DEFENSE THREAT REDUCTION AGENCY

BROAD AGENCY ANNOUNCEMENT

HDTRA1-11-21-BRCWMD-BAA

Amendment 5 (December 2015)

Research and Development Directorate

Basic and Applied Sciences Department

Basic Research for Combating Weapons of Mass Destruction (C-WMD)

Original Posting Date: March 2011

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OVERVIEW INFORMATION

1. Federal Agency Name:

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

2. Funding Opportunity Title:

   FY2011 – 2021 Basic Research for Combating Weapons of Mass Destruction (C-WMD) Broad Agency Announcement (BAA)

3. Announcement Type:

   The BAA, which is in effect from March 2011 through September 2021, established the multi-year process and served as the announcement for the first round of submissions (referred to as "periods").

   Over this timeframe there will be multiple opportunities/periods to electronically submit research ideas. Each period will have a two-phased submission process. *Phase I* is the pre-application white paper submission and is open to all qualified entities; *Phase II* is an invitation-only full proposal submission resulting from Phase I pre-application white paper review as decided by the DTRA Selection Authority.

   This Amendment alerts applicants to several administrative updates to the BAA and serves as the announcement for the next round of submissions.

4. Funding Opportunity Number:

   HDTRA1-11-21-BRCWMD-BAA

5. Catalog of Federal Domestic Assistance (CFDA) Number:

   12.351

6. Dates:

   This BAA will have multiple, consecutive opportunities/periods which are not predetermined; however, it is anticipated that there will be at least one opportunity for each year announced in the December timeframe; there may be additional opportunities/periods in any year. Subsequent submission opportunities/periods with corresponding topics, application packages, applicable deadlines, will be published via amendments to this BAA.

The Phase I (pre-application white paper) and Phase II (invitation-only proposal) submission deadlines are/will be shown in Table 1 (below and in Section IV.3.3). The Tables will be updated (by amendments to this BAA) as changes are made to the schedule.

All submissions (pre-application white papers and invited proposals) must be made in accordance with the submission instructions in this BAA through Grants.gov using the application packages provided with this BAA. Applicants are responsible for ensuring compliant and final submission of their Phase I pre-application white papers and Phase II 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.

Date	Event
Period F	
1 December 2015	Amendment to the BAA announced on Grants.gov with Period F topics, application packages, and applicable deadlines
1 February 2016	Phase I pre-application white paper receipt deadline
11:59pm EST, Not prior to 2 May 2016, and not later than 31 May 2016 *	Phase II invitation-only proposal receipt deadline
October—December 2016	Period F Grants scheduled to be awarded

Table 1: List of important dates. (This is a condensed version of Table 5, located in Section IV.3.7.)

ADDITIONAL OVERVIEW CONTENT

This BAA is focused on soliciting **basic research** projects that support the DTRA mission to safeguard America and its allies from WMD (e.g., chemical, biological, radiological, nuclear, and high-yield explosives) by providing capabilities to reduce, eliminate, and counter the threat and mitigate its effects. To this end, DTRA seeks research across broad strategic thrust areas:

- ***Science of WMD Sensing and Recognition***
- ***Cognitive and Information Science***
- ***Science for Protection***
- ***Science to Defeat WMD***
- ***Science to Secure WMD***

Detailed descriptions of these thrust areas can be found in Section I.3. The specific research opportunities (topics) for each period that align to these thrust areas are listed in Section VIII. Research topics are only valid for the submission period in which they are posted, and only pre-application white papers responsive to the topics posted for a given submission period will be considered.

Resulting awards from this announcement will be **grants only**. These grants will be paid in advance, subject to the conditions described in 2 CFR 215.22(b).

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 will reflect DoD implementation of 2 CFR part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards."

I. FUNDING OPPORTUNITY DESCRIPTION

I.1. This BAA is an extramural endeavor that combines basic research needs of DTRA and the Joint Science and Technology Office for Chemical and Biological Defense (JSTO-CBD) to address the full spectrum of counter-WMD challenges. Both DTRA and JSTO-CBD share the mission to safeguard America and its allies from WMD and provide capabilities to reduce, eliminate, and counter the threat and effects from chemical, biological, radiological, nuclear, and high-yield explosives. Each seeks to identify, adopt, and adapt emerging and revolutionary sciences that may demonstrate high payoff potential to counter-WMD threats.

