if the proposal is successful.
  - Animal Use. For full discussion, see Section 6.2.3. If the proposed research involves animal use, applicants are asked to justify the use of animals. Any proposals involving animal studies or animal work must include detailed information on the animal protocols to be used and verify the location where the studies will be conducted. Animal studies are subject to review and approval for safety and adherence to regulations. Applicants shall submit with the full proposal package written evidence, to include a provisional protocol number and Institutional Animal Care and Use Committee (IACUC) point of contact information, that a vertebrate animal use protocol has been submitted to, and is pending approval by, a qualified IACUC. Further information may be required if the proposal is successful.
- *Performance Schedule*. Provide a table of tasks and sub-tasks and the duration of performance of each in a Gantt or other suitably formatted chart.
- *References.* List any relevant documents referenced.

<u>Disclosure of Lobbying Activities (SF-LLL) Form:</u> The Disclosure of Lobbying Activities Standard Form-LLL, if applicable, should be completed.

<u>Attachments Form</u>: The attachments form should be used to include the following three items with the application:

**Attachment 1 – SOW.** The SOW does not have a page limit, but should be approximately 3-5 pages in length for incorporation into an award document. The SOW should not contain any proprietary data or markings. Pages should be numbered and the initial page should have a date

(document date) shown under the title (the title of the SOW should match that of the proposal). The SOW must be provided in portrait layout. A template for the SOW format may be found online at the DTRA website (www.dtra.mil) (MS Word format).

The proposed SOW must accurately describe the research to be performed. The proposed SOW must also contain a summary description of the technical methodology as well as the task description, but not in so much detail as to make the SOW inflexible. The SOW format/guidance is as follows:

- *Objective:* Brief overview of the specialty area. Describe why the research is being pursued and what knowledge is being sought.
- *Scope:* Include a statement of what the SOW covers including the research area to be investigated, objectives/goals, and major milestones and schedule for the effort.
- *Background:* The applicant must identify appropriate documents, including publications that are applicable to the research to be performed. This section includes any information, explanations, or constraints that are necessary in order to understand the hypothesis and scientific impact on capabilities needed to reduce, eliminate, and counter the threat, and also mitigate the effects of WMD. It may also include previously performed relevant research and preliminary data.
- Tasks/Scientific Goals: This section contains the detailed description of tasks which represent the research to be performed that are contractually binding. Thus, this portion of the SOW should be developed in an orderly progression and presented in sufficient detail to establish the methodology and feasibility of accomplishing the overall program goals. The work effort should be segregated by performance period for all tasks to be performed and anticipated milestones realized in that year (e.g., Year 1, Year 2, etc., should be detailed separately). Identify the major tasks in separately numbered sub-paragraphs. Each major task should delineate, by subtask, the research to be performed by year and number each task using the decimal system (e.g., 4.1, 4.1.1, 4.1.1.1, 4.2, etc.). The sequence of performance of tasks and achievement of milestones must be presented by project year and task in the same sequence as in the Project Narrative/Technical Proposal. The SOW must contain every task to be accomplished to include a detailed schedule.
- The tasks must be definite, realistic, and clearly stated. Use "the awardee shall" whenever the work statement expresses a provision that is binding. Use "should" or "may" whenever it is necessary to express a declaration of purpose. Use active voice in describing work to be performed. Do not use acronyms or abbreviations without spelling out acronyms and abbreviations at the first use; place the abbreviation in parenthesis immediately following a spelled-out phrase. If presentations/meetings are identified in your schedule, include the following statement in your SOW: "Conduct presentations/meetings at times and places specified in the grant schedule."
- *Deliverables:* Thrust Area 6 <u>requires</u> several additional items be included in the SOW. These items are as follows:
  - O Submission of annual sample repository information using a DTRA-specified format (for an example, please see the DTRA website (www.dtra.mil)).
  - o Access to all samples collected and data generated during the course of the project, up to

and including at least 12 months after the project end date.

Attachment 2 – Quad Chart. The quad chart must be presented on one (1) page. The quad chart must not contain any proprietary data or markings. The quad chart must be provided in landscape layout. A template for the quad chart format may be found online at the DTRA website (www.dtra.mil) (MS PowerPoint format). The inclusion of the DTRA logo is not required. The quad chart should be uploaded as "Attachment 2" of the Attachments Form.

Attachment 3 – Supporting Documentation. For Thrust Area 6 proposals ONLY. Thrust Area 6 narratives must also describe an operational framework to support the proposed work. This includes, but is not limited to the following: the extent and duration of the relationship/collaboration between the universities/institutes/entities and/or scientists. Teams with pre-existing collaborative research relationships and those which propose to establish new collaborations will be considered, provided teams can supply documentation to demonstrate that an operational framework exists to support the proposed work. Each of the following should be concatenated into a single document, in the order specified:

- Specific identification of foreign Principal Investigators (PIs) and number of/job title for other members of the foreign research team.
- Detailed description of the relationship between the proposed research project and current research efforts at the foreign institution.
- Description of facilities and any other evidence of suitability of foreign collaborators and sites. In the event that the foreign research component will involve human or other vertebrate animal use, appropriate facilities compliance and certifications documents must be provided. Refer to <u>Section 6.2.2</u> and <u>Section 6.2.3</u> for specific information on required approvals and documentation.
- Foreign PI letter of collaboration describing, at minimum, the suitability of the proposed work with respect to ongoing research efforts at the foreign institution, merit of the proposed collaboration, and the expected mutual benefits.

<u>Protocol Risk Assessment Tool (PRAT).</u> For Thrust Area 6 proposals ONLY. Applicants <u>must</u> download the PRAT from the DTRA website (<u>www.dtra.mil</u>) and complete it in its entirety for <u>each</u> foreign institution participating in the project. Additional instructions for completing the PRAT may be found within the file. The completed PRAT file(s) should be emailed as a Portable Document File (PDF) format to <u>HDTRA1-FRCWMD-A@mail.mil</u> within two (2) weeks of the full proposal submission. <u>DO NOT</u> attempt to attach the PRAT(s) to the <u>www.grants.gov</u> submission.

4.2.7. Phase II - Additional Information Requests by DTRA. A revised proposal may be requested based on the review of the original proposal. Revised proposals will be requested when changes to the project scope, technical approach, and/or cost are required before the proposal could be further considered for an award. Applicants whose proposals are of interest to DTRA may be contacted to provide additional information or to make requested revisions prior to the final decision on funding. This request for further information may include revised budgets or budget explanations, revised SOWs, and other information, as applicable, to the proposed award. Applicants who are not responsive to Government requests for information in a timely manner, defined as meeting Government deadlines established and communicated with the request and not making satisfactory updates as requested, may be removed from award

consideration. Applicants may also be removed from award consideration if the applicant and the Government fail to negotiate mutually agreeable terms within a reasonable period of time.

Re-submissions should be made with the appropriate Phase II application package for the thrust area or topic of interest and should be completed in accordance with the instructions provided in the notification email.

The DTRA-specific instructions for completing a proposal re-submission are the same as for the original submission, except the SF 424 (R&R) Application for Federal Assistance should be marked as follows:

- Block 1 Type of Submission. Applicants should indicate the Phase II submission is a "Changed/Corrected Application."
- Block 4b Agency Routing Identifier. Enter the corresponding Phase I Grant ID.
- Block 4c Previous Grants.gov Tracking ID. Enter the Phase II Grant ID for the original Phase II submission.

#### 4.2.8. File Format.

Documents should be uploaded as a Portable Document File (PDF) format. Perform a virus check before uploading any files to <a href="www.grants.gov">www.grants.gov</a> as part of your application package. If a virus is detected, it may cause rejection of the file.

Do not lock or encrypt any files you upload to <a href="www.grants.gov">www.grants.gov</a> as part of your application package. Movie and sound file attachments will not be accepted.

- 4.2.9. All submissions must be UNCLASSIFIED.
- 4.2.10. Confirmed Proposal Expiration Date. Applicants requesting contracts must provide written confirmation that holds the proposal, to include proposed costs, firm for 180 days after the submission due date, as included in the invitation to submit a full proposal. This information must be included in the text of the technical proposal.
- 4.2.11. Withdrawal of Proposals. Proposals may be withdrawn by written notice received at any time before award. Withdrawals are effective upon receipt of notice by the Grants/Contracting Officer via the administrative e-mail address listed in Section 7.

#### 4.3. Submission Dates and Times.

Coordination of abstracts may be accomplished at any time that this BAA is in effect, unless otherwise stated as part of a specific topic. Once an applicant has been notified that a preapplication white paper is welcomed, the white paper should be submitted within 60 days. If the white paper is not submitted within 60 days, DTRA reserves the right to require the applicant to re-initiate the process with another abstract coordination.

Pre-application white papers may be submitted anytime that this BAA is in effect (as long as it occurs within the 60 day window following pre-coordination of the abstract), unless otherwise stated as part of a specific topic. Pre-application white papers may be evaluated at any time after submission and invitations for full proposal submission may occur any time after pre-application white paper evaluation. Note that proposal invitations may be limited to available program funds.

The due date for the Phase II invited proposal submissions will be provided in the letter of

invitation. The applicant will not be allowed less than 45 days to prepare a full proposal submission; there is no penalty for early submissions. An extension for submission of the Phase II proposal submission may be requested by emailing the administrative email address in <u>Section 7</u> prior to the deadline for the proposal submission. Full proposals may be evaluated at any time after submission, but generally are reviewed within 60 days.

Applicants are responsible for submitting all materials to <a href="www.grants.gov">www.grants.gov</a>. When sending electronic files, the applicant should allow for potential delays in file transfer from the originator's computer server to the <a href="www.grants.gov">www.grants.gov</a> website/computer server, as well as the delay associated with the <a href="www.grants.gov">www.grants.gov</a> validation of applications, which may be up to 48 hours. Applicants are encouraged to submit their proposals early to avoid issues with file transfers, rejection of applications by <a href="www.grants.gov">www.grants.gov</a>, and delays due to high website demand.

Acceptable evidence to establish the time of receipt at the Government office includes documentary and electronic evidence of receipt maintained by DTRA. Applicants should also print, and maintain for their records, the electronic receipt following submission of a proposal to www.grants.gov.

Applicants should note that DTRA uses a system that pulls applications from <a href="www.grants.gov">www.grants.gov</a> en masse, but this system does not mark applications as "retrieved" on <a href="www.grants.gov">www.grants.gov</a>. As a result, when applicants check the status on <a href="www.grants.gov">www.grants.gov</a> the applications will always look like they have not been retrieved by DTRA. Should you require confirmation of receipt by the Agency, you may request such via the administrative email address provided in <a href="Section 7">Section 7</a>. Note that such requests will generally be treated with low priority by the Agency.

Please note 15 U.S.C. 260a establishes daylight saving time as the standard time during the daylight saving period.

If the application package and required attachments are submitted to <a href="www.grants.gov">www.grants.gov</a> after the exact time and date specified in this announcement or in any written communications provided by DTRA, the application may be considered "late" and may not be reviewed.

If an emergency or unanticipated event interrupts normal Government processes so that proposals cannot be submitted to <a href="www.grants.gov">www.grants.gov</a> by the exact time specified by DTRA correspondence, the time specified for receipt of applications will be deemed to be extended to the same time of day specified in the BAA or in the letter of invitation on the first work day on which normal Government processes resume.

- 4.4. Intergovernmental Review. Not Applicable.
- 4.5. Other Submission Requirements.
- 4.5.1. Registration with <a href="www.grants.gov">www.grants.gov</a>. Applicants should note that each organization must complete a one-time registration in order to submit its pre-application white paper(s) and full proposal(s) through <a href="www.grants.gov">www.grants.gov</a>. Please see the following web link on information about registering with <a href="www.grants.gov">www.grants.gov</a>. <a href="http://www07.grants.gov/applicants/applicants.jsp">http://www07.grants.gov/applicants/applicants.jsp</a>. If your organization is already registered in <a href="www.grants.gov">www.grants.gov</a>, no further action should be required.

The registration process may take up to **four (4) weeks** to complete depending on your organization and requires multiple steps, some of which are detailed below.

• Identifying the Data Universal Number Systems (DUNS) number or registering for one with Dun & Bradstreet at <a href="http://fedgov.dnb.com/webform/displayHomePage.do">http://fedgov.dnb.com/webform/displayHomePage.do</a> if your

- organization does not have a DUNS number.
- Registering with the System for Award Management (SAM) by calling the SAM Assistance
  Center at 1-866-606-8220, or you may register online at <a href="www.sam.gov">www.sam.gov</a>. You will NOT be
  able to complete your SAM registration until SAM has confirmed your Employer
  Identification Number (EIN) or Taxpayer Identification Number (TIN) with the Internal
  Revenue Service (IRS).
- 4.5.2. Compliance with Appendix A to 32 CFR 28. All awards require certifications of compliance with Appendix A to 32 CFR 28 regarding lobbying. The full text of this certification is available at the DTRA website (<a href="www.dtra.mil">www.dtra.mil</a>). Proposers are certifying compliance with this regulation by submitting the invited proposal. It is not necessary to include the certification text with your invited proposal. If applicable, proposers should submit the Disclosure of Lobbying Activities (SF-LLL) Form in accordance with Section 4.2.6.
- 4.5.3. Marking Guidance for Pre-Application White Paper and Invited Proposal and Disclosure of Proprietary Information other than to the Government. The pre-application white papers and invited proposals submitted in response to this BAA may contain technical and other data that the applicant does not want disclosed to the public or used by the Government for any purpose other than application evaluation. Public release of information in any pre-application white paper and invited proposal submitted will be subject to existing statutory and regulatory requirements.

If proprietary information which constitutes a trade secret, proprietary commercial or financial information, confidential personal information, or data affecting national security, is provided by an applicant in a pre-application white paper and/or invited proposal, it will be treated in confidence, to the extent permitted by law, provided that the following legend is included on the front page of the pre-application white paper and/or invited proposal:

"For any purpose other than to evaluate the pre-application white paper and/or proposal, this data shall not be disclosed outside the Government and shall not be duplicated, used, or disclosed in whole or in part, provided that if an award is made to the applicant as a result of or in connection with the submission of this data, the Government shall have the right to duplicate, use or disclose the data to the extent provided in the agreement. This restriction does not limit the right of the Government to use information contained in the data if it is obtained from another source without restriction. The data subject to this restriction is contained in page(s) \_\_\_\_\_ of this preapplication white paper and/or proposal."

Any other legend may be unacceptable to the Government and may constitute grounds for removing the pre-application white paper and/or invited proposal from further consideration without assuming any liability for inadvertent disclosure.

The Government will limit dissemination of properly marked information to within official channels. In addition, the pages indicated as restricted must be marked with the following legend:

"Use or disclosure of the pre-application white paper and/or proposal data on lines specifically identified by asterisk (\*) are subject to the restriction on the front page of this pre-application white paper and/or proposal."

The Government assumes no liability for disclosure or use of unmarked data and may use or

disclose such data for any purpose.

In the event that properly marked data contained in a pre-application white paper and/or invited proposal submitted in response to this BAA is requested pursuant to the Freedom of Information Act (FOIA), 5 U.S.C. § 552, the applicant will be advised of such request and prior to such release of information, will be requested to expeditiously submit to DTRA a detailed listing of all information in the pre-application white paper and/or invited proposal which the applicant believes to be exempt from disclosure under the Act. Such action and cooperation on the part of the applicant will ensure that any information released by DTRA pursuant to the Act is properly identified.

By submission of a pre-application white paper and/or invited proposal, the applicant understands that proprietary information may be disclosed outside the Government for the sole purpose of technical evaluation. DTRA will obtain a non-disclosure agreement from the evaluator that proprietary information in the pre-application white paper and/or invited proposal will only be used for evaluation purposes and will not be further disclosed or utilized.