I.2. This announcement solicits pre-application white papers for long-term challenges in specific fundamental areas of basic research that offer a significant contribution to the current body of knowledge or further the understanding of phenomena and observable facts and may have impact on future capabilities that support the DTRA and JSTO-CBD missions. Responses to this BAA must address **only basic research**. Pre-application white paper and proposal submissions that address applied research, advanced technology development, or combine basic research with applied research and/or advanced technology development will be considered not responsive and will not be evaluated further.

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.[1]

In contrast to basic research, applied research is the systematic study to understand the means to meet a recognized and specific need. It is a systematic expansion and application of knowledge to develop useful materials, devices, and systems or methods. The boundary between basic research and applied research occurs at the point when sufficient knowledge exists to support a hypothesis involving a specific application.[2]

[1] DoDI 3210.1, September 16, 2005

[2] DoD Financial Management Regulation Volume 2B, Chapter 5

I.3. DTRA seeks unclassified basic research across five major functional counter-WMD research thrust areas. Specific research topics that align to one or more thrust areas are presented in Section VIII. The five thrust area descriptions are outlined below.

- ***Thrust Area 1—Science of WMD Sensing and Recognition:*** The basic science of WMD sensing and recognition is the fundamental understanding of materials that demonstrate measurable changes when stimulated by energy, molecules, or particles from WMD in the environment. This research thrust involves exploration and exploitation of interactions between materials and various electromagnetic frequencies, molecules, nuclear radiation or particles. These interactions and the specific form of recognition they provide are used for subsequent generation of information that provides knowledge of the presence, identity, and/or quantity of material or energy in the environment that may be significant.
- ***Thrust Area 2—Network Sciences:*** The basic science of network science is the convergence of computer, information, mathematical, networks, natural, and social science. This research thrust expands our understanding of social networks and advances knowledge of adversarial intent with respect to the acquisition, proliferation, and potential use of WMD. The methods may include analytical, computational or numerical, or experimental means to integrate knowledge across disciplines and improve rapid processing of intelligence and dissemination of information.
- ***Thrust Area 3—Science for Protection:*** Basic science for protection involves advancing knowledge to protect life and life-sustaining resources and networks. Protection includes threat containment, decontamination, threat filtering, and shielding of systems. The concept is generalized to include fundamental investigations that reduce consequences of WMD, assist in the restoration of life-sustaining functions, and support forensic science.
- ***Thrust Area 4—Science to Defeat WMD:*** Basic science to defeat WMD involves furthering the understanding of explosives, their detonation, and problems associated with accessing target WMDs. This research thrust includes the creation of new energetic materials or physical approaches that enhance the defeat of WMDs by orders of magnitude, the improvement of modeling and simulation of these materials and various phenomena that affect success and estimate the impact (lethality) of defeat actions, including the assessment of event characteristics using various dynamic analytical methods.
- ***Thrust Area 5—Science to Secure WMD:*** Basic science to support securing WMD includes: (a) environmentally responsible innovative processes to neutralize chemical, biological, radiological, nuclear, or explosive (CBRNE) materials and components; (b) discovery of revolutionary means to secure components and weapons; and (c) studies of scientific principles that lead to novel physical or other tags and methods to monitor compliance and disrupt proliferation pathways. The identification of basic phenomena that provide verifiable controls on materials and systems also helps arms control.

I.4. DTRA seeks unclassified basic research ideas that are responsive to the goals and objectives of the topics outlined in Section VIII. The topics labeled "PerF" are only valid for Period F of this BAA. Only pre-application white papers responsive to the topics posted for Period F and submitted by the Period F deadline will be considered. A new list of topics will be posted for subsequent periods with corresponding pre-application white paper due dates. Note that topics from the original solicitation and Amendments 1, 2, 3, and 4, labeled "PerA", "PerB", "PerC", "PerD", and "PerE" are NOT valid topics for "PerF". Pre-application white papers that address "PerA", "PerB",

“PerC”, “PerD”, and “PerE” topics will not be reviewed by DTRA.

II. AWARD INFORMATION

II.1. Resulting awards from this BAA will be **grants only**. These grants will be paid in advance, subject to the conditions described in 2 CFR 215.22(b).