- 4.6. Applicants that Propose Use of Contracts or OTAs.
- 4.6.1. Recommended Procurement Instrument and Pricing Arrangement. Applicants that propose use of contracts or OTAs must provide a summary of their recommended procurement instrument and pricing arrangement as part of the Phase II proposal. However, the Government reserves the right to negotiate and award the types of instruments determined most appropriate under the circumstances. It is anticipated that most instruments will be grants.
- 4.6.2. Representations and Certifications. Representations and Certifications must be completed at the time of Phase II submission. The applicant must complete the annual representations and certifications electronically via the System for Award Management (SAM) website at https://www.sam.gov/portal/SAM/#1#1. After reviewing their information, the applicant verifies by submission of the application that the representations and certifications currently posted electronically have been entered or updated within the last 12 months.
- 4.6.3. Organization Conflict of Interest Advisory. Certain post-employment restrictions on former federal officers and employees may exist, including special Government employees (including but not limited to 18 U.S.C § 207, the Procurement Integrity Act, 41 U.S.C. § 2101 et.seq). If a prospective applicant believes that a conflict of interest exists, the situation should be raised to the DTRA Contract/Grant Officer before time and effort are expended in preparing a proposal. All applicants and proposed sub-contractors must therefore affirmatively state whether they are providing scientific, engineering and technical assistance (SETA), advisory and assistance services (A&AS) or similar support, through an active contract or subcontract, to any DoD technical office to include, but not limited to, the Joint Program Executive Office (JPEO), the Office of the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs (ASD-NCB), or the Office of the Special Assistant for Chemical and Biological Defense and Chemical Demilitarization Programs (OSA (CBD&CDP)). This information must be included in Technical Proposal of the Phase II full submission. All affirmations must state which office(s) the applicant(s) supports, and identify the prime contract number. Affirmations must be furnished at the time of Phase II full proposal submission. All facts relevant to the existence or potential existence of organizational conflicts of interest, including but not limited to those arising out of activities with the above-referenced organizations, must be disclosed. The disclosure must include a description of the action the applicant has taken or proposes to take to

avoid, neutralize, or mitigate such conflict.

- 4.6.4. Contracts with Subcontracts. Any applicant, other than small businesses, submitting a proposal that exceeds \$650,000.00 must submit a subcontracting plan in accordance with FAR 19.704(a) (1) and (2). This information must be included in Technical Proposal of the Phase II full submission. The plan format is outlined in FAR 19.704. Pursuant to Section 8(d) of the Small Business Act (15 U.S.C. § 637(d)), it is the policy of the Government to enable small business and small disadvantaged business concerns to be considered fairly as subcontractors to contractors performing work or rendering services as prime contractors or subcontractors under Government contracts, and to assure that prime contractors and subcontractors carry out this policy.
- 4.6.5. Limitations on OTAs. Applicants are advised that an Other Transaction for Research Agreement (10 U.S. Code § 2371) will only be awarded if the use of a standard contract or CA is not feasible or appropriate. Applicants are advised that an Other Transaction for Prototype Agreement (P.L. Law 103-160 § 845) will only be awarded if there is:
- a. At least one nontraditional defense contractor participating to a significant extent in the prototype project, or
- b. No nontraditional defense contractor is participating to a significant extent in the prototype project, but at least one of the following circumstances exists:
  - At least one-third of the total cost of the prototype project is to be paid out of funds provided by the parties to the transaction other than the Federal Government. The cost share should generally consist of labor, materials, equipment, and facilities costs (including allocable indirect costs).
  - Exceptional circumstances justify the use of a transaction that provides for innovative business arrangements or structures that would not be feasible or appropriate under a procurement contract.
- c. Although use of one of these options is required to use an Other Transaction for Prototype agreement as the procurement vehicle, no single option is encouraged or desired over the others.
- d. NOTE: For purposes of determining whether or not a participant may be classified as a nontraditional defense contractor and whether or not such participation is determined to be participating to a significant extent in the prototype project, the following definitions are applicable:
  - "Nontraditional defense contractor" means an entity that is not currently performing or has not performed, for at least the one-year period preceding this solicitation, any of the following for the Department of Defense:

- i. any contract or subcontract that is subject to full coverage under the cost accounting standards prescribed pursuant to section 26 of the Office of Federal Procurement Policy Act (41 USCS §§ 1501 et seq.) and the regulations implementing such section; or
- ii. any other contract in excess of \$500,000 under which the contractor is required to submit certified cost or pricing data under section 2306a of this title (10 USCS § 2306a).
- "Participating to a significant extent in the prototype project" means that the nontraditional defense contractor is supplying a new key technology or product, is accomplishing a significant amount of the effort wherein the role played is more than a nominal or token role in the research effort, or in some other way plays a significant part in causing a material reduction in the cost or schedule of the effort or an increase in performance of the prototype in question.
- e. NOTE: Applicants are cautioned that if they are classified as a traditional defense contractor, and propose the use of an Other Transaction for Prototype Agreement, the Government will require submittal of both a cost proposal under the guidelines of the FAR/DFARS, and a cost proposal under the proposed Other Transaction for Prototype Agreement, so that an evaluation may be made with respect to the cost tradeoffs applicable under both situations. The Government reserves the right to negotiate either a FAR based procurement contract, or Other Transaction for Prototype Agreement as it deems is warranted under the circumstances.

#### 5. APPLICATION REVIEW INFORMATION

- 5.1. Evaluation Criteria. The four evaluation criteria to be used for responses received to this BAA are as follows:
- 1. Scientific and Technical Merit. The objective of this criterion is to assess the extent to which the applicant presents ideas that are innovative and/or unique with the potential for high payoff in the science area and details a comprehensive technical approach based on sound scientific principles. Innovation will be judged contextually against the white paper's/proposal's scope, goals, and setting. To the extent possible, the technical risks, including those of biosafety and security, to accomplish the research or project should be identified with appropriate mitigation/management details.
  - For Thrust Area 6 white papers/proposals, innovation will also be considered with respect to partner country capabilities.
- 2. Value to Mission Goals. The objective of this criterion is to assess the extent to which the applicant demonstrates an understanding of the C-WMD research or mission challenges and the contribution to the C-WMD research or mission needs of that thrust area/topic. White papers/proposals must detail research or a project that is responsive to the thrust area/topic as presented in this solicitation. This criterion also addresses the benefit of the proposed effort on enabling knowledge, technology, or capabilities over current methods and/or practices and on the transition potential that is appropriate to the proposed effort. Applicants must also demonstrate an impact of the proposed effort on the institution's ability to perform research

relevant to reducing the global WMD threat; and/or to train, through the proposed effort, students and/or partner scientists in science, technology, engineering and/or mathematics.

Thrust Area 6 white papers/proposals must demonstrate an understanding of the CBEP priorities and mission. As such, the degree to which the proposed collaborations may lead to long-term partner country self-sufficiency and sustainment of the jointly developed capabilities will be considered.

- 3. Capability of the Personnel and Facilities to Perform the Proposed Effort. The objective of this criterion is to assess the extent to which the applicant's team has the requisite expertise, skills and resources necessary to perform the proposed program. This includes an assessment of the team's management construct, key personnel, facilities and past technical experience in conducting similar efforts of the proposed scope. Applicants must demonstrate that their team has the necessary background and experience to perform this project. Facilities should be detailed with discussion of any unique capabilities pertinent to the research. Subcontractors may include Government facilities or Agencies; however the unique expertise or specialized facilities provided through their inclusion must be clearly presented and the validity of the proposer-Governmental relationship must be clearly documented.
- 4. Cost Realism Evaluation. The objective of this criterion is to establish that the proposed costs are reasonable, realistic, and justified for the technical approach offered and to assess the applicant's practical understanding of the scope of the proposed effort.

#### 5.2. Review and Selection Process.

The pre-application white paper and proposal selection process will be conducted based upon a technical review as described in the DoDGARs (32 CFR 22.315(c)) and includes the use of non-Government peer-reviewers.

Each pre-application white paper and invited proposal submitted to a general TA will be reviewed on a rolling basis; topic-based submissions will be reviewed as a batch following receipt deadlines. All applications will be reviewed based on the merit and relevance of the specific pre-application white paper/proposal as it relates to the DTRA program, rather than against other pre-application white papers/proposals for research in the same general area.

Pre-application white paper (Phase I) evaluation will be based on the two (2) equally weighted criteria of (1) Technical/Scientific Merit and (2) Value to Mission Goals. The criteria will be scored as Outstanding (O), Good (G), Acceptable (A), Marginal (M) or Unacceptable (U). Any criterion scored as "Unacceptable (U)" will render the pre-application white paper "Not Selectable," and the pre-application white paper will not be considered further.

The full proposal evaluation will be based on the four criteria listed above. The first three criteria will be scored Outstanding (O), Good (G), Acceptable (A), Marginal (M) or Unacceptable (U). The fourth criterion will be scored as either Acceptable (A) or Unacceptable (U). Any criterion scored as "Unacceptable (U)" will render the proposal "Not Selectable," and the proposal will not be considered further.

Other factors that may be considered are duplication with other research, program balance, past performance and budget limitations. Prior to award, the Government reserves the right to perform a review of past performance. Sources that may be used for past performance review may include the Past Performance Information Retrieval System (PPIRS) and the Federal Awardee Performance and Integrity Information System (FAPIIS). The Government will also

evaluate the impact of any proposed limitations to the use of intellectual property (e.g. asserted technical data/computer software restrictions or patents) during the selection and/or negotiation process, and may request additional information from the applicant, as may be necessary, to evaluate the applicant's assertions. Accordingly, proposals may be selected for funding which are not reviewed as highly as others, which are of higher risk and/or which may be of a higher cost.

The Government reserves the right to select all, some, or none of the proposals, or any part of any proposal received in response to this BAA and to make awards without discussions with applicants; however, the Government reserves the right to conduct discussions if determined necessary.

- 5.3. DTRA anticipates that the total Federal share of awards made under this announcement will be greater than the simplified acquisition threshold over the period of performance (see §200.88 Simplified Acquisition Threshold). Therefore, in accordance with Appendix I to 2 CFR Part 200, Section E.3, this section serves to inform applicant:
  - i. That DTRA, prior to making a Federal award with a total amount of Federal share greater than the simplified acquisition threshold, is required to review and consider any information about the applicant that is in the designated integrity and performance system accessible through SAM (currently Federal Awardee Performance and Integrity Information System (FAPIIS)) (see 41 U.S.C. 2313);
  - ii. That an applicant, at its option, may review information in the designated integrity and performance systems accessible through SAM and comment on any information about itself that a Federal awarding agency previously entered and is currently in the designated integrity and performance system accessible through SAM;
- iii. That DTRA will consider any comments by the applicant, in addition to the other information in the designated integrity and performance system, in making a judgment about the applicant's integrity, business ethics, and record of performance under Federal awards when completing the review of risk posed by applicants as described in §200.205 Federal awarding agency review of risk posed by applicants.
- iv. For awards that exceed \$500,000 over the period of performance, DTRA will employ the additional post-award reporting requirements reflected in Appendix XII—Award Term and Condition for Recipient Integrity and Performance Matters of 2 CFR 200.
- 5.4. Technical and Administrative Support by Non-Government Personnel.

It is the intent of DTRA to use both Government and non-Government personnel to assist with the review and administration of submittals for this BAA. All pre-application white papers and invited proposals may be reviewed by subject matter experts, including, but not limited to, peer reviewers from across the academic and industrial community, as applicable to the research proposed.

Further, participation in this BAA requires DTRA support contractors to have access to preapplication white paper and invited proposal information including information that may be considered proprietary or otherwise marked with restrictive legends. Existing DTRA contractors include but may not be limited to the following: TASC, an Engility Company (Advisory & Assistance Services) and their subcontractors, JAB Innovative Solutions, LLC, Tenica and Associates LLC, and TFAB Ground Systems LLC (contract specialist support) and their subcontractors, SBG Technology Solutions (automated solicitation proposal management system [ASPMS] support) and their subcontractors, and Terremark Worldwide Inc (ASPMS support). Each contract contains organizational conflict of interest provisions and/or includes contractual requirements for non-disclosure of proprietary contractor information or data/software marked with restrictive legends. The Offeror, by submitting a white paper or proposal, is deemed to have consented to the disclosure of its information to the aforementioned contractors under the conditions and limitations described herein.

All individuals—including subject matter experts and support contractors—having access to any proprietary data must certify that they will not disclose any information pertaining to this BAA including any submittal, the identity of any submitters, or any other information relevant to this BAA. All applicants to this BAA consent to the disclosure of their information under these conditions.

#### 6. AWARD ADMINISTRATION INFORMATION

6.1. Award Notices. Applicants will be notified regarding the status of their applications (invitation/non-invitation for full proposals, re-submission of white papers, selection/non-selection for award, etc.) via e-mail to the BPOC listed in Block 5 of the SF-424 and the PI listed in Block 14 of the SF-424 provided at the time of submission. A debrief summary will be provided as part of all notification e-mails.

A notice of selection should not be construed as an obligation on the part of the Government; only duly authorized procurement personnel may commit resources, this will be done by issuing a grant or contract document to the selected applicant. Also, this notification must not be used as a basis for accruing costs to the Government prior to award. Selected applicants are not authorized to begin work, as any award is subject to successful negotiations (if determined necessary by DTRA) between the DTRA contracting division and the selected organization, and to the availability of funds.

All notifications will be made from <a href="mailto:notification@dtrasubmission.net">notification@dtrasubmission.net</a>. **E-mails to this e-mail** address will not be answered or forwarded.

Applicants must be aware that it is their responsibility to ensure: (1) correct e-mail addresses are provided at the time of submission, (2) this e-mail notification reaches the intended recipient(s), and (3) the e-mail is not blocked by the use of 'spam blocker' software or other means that the recipient's Internet Service Provider may have implemented as a means to block the receipt of certain e-mail messages.

If for any reason there is a delivery failure of these e-mail notices, DTRA retains the right to not make further attempts to contact the applicants.

6.2. Administrative and National Policy Requirements. The DTRA Grant Terms and Conditions may be found online at the DTRA website (<a href="www.dtra.mil">www.dtra.mil</a>). There are different versions for different recipients. As the Terms and Conditions are updated, they will be posted on the DTRA website (<a href="www.dtra.mil">www.dtra.mil</a>). All awards require certifications of compliance with national policy requirements. Statutes and Government-wide regulations require some certifications to be submitted at the time of proposal submission. See <a href="Section 4.5.2">Section 4.5.2</a> and <a href="Section 4.5.2">Section 4.5.2</a> and <a href="Section 4.6.2">Section 4.6.2</a> for the certification(s) required at the time of submission.

This BAA focuses on fundamental research in a DoD contractual context, which was defined in Section 1.2 of this BAA. Per DoD policy<sup>1</sup>, "...products of fundamental research are to remain unrestricted to the maximum extent possible." Furthermore, "The DoD will place no other restrictions on the conduct or reporting of unclassified fundamental research, except as otherwise required by statue [sic], regulation, or Executive Order." As such, fundamental research is normally exempt from controls under the International Traffic in Arms Regulation (ITAR) (22 CFR Parts 120-130) and/or the Department of Commerce regarding the Export Administration Regulations (15 CFR Parts 730-774), but the DoD rule recognizes that there are "rare" situations where export-controlled information or technology may be used in fundamental research that may require a license(s) or restrictions on products.

- 6.2.1. Export Control Notification. Applicants are responsible for ensuring compliance with any export control laws and regulations that may be applicable to the export of and foreign access to their proposed research. Applicants may consult with the Department of State with any questions regarding the International Traffic in Arms Regulation (ITAR) (22 CFR Parts 120-130) and/or the Department of Commerce regarding the Export Administration Regulations (15 CFR Parts 730-774). Please note that the prime awardee is responsible for monitoring ITAR compliance of all subawardees.
- 6.2.2. Protection of Human Subjects. If the proposed research involves human subjects or materials, applicants are asked to: a) justify the use of human subjects, b) outline the human use, and c) include the source of the human subjects or materials involved in the research. As a condition precedent to receipt of DTRA funding, applicants must ensure that the basic rights and welfare of human subjects are protected. Applicants shall submit with the full proposal package written evidence, to include a provisional protocol number and Institutional Review Board (IRB) point of contact information, that a human use protocol has been submitted to, and is pending approval by, a qualified IRB. Further information may be required if the proposal is successful.

All research under any award made under this BAA involving human subjects must be conducted in accordance with 32 CFR 219, 10 U.S.C. § 980, and DoD Instruction 3216.02, and, as applicable, 21 CFR parts 11, 50, 56, Good Clinical Practice, the ICH, as well as other applicable federal and state regulations. Awardees must be cognizant of and abide by the additional restrictions and limitations imposed on the DoD regarding research involving human subjects, specifically as regards vulnerable populations (32 CFR 219 modifications to subparts B-D of 45 CFR 46), recruitment of military research subjects (32 CFR 219), and surrogate consent (10 U.S.C. § 980).

DTRA Directive 3216.01 of June 9, 2010, modified March 18, 2015, established the DTRA Human Subjects Protection Program, set forth the policies, defined the applicable terms, and delineated the procedures necessary to ensure DTRA compliance with federal and DoD regulations and legislation governing human subject research. The regulations mandate that all DoD activities, components, and agencies protect the rights and welfare of human subjects of study in DoD supported research, development, test and evaluation, and related activities hereafter referred to as "research." The requirement to comply with the regulations applies to

<sup>&</sup>lt;sup>1</sup> Under Secretary of Defense for Acquisition, Technology and Logistics Memorandum, SUBJECT: Contracted Fundamental Research, dated 26 Jun 2008

new starts and to continuing research.