II.2. The period of performance (POP) for the Single Scope Awards, the Multidisciplinary Awards, and the Young Investigator Awards (all types of awards are detailed in Section II.6) may be up to five (5) years. Awards may be for a base period of one (1) year with up to four (4) additional years as possible options, a base period of two (2) years with up to three (3) additional years as possible options, or a base period of three (3) years with up to two (2) additional years as possible options. The base period and option combination(s) will be specifically detailed in each and every topic. Pre-application white papers and proposals that outline scope and effort for only the base period and do not propose options are also acceptable. Additional guidance on the POP may be provided with the topic description or in the letter of invitation for the full proposal. Each of these supersedes the guidance provided here.

II.3. The POP for the Seed Awards will be for one (1) year or less. Seed Awards may not include option years.

II.4. The final number of grants and the amount of funds allocated for each period will be determined after all pre-application white papers and invited proposals are received and evaluated. On average DTRA may make up to award 50-75 grants annually for a maximum total grant value of approximately $66M. 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 will reflect DoD implementation of 2 CFR part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards."

II.5. The Government actions under this BAA shall adhere to the requirements of the Department of Defense (DoD) Grant and Agreement Regulations (DoDGARs). DoDGARs can be accessed online at http://www.gpo.gov/fdsys/pkg/CFR-2011-title32-vol1/xml/CFR-2011-title32-vol1-subtitleA-chapI-subchapC.xml. See also 32 Code of Federal Regulations (CFR) 22, which can be accessed online at http://www.gpo.gov/fdsys/granule/CFR-2011-title32-vol1/CFR-2011-title32-vol1-part22.

II.6. There are four (4) categories of awards, which are detailed below. The applicant does not need to specify the type of award sought. It will be inferred by the dollar amount requested and/or the topic to which the pre-application white paper is submitted.

1. Single Scope Awards: Research projects that focus on exploratory aspects of a unique problem, a high-risk approach, or innovative research in subjects with potential for high impact to C-WMD science. Research must support undergraduate, and/or graduate students, and/or postgraduate students.

   Single Scope Awards may have Co-Principal Investigators (Co-PIs) and subawards (grants and/or contracts). Single Scope Awards will be made by a single grant to the lead organization. Subawards, including all grants and contracts, are the responsibility of the award recipient; exceptions will not be made.

   Single Scope Awards will average $150K per year for DTRA sponsored topics and $250K per year for JSTO-CBD Program sponsored topics (average award values include both direct and indirect costs). Additional guidance for the average dollar value may be provided in the topic description or in the letter of invitation for the full proposal. Each of these supersedes the guidance provided here.

   The predominance of awards will be Single Scope Awards.

2. Multidisciplinary Awards: Research projects that involve a comprehensive program of innovative research in an interdisciplinary area with potential for high impact. The proposed research must involve fundamental contributions in research by multiple investigators from diverse disciplines (proposal **must** be multidisciplinary). Investigators may be from a single institution or multiple institutions. Research must support multiple undergraduate, and/or graduate students, and/or postgraduate students.

   Authors of these pre-application white papers and invited proposals must take great care to clearly outline the impact to C-WMD science that is to be gained from the higher dollar amount investment and justify the scientific contribution from each investigator.

   Proposals submitted under this category must have a single lead organization and single submission for the pre-application white paper and the invited proposal. Multidisciplinary Awards will be made by a single grant to the lead institution. Subawards, including all grants and/or contracts, are the responsibility of the award recipient; exceptions will not be made.

   Multidisciplinary Awards will average $350K per year for DTRA sponsored topics and $500K per year for JSTO-CBD Program sponsored topics (average award values include both direct and indirect costs). Additional guidance for the average dollar value may be provided in the topic description or in the letter of invitation for the full proposal. Each of these supersedes the guidance provided here.

3. Young Investigator Awards: Research projects that focus on exploratory aspects of a unique problem, a high-risk approach, or innovative research in subjects with potential for high impact to C-WMD science from individuals 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 pre-application white paper submission.

Young Investigator Awards may have subawards; however, subawards that transfer substantive programmatic activity will be considered non-responsive to the Young Investigator topics. Young Investigator Awards will be made by a single grant to the lead organization. Subawards, including all grants and/or contracts, are the responsibility of the award recipient; exceptions will not be made.

Young Investigator Awards will average $100K per year (average award values include both direct and indirect costs).

4. Seed Awards: Research projects that focus on the exploratory aspects of a research hypothesis or on the development of a high-risk approach with potential for high impact to C-WMD science.

   Seed Awards may have Co-PIs and subawards. Seed Awards will be made by a single grant to the lead organization. Subawards, including all grants and/or contracts, are the responsibility of award recipient; exceptions will not be made.

   Seed awards will be less than $75K (average award values include both direct and indirect costs).

II.7. Funding for participation in this program is highly competitive and the cost of proposed research should strictly be maintained in the award amounts outlined for each award type and for each topic. Under no circumstances will awards exceed 10% of the averages as outlined for each award type and for each topic. Exceptions will not be made.

II.8. Subawards (grants and/or contracts) are permitted. Subawards may be used to carry out a portion of the research. In instances where the lead applicant is an accredited degree-granting college and/or university, applicants should note that substantive programmatic activity must be maintained at accredited degree-granting colleges and universities. DTRA will review and consider the proposed subawards for all pre-application white papers and proposals on a case-by-case basis.

II.9. Applications for renewal or supplementation of existing DTRA funded projects are not eligible to compete with applications for new awards.

II.10. The Government will not provide any hardware or software to execute the proposed research. Exceptions will not be made.

II.11. 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 or fully fund any or all awards under this BAA. All awards are subject to the availability of funds.

III. ELIGIBILITY INFORMATION

III.1. Pre-application white papers and proposals submitted for this BAA will be considered from the following U.S. and foreign-based equivalents:

- Accredited degree-granting colleges and universities.

- Industrial/commercial basic research centers, including small businesses with a portfolio predominantly in basic research proposing a project with significant participation (minimum 30% of total effort value on the proposed project) by one or more accredited degree-granting colleges and/or universities. Note: ***Not eligible for Young Investigator Awards.***

- Not-for-profit organizations/basic research centers with a portfolio predominantly in basic research proposing a project with significant participation (minimum 30% of total effort value on the proposed project) by one or more accredited degree-granting colleges and/or universities. 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. Note: ***Not eligible for Young Investigator Awards.***

III.2. The following entities may not participate as prime grantees for awards made under this BAA, but may act as collaborators, including as Co-PIs, and/or subawardees:

- Federal laboratories (including DoD and Department of Energy (DOE)[3] laboratories), Federal academic institutions, Federal agencies, and Federal organizations.

- 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[4].

- Foreign government-owned institutions.

- Industrial/commercial firms other than those outlined in Section III.1.

Note: DoD degree-granting academic institutions that are Federal government organizations, e.g. United States Military Academy at West Point, The Air Force Institute of Technology, etc., are eligible to submit pre-application white papers and proposals in response to the intramural Service Call issued by the DTRA Basic and Applied Sciences Department, see http://www.dtrasubmission.net and after logging in, follow the link to the 'FY11-16 Basic Research for Combating Weapons of Mass Destruction (WMD) Service Call for DoD Degree-Granting Academic Institutions'. Please note that the Service Call link will also contain the submission periods. Eligibility requirements under the Service Call are subject to change.

III.3. Cost sharing and/or matching is not required.

III.4. Other.

[3] DOE-sponsored laboratories must obtain authorization from the DOE sponsor. DTRA does not require documentation of this authorization.

[4] DOE-sponsored FFRDCs must obtain authorization from the DOE sponsor. DTRA does not require documentation of this authorization.

III.4.1. DTRA uses the Excluded Parties List System (EPLS) to exclude recipients ineligible to receive Federal awards. EPLS can be accessed online at http://epls.arnet.gov (Reference 2 CFR 1125).

III.4.2. There is no limit on the number of pre-application white papers and invited proposals that an applicant (PI/Co-PIs) may submit in response to this BAA.

- Applicants (PI/Co-PIs) may submit pre-application white papers and invited proposals to one or more topics.

- Applicants (PI/Co-PIs) may submit pre-application white papers and invited proposals to one or more periods under this BAA, regardless of a previous submission's disposition.