The DTRA Directive requires that research using human subjects may not begin or continue until the DTRA Research Oversight Board (ROB) has reviewed and approved the proposed protocol. Contractors and subcontractors are required to submit a valid federal assurance for their organization (institution, laboratory, facility) that has been issued by either DoD or the Department of Health and Human Services, and documentation of review of proposed protocols by the local IRB to include consent forms for any planned research using human subjects to the DTRA ROB for its review through the contracting officer's representative (if assigned) or the contracting officer. The ROB review is separate from, and in addition to, local IRB review.

A study is considered to involve human research subjects if: 1) there is interaction with the subject (even simply talking to the subject qualifies; no needles are required); and 2) if the study involves collection and/or analysis of personal/private information about an individual, or if material used in the study contains links to such information.

Written approval to begin research or to subcontract for the use of human subjects under the proposed protocol will be provided in writing from the DTRA ROB, through the contracting officer. Both the contractor and the Government must maintain a copy of this approval. Any proposed modifications or amendments to the approved protocol or consent forms must be submitted to the local IRB and the DTRA ROB for review and approval. Examples of modifications/amendments to the protocol include, but are not limited to:

- a change of the Principal Investigator;
- changes in duration or intensity of exposure to some stimulus or agent;
- changes in the information requested of volunteers, or changes to the use of specimens or data collected; or
- changes in perceived or measured risks or benefits to volunteers that require changes to the study.

Research pursuant to such modifications or amendments must not be initiated without IRB and ROB approval except when necessary to eliminate apparent and immediate hazards to the subject(s).

Research projects lasting more than one year require IRB review at least annually, or more frequently as required by the responsible IRB. The contractor or subcontractor must provide documentation of continued IRB review of protocols for ROB review and approval in accordance with the Contract Data Requirements List. Research changes must be reviewed by the IRB and ROB in advance unless necessary to eliminate apparent and immediate hazards to the subject(s).

A clause regarding human subjects research will be included in all contracts involving human subjects research. Non-compliance with any provision of this clause may result in withholding of payments under the contract pursuant to the contract's payments clause(s) and/or contract termination pursuant to the contract's termination clause(s). The Government shall not be responsible for any costs incurred for research involving human subjects prior to protocol approval by the ROB.

6.2.3. Animal Use. If the proposed research involves the use of live nonhuman vertebrate

animals, applicants are required to justify the use of animals by providing detailed information on the proposed animal use, to include the proposed species and number of animals planned, along with the location(s) where the animal study(ies) is planned. . Additional information will be required if the proposal is selected for award subject to successful negotiations. The Animal Care and Use Review Office (ACURO), a component of the USAMRMC Office of Research Protections (ORP), must review and approve all animal use prior to the start of working with animals. Therefore, Principle Investigators will be required to complete and submit the animal use appendix titled "Research Involving Animals", after award of the procurement instrument, which is available on the ACURO website

(http://mrmc.amedd.army.mil/index.cfm?pageid=research\_protections.acuro). Allow 2 to 4 months for regulatory review and approval processes for animal studies. Applicants are to build this review time into their project schedules.

DoD Instruction 3216.01, dated September 13, 2010, provides policy and requirements for the use of animals in DoD-funded research based on Army Regulation (AR) 40-33. The DoD definition of animal is any live nonhuman vertebrate. All proposals that involve the use of animals must be in compliance with DoD Instruction 3216.01 and AR 40-33. DTRA requires that research using animals not begin or continue until the ACURO has reviewed and approved the proposed animal use. For animals, the provisions include rules on animal acquisition, transport, care, handling, and use in: (i) 9 CFR parts 1-4, Department of Agriculture rules that implement the Laboratory Animal Welfare Action of 1966 (U.S.C. 2131-2156); and (ii) the "Guide for the Care and Use of Laboratory Animals," National Institutes of Health Publication No. 86-23.

6.2.4. Biological Defense Research Program (BDRP) Requirements: BioSurety and Select Agent Use.

Proposals must specify what Select Agent work will be conducted at the applicant's facility and what Select Agent work will be performed in other facilities. Proposals also must provide the source of the Select Agent(s), any appropriate registration information for the facilities, and specify the Laboratory Bio-safety Level. All Select Agent work is subject to verification of information and certifications. Further information may be required if the proposal is successful.

For those institutions in which PI's are conducting research with Bio-safety Levels 3 and 4 material, a Facility Safety Plan must be prepared and made available during the project award phase in accordance with 32 CFR 626.18. For grants awarded to foreign institutions, you must follow either local or U.S. laws (as stated above) depending on which laws provide stronger protection. (DTRA requires that research using Select Agents not begin or continue until DTRA has reviewed and approved the proposed agent use. See URL:

https://www.gpo.gov/fdsys/pkg/CFR-2002-title32-vol3/pdf/CFR-2002-title32-vol3-sec626-18.pdf for a copy of 32 CFR 626.18, Biological Defense Safety Program.)

For projects that will employ the use of chemical agents, either neat agent or dilute agent, the offeror must provide approved Facility Standard Operating Procedures that conform to Federal, State and local regulations and address the storage, use and disposition of these chemical materials.

6.2.5. Dual-Use Potential. In accordance with National Science Advisory Board for Biosecurity (NSABB) recommendations, DTRA will not support research that, based on current understanding, can reasonably be anticipated to provide knowledge, information, products, or

technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security. Research involving select agents and toxins is within scope of the DTRA mission; however, the use of select agents and toxins in certain experimental categories is considered "dual-use research of concern" (DURC) according to U.S. policy. (<a href="http://www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf">http://www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf</a>) Proposals that contain DURC will not be funded. Dual-use potential will be assessed based on application of the following criteria:

- Use of select agents or toxins. This factor evaluates whether the proposed research involves use of one or more select agents or toxins [as identified by the Select Agent Program under Federal Law (7 C.F.R. part 331, 9 C.F.R. part 121, and 42 C.F.R. part 73)] which pose significant risk of deliberate misuse with potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence.
- Scope of proposed experiments. This factor evaluates whether the proposed research involves experiments that will produce, aim to produce, or is reasonably anticipated to produce: (a) Enhanced harmful consequences of the agent or toxin; (b) Disruption of immunity or effectiveness of an immunization against the agent or toxin without clinical or agricultural justification; (c) Conferred resistance by the agent or toxin to clinically or agriculturally useful prophylactic or therapeutic interventions against the agent or toxin, or facilitated ability to evade detection methodologies; (d) Increased stability, transmissibility, or dissemination ability of the agent or toxin; (e) Altered host range or tropism of the agent or toxin; (f) Enhanced susceptibility of a host population to the agent or toxin; or (g) Eradicated or extinct select agents or toxins.
- 6.2.6. Military Recruiting. This is to notify potential applicants that each award under this announcement to an institution of higher education, with exception of any grants awarded to institutions of higher education entirely located outside the United States and/or its territories, must include the following term and condition: "As a condition for receipt of funds available to DoD under this award, the recipient agrees that it is not an institution of higher education (as defined in 32 CFR 216) that has a policy of denying, and that it is not an institution of higher education that effectively prevents, the Secretary of Defense from obtaining the following for military recruiting purposes: (A) entry to campuses or access to students on campuses; or (B) access to directory information pertaining to students. If the recipient is determined, using procedures in 32 CFR 216 to be such an institution of higher education during the period of performance of this agreement, and therefore to be in breach of this clause, the Government will cease all payments of DoD funds under this agreement and all other DoD grants and CAs, and it may suspend or terminate such grants and agreements unilaterally for material failure to comply with the terms and conditions of award." 32 CFR 216 may be accessed electronically at <a href="http://www.ecfr.gov/cgi-bin/text-">http://www.ecfr.gov/cgi-bin/text-</a>

idx?SID=ee45add5e352854b7089ce420c7fd0a6&mc=true&tpl=/ecfrbrowse/Title32/32cfr216 m ain 02.tpl. If your institution has been identified under the procedures established by the Secretary of Defense to implement Section 558 of Public Law 103-337, then: (1) no funds available to DoD may be provided to your institution through any grant, including any existing grant; and (2) your institution is not eligible to receive a grant in response to this BAA. This is to notify potential applicants that each award under this announcement to an institution of higher education, with exception of any grants awarded to institutions of higher education entirely

located outside the United States and/or its territories, must include the following clause: 32 CFR 22.520 (DoDGARS 22.520), Military Recruiting and Reserve Officer Training Corps Program Access to Institutions of Higher Education.

- 6.2.7. Combating Trafficking in Persons. The recipient agrees to comply with the trafficking in persons requirement in Section 106(g) of the Trafficking Victims Protection Act of 2000 (TVPA), as amended (22 U.S.C. 7104(g)).
- 6.2.8. Reporting Subawards and Executive Compensation. The recipient agrees to ensure they have the necessary processes and systems in place to comply with the reporting requirements of the Transparency Act, as defined at 2 CFR 170.320, unless they meet the exception under 2 CFR 170.110(b).
- 6.2.9. Representation Regarding the Prohibition on Using Funds under Grants and Cooperative Agreements with Entities that Require Certain Internal Confidentiality Agreements. By submission of its proposal or application, the applicant represents that it does not require any of its employees, contractors, or subrecipients seeking to report fraud, waste, or abuse to sign or comply with internal confidentiality agreements or statements prohibiting or otherwise restricting those employees, contractors, or subrecipients from lawfully reporting that waste, fraud, or abuse to a designated investigative or law enforcement representative of a Federal department or agency authorized to receive such information. Note that: (1) the basis for this representation is a prohibition in section 743 of the Financial Services and General Government Appropriations Act, 2015 (Division E of the Consolidated and Further Continuing Appropriations Act, 2015, Pub. L. 113-235) and any successor provision of law on making funds available through grants and cooperative agreements to entities with certain internal confidentiality agreements or statements; and (2) section 743 states that it does not contravene requirements applicable to Standard Form 312, Form 4414, or any other form issued by a Federal department or agency governing the nondisclosure of classified information.
- 6.3. Reporting. General requirements are provided below; however, each awardee should check the award agreement and its contract data requirements list (CDRLs) and/or terms and conditions to determine the requirements for that specific award.
- 6.3.1. Annual Reports. Annual Reports will be due no later than 1 July of each year. Awards effective after 31 January will not require an Annual Report until 1 July of the following year. The Annual Report is *not* a cumulative report.
- 6.3.2. Final Technical Reports. A comprehensive final technical report is required prior to the end of an effort, due on the date specified in CDRLs and/or the terms and conditions of the award document. The purpose of the Final Report is to document the results of the effort. The Final Report *is* a cumulative report.

The final report will always be sent to the Defense Technical Information Center (DTIC) and reports may be available to the public through the National Technical Information Service (NTIS).

- 6.3.3. Financial Reports. Federal Financial Reports (SF-425) are due no later than 1 July of each year. Grants effective after 31 January will not require a Federal Financial Report until 1 July of the following year.
- 6.3.4. Foreign Travel Reports. Within thirty (30) days after returning to the United States from foreign travel, the PI may be required to submit an acceptable trip report summarizing the

highlights of the trip. For grants, contracts, or OTAs awarded to institutions entirely located outside the United States and/or its territories, this is not required.

6.4. After-the-Award Requirements for *Grants*. Closeout, subsequent adjustments, continuing responsibilities, and collection of amounts due are subject to requirements found in 32 CFR 32.71 – 73 (Institutions of Higher Education, Hospitals, and Other Non-Profit Organizations) and 32 CFR 34.61 – 63 (For-Profit Organizations).

#### 7. AGENCY CONTACTS

Administrative Correspondence and Questions	HDTRA1-FRCWMD-A@mail.mil
Thrust Area 1: Science of WMD Sensing and Recognition	HDTRA1-FRCWMD-TA1@mail.mil
Thrust Area 2: Network Sciences	HDTRA1-FRCWMD-TA2@mail.mil
Thrust Area 3: Science for Protection	HDTRA1-FRCWMD-TA3@mail.mil
Thrust Area 4: Science to Defeat WMD	HDTRA1-FRCWMD-TA4@mail.mil
Thrust Area 5: Science to Secure WMD	HDTRA1-FRCWMD-TA5@mail.mil
Thrust Area 6: Cooperative Counter WMD Research with Global Partners	HDTRA1-FRCWMD-TA6@mail.mil
Thrust Area 7: Fundamental Science for Chemical and Biological Defense	HDTRA1-FRCWMD-TA7@mail.mil

Table 6: Agency Contacts.

- 7.1. Questions regarding administrative content of this BAA must be addressed to the administrative e-mail address listed above.
- 7.2. Questions regarding technical content of this BAA must be referred to the technical staff responsible for the relevant thrust areas.

DTRA will not release employee personal contact information.

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#### 8. OTHER INFORMATION

Topics from previous periods may or may not be repeated. DTRA will not provide additional information regarding the posting of future topics, including dates for posting, the potential for a topic to be repeated in out years, the potential for similar topics to be posted, and/or topic details in advance of issuance of an amended BAA.

#### ATTACHMENT 1: SPECIFIC TOPICS

Thrust Area 6 has no specific topics at this time. Submissions to the general thrust area description in accordance with the requirements detailed in this BAA are welcome.

Thrust Areas 1, 2, 3, 4, 5, and 7 have specific topics—Topics G1-G19—detailed below. Submissions to the general thrust area descriptions for these thrust areas in accordance with the requirements detailed in this BAA are also welcome. However, great care must be taken to use the appropriate application package:

- If <u>NOT</u> submitting to one of the specific topic numbers detailed below, use one of the **Thrust Area N <u>NO TOPIC</u>** packages
- If you <u>ARE</u> submitting to one of the specific topic numbers detailed below, use the applicable <u>Basic Research-Thrust Area N-Topic G1 to G19</u> package

### \*\*\*BASIC RESEARCH TOPICS G1-G19\*\*\*

In accordance with <u>Section 4.2.1</u>, the requirement for abstract pre-coordination is waived for Topics G1-G19; these topics do NOT require pre-coordination of an abstract prior to the submission of pre-application white papers.

The pre-application white paper deadline for Topics G1-G19 is 1 February 2017. NOTE: An amendment to this BAA will be posted on 2 February 2017 removing Topics G1-G19. **PRE-APPLICATION WHITE PAPERS FOR THESE TOPICS MUST BE SUBMITTED BY 11:59 PM (MIDNIGHT) EST ON 1 FEBRUARY 2017.** White papers may not be considered if they are received after this deadline.

Responses to Topics G1-G19 must address only basic research. Basic research is the systematic study directed toward greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications toward processes or products in mind. It includes all scientific study and experimentation directed toward increasing fundamental knowledge and understanding in those fields of the physical, engineering, environmental, and life sciences related to long-term national security needs. It is farsighted, high payoff research that provides the basis for technological programs.<sup>2</sup>

Topics G1-G19 are interested in research projects that span from those that focus on exploratory aspects of a unique problem or a high-risk approach to those that involve a comprehensive program with interdisciplinary areas. Consistent across all proposals should be the focus on innovative research with the potential for high impact to C-WMD science.

DTRA anticipates that the predominance of awards made under Topics G1-G19 will be grants. Pre-application white papers and proposals submitted to Topics G1-G19 must have a single lead organization and single submission for the pre-application white paper and the invited proposal. Awards will be made by a single award to the lead institution. Subawards, including all grants and/or contracts, are the responsibility of the award recipient; exceptions will not be made.

<sup>&</sup>lt;sup>2</sup> DoDI 3210.1, September 16, 2005

### Basic Research-Thrust Area 1-Topic G1: Early Time Signatures of a Nuclear Attack

Award Amounts for this topic are anticipated to be between \$150,000 and \$350,000 per year (total dollar value = direct and indirect costs). Larger value efforts (i.e., \$350, 000 per year) that are university led, include multiple PIs (at either a single or at multiple organizations), and provide training opportunities are encouraged. In all cases, the proposed award value should be clearly substantiated by the scope of the effort.

Proposals from Young Investigators will be considered for this topic. Young Investigator proposals should be clearly marked as such and include a scope of work commensurate with a \$100,000 award (total dollar value = direct and indirect costs). Young Investigators are defined as individuals who are currently employed by a U.S. accredited degree-granting college or university who received a Ph.D. or equivalent degree within five (5) years of the date of the preapplication white paper submission. Pre-application white papers and proposals from Young Investigators will be given preference.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** Following a nuclear attack, a variety of complex nuclear and chemical processes occur that envelop the bomb materials, the surrounding air, and the local environment. Understanding these processes provides insight into the device composition and origins, useful for post-detonation nuclear forensics. The emission and detection of prompt signatures (optical, gamma, shock wave, etc.) can give valuable information before the material collection and analysis process has begun. However, interpreting these signals can be difficult due to limits in knowledge of the fundamental processes leading to their creation and propagation.