- Applicants (PI/Co-PIs) are **strongly** encouraged to minimize overlap in scope and level of effort if multiple projects are submitted for pre-application white papers and invited proposals. Further, individual PIs and Co-PIs are discouraged from repackaging research and submitting multiple redundant Phase I submissions in any given period of this BAA.

IV. APPLICATION AND SUBMISSION INFORMATION

IV.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 www.dtrasubmission.net/portal for applicant use, as noted in the text of this announcement. 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.

IV.1.1. The required application packages for the pre-application white papers are provided with this announcement. Note that each topic outlined in Section VIII has a unique application package posted with this BAA. **The application package corresponding to the topic of interest should be used for submission of pre-application white papers.**

IV.1.2. The required application packages for the invited proposals will be posted at a later date. As with the Phase I submissions, each topic outlined in Section VIII will have a unique application package**. The application package corresponding to the topic of interest should be used for submission of invited proposals.** Application packages for Phase II submissions will be posted following the notification of invitation for proposals.

IV.1.3. While the review of all submissions is at the discretion of DTRA, in general, DTRA will not consider the following:

- Pre-application white papers that attempt to address multiple topics.

- Pre-application white papers that are submitted to topics from previous periods.

- Application packages and proposals for Phase II submissions that were not invited.

IV.1.4. The application packages posted to www.Grants.gov consist of the forms detailed in Table 2, which must be completed as part of the submission process. Additional files are required to be uploaded as attachments. Refer to Section IV.2.3 for more information on Phase I requirements and Section IV.2.4 for more information on Phase II requirements:

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 Form	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://www07.grants.gov/agencies/forms_instruction_information.jsp.

IV.2. Content and Form of Application Submission. Each period of 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, invited proposal submission, will be based on the evaluation results of the Phase I pre-application white paper. Pre-application white papers and invited proposals **must be** submitted electronically using Grants.gov and the corresponding application packages provided with this BAA on Grants.gov.

Applicants are responsible for ensuring compliant and final submission of their Phase I pre-application 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.

IV.2.1. Phase I Pre-Application White Paper Submission and Content.

Each pre-application white paper must address only one of the research topics detailed in Section VIII for the relevant period. Each pre-application white paper must use the application package for the specific topic number as presented in Section VIII of this BAA.

Each Phase I application package contains the following form (Note: all other BAA guidelines must also be met to be considered a true complete package):

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.

DTRA-specific instructions for completing the SF 424 (R&R) Application for Federal Assistance are below, general application instructions can be found on 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. 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 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 1/2 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 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). Note that dollar values in the BAA

include both direct and indirect costs.

- 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.

- The topic number and name should be included as a header on the white paper and in the text of the white paper.

IV.2.2. Phase II - Invited Proposal Submission and Content.

Each invited proposal must address the research topic for the corresponding Period that was the subject of the corresponding pre-application white paper, as detailed in Section VIII. Each invited proposal must use the application package for the specific topic number as presented in Section VIII of this BAA.

Each Phase II application package contains the following forms (Note: all other BAA guidelines must also be met to be considered a true complete package):

Form	Attachment	Action
SF-424 (R&R) Application for Federal Assistance Form		Enter the appropriate information in data fields
RR Budget Form	Budget Justification for entire performance period	Attach to Section K in budget period one
R&R 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
	Technical Proposal	Attach to Block 8

		Project Narrative
Disclosure of Lobbying Activities (SF-LLL)	N/A	N/A
Attachments Form	Attachment 1 – SOW	Upload as Attachment 1
	Attachment 2 – Quad Chart	Upload as Attachment 2

Table 4: Phase II Proposal Package Chart.

SF 424 (R&R) Application for Federal Assistance. DTRA-specific instructions for completing the SF 424 (R&R) are below, general application instructions can be found on 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 4c – Previous Grants.gov Tracking ID. Enter the Phase I Grant ID.
- 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.*

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 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. DTRA encourages graduate students to attend the Annual Technical Review.

Budget Justification. 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 must include a statement discussing how the subawardee(s) was determined to be fair and reasonable.

R&R Subaward Budget Attachment(s) Form (if applicable). Detailed cost estimates and budget justifications 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. 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 all grants and contracts through which each PI and Co-PI is currently receiving or may potentially receive financial support to be disclosed.

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. This information will include the abstract submitted to Block 7 of the SF 424.

  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. 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 www.dtrasubmission.net/portal (MS Word format).

The technical proposal must include the following components:

- Abstract.
- 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 higher dollar amount investment and justify the scientific contribution from each investigator.
- 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.
- Performance Schedule. Provide a table of tasks and subtasks and the duration of performance of each in a Gantt or other suitably formatted chart.
- References. List any relevant documents referenced.

Disclosure of Lobbying Activities (SF-LLL) Form. The Disclosure of Lobbying Activities Standard Form-LLL, if applicable, should be completed.

Attachments Form.

- **Attachment 1 – SOW.** The SOW does not have a page limit, but should be approximately 3-5 pages in length and appropriate for incorporation into the grant 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 https://www.dtrasubmission.net/portal/Forms.aspx (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 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 grantee 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 parentheses 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."

- **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 https://www.dtrasubmission.net/portal/Forms.aspx (MS PowerPoint format). A pictorial representation of the quad chart is provided herein and includes the relevant fields that must be included in the Phase II proposal submission. The inclusion of the DTRA logo is not required. The quad chart should be uploaded as "Attachment 2" of the Attachments Form.

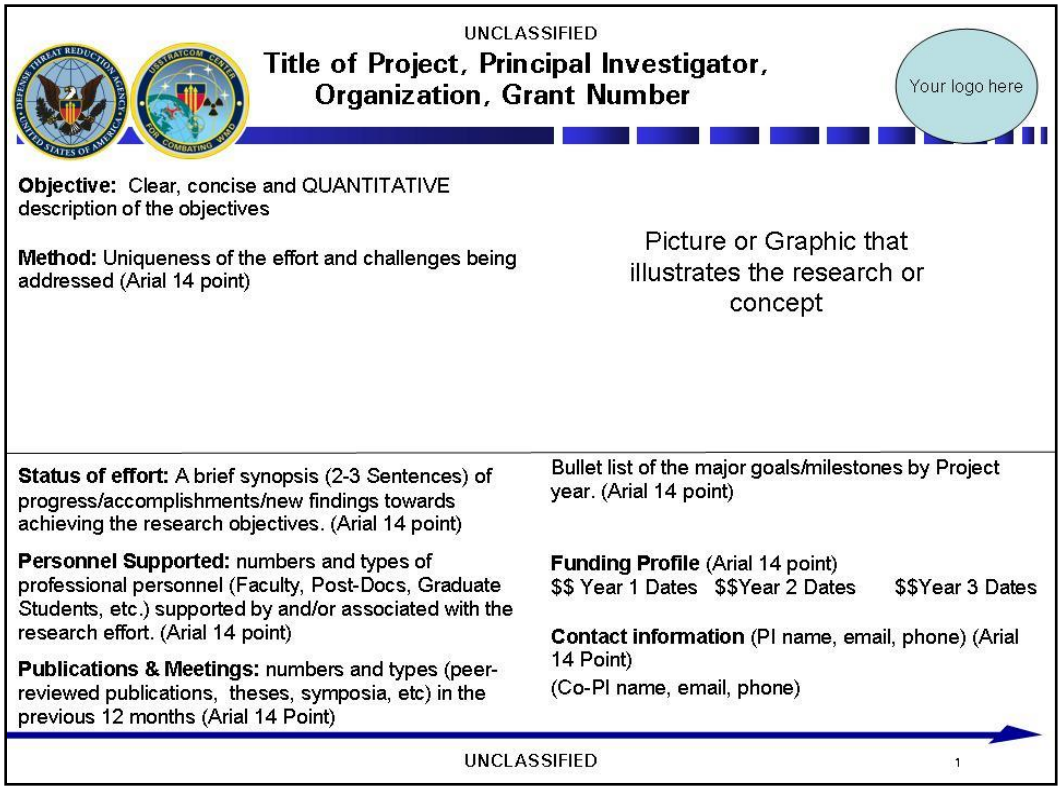

Figure 1: Sample Quad Chart.

IV.2.3. File Format.

Documents should be uploaded as a Portable Document File (PDF) format. Perform a virus check before uploading any files to www.grants.gov 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 www.grants.gov as part of your application package. Movie and sound file attachments will not be accepted.