DTRA is responsible for research and development efforts for post-detonation nuclear forensics within the DoD. In this topic, DTRA seeks basic research to understand the formation and propagation of prompt signals as well as the identification of new signatures that occur during the early interactions of a nuclear detonation with the surrounding environment. Possible research areas could include air chemistry, nuclear or non-nuclear interactions of the blast with surrounding materials (particularly urban materials) or nuclear data associated with relevant nuclear reactions.

**Impact:** The development of advanced post detonation forensics addresses DTRA's C-WMD need to enable: prevention of future detonations; identification of those responsible; and improvement in response and recovery efforts. A better interpretation of early-time interactions would provide situational information quicker, inform material analysis and guide a more efficient response. In addition, an understanding of surrounding air chemistry, signature transport and the underlying nuclear reactions helps to better inform modeling and analysis efforts.

**Objective:** This topic seeks research to study the early-time signatures (from T=0 to several hours) of a nuclear blast and their propagation in the surrounding environment. We seek to

better comprehend the air chemistry and nuclear effects that result in the production and propagation of prompt signatures (speed of light, speed of sound). Additionally, this topic seeks to uncover new signatures, resulting from the blast's effect on nearby materials, that haven't been explored previously because of constraints in accessing detonation sites. These signatures would potentially be measureable for a period of several hours after the blast. The research should identify and characterize these signatures, but not focus on developing a specific detection scheme. Possible research areas may include, but are not limited to:

- Experimental and modeling studies of air chemistry and urban effects including:
  - Radiation transport
  - Optical transport
  - o Dynamic particle chemistry and physics
  - Non-equilibrium dynamics
- Nuclear data experimental measurements. Data of particular interest include:
  - o Fission product yields
  - o Prompt-fission gamma yields
- Material interactions
  - Activation of urban materials
  - Characterization of material morphology

# <u>Basic Research-Thrust Area 1-Topic G2: Energy-Efficient Physical and Algorithmic Methods</u> for Detection, Localization, and Isotope Identification

Award Amounts for this topic are anticipated to be between \$150,000 and \$350,000 per year (total dollar value = direct and indirect costs). Larger value efforts (i.e., \$350, 000 per year) that are university led, include multiple PIs (at either a single or at multiple organizations), and provide training opportunities are encouraged. In all cases, the proposed award value should be clearly substantiated by the scope of the effort.

Proposals from Young Investigators will be considered for this topic. Young Investigator proposals should be clearly marked as such and include a scope of work commensurate with a \$100,000 award (total dollar value = direct and indirect costs). Young Investigators are defined as individuals who are currently employed by a U.S. accredited degree-granting college or university who received a Ph.D. or equivalent degree within five (5) years of the date of the preapplication white paper submission. Pre-application white papers and proposals from Young Investigators will be given preference.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be

considered.

**Background:** Capabilities in the detection of nuclear materials in mobile scenarios are limited by power-consumption of sensor-supporting electronics for signal amplification, processing, and algorithmic computation. Algorithm computation becomes a nebulous area of research employing many techniques and many levels of fidelity spanning between gross-count alarms for initial detection and isotope identification. To minimize size, weight, and power for mobile detection systems, these computational methods must be transitioned to embedded, chip-scale, hardware. Thus, basic research is sought to explore the theoretical minimum amount of electrical power necessary to achieve algorithmic output from spectroscopic sensor data for a given physical architecture. This data may include spectral histograms or list-mode data received event by event. Solutions to decrease power consumption may be found in both algorithmic and physical approaches.

**Impact:** Advancements in fundamental science may foster future technologies and analysis methodologies that require fewer power resources, help discriminate between background response and signatures of interest, and enhance range-of-detection of illicit nuclear materials. These advancements will also engender processes that extend both the minimal detectable activity and minimal rate of false alarms and false identifications. It is desirable to advance knowledge of embedded computational techniques that minimize power resources and size of supporting electronics. Scientific and technical approaches should enable smarter sensor components and reduce communication resources for exfiltration in a global network by means of transmitting high-fidelity information as opposed to raw sensor data.

**Objective:** This topic seeks research to foster physical and algorithmic methods that make computational capability more power-efficient in embedded systems. More efficient systems will provide smarter sensing instrumentation on the ground, producing higher information density output and communicating higher-level information while consuming fewer power resources. Successful results may be applicable across multiple uses including ground or airborne radiation/nuclear detection networks, mobile or fixed. Possible research areas may include, but are not limited to:

- Conducting theoretical, computational, or experimental studies of fundamental computational
  methods to reduce the number of math operations required to achieve algorithmic output for
  mobile detection and isotope identification with minimal false alarm rates.
- Exploring chip-scale architectures and assemblies that may reduce the power consumed to execute algorithmic calculations, including the reduction of clock-cycles and memory.
- Enhancing understanding of sensor signal fidelity in time and space to exploit minimal effort in computation in distinguishing radiological features of interest from background signatures.
- Investigate additional approaches beyond algorithms to find efficiencies in lowering power
  for radiation detection analyses; e.g., power saving advances with neuromorphic computing,
  low-power concepts analogous to advances demonstrated with the introduction of GPUs, or
  other novel approaches.

Note: Submissions proposing a repackaging of existing processing systems will not be considered.

## <u>Basic Research-Thrust Area 1-Topic G3: Robust Organic Scintillators and Algorithms to</u> Advance Autonomous RN Search

Award Amounts for this topic are anticipated to be between \$150,000 and \$350,000 per year (total dollar value = direct and indirect costs). Larger value efforts (i.e., \$350, 000 per year) that are university led, include multiple PIs (at either a single or at multiple organizations), and provide training opportunities are encouraged. In all cases, the proposed award value should be clearly substantiated by the scope of the effort.

Proposals from Young Investigators will be considered for this topic. Young Investigator proposals should be clearly marked as such and include a scope of work commensurate with a \$100,000 award (total dollar value = direct and indirect costs). Young Investigators are defined as individuals who are currently employed by a U.S. accredited degree-granting college or university who received a Ph.D. or equivalent degree within five (5) years of the date of the preapplication white paper submission. Pre-application white papers and proposals from Young Investigators will be given preference.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** DTRA develops technology to search for, locate, and characterize radiological/nuclear (RN) materials and WMD. However, detection of many materials, particularly Special Nuclear Material (SNM), can be difficult due to weak radioactive signatures. In many cases, close quarters search with hand-held detectors is necessary. One possible solution to remove the warfighter from these searches, as well as to increase search speed and accuracy, could be to equip unmanned vehicles (UAV, UGV) to search autonomously. However, current radiation detectors and algorithms limit the possibilities for autonomous RN search.

This topic seeks research into novel organic radiation sensor materials that provide improved efficiency and energy resolution but also offer superior robustness over current materials. Current sensor materials are either bulky or brittle (NaI, HPGe), are limited in size due to growth constraints (CZT), or possess poor energy resolution and efficiency for gamma-rays (plastic scintillators). We envision a new class of materials that possess excellent response (resolution and efficiency) and are also mechanically robust, lightweight, and have the versatility to be produced in a variety of unconventional sizes and shapes. Potential research could investigate material interaction with gamma and neutron radiation, light collection and photodetection for scintillator materials, new or innovative material growth methods, or physical and mechanical material properties.

In addition to materials research, the development of advanced algorithms for gamma-ray spectrum analysis and real-time RN threat mapping is essential to improving RN search capabilities. Previous work has shown that algorithms that target spectral anomalies through a variety of mathematical techniques can improve sensitivity and source localization while reducing false alarms. Through this topic, we seek additional work on algorithms to improve the

sensitivity, incorporate multimodal information (e.g. 3D mapping and source tracking), and enable real-time autonomous path planning for RN search. The algorithm work, conducted in collaboration with the material development, should be targeted towards the signals created by the new materials developed under this project.

**Impact:** Efficient, lightweight organic radiation detectors and innovative algorithms for detection would enable new capabilities for RN search. These combined capabilities could increase the speed, sensitivity, and accuracy of these searches while reducing the operational burden and danger to the warfighter.

**Objective:** This topic seeks research to advance the current state of RN materials search. This research should focus on the development of novel radiation sensor materials that will enable the creation of lightweight, mechanically robust detectors and the advancement of algorithms for RN search. This topic is not seeking a final detector product but, rather, research to investigate the fundamental material properties of such a sensor, and the algorithms necessary to analyze RN and multi-modal signatures. Possible research areas may include, but are not limited to:

- Materials development of high-efficiency solid-organic or plastic scintillators
- Fabrication methods to develop unconventional detector shapes and designs
- Investigations into increasing the structural robustness of detector materials
- Methods to improve light collection in scintillators of novel composition and geometry
- Novel, adaptable, robust photodetector designs; photodetectors using flexible substrates
- Algorithm development for autonomous RN threat identification, mapping and path planning

## <u>Basic Research-Thrust Area 2-Topic G4: Behavior Regime Analysis and Model Order</u> Reduction (MOR) for Nuclear Weapons Effects (NWE)

Award Amounts for this topic are anticipated to be between \$150,000 and \$350,000 per year (total dollar value = direct and indirect costs). Larger value efforts (i.e., \$350, 000 per year) that are university led, include multiple PIs (at either a single or at multiple organizations), and provide training opportunities are encouraged. In all cases, the proposed award value should be clearly substantiated by the scope of the effort.

Proposals from Young Investigators will be considered for this topic. Young Investigator proposals should be clearly marked as such and include a scope of work commensurate with a \$100,000 award (total dollar value = direct and indirect costs). Young Investigators are defined as individuals who are currently employed by a U.S. accredited degree-granting college or university who received a Ph.D. or equivalent degree within five (5) years of the date of the preapplication white paper submission. Pre-application white papers and proposals from Young Investigators will be given preference.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white

papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** Current state of the art analysis methods for NWE do not have sufficient flexibility to meet the wide range of mission needs. Analysis methods currently used for NWE generally fall into one of two general categories: either very high fidelity first principles-based approaches with long computation time (resource heavy high fidelity or completely intractable) or very simple with short computation time (resource light with low fidelity or simply a look-up table). Current missions require analysis methods with flexible levels of fidelity and corresponding resource usage (manpower and computation appropriate), that vary on a continuum between the very high and very low fidelity methods available now. Specific research on determination of various behaviors at regime boundaries and simplified characterizations of NWE would help fill in the capability space with more appropriate fidelity approaches better suited to DTRA missions.

**Impact:** Advances in the understanding of NWE in various regimes of behavior and the development of NWE characterizations with adjustable fidelity in different regimes, would allow for the appropriate scaling and implementation of theory, modeling, and simulation tools to better meet analysis for mission needs to support national decision makers. Analysts are currently forced to rely on NWE analysis tools with fidelities that may be inappropriate to the problems decision makers confront. NWE analysis tools of varying fidelity could be better matched to mission needs. This flexibility would in turn allow NWE analysts to provide better quality results with greater confidence to national decision makers at appropriate levels of complexity, resource usage and uncertainty.

**Objective:** The objective of this topic is to fill in the NWE analysis capability space between very high fidelity and very simple methodologies. Development of simplified characterizations of NWE and of research to understand NWE regime behavior focusing on boundary behavior will allow for appropriate fidelity approaches to be developed. Research for this topic may focus specifically on single NWE or be more broadly applicable to multiple NWE. Possible research areas may include, but are not limited to:

- Reduced state and mission-appropriate fidelity of NWE focusing on exploration of physical behavior similitudes and scaling.
- NWE regime determination (phase transition analysis) focusing on boundary behavior (phase changes and emergent behavior).
- Rules of thumb for NWE modeling obtained from ab-initio and/or data driven modeling. Easy user friendly visualization of complex phenomena using these rules
- Surrogate modeling and Simplified Order Modeling (SOM) for NWE that may include kernel PCA, ICA, maximum likelihood, semi-empirical, machine learning, adaptive data driven modeling, and other methods and approaches for reduced order modeling (parametric and non-parametric) are welcomed.

Investigators should propose their own NWE high fidelity model to work with, for example, Boltzmann transport, Navier-Stokes, Maxwell's equations, reaction-diffusion equations, etc. Investigators may also propose a model order reduction methodology that builds hybrid semi-empirical modeling schemes based upon data-driven modeling of some more difficult to calculate terms in first principles calculations. Regardless of approach, all investigators may

request unclassified data sets for use in the research. The end result is to have a methodology to create a continuum of modeling approaches of various levels of fidelity, various levels of tractability, various levels of computational scaling, and various levels of transferability in between regimes for a given NWE simulation system (e.g. simulation of a fireball). The resultant approaches will provide a wider selection of theory, modeling and simulation solutions for the analyst to choose from.

# <u>Basic Research-Thrust Area 3-Topic G5: Formation, Evolution, and Conductivity of X-Ray Generated Warm Dense Plasma</u>

Award Amounts for this topic are anticipated to be between \$150,000 and \$350,000 per year (total dollar value = direct and indirect costs). In all cases, the proposed award value should be clearly substantiated by the scope of the effort.

Proposals from Young Investigators will be considered for this topic. Young Investigator proposals should be clearly marked as such and include a scope of work commensurate with a \$100,000 award (total dollar value = direct and indirect costs). Young Investigators are defined as individuals who are currently employed by a U.S. accredited degree-granting college or university who received a Ph.D. or equivalent degree within five (5) years of the date of the preapplication white paper submission. Pre-application white papers and proposals from Young Investigators will be given preference.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** Satellites are a critical part of DoD communication, reconnaissance, and guidance systems. The majority of these satellites are powered by photovoltaic arrays due to their superior combination of cost, weight, stability, and risk. In order to work effectively solar arrays need to have a large surface area exposed to sun light. The large exposed surface area makes them potentially vulnerable to prompt radiation from a high altitude nuclear explosion. The large surface area of modern solar arrays also means that adding even transparent thin films for protection can add significant weight, and the need for direct sunlight exposure in non-concentrator designs precludes shielding-based protection strategies. While surface charging, displacement damage, and total ionizing dose have been studied in solar arrays, the effects of prompt cold X-rays are not well understood.

Prompt X-ray exposures with pulses of less than 100 nanoseconds and with photon energies below ~1 keV can generate high-density surface plasmas due to the vaporization and ionization of the first few microns of surface materials. This warm dense plasma can span the dielectric surfaces and couple the biased solar cells to each other, to spacecraft structures, or to the space plasma itself. The formation and temporal behavior of the plasma, as well as the effective conductivity and coupling to exposed conductors, are not well understood or modeled.

For example, formation of a highly conductive plasma layer has been observed in experiments

using the Omega laser at the University of Rochester Laboratory for Laser Energetics. X-rays pulses of  $\sim$ 2 nanoseconds were created using standard laser pulse widths and targets at the Omega laser system. Langmuir probes biased at 10-30 V and solar cells biased at 100 V were used to measure the effects of plasma blow-off. The fluence at the probes and cells of X-rays with energies below  $\sim$ 1 keV ranged from 0.003 – 0.03 Joule/cm². In almost all cases, the probes and solar cells exhibited the effects of a conductive surface plasma that allowed discharges with voltage drops <10 V.

**Impact:** This effort will increase understanding of the potential impacts of prompt X-rays on satellite solar array performance, reliability, and lifetime though fundamental physics modeling of the formation, time evolution, and conductivity of warm dense surface plasmas generated by prompt X-rays. This will lead to more cost-effective designs for future survivable solar arrays.

**Objective:** This topic seeks research to study the fundamental physics of the generation, temporal evolution, and properties of the warm dense plasma that can be generated by X-ray exposures. Experimental, theoretical, modelling, and computational efforts that fundamentally describe, predict, and replicate the phenomenon are of interest. Efforts should be focused on discovering the fundamental science that explains the formation and evolution of warm dense surface plasmas and physical and electrical properties of the plasma and its electrical connection to conductive surfaces, not on engineering approaches that seek to develop new methods for mitigation or new solar array designs. This topic is also not interested in solar array ESD (electrostatic discharge) due to natural space environments. Possible research areas may include, but are not limited to:

- The time-dependent interaction of x-rays (with a range of effective blackbody temperatures from 100 to 1000 eV) with both metallic and insulating materials typical of solar arrays that drive the formation warm dense surface plasmas
- Time dependent warm dense surface plasma evolution and conductivity
- The nature of electrical conduction properties of the two solid conductors bridged by surface plasma generated in the aforementioned range for discharges driven by the voltages and currents typically generated by a solar array
- Thermal and electrical transport between cold metals and warm dense surface plasmas
- Changes in x-ray absorption during material blow-off and plasma generation
- Macroscopic property of effective conductivity across an insulating surface and the transition to a sustained arc

Experimental data may be available as Government-Furnished Information during the period of performance of the award for model validation.

## <u>Basic Research-Thrust Area 3-Topic G6: Modeling Infectious Disease Kinetics and the Host Immune Response</u>

Award Amounts for this topic are anticipated to be between \$150,000 and \$350,000 per year (total dollar value = direct and indirect costs). Larger value efforts (i.e., \$350, 000 per year) that are university led, include multiple PIs (at either a single or at multiple organizations), and provide training opportunities are encouraged. In all cases, the proposed award value should be clearly substantiated by the scope of the effort.

Proposals from Young Investigators will be considered for this topic. Young Investigator proposals should be clearly marked as such and include a scope of work commensurate with a \$100,000 award (total dollar value = direct and indirect costs). Young Investigators are defined as individuals who are currently employed by a U.S. accredited degree-granting college or university who received a Ph.D. or equivalent degree within five (5) years of the date of the preapplication white paper submission. Pre-application white papers and proposals from Young Investigators will be given preference.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** DTRA Reachback provides continuous support and assistance to combatant commands and other customers for all WMD-related matters and natural disasters that involve the release of CBRN materials. DTRA Reachback is called upon to predict the impact of countermeasures for infectious diseases that could impact military operations or in cases where the military is called upon to assist in humanitarian responses. Additionally, DTRA Reachback is asked to provide guidance for a variety of emerging infectious diseases as well as category A bioagents. In order to provide guidance or answer questions for these heterogeneous populations, it is necessary to consider the impact of differing host factors (e.g. age, gender, genetic, malnutrition) on disease pathogenesis and the host immune response. Models that incorporate the impact of differing host factors can aid DTRA Reachback in predicting the severity of consequences for these heterogeneous populations with and without appropriate medical countermeasures. From the cellular to the tissue level, models have been developed to simulate pathogen infection kinetics and the host immune response. 1-5 Examples include models of viral infection kinetics and sepsis. Some models have begun to incorporate therapeutic treatments, which open the possibility to predicting the performance of different therapeutic dosing regimens, and some researchers have begun modeling the role of host factors such as age on pathogen infection dynamics. Framing such models appropriately poses many challenges, including those associated with determining the appropriate level of abstraction (e.g., whether or not to incorporate specific granulocytes, monocytes, lymphocytes and cytokine/chemokine networks). Quantitatively validating models with experimental data is likewise a significant challenge, as is the computational tractability of modeled systems as they increase in complexity and size. However, before conducting additional targeted experiments, it is prudent to integrate the use of existing in vitro and in vivo data of disease infection kinetics, host immune response including both cellular (T cell) and humoral (antibodies) arms, and therapeutic treatments.

**Impact:** This work focuses on modeling pathogen-host interactions. This will provide deeper insights regarding the establishment of infections and help predict the severity of consequences both with and without appropriate medical treatment. Research conducted herein will enable DTRA Reachback to predict the performance of differing therapeutic dosing regimens for heterogeneous populations.

**Objective:** The overarching research goal is to gain further understanding of infectious disease kinetics and host immune response dynamics by modeling the emergent system behavior (e.g. viral load, immunoglobulin levels, cellular lysis, etc.). Synthesis of existent data is desirable in order to identify critical gaps in knowledge and provide an analytical framework to guide future research. Proposals should utilize, to the extent possible, data generated by previous studies. Proposals that include experimental testing should provide clear rationale for doing so. In particular, approaches that establish validity using a single model system that lends itself to comparisons with other emerging pathogens or Category A agents containing similar host-pathogen dynamics are of interest. Successful programs under this topic should address a majority of the following concerns:

- Develop approaches to incorporate and predict the impact of differing host factors on disease pathogenesis and the host immune response
- Develop approaches to incorporate and predict the impact of differing therapeutic dosing regimens on disease pathogenesis
- Incorporate disparate data sources as well as develop methods to analyze datasets with missing or incomplete data
- Address potential computational tractability issues and, if appropriate, develop methods to overcome these issues
- Verify if parameters in their chosen model or simulation are identifiable<sup>4</sup>
- Delineate and justify assumptions, including those associated with hypothetical cause-andeffect relationships
- Provide rationale for selection of data types (e.g. choice of cell type), choice of system (e.g. human, rat, etc.), selection of therapeutic (e.g. antibiotic), and selection of computational approaches
- Incorporate sensitivity analysis and risk mitigation plans, especially for cases where small changes to assumptions may result in large changes to end-state predictions
- Explain methods that will be used or developed to quantify uncertainties

A multidisciplinary team with strong backgrounds in medical, immunological, and computational sciences is preferred.

#### **References:**

- 1. http://www.dtra.mil/Portals/61/Documents/Shield\_spring\_2011\_12mb.pdf
- 2. Shi, Zhen Z., Chih-Hang Wu, and David Ben-Arieh. "Agent-based model: a surging tool to simulate infectious diseases in the immune system." *Open Journal of Modelling and Simulation* 2014 (2014).

- 3. Boianelli, Alessandro, et al. "Modeling influenza virus infection: A roadmap for influenza research." *Viruses* 7.10 (2015): 5274-5304
- 4. Nguyen, Van Kinh, et al. "Ebola virus infection modeling and identifiability problems." *Frontiers in microbiology* 6 (2015): 257.
- 5. Pollmächer, Johannes, and Marc Thilo Figge. "Deciphering chemokine properties by a hybrid agent-based model of Aspergillus fumigatus infection in human alveoli." Frontiers in microbiology 6 (2014): 503-503.
- 6. Schirm, Sibylle, et al. "A biomathematical model of pneumococcal lung infection and antibiotic treatment in mice." *PloS one* 11.5 (2016): e0156047.
- 7. Uvarovskii, Ted M. Ross, et al. "Effects of Aging on Influenza Virus." J. Virol 88.8 (2014): 4123.

# <u>Basic Research-Thrust Area 3-Topic G7: Radiation Effects in 3D and Vertically Integrated</u> <u>Microelectronics</u>

Award Amounts for this topic are anticipated to be up to \$1,000,000 per year (total dollar value = direct and indirect costs). All efforts must be multidisciplinary. Preference will be given to multi-institution proposals; however, multiple PIs from a single organization are also eligible to apply. Further preference will be given to teams that have a university as the lead organization, maintain significant amounts of research at one or more universities, and include multiple opportunities for training. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** Highly integrated micro/nanoelectronic components in satellites, robots, and unmanned vehicles may be required to operate reliably and predictably in natural and manmade high radiation environments. As the electronics, circuits, and sensors become integrated in three dimensions on the same chip or in the same package, understanding, modeling, predicting, and testing the effects of radiation becomes increasing challenging and complicated.

As micro/nanoelectronic device scaling becomes more technologically challenging and less cost effective, manufacturers are increasingly turning to vertical integration to increase device density, improve efficiency, and add functionality. This three dimensional (3D) integration also adds complexity and cost to the design and fabrication process that could limit adoption. The degree of vertical integration possible is currently limited by the fabrication process (e.g. temperature limits, yield), by chip limits (heat removal, IO), and by the cost-to-benefit ratio. The ideal level of 3D integration is currently unknown and application specific, but there is increasing interest in and availability of vertically integrated devices for space and DoD applications.

There are multiple approaches to achieving 3D integration. Some approaches look to combine different device types, for example MEMS devices using the BEOL (back end of the line) process have been stacked on conventionally fabricated CMOS circuits. Some approaches create multiple layers of the same devices, for example 3D NAND Flash is already commercially available with 32 device layers and V-NAND Flash is available with 48 layers. Other efforts are underway to stack photonic devices or non-silicon devices with silicon CMOS.

A few initial studies have been done on the effects of radiation on stacked devices. One of the first studies by Gouker *et al.* looked at three layers of fully depleted 150nm SOI SRAM fabricated by oxide to oxide wafer bonding. They showed that there were no tier-to-tier effects and radiation effects were comparable between 2D and 3D SRAM. In subsequent studies Re *et al.* showed no additional TID effects in wafer bonded 130 nm bulk CMOS layers due to stacking. Single event effects (SEE) in two 90 nm COTS SRAM stacked dice separated by ~250µm were investigated by Gupta *et al.* They found a negligible increase in predicted proton SEE rates versus a single layer device. While these initial studies are promising for 3D ICs operating in high radiation environments, there are a number of unanswered questions that require further investigation.

**Impact:** Multi-layer stacked and 3D integrated chips have significant potential benefits for space and DoD applications, including increased power efficiency, increased device density, and added chip level functionality. However, the effect of stacking and integrating multiple technologies and materials on their radiation response is largely unknown.

**Objective:** This topic seeks, through experimentation and modeling, to develop a fundamental knowledge of the effects of radiation on multiply stacked and 3D integrated micro/nanoelectronic device and circuits. This topic is interested in both innovative and efficient ways to model and test radiation effects in 3D integrated devices as well as the results (underlying physics) of radiation testing and modeling. This topic is NOT interested in developing 3D IC technology. Of particular interest:

- Innovative radiation testing approaches to overcome the limitations of conventional testing facilities to effectively penetrate multiple layers
- Innovative radiation effects modeling approaches to address the challenges of efficiently modeling across multiple layers, both radiation/charge transport and circuit level
- Effect of integrating non-silicon materials and layers on radiation response
- Effect of integrating MEMS, photonic, or sensor devices and layers on radiation response
- Effect of device and layer scaling on radiation response
- Radiation effects in nanowire and gate all around (GAA) devices
- Impact of 3D transmission lines and through silicon vias on radiation response
- Probability and consequences of SEEs across multiple layers
  - o Does RHBD need to be three dimensional?
- Impact of radiation strike angle

#### **References:**

- 1. P. M. Gouker *et al.*, "Radiation Effects in 3D Integrated SOI SRAM Circuits," in *IEEE Transactions on Nuclear Science*, vol. 58, no. 6, pp. 2845-2854, Dec. 2011.
- 2. V. Re, L. Gaioni, A. Manazza, M. Manghisoni, L. Ratti and G. Traversi, "Radiation Tolerance of Devices and Circuits in a 3D Technology Based on the Vertical Integration of Two 130-nm CMOS Layers," in *IEEE Transactions on Nuclear Science*, vol. 60, no. 6, pp. 4526-4532, Dec. 2013.
- 3. V. Gupta *et al.*, "SEE on Different Layers of Stacked-SRAMs," in *IEEE Transactions on Nuclear Science*, vol. 62, no. 6, pp. 2673-2678, Dec. 2015.

### <u>Basic Research-Thrust Area 4-Topic G8: Dynamic Characterization of Shock Induced</u> Fragmentation and Reactions Involving Reactive Materials upon Impact

Award Amounts for this topic are anticipated to be between \$150,000 and \$250,000 per year (total dollar value = direct and indirect costs). Larger value efforts (i.e., \$250, 000 per year) that are university led, include multiple PIs (at either a single or at multiple organizations), and provide training opportunities are encouraged. In all cases, the proposed award value should be clearly substantiated by the scope of the effort.

Proposals from Young Investigators will be considered for this topic. Young Investigator proposals should be clearly marked as such and include a scope of work commensurate with a \$100,000 award (total dollar value = direct and indirect costs). Young Investigators are defined as individuals who are currently employed by a U.S. accredited degree-granting college or university who received a Ph.D. or equivalent degree within five (5) years of the date of the preapplication white paper submission. Pre-application white papers and proposals from Young Investigators will be given preference.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** Reactive materials are solids such as metals and metal oxides that are capable of releasing large amounts of thermodynamic energy very rapidly. The individual constituents are mixed together in solid form and compacted into structures. Impact induced reactions of reactive fragments are caused by high velocity (~1-2 km/s) impact of composite materials of metal components on solid walls. These composite metal pieces generally range in size from millimeters to a few centimeters. Many aspects of the impact process between the composite metal pieces and solid walls, and the constituent spatiotemporal and thermochemical processes are not well characterized, along with the resulting fragmentation, rebound velocities and direction of the resulting fragments, their sizes, their temperature, their ignition, and combustion in air.

As another example, shock induced fragmentation of weapon case metals is generally accepted

to proceed through crack nucleation, growth, coalescence, and culminating in fragmentation; however, limited dimensionality of data collection and *post mortem* sample collection and analysis further limit the understanding of this fundamental process. Limitations in detection capabilities still present a significant hurdle to providing a complete mapping of the spatiotemporal evolution of these processes. Methods that allow observation of the dynamics of these fundamental constituent processes involving reactive fragments are highly desired.

Experimental facilities/tools now couple high intensity and high flux x-ray capabilities with impact drivers (e.g. lasers, gas guns, etc.), so opportunities now exist for directly probing material fracture mechanisms and particle dispersal under extreme loading/unloading conditions. In addition to fragmentation, enhancing the capability to measure processes including the dynamics of metal particle dispersal as well as diagnosing temperature and reaction mechanisms of metals upon impact is desired. Intensity and phase dependent imaging techniques at both x-ray and optical wavelengths may offer the ability to fully characterize some of these processes with a high degree of spatiotemporal resolution. Additionally, time resolved x-ray diffraction (XRD) at high repetition rates would allow for investigating the thermodynamic pathways of metal composite material reactions of interest.

**Impact:** Currently, hydrodynamic / multiphysics codes far exceed the experimental capabilities to examine the overall complex nature of fragmentation and breakup evolution to particles, high velocity particle transit and finally impact induced reaction involving reactive materials. Being able to characterize the dynamic breakup and reactions of reactive materials upon impact may lead to better understanding of how to utilize casing materials to react with and control agents and agent simulants.

**Objective:** Overall, the intent is to develop advanced characterization methodologies to measure and visualize the development of fragmentation, particle dispersal, and impact induced reactions of reactive materials. The primary objective of interest is to develop a comprehensive methodology to examine a dense reacting particle flow upon secondary fragmentation of a reactive material hitting an anvil, thereby allowing for characterizing ignition and combustion of metal/metal alloy systems. The secondary objective is to develop methods to characterize the initial fracture behavior (e.g. case breakup) and relate it back to fundamental fracture theory and modeling capabilities. Possible research areas may include, but are not limited to:

- Fully characterize size, size distribution, dispersal and mass of fast moving particles traveling at high velocities (~1-2 km/s) before impact and the resulting fragments after impact
- Characterize conditions for driving ignition and burn of fragments
- Use techniques such as time resolved XRD to characterize ignition and combustion reactions of metals/metal alloys upon impact
- Evaluate *in situ* fragment temperature upon high velocity impact via material or photon based techniques, allowing for measuring reaction thermodynamic pathways
- Utilize intensity and phase dependent techniques (both x-ray and optical) in multiple dimensions to characterize the evolution of processes that include fragmentation and particle dispersal
- Utilize advanced imaging techniques (e.g. plenoptic techniques) to evaluate material failure and transit of particles (including particle velocity vectors) of different sizes and distributions

across a 2D plane or 3D volume with high spatiotemporal resolution

### **References:**

1. "Material Development for Enhanced X-ray Detection of Dynamic Material Events under High Loading Rates", SBIR Topic: DTRA-T152-002

## <u>Basic Research-Thrust Area 4-Topic G9: Evaluating High Strain Rate Mechanical Response</u> <u>and Chemical Reactivity of Energetic/Reactive Composite Materials Produced via Additive</u> <u>Manufacturing</u>

Award Amounts for this topic are anticipated to be up to \$1,000,000 per year (total dollar value = direct and indirect costs). All efforts must be multidisciplinary. Preference will be given to multi-institution proposals; however, multiple PIs from a single organization are also eligible to apply. Further preference will be given to teams that have a university as the lead organization, maintain significant amounts of research at one or more universities, and include multiple opportunities for training. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** It is desired to neutralize WMD using air-dropped ordnance that must penetrate or otherwise gain entry into WMD locations, activate a dispersal mechanism (typically driven by high explosives), couple with WMD targets, and neutralize these targets. Current inventory munitions impact targets at rates of ~1 km/s. Fragments driven by high explosives have initial velocities of 1,000 - 2,000 m/s. Shaped charges travel on the order of multiple km/s. As a result, C-WMD events occur at high rates  $(10^2 - 10^7 \text{ s}^{-1})$  where physical and chemical changes can take place as fast as nanosecond time scales, and necessarily involve a wide variety of highly-heterogeneous particulate materials.

Additive manufacturing (AM) is a material production technique that dates back nearly three decades. AM offers advantages in performance, innovation, and flexibility and its attractiveness lies in its customization and cost effectiveness, increasing efficiency and time. Research in AM energetics presents an intersection between pure plastic and metal AM research. These composite materials have unique characteristics due to having organic crystals and metal particles in a low total mass composition polymeric binder. AM energetics efforts are currently focused on understanding the build process of materials (e.g. real time build quality and effect of build parameters) and understanding the product (e.g. quasistatic mechanical properties, safety). Additionally, most studies on the properties of printed materials have been on single material builds and not complex composites. The use of AM for the production of energetic materials is feasible; however, production of materials with consistent material properties, and understanding the factors that give these material properties, is a challenge. A better understanding of a material's mechanical properties under load and in shock conditions is an integral component in

better weapons design. WMD-defeating systems are designed by using engineering hydrocodes that simulate the behavior of proposed weapon designs and troubleshoot solutions prior to the performance of expensive mid/full-scale tests. The hydrocodes can produce excellent results if high-fidelity material models are available. These material models require the kind of information being sought after in this topic.

Testing standards for materials are not necessarily appropriate for AM materials (e.g. ASTM standards). For example, in the case of high strain rate testing, velocimetry techniques are used to map behavior of ideally 1D materials as a function of time to yield information such as elastic to plastic transformation behavior and fracture in compression or tension. Additionally, *post-mortem* material characterization is used to complement velocimetry analysis. Characterizing mechanical behavior at fast rates must go beyond these historically used techniques. Both localized material based sensing (mechanosensors) and dynamic x-ray characterization may provide enhanced characterization of high rate material deformation.

Impact: The immediate potential payoff of these research efforts is expected to be the extraction of mechanical property data at high strain rates that will feed into multiphysics and hydrocode models and ultimately provide vast improvement of blast and weapon modeling essential to new weapons design for various C-WMD applications. Being able to link modeling and simulation with experimental results would lead towards optimal designs for both AM structure and structural/energetic performance. Knowledge of a materials' properties including deformation at high strain rates, bonding chemistry, anisotropic nature under shock rates, etc. are critical for better predicting a weapon's effectiveness and lethality against WMD-containing targets. A better understanding of material's mechanical and energetic response will result in better designed agent defeat weapons that can achieve higher agent lethality. This will improve weapon and target planning for defeat of WMDs containing biological and chemical weaponized agents, reduce or eliminate collateral effects and enhance post-strike assessments, in all attempts to successfully destroy WMD in hostile environments.

**Objective:** This topic seeks research in characterizing mechanical properties and chemical reactivity of energetic and reactive materials produced by AM across high strain rate regimes (10<sup>2</sup> - 10<sup>7</sup> s<sup>-1</sup>). These AM materials would be highly solids-loaded polymers, i.e., polymers incorporating various additives - metals, alloys, energetic crystals, thermites, binders, biocidals/chemicidals etc. More specifically, we want to address the following: (1) experimental techniques and characterization of material mechanical response and chemical/metal reactivity to fast rate loading, (2) computational tools that lead to development of predictive models, and (3) validate physics- and chemistry-based predictive models for energetic and reactive materials prepared through AM. Pre-deformation characterization (e.g. void density) of AM materials will be an important, supporting aspect of the research. The focus of this topic is to emphasize experimental characterization efforts that will help build and validate computational models with less emphasis on new material synthesis or development. Possible research areas may include, but are not limited to:

- Using AM prepared energetic composite samples with similar properties, measure mechanical properties of solids-loaded polymers (e.g. polymers mixed with metals, alloys, thermites, biocidals/chemicidals, etc.) under fast rate loading (e.g. dynamic Brazilian, Hopkinson bar, Shock gun)
- Quantify the anisotropic nature of mechanical deformation for AM solid binders up to shock

loading rates.

- Characterize dynamic changes in mechanical deformation under both compressive and tensile loads
- Develop performance criteria for mixed composite materials (e.g. detonation pressure, detonation velocity, and shock sensitivity)
- Investigate energetic performance of AM composite materials under fast loading rates
- Incorporate dynamic characterization methodologies (including x-ray, optical, and material sensors) to measure localized pressure/strain, temperatures and chemical reactions of energetic/reactive material composite AM systems
- Characterize time-resolved chemical interactions (e.g. interaction involving biocidal/chemicidal additives) of AM energetic composites
- Examine these concepts with solids composed of multiple composite materials with complex geometry builds i.e. patchwork build made up of explosive composition A and explosive composition B

#### **References:**

- 1. ASTM WK43112. New Guide for Evaluating Mechanical Properties of Metals Made via Additive Manufacturing Processes. American Society for Testing and Materials, West Conshohocken, PA, 2014a, astm.org/WorkItems/WK43112.htm.
- 2. Hawreliak, J.A. et al. "Dynamic Behavior of Engineered Lattice Materials", *Scientific Reports*, 6:28094: doi:10.1038/srep28094

### Basic Research-Thrust Area 5-Topic G10: Noble Gas Biodetection

Award Amounts for this topic are anticipated to be between \$150,000 and \$350,000 per year (total dollar value = direct and indirect costs). Larger value efforts (i.e., \$350, 000 per year) that are university led, include multiple PIs (at either a single or at multiple organizations), and provide training opportunities are encouraged. In all cases, the proposed award value should be clearly substantiated by the scope of the effort.

Proposals from Young Investigators will be considered for this topic. Young Investigator proposals should be clearly marked as such and include a scope of work commensurate with a \$100,000 award (total dollar value = direct and indirect costs). Young Investigators are defined as individuals who are currently employed by a U.S. accredited degree-granting college or university who received a Ph.D. or equivalent degree within five (5) years of the date of the preapplication white paper submission. Pre-application white papers and proposals from Young Investigators will be given preference.

The preferred award structure for this topic is a base period of three (3) years with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Pre-application white papers and proposals that outline scope and effort for different base period and option combinations may also be considered; however, note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be

considered.

**Background:** Many nation states conduct nuclear activities for legitimate peaceful purposes as well as for acknowledged defense programs within the international norms established by current non-proliferation and arms control treaties or agreements. However, discriminating between legitimate activities and activities prohibited by international agreements, or nefarious nuclear activities conducted by non-state actors, poses significant challenges to current monitoring and analysis methods. Extant nuclear detection technologies often require sample collection near a suspected activity, and transport to an off-site laboratory for analysis, resulting in substantial time-to-answer delays. Other methods rely upon unwieldy sampling architectures with high power requirements that limit the number and location of such detection systems. In the latter case, reliable detection of specific "smoking gun" signatures is further hampered by uncertainties in establishing background levels because of contributions from other processes (e.g., medical isotope production). Collection and detection motifs that would allow greater proximity to suspect activities in order to improve the signal-to-noise ratio and provide near real-time information are desirable to serve a cueing function that can direct more granular collections.

Radioisotopes of noble gases, like xenon, argon, and krypton, are produced in relatively high abundances during nuclear fission and may also be produced by activation of surrounding materials in both nuclear power plants and nuclear explosions. The elevation of noble gas isotope concentration above regional background (e.g., natural xenon atmospheric concentration is estimated to range from about 50 - 100 ppb depending upon the source of the information)<sup>2</sup> provides strong indication of nuclear activity. Therefore, the collection and measurement of these gases may assist in detecting and locating activities associated with the production of materials for nuclear weapons or weapons testing. These elemental gases are chemically inert yet, paradoxically, noble gases display a remarkable spectrum of biological properties, including a number of health-benefiting qualities which make them clinically relevant.<sup>3</sup> Noble gas atom size, and both chemical and physical properties make them available to a variety of biochemical and biophysical reactions. For example, xenon is regularly used in biochemical and structural studies of proteins because of its known affinity for the hydrophobic cavities in macromolecular interiors. X-ray crystallography studies have characterized gas-binding properties in different domains of model transmembrane proteins to better understand the means by which inert gases produce pharmacological action. <sup>4,5,6</sup> Xenon also has a low blood-gas partition coefficient that affords rapid induction and emergence times which make it a nearly ideal anesthetic agent. Likewise, xenon has analgesic and neuroprotective properties. <sup>2,3,8</sup> It acts as an antagonist to the excitatory N-methyl-D-aspartate receptor, although contributing mechanisms and pathways have not been fully elucidated. <sup>2,9,10</sup> Argon and xenon have been shown to impact inflammation <sup>11</sup> and apoptosis signal transduction pathways induced by the broad-spectrum tyrosine kinase inhibitor staurosporine. 12 Such properties also have been investigated for krypton and argon, albeit to a lesser extent. Despite the extensive prospects for clinical applications of noble gases, fundamental biochemical studies which would provide the basis for broader use are lacking.

The present topic seeks deeper understanding of the means by which biological systems interact with noble gases, with the aim of developing novel collection, separation, concentration and/or detection motifs that can report local elevations of noble gas.

**Impact:** The fundamental knowledge generated as a result of this research will be broadly applicable to core DTRA capability requirements for detecting, locating, identifying, characterizing and assessing foreign nuclear materials production and weaponization in support

of C-WMD operations. In addition, the research could further understanding of the direct and indirect effects of human exposure to certain noble gases, and thus will address Force Protection requirements for conducting operations in contaminated environments. The described work also will contribute to better understanding of the basis for clinically important effects mediated by noble gases and potential applications to mitigate or reverse impacts from traumatic injuries to warfighters. Research likewise will support development of better noble gas recapture technologies. Finally, the development of detection technologies to address a number of diverse mission needs is of paramount interest to the DoD and is critical to developing disruptive technologies that will enable game-changing C-WMD capabilities.

**Objective:** This topic seeks research to investigate interactions with, and reactions to, xenon by biological systems. Different lines of research could contribute to the overall aims by: (1) identifying macromolecular structures that are uniquely suited to bind xenon and are compatible with emplacement on or in standard detection architectures, or (2) characterizing chemical and physical properties of cellular compartments that could be replicated for development of novel collection and/or detection motifs. Topic focus is on discrete structures and compartments affecting the collection and concentration of xenon rather than on whole-cell or -organism systems. Although such systems may be used as the basis for establishing basic principles on likely modes of interaction, efforts specifically concerned with modifying or engineering whole-cell or -organism systems will not be considered. Possible research areas may include, but are not limited to:

- Experimentally characterize the gas-binding properties of **macromolecules** (e.g., proteins) known to interact with xenon and identify specific domains which demonstrate particular proficiency. Establish the likely basis for such interactions as it relates to specific structures (e.g., side chain residues) within the respective domains. Develop actual or propose hypothetical macromolecules that leverage properties of domains with high binding proficiency, and promote higher binding efficiency beyond the capacity that was experimentally observed in order to increase local concentrations and retention times.
- Identify and characterize **cellular compartments** in which xenon is preferentially sequestered. Establish contributing chemical and/or physical processes and determine retention times. Develop [biotic-abiotic] hybrid or synthetic collection architectures based upon experimental observations of biological systems as noted above and supported by molecular modeling and simulation where practical, with the specific goal of increasing local concentrations and retention times.

Collaborative efforts between life scientists and nuclear or chemical engineers working in the nuclear industry are particularly encouraged in order to establish relevance of exposure levels to anticipated "real-world" scenarios.

#### **References:**

- 1. Bowyer TW. 2002. Detection and analysis of xenon isotopes for the comprehensive nuclear-test-ban treaty international monitoring system. *J Environmental Radioactivity* 59:139-151.
- 2. Jordan BD, Wright EL. 2010. Xenon as an anesthetic agent. AANA 78:387-392.
- 3. Sanders RD, Ma D, Maze M. 2005. Xenon: elemental anaethesia in clinical practice. *British Medical Bulletin* 71:115-135.

- 4. Tanwar AS et al. 2013. Importance of hydrophobic cavities in allosteric regulation of formylgycinamide synthetase: insight from xenon trapping and statistical coupling analysis. *PLoS One* 8:e77781.
- 5. Colloc'h N, Marrasio G, Prangé T. 2011. Protein-noble gas interactions investigated by crystallography on three enzymes implication on anesthesia and neuroprotection mechanisms. *Current Trends in X-Ray Crystallography* ed. Chandrasekaran A, ISBN: 978-953-307-954-3.
- 6. Sauguet L et al. 2016. Structural basis for xenon inhibition in a cationic pentameric ligand-gated ion channel. *PLoS One* DOI: 10.137/journal.pone.0149795.
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- 8. Winkler DA et al. 2016. The diverse biological properties of chemically inert noble gases. *Pharmacol Thera* 160:44-64.
- 9. Weinrich M, Worcester DL. 2013. Xenon and other volatile anesthetics change domain structure in model lipid raft membranes. *J Phys Chem B* 117:16141-16147.
- 10. Gruss M et al. 2004. Two-pore domain K<sup>+</sup> channels are a novel target for the anesthetic gases xenon, nitrous oxide, and cyclopropane. *Mol Pharmacol* 65:443-452.
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- 12. Spaggiari S et al. 2013. Antiapoptotic activity of argon and xenon. Cell Cycle 12:2636-2642.

## <u>Basic Research-Thrust Area 7-Topic G11: Critical Requirements for Effective Single-Dose</u> Vaccines

Award Amounts for this topic are anticipated to be between \$750,000 and \$1,000,000 per year (total dollar value = direct and indirect costs). The larger value efforts (i.e., \$1,000,000 per year) should be multi-disciplinary. Further guidance on scope and cost may be provided in the debrief summary for full proposal invitations. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of one (1) year with up to four (4) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** The current immunization schedule for many childhood and adult vaccines in the U.S. consists of multiple doses, with time between priming and boosting ranging from one to several months, or even years. For military operations, however, an ideal vaccine is one that can provide 1+ year of protection after a single dose. While live attenuated vaccines are typically effective as single-dose vaccines due to their ability to replicate, non-replicating vaccines such as subunit, inactivated, or nucleic acid vaccines require one or more boosts. Controlled release of non-replicating vaccines has been identified as a potential single-dose prime-boost technology. An example is an injectable controlled-release microsphere formulation containing vaccine

antigen that can be released as a pulse one to six months after injection, and with continuous release of antigen by particulate platforms. However, further development of these encapsulation technologies (pulsed and continuous) and translation of their feasibility in animal models and human trials have been hindered for a number of reasons, including antigen thermostability at body temperature over time, encapsulation material and size, antigen loading and dose control, and full characterization of the immune response.

**Impact:** Safe and protective vaccines that can be administered in one dose would be conducive to military operational deployment. Understanding what is required for an effective single-dose vaccine will support the development of future single-dose vaccine candidates that will be compatible with military operations.

**Objective:** The goal of this topic is to identify optimal requirements for effective, non-replicating single-dose vaccines by examining the knowledge gaps in controlled-release antigen delivery and ways to enhance timing and duration of antigen exposure. Specifically, research to understand and identify the critical requirements to make single-dose, non-replicating vaccines effective using a viral biowarfare (BW) pathogen, or a non-BW pathogen that has similarities to a viral BW agent as a model is of interest. The pathogen of choice should have the necessary tools (i.e. established animal model, non-replicating vaccine(s) candidate, live attenuated vaccine(s) candidate) available to make sound comparisons between single-dose, multi-dose or live-attenuated vaccine effectiveness, such as Yellow Fever virus. Possible research areas may include, but are not limited to:

- Characterization of the immune response to pulsatile versus continuous antigen release
- The effect of antigen release rate and timing on the magnitude and type of immune response elicited
- Understanding the requirements for enhanced onset to immunity
- Novel methods to control the timing and duration of antigen exposure. This can include, but is not limited to: novel materials and encapsulation techniques, techniques to enhance antigen stability over time at body temperature, and other single-dose technologies that have not established a proof-of-concept

Proposals that detail development and advancement of a vaccine candidate will not be considered. Any proposed in vivo animal studies should be conducted in small animal models, not non-human primates. Moreover, proposed animal studies should use both male and female animals, and include any statistical gender differences. In addition, applicants who are selected for funding under this Topic will be encouraged to share data with other grantees funded under this Topic, as well as those funded under TA7-BR-Topic G14: Generating Cross-Reactive Antibodies Following Single-Dose Vaccination (Thrust Area 7), detailed below.

#### **References:**

- 1. Walters, Krastev, et al. Journal of Pharmacy and Pharmacology, Vol 67, 400-408, 2014.
- 2. Alonso, et al. Vaccine, 12: 299-306, 1994.
- 3. Sanchez, et al. J Pharm Sci, 85(6): 547-52, 1996.

# Basic Research-Thrust Area 7-Topic G12: Discovery of Novel Methods to Ameliorate the Effects of Nerve Agent Exposure

Award Amounts for this topic are anticipated to be \$350,000 per year (total dollar value = direct and indirect costs); awards are anticipated to be multidisciplinary. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of two (2) years with up to one (1) additional year as a possible option. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of three (3) years will not be considered.

**Background:** Organophosphorus (OP) agents act by inhibition of acetylcholinesterase (AChE) resulting in reduced hydrolysis of the neurotransmitter, acetylcholine, causing overstimulation of the acetylcholine receptor. Physiological responses comprise hypotension, rhinorrhea, wheezing, and diarrhea among other symptoms, with severe exposures leading to death. OP intoxication poses a significant threat to military forces and agricultural workers. In the military, current medical countermeasures constitute: 1) pralidoxime (2-PAM), a charged oxime reactivator of OP-inhibited AChE, 2) atropine, an antimuscarinic agent that blocks the acetylcholine receptor, and 3) diazepam, to treat seizures resulting from excess acetylcholine in the central nervous system by enhancing the inhibitory effects of gamma-aminobutyric acid in the brain. A majority of research within this arena target reactivation of OP-inhibited AChE using oxime-based compounds. Few groups have explored AChE reactivators containing different functional moieties, or pursued targets other than AChE and the acetylcholine receptor to treat OP intoxication. Novel approaches to treat OP agent intoxication are desired with focus on a wider spectrum of targets involved in the biological cascade resulting from exposure.

**Impact:** OP agents continue to be a threat to the Armed Forces and agricultural workers, against which there are no broad spectrum medical countermeasures. Addressing causal agents that lead to symptoms of OP exposure will provide more insight into the short-term and long-term effects resulting from OP intoxication.

**Objective:** This topic seeks proposals that identify new and innovative methods of treating nerve agent exposure. Core focus should be on elimination or inactivation of causal agents rather than treating the symptoms of OP exposure. Possible strategies may include, but are not limited to:

- Sequestration and/or hydrolysis of excess acetylcholine
- Induced temporary expression of AChE to moderate accumulation of acetylcholine
- Reactivation of AChE inhibited by a broad range of OP agents, through use of non-oxime based reactivators

As an example, the above aims may be achieved via discovery of novel small molecules, peptides, peptidomimetics, or proteins. Proposals detailing new methods of AChE reactivation will be considered if the strategy is novel and unpublished, with the proviso that oxime-based reactivators will not be considered. This topic is not interested in pursuit of acetylcholine receptor inhibitors, AChE inhibitors, new anticonvulsants or GABA receptor modulators.

#### **References:**

- 1. Bhattacharjee, *et al.* "Discovery of non-oxime reactivators using an *in silico* pharmacophore model of oxime reactivators of OP-inhibited acetylcholinesterase" *Eur. J. Med. Chem.* **2012**, 49, 229-238.
- 2. Katz, *et al.* "Discovery of New Classes of Compounds that Reactivate Acetylcholinesterase Inhibited by Organophosphates" *ChemBioChem*, **2015**, *16*, 2205-2215.

# <u>Basic Research-Thrust Area 7-Topic G13: Environmental Factors and the Viable but Non-Culturable State of Francisella tularensis</u>

Award Amounts for this topic are anticipated to be between \$500,000 and \$750,000 per year (total dollar value = direct and indirect costs). The larger value efforts (i.e., \$750,000 per year) should be multi-disciplinary. Further guidance on scope and cost may be provided in the debrief summary for full proposal invitations. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of two (2) years with up to one (1) additional year as a possible option. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of three (3) years will not be considered.

**Background:** Category A agents Francisella tularensis, Burkholderia psuedomallei and Yersinia pestis enter into viable but non-culturable (VBNC) state (Sinclair et al., 2008). This state allows bacteria to persist in an environment with unfavorable conditions until they can resuscitate under more favorable conditions. It is unclear what specific environmental factors induce pathogenic bacteria F. tularensis to enter into the VBNC state. Other bacteria enter the VBNC state when exposed to certain temperatures, levels of salinity or acidic conditions. It can be projected that these factors also effect F. tularensis, but under what levels? A systematic approach of testing the various environmental factors known for inducing the VBNC state in other bacteria would help elucidate under what conditions F. tularensis may be persisting in the environment as VBNC bacteria. Additionally, the behavior of F. tularensis in the environment while it is in the VBNC state has yet to be explored (Oliver 2010; Li 2014). Bacteria behave differently under stressful conditions while they are entering the VBNC state. For instance, B. psuedomallei forms biofilms under nutrient-limited conditions and enters the VBNC state. Certain concentrations of iron and salt also trigger this behavior (Kamjumphol et al., 2015). The formation of biofilms is considered problematic since biofilms protect the bacteria from antibiotics and decontamination, promoting continued persistence in the environment (Oliver 2010). Additionally, bacteria in the VBNC state could have properties allowing it to transport to more favorable conditions, spreading the pathogenic bacteria to new areas, or the bacteria may adhere to various surfaces like clay particles.

**Impact:** Overall impact of this research includes providing possible targets for detection, understanding how *F. tularensis* could transport to other locations helping explain current disease incident research, and inform on general persistence of the bacteria in the environment for future prediction models.

**Objectives:** There are four objectives to this topic:

- 1) Systematically determine what environmental factors induce *F. tularensis* to enter the VBNC state. Offerors should provide details on measuring the VBNC state and propose a systematic approach to test these factors, including testing their effects individually and combined.
- 2) Understand *F. tularensis* behavior in the environment while it is in the VBNC state, e.g., can the bacteria form biofilms, do the cells adhere to surfaces such as soil minerals or other organisms like amoebas?
- 3) Understand what conditions resuscitate *F. tularensis* so that it is viable, e.g., can the *F. tularensis* cell resuscitation from the VBNC state be reliably quantified?
- 4) Determine which genes, if any, are transcribed while *F. tularensis* is in the VBNC state allowing it to survive.

#### **References:**

- 1. Li, L., N. Mendis, H. Trigul, J. D. Oliver, and S. P. Faucher. The importance of the viable but non-culturable state in human bacterial pathogens. Frontiers in Microbiology. 5:72-91.
- 2. Kamjumphol, W., P. Chareonsudjai, S. Taweechaisupapong, and S. Chareonsudjai. 2015. Morphological alteration and survival of *Burkholderia pseudolmallei* in soil microcosms. The American Journal of Tropical Medicine and Hygiene. 93: 1058-1065.
- 3. Oliver, JD. 2010 Recent findings on the viable but nonculturable state in pathogenic bacteria. FEMS Microbiology Reviews. 34:415-425
- 4. Sinclair R, S. A. Boone, D. Greenberg, P. Keim, and C. P. Gerba. 2008. Persistence of category A select agents in the environment. Applied and Environmental Microbiology. 74: 555-563.

# <u>Basic Research-Thrust Area 7-Topic G14: Generating Cross-Reactive Antibodies Following Single-Dose Vaccination</u>

Award Amounts for this topic are anticipated to be between \$500,000 and \$1,000,000 per year (total dollar value = direct and indirect costs). The larger value efforts (i.e., \$1,000,000 per year) should be multi-disciplinary. Further guidance on scope and cost may be provided in the debrief summary for full proposal invitations. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of one (1) year with up to four (4) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** A single-dose vaccine that can protect against multiple bacterial or viral pathogenic strains is a desired, yet challenging goal. It's well established that antibody responses are typically required for protective vaccines, however immunization with a single antigen variant results in strain-specific antibodies, suggesting that vaccination with multiple antigen

variants is required to generate cross-reactive antibodies. Affinity maturation (AM) is a key process that drives the fine specificity of a protective humoral response. Studies to understand how AM takes place in the presence of variants of the same antigen revealed that administration with a cocktail of antigen variants frustrated AM resulting in a low probability of cross-reactive antibody generation, whereas sequential administration of multiple antigen variants can generate cross-reactive antibodies that focus on conserved residues. Controlled-release of antigen after a single dose has been shown to mimic multiple, sequential doses, however how controlled-release of multiple antigen variants affect AM and the generation of cross-reactive antibodies remains elusive. Based on these phenomena and the need for broadly protective single-dose vaccines, this topic seeks to understand how to generate cross-reactive antibodies after a single vaccination and to determine how controlled-release of antigen, or other single-dose technology, can be used to generate a broadly protective humoral response.

**Impact:** Single-dose vaccines that can protect against multiple pathogenic strains would be conducive to military operational deployment. Understanding how to generate a broadly protective immune response after a single administration will support the development of future single-dose vaccine candidates that will be compatible with military operations.

**Objective:** This topic seeks research to understand how to generate cross-reactive antibodies after a single-dose vaccination and to determine how controlled-release of antigen, or other single-dose technologies, can be used to generate a broadly protective humoral response using antigens from a viral biowarfare (BW) pathogen, or a non-BW pathogen that has similarities to a viral BW agent. Possible research areas may include, but are not limited to:

- Understanding how controlled-release of multiple variants of the same antigen affect affinity maturation and the generation of cross-reactive antibodies
- Understanding how epitope valence, or concentration, of multiple antigen variants influences AM and the generation of cross-reactive antibodies after a single vaccination
- Identifying other innovative strategies to generate cross-reactive antibodies after a single vaccination

Proposals that detail development of a vaccine candidate will not be considered and any *in vivo* animal studies should be conducted in small animal models, not non-human primates. Moreover, any proposed animal studies should use both male and female animals, and include any statistical gender differences in humoral responses. In addition, applicants who are selected for funding under this topic will be encouraged to share data with other grantees funded under this topic, as well as those funded under TA7-BR-Topic G11: Critical Requirements for Effective Single-Dose Vaccines (Thrust Area 7), detailed above.

### **References:**

- 1. Liao, et al. Nature, 496, 469-476, 2013.
- 2. Wang, Shenshen et al. Cell, Volume 160, Issue 4, 785-797, 2015.
- 3. Walters, Krastev et al. Journal of Pharmacy and Pharmacology, Volume 67, 400-408, 2014.

# Basic Research-Thrust Area 7-Topic G15: Non-Invasive Cell-Free Nucleic Acid for Companion Diagnostics (NICNAC)

Award Amounts for this topic are anticipated to be between \$500,000 and \$1,000,000 per year (total dollar value = direct and indirect costs). The larger value efforts (i.e., \$1,000,000 per year) should be multi-disciplinary. Further guidance on scope and cost may be provided in the debrief summary for full proposal invitations. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of two (2) years with up to one (1) additional year as a possible option. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of three (3) years will not be considered.

**Background:** Given that only a small percentage of the transcribed human genome is actually translated into protein, there has been a surge of interest in the role of the non-coding RNA transcriptome and its contribution to pathogenesis. While RNA sequencing (RNA-Seq) molecular genomic approaches have studied RNA differential expression in several body fluids, most of these studies have focused on analyses of miRNAs and mRNAs. The recent discovery of a significant number of other cell-free small non-coding RNA species suggests an additional pool of potential host biomarkers of exposure to infectious disease pathogens. Some examples of recent discoveries include:

- A significant number of extracellular circular RNAs (cirRNAs) have recently been identified; their biogenesis are formed by back-splicing events in higher eukaryotic cells and are extremely stable in clinical body fluids. However, little is known about how circRNAs are regulated, cleared or foster cell-to-cell communication.<sup>1-3</sup>
- Piwi-interacting RNAs (piRNAs) are small (26–31nt) non-coding cell-free RNA molecules expressed in animal cells that form RNA-protein complexes. Originally described in the germline, there are many piRNA genes in the human genome that are involved in the epigenetic silencing of transposable elements in addition to the transcriptional regulation of genes.<sup>4</sup>
- Some miRNAs are hypothesized to act as signaling molecules via binding to intracellular Toll-like receptors (TLRs); characteristic of immune cells involved in the innate immune system.<sup>5</sup>
- A recent study characterizing extracellular small non-coding RNA in human saliva identified approximately 400 circRNAs in cell-free saliva. The results also indicated that that piRNAs were surprisingly abundant in cerebrospinal fluid (CSF) when compared with other body fluid or intracellular samples.<sup>6</sup>
- "Liquid biopsy" targeting of extracellular sequence mutations as cancer genotyping biomarkers for several somatic mutations derived from malignant tumors.<sup>7</sup>
- Pathogen small RNAs colonizing strains have been discriminated in saliva from strains in patients with bloodstream infections, including patients with sepsis and septic shock using pathogens small RNAs.<sup>8</sup>
- Invasive blood collection, transport, preservation and sample processing, nucleic acid

extraction, and assessment of sample quality are major hindrances on time, cost, and applicability of standard molecular diagnostics of early warning biomarkers diagnosis of exposure/disease. Thus, alternative sample matrix (e.g. saliva) as part of a "liquid biopsy" could provide a more subject- and user-friendly system.

**Objectives:** The goal of this topic is to provide a fundamental scientific understanding of cell-free non-coding RNA (cfNCR) species. Responsive proposals should address the following aims:

- 1. Discovery, survey and catalogue of presence, state (free versus bound), and range determination of analytical attributes of novel cfNCR species as potential biomarkers of infectious disease and therapeutic targets for companion diagnostics in non-traditional clinical matrices.
  - a. Development and enhancement of catalogue of cfNCR species in non-invasively sampled body fluid (i.e. saliva) and investigation into their potential as biomarkers.
  - b. Characterization of the normal range/variability of cfNCR species.
  - c. Determine most up- or down-regulated RNAs in exposed saliva and corresponding serum (properly preserved bio-banked samples are acceptable).
  - d. Perform preliminary determination of the diagnostic/prognostic windows of the biomarkers in non-traditional clinical matrices.
- 2. Method development and determination by enriched sensitivity, un-biased, broad spectrum analytical approaches. In order to detect down-regulated cell-free RNAs, a high analytical sensitivity (limit of detection) will be required.
- 3. Determination of a panel of candidate cfNCR circulating and exosomal nucleic acids of both:
  - a. Host response to infectious disease (e.g. respiratory tract, GI tract, etc.) and;
  - b. RNAs secreted/shed directly from causative infectious agent or surrogate (at least one virus and one bacteria).
- 4. Identify role/mechanism of  $\geq$  4 most dysregulated species.
  - a. Determination of the mechanisms of host, as well as pathogen-shed, extracellular RNA, and protein/peptide biomarkers generation, secretion, and transport.

### **References:**

- 1. Salzman J, Chen RE, Olsen MN, Wang PL, Brown PO (2013) Cell-Type Specific Features of Circular RNA Expression. PLoS Genet.
- 2. Salzman J, (2012) Circular RNAs Are the Predominant Transcript Isoform from Hundreds of Human Genes in Diverse Cell Types. PLoS ONE.
- 3. Lasda E, Parker R (2016) Circular RNAs Co-Precipitate with Extracellular Vesicles: A Possible Mechanism for circRNA Clearance. PLoS ONE 11(2): e0148407. doi:10.1371/journal.pone.0148407.
- 4. Biology of PIWI-interacting RNAs: new insights into biogenesis and function inside and outside of germlines (2012) Genes & Development.
- 5. Fabbri, M et al. (2012) MicroRNAs bind to Toll-like receptors to induce prometastatic

- inflammatory response. PNAS.
- 6. JH Bahn et al. (2015) The Landscape of MicroRNA, Piwi-Interacting RNA, and Circular RNA in Human Saliva. Clin Chem.
- 7. F Wei, et al. 2014. Detecting EGFR Mutations in Saliva. Am J Respir Crit Care Med.
- 8. V Bordeau et al. 2016. Staphylococcus aureus Regulatory RNAs as Potential Biomarkers for Bloodstream Infections. Emerg Infect Dis.

## <u>Basic Research-Thrust Area 7-Topic G16: Novel Technologies to Target Encephalitic</u> Alphavirus Infections

Award Amounts for this topic are anticipated to be between \$500,000 and \$750,000 per year (total dollar value = direct and indirect costs). The larger value efforts (i.e., \$750,000 per year) should be multi-disciplinary. Further guidance on scope and cost may be provided in the debrief summary for full proposal invitations. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of one (1) year with up to four (4) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** The new-world alphaviruses, including Venezuelan equine encephalitis virus (VEEV), eastern equine encephalitis virus (EEEV), and western equine encephalitis virus (WEEV), cause disease in humans and pose a grave threat to the warfighter as an engineered biological weapon. The susceptibility of humans to aerosol infection evident in reported cases of laboratory infections by VEEV, EEEV, and WEEV raises the level of concern. No licensed vaccines or specific therapies exist to prevent or treat human infections for VEEV, EEEV, or WEEV due in part to the challenges of addressing multiple viral serotypes, the rapid transmission of the viruses to the brain, and associated difficulty of getting a therapeutic across the blood brain barrier (BBB). In an ever-changing threat environment, the "one bug" one drug, pathogen-targeted approach is prohibitively slow and expensive; the warfighter requires a broad spectrum antiviral. Therefore, the goal of this topic is to discover novel, medically relevant technologies such: a) Host protein targets that can lead to a broad spectrum antiviral; and b) Proteins capable of targeting viral dsRNA and treating the encephalitic alphaviruses. All technologies need to be capable of crossing the BBB.

**Impact:** Identification and development of broad-spectrum antiviral therapeutics derived from host target proteins and proteins targeting viral dsRNA will lead to safe therapeutics that treat the encephalitic alphaviruses. These therapeutics will provide the warfighter with a key medical countermeasure to combat emerging biological threats as there are no current licensed therapeutics for the treatment of alphavirus infection.

**Objective:** The goal of this topic is to: a) identify host cell proteins that can serve as targets for therapeutics in treating alphavirus encephalitic virus infection; and b) identify and understand proteins capable of targeting long-stranded viral dsRNA to treat alphavirus encephalitic virus infection. The goal of this topic is identification and understanding of the interactions between

host cell proteins and alphavirus proteins necessary for replication. Development of therapeutics focused on targeting viral proteins has not produced promising therapeutic candidates in part due to structural complexity and diversity. Focusing on host proteins/pathways required for EEEV, VEEV, and WEEV replication provide an opportunity to develop antivirals capable of treating all encephalitic alphaviruses. Additionally, an added benefit of focusing on host cell proteins should be reduced viral resistance since the proteins being targeted are from the host and not the virus. Previous studies have shown that both DNA and RNA viruses can be inhibited using host protein targets. Applicants should seek to identify and understand host proteins required for replication and interactions with EEV, VEEV, and WEEV viral proteins. Proof of concept will include in vivo testing.

Only proposals addressing the encephalitic alphaviruses will be considered. Monoclonal antibody proposals will not be entertained.

## <u>Basic Research-Thrust Area 7-Topic G17: Organophosphate Poisoning—Novel Detoxifying</u> Mechanisms in Animal Systems

Award Amounts for this topic are anticipated to be \$600,000 total (total dollar value = direct and indirect costs). Further guidance on scope and cost may be provided in the debrief summary for full proposal invitations. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of one (1) year with a 6-month possible option. The base period of the effort should be focused on exploration and identification of OP resistant animal species and the option should be focused on determination of the mechanism of OP resistance and proof of concept experiments. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of 18 months will not be considered.

**Background:** Animal species, including many invertebrates, have a robust innate protection mechanism against organophosphate (OP) poisoning, while others have the ability to develop resistance towards OP toxicosis within their respective environment. For example, this phenomenon can be observed in the necessity of repeated OP pesticide application in agriculture. Carboxylesterase degradation of the OPs appears to be the most common mechanism of this resistance. The Australian Blowfly, for instance, contains within its hemolymph a type of carboxylesterase which is not only capable of efficiently detoxifying the most common OP containing pesticides, but is also modified by the insect to detoxify newly developed OP pesticides as well. However, additional physiological processes of OP resistance or detoxification might exist in insects or other animal species waiting to be discovered.

The chemical structures and general modes of action of OP pesticides and organophosphate nerve agents (OPNAs) are related. Therefore, if additional novel OP detoxifying mechanisms exist they could eventually be exploited to develop medical countermeasures that are effective against OPNA compounds.

Medical countermeasure development against chemical WMD is a major focus of the Chemical and Biological Defense Program. Thus, a systematic discovery study designed to identify unique endogenous systems that may protect against OPs and possibly OPNAs apart from the carboxylesterase enzyme systems would not only be of general scientific interest but also of

great utility. Current systems have severe limitations in therapeutic as well as prophylactic applications. Carboxylesterase enzymatic systems such as PON1, OPAA, and OPH suffer from limitations such as low  $LD_{50}$ , inadequate bioavailability (no access to the central nervous system), lack of broad spectrum reactivity against multiple OPNAs, immunogenicity, and high cost of production. Therefore, new approaches are needed.

**Impact:** Discovery and identification of novel organophosphate protection mechanisms could provide alternative means for medical chemical countermeasure development to address current capability gaps.

**Objective:** The goal of this topic is discovery of novel mechanisms of OP detoxification leading to survivability. Proposals describing work on known carboxylesterases such as OPH, OPAA, etc., will not be considered. For the purpose of this topic, animal species will be limited to invertebrates that are known to be able to survive high levels of OP exposure. Consideration will be given to proposals that:

- Cogently define those experiments that will lead to a demonstration of proof of concept in the timeframe of the period of performance
  - Studies that make use of modern genetic technologies that will "silence" or significantly knock down the production of the known pathways would be favored
- Include discussion of methods for the identification of the specific pathway(s) or endogenous peptide, protein or natural product leading to survivability
- Indicate strategies for moving forward if the research is successful. For example, how the information discovered will be capitalized on and how it can lead to the development of a medical countermeasure

#### **References:**

- 1. Maxwell DM, Brecht KM, O'Neill BL. *The effect of carboxylesterase inhibition on interspecies differences in soman toxicity*. Toxicol Lett. 1987;39:35–42.
- 2. Ranson H, et al. *Evolution of supergene families associated with insecticide resistance*. Science. 2002;298(5591):179–181.
- 3. Jackson CJ, et al. Structure and function of an insect  $\alpha$ -carboxylesterase ( $\alpha$ *Esterase*7) associated with insecticide resistance. Proc Natl Acad Sci USA. 2013 Jun 18; 110(25): 10177–10182.
- 4. 4. Kikuchi, Y., Hayatsu, M., Hosokawa, T., Nagayama, A., Tago, K., & Fukatsu, T. (2012). Symbiont-mediated insecticide resistance. Proceedings of the National Academy of Sciences, 109(22), 8618-8622.

# <u>Basic Research-Thrust Area 7-Topic G18: Photonic Transducers for Chemical Threat Sensing</u>

Award Amounts for this topic are anticipated to be between \$350,000 and \$750,000 per year (total dollar value = direct and indirect costs). The larger value efforts (i.e., \$750,000 per year) should be multi-disciplinary. Further guidance on scope and cost may be provided in the debrief summary for full proposal invitations. The proposed award value should be clearly substantiated

by the scope of the effort.

The preferred award structure for this topic is a base period of one (1) year with up to two (2) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of three (3) years will not be considered.

**Background:** Spectroscopic sensing techniques offer promise for low-power, low-consumable chemical detection. Recent advances in materials design and fabrication have improved the feasibility of small, multiplexed photonic detection devices. Whispering gallery mode resonators can significantly amplify signals from highly dilute samples due to the recirculation of light via continuous total internal reflection, and these resonators have been demonstrated for chemical detection via absorption methods<sup>1</sup> or through shifts in the refractive index.<sup>2</sup> Expanding the selectivity and availability of these photonic chemical sensing approaches is desired, as detection of low levels of threat compounds in highly cluttered backgrounds remains a significant challenge.

**Impact:** It is anticipated that the new photonic transduction approaches enabled by this topic will enable more sensitive, selective, and low-cost sensing of chemical threat materials. The comparative simplicity of a system based on these new approaches may also decrease the overall logistical burden when compared to current detection methods.

**Objective:** The goal of this topic is to develop and demonstrate the scientific underpinnings and design principles for miniaturized photonic transducers, in order to enable new approaches to chemical threat sensing.

Research areas of interest include:

- Understanding design features to ultimately improve selectivity, sensitivity, and/or
  affordability compared to current optical or photonic sensing approaches.. Initial analytes of
  interest are chemical warfare agent simulants/surrogates, precursors, breakdown products,
  and toxic industrial chemicals.
- Development of the fundamental understanding of the key phenomena and principles of photonic transducers to enable new approaches to chemical threat sensing, such as the effects of size, shape, and composition.

Where possible, relevant data from experiments and related publications should be included and explained. Submissions should include order-of-magnitude estimates of the predicted capability improvements for the proposed approach. Priority will be given to proposals that couple experimental observation with theoretical grounding. Proof-of-concept experimentation is expected; however, this is not an instrument development program and proposals in that vein will not be considered. Approaches aimed at specific applications not relevant to sensing of chemical threats (i.e., biological detection) will likewise not be considered.

#### References:

1. Todd H. Stievater, Marcel W. Pruesnner, Doweon Park, William S. Rabinovitch, R. Andrew McGill, Dmitry A. Kozak, Robert Furstenberg, Scott A. Holmstrom, and Jacob B. Khurgin, "Trace gas absorption spectroscopy using functionalized microring resonators," *Optics Letters* v. 39 (2014), p. 969.

2. Daniel C. Kim and Robert C. Dunn, "Integrating Whispering Gallery Mode Refractive Index Sensing with Capillary Electrophoresis Separations Using Phase Sensitive Detection," *Analytical Chemistry* v. 88 (2016), p. 1426

## <u>Basic Research-Thrust Area 7-Topic G19: Robust and Efficient Catalytic Systems for</u> Degradation of Organophosphorus Nerve Agents

Award Amounts for this topic are anticipated to be between \$400,000 and \$600,000 per year (total dollar value = direct and indirect costs). The larger value efforts (i.e., \$600,000 per year) should be multi-disciplinary. Further guidance on scope and cost may be provided in the debrief summary for full proposal invitations. The proposed award value should be clearly substantiated by the scope of the effort.

The preferred award structure for this topic is a base period of two (2) years with up to three (3) additional years as possible options. However, pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Note that pre-application white papers and proposals that outline scope and effort that exceed a total of five (5) years will not be considered.

**Background:** Naturally occurring enzymes that are capable of catalytic degradation of OPNAs are scarce and their use for countermeasure applications is limited due to their high cost, fragility, and inefficiency (especially towards more toxic OPNA isomers). Many organisms have evolved to develop enzymes for survival purposes, and in the process have attained high catalytic efficiencies that approach diffusion limits. However, OPNAs are a recent development and therefore the OPNA-degrading activities of naturally occurring enzymes are relatively low. Different approaches have been undertaken to address these shortcomings (e.g., directed evolution of natural OPNA enzymes and of unrelated enzyme scaffolds redesigned with new catalytic sites). Also, efforts have been undertaken to develop biomimetic abiotic catalysts. Although much progress has been made, the results are still inadequate to meet warfighter needs. Nevertheless, the knowledge provided by these undertakings (including designing catalytic enzymes for OPNA stereo-selective hydrolysis and robust catalytic organometallics, advances in parametric protein design, and the advent of high-throughput enabling methods for screening genomic libraries and for determining 3-D protein structures) have provided a unique opportunity to pursue computational design approaches for catalytic OPNA-degrading catalytic systems and develop deeper understanding for the underlying structure-activity and structurestability relationships. These insights could enable better biomimetic abiotic or bio-abiotic hybrid catalytic systems for OPNA degradation.

**Impact:** The success of the research under this topic would enable rational design and production of efficient, rugged, and inexpensive catalytic bio and abiotic systems for OPNA degradation.

**Objective:** The goal of this topic is to develop and utilize an advanced fundamental mechanistic understanding of high-efficiency hydrolytic and hyper-stable OPNA-degrading abiotic catalysts or bio-abiotic hybrids. The research should be targeted so the results can inform design and construction of catalytic systems for OPNA hydrolysis that are highly efficient, thermostable, small, and functional even when exposed to mixed solvents or reaction byproducts.

Highest consideration will be given to proposals based on an iterative (spiral) approach to

understand the underlying structure-activity and structure-stability relationships and can provide confirmation of the developed catalytic system's effectiveness on live agents. Proposals offering only theoretical approaches (e.g., modeling) or approaches to improve existing natural enzymes will not be entertained.

Possible research areas may include, but are not limited to:

- Studies of high efficacy mechanisms of catalytic constructs' interactions with targets (e.g., binding, transition state stabilization, product release)
- Studies of the mechanisms of high catalytic efficiency and hyperstability phenomena of rationally designed biomimetic constructs and beyond on abiotic catalysts, such as completely *de novo* designed small proteins, proteomimetic and organometallic catalysts
- Studies of synergistic combinations of bio and abiotic catalytic systems
- Predictive models with experimental validation for binding and catalysis using modern computational methods
- Design imparting high stability against time, heat, mixed solvents, and reaction byproducts

### ATTACHMENT 2: INTELLECTUAL PROPERTY

(Applies to FAR Contracts & OTAs)

Applicants must describe any limitations on the use of any intellectual property (patents, inventions, trade secrets, copyrights, trademarks, technical data or computer software) that will impact the offeror's performance of the contract or impact the Government's subsequent use of any deliverable under the contract. In particular, the applicant must describe the intellectual property in sufficient detail and describe the limitations on its use (potential patent licenses required by the Government, data assertions of the offeror or any subcontractor, etc.) and describe how the Government can accomplish the stated objectives of this BAA with the limitations described or proposed by the offeror.

<u>Patents.</u> Applicants must list any known patents, patent applications, or inventions which the offeror may be required to license in order to perform the work described in the Applicant's proposal, or which the Government may be required to license to make or use the deliverables of the contract should the Applicant's proposal be selected for award. For any patent, patent application or invention listed, the Offeror must provide the invention title, a summary of the invention, patent number, patent application publication number, or provisional patent application number, and indicate whether the offeror is the patent or invention owner. If a patent or invention is in-licensed by the offeror, identify the licensor.

If any listed patent, patent application or invention is owned or licensed by the applicant, the applicant must provide a statement, in writing, confirming that it either owns or possesses the appropriate licensing rights to patent, patent application or invention to perform the work described in the proposal and/or to grant the Government a license to make or use the deliverables for this program. If any listed patent, patent application or invention is not owned or licensed by the applicant, then the applicant must explain how it will obtain a license, how the Government may obtain a license and/or whether the offeror plans to obtain these rights on behalf of the Government.

Be advised that no patent, patent application, or invention disclosure will be accepted if identified in the Data Rights Assertion list. The list of patents, patent applications, and inventions of this section must be a separate list from the Data Rights Assertion list.

Government rights in any technology that might be invented or reduced to practice under the contract are addressed in the patent rights clause to be included in the contract.

<u>Data Rights.</u> Applications submitted in response to this BAA shall identify, to the extent known at the time an offer is submitted to the Government, the technical, the technical data, or computer software that the Offeror, its subcontractors or suppliers, or potential subcontractors or suppliers assert should be furnished to the Government with restrictions on use, release, or disclosure, in accordance with DFARS 252.227-7017, Identification and Assertion of Use, Release or Disclosure Restrictions, and DFARS 252.227-7028, Technical Data or Computer Software Previously Delivered to the Government. The applicant's assertions, including the assertions of its subcontractors or suppliers or potential subcontractors or suppliers, shall be submitted in the following format, dated and signed by an official authorized to contractually obligate the applicant. If the applicant will deliver all technical data and computer software to the Government without restrictions, enter "NONE" in this table under the heading "Technical Data or Computer Software to be Furnished with Restrictions."

## Identification and Assertion of Restrictions on the Government's Use, Release, or Disclosure of Technical Data or Computer Software.

The applicant asserts for itself, or the persons identified below, that the Government's rights to use, release, or disclose the following technical data or computer software should be restricted:

Technical Data or			
Computer			Name of Person
Software	Basis for	Asserted Rights	Asserting
to be Furnished	Assertion**	Category***	
With Restrictions*			Restrictions****
(LIST)****	(LIST)	(LIST)	(LIST)

<sup>\*</sup>For technical data (other than computer software documentation) pertaining to items, components, or processes developed at private expense, identify both the deliverable technical data and each such item, component, or process. For computer software or computer software documentation identify the software or documentation.

\*\*Generally, development at private expense, either exclusively or partially, is the only basis for asserting restrictions. For technical data, other than computer software documentation, development refers to development of the item, component, or process to which the data pertain. The Government's rights in computer software documentation generally may not be restricted. For computer software, development refers to the software. Indicate whether development was accomplished exclusively or partially at private expense. If development was not accomplished at private expense, or for computer software documentation, enter the specific basis for asserting restrictions.

\*\*\*Enter asserted rights category (e.g., government purpose license rights from a prior contract, rights in SBIR data generated under another contract, limited, restricted, or government purpose rights under this or a prior contract, or specially negotiated licenses).

****Corporation, individual, or other pers	on, as appropriate.
*****Enter "none" when all data or softw	are will be submitted without restrictions.
Date	
Printed Name and Title	
Signature	

Applicants responding to this BAA requesting an Other Transaction or Other Transaction for Prototype shall specifically identify any asserted restrictions on the Government's use of intellectual property contemplated under those award instruments. For this purpose, offerors must propose specific Intellectual Property terms and conditions and a data deliverable list. Further, the offerors must explain why an Other Transaction is necessary and, in particular, how the intellectual property terms and conditions proposed will meet the objectives of this BAA.