IV.2.4. All submissions must be UNCLASSIFIED.

IV.3. Submission Dates and Times.

Phase I pre-application white papers will be accepted based on periods as outlined in Table 5. A Phase II "receipt window" of 4 to 6 weeks will be provided in Table 5, however, the specific due dates for the Phase II invited proposal submissions will be provided in the letters of invitation. (The window is strictly for informational purposes only, to provide 'not prior to' and 'not later than' dates.) After the deadline date provided for a given period, the application packages will no longer be available for

download from Grants.gov. Most importantly, applications received after these deadlines will only be reviewed under extremely limited circumstances, at the discretion of DTRA.

When sending electronic files, the applicant should allow for potential delays in file transfer from the originator's computer server to the Grants.gov website/computer server, as well as the delay associated with the Grants.gov 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 Grants.gov, and delays due to high demand encountered as the submission deadline approaches.

Applicants are responsible for submitting fully compliant pre-application white papers and invited proposals so as to be received by Grants.gov no later than the time and dates listed in Table 5 and the letter of invitation for proposals, respectively.

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 Grants.gov.

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

Additional timeline details are available to all applicants at the DTRA Basic and Fundamental Research Community Portal (www.dtrasubmission.net/portal), e.g., estimated notification date for proposal invitations. Applicants are responsible for checking www.dtrasubmission.net/portal for changes and updates to the schedule.

Additional opportunities for pre-application white paper submissions with applicable topics, due dates, and application packages will be posted as amendments to this BAA. Schedules of future amendments, topic information, and due dates will not be provided and questions requesting information relevant to future amendments, schedules, and/or topics will not be answered in advance of an amendment.

Date	**Event**
1 March 2011	BAA announced on Grants.gov
Period A, Period B, Period C, Period D, and Period E are CLOSED	
Period E Grants are scheduled to be awarded October-December 2015	
Period F	
1 December 2015	Amendment to the BAA announced on Grants.gov with Period F topics, application packages, and applicable deadlines
1 February 2016	Phase I pre-application white paper receipt deadline
11:59pm EST, Not prior to 2 May 2016, and not later than 31 May 2016 *	Phase II invitation-only proposal receipt deadline

October—December 2016	Period F Grants scheduled to be awarded
Period G	
TBD	Amendment to the BAA announced on Grants.gov with Period G topics, application packages, and applicable deadlines
TBD	Phase I pre-application white paper receipt deadline
TBD	Phase II invitation-only proposal receipt deadline
TBD	Period G Grants scheduled to be awarded
Period H	
Period I	
Period J	
……	
Period 'n'	

Table 5: List of important dates. (This is an expanded version of Table 1, located in the Overview Information.)

If the application package and required attachments are submitted to Grants.gov after the exact time and date specified in this BAA for the pre-application white paper (Phase I) and/or the letter of invitation for the invited proposal (Phase II), the application is "late". Applications that are "late" will only be reviewed under extremely limited circumstances, at the discretion of DTRA.

If an emergency or unanticipated event interrupts normal Government processes so that proposals cannot be submitted to Grants.gov by the exact time specified in this BAA for the pre-application white paper and/or the letter of invitation for the invited proposal, and urgent Government requirements preclude amendment of the BAA closing date, the time specified for receipt of applications will be deemed to be extended to the same time of day specified in the BAA on the first work day on which normal Government processes resume.

IV.4. Intergovernmental Review. Not Applicable.

IV.5. Funding Restrictions. There are no known funding restrictions at this time.

IV.6. Other Submission Requirements.

IV.6.1. Phase I and Phase II applications must be made through www.grants.gov using the application package specific to the period/phase/topic of interest. Application packages for a *particular period* are posted with the announcement of the particular period (i.e., Period A was announced by the original posting of the BAA and the application packages were posted with it. When a new period is announced, an amendment will be published with new application packages). Applicants should take care to use the application package associated with the topic for which an application is being made.

Phase I and Phase II submissions made via any other means (e.g., hand-carried, postal service, commercial carrier, e-mail, etc.) will NOT be considered under any circumstances.

IV.6.2. Applicants should note that each organization must complete a one-time registration in order to submit its pre-application white paper(s) and application(s) through www.grants.gov. Please see the following web link on information about registering with Grants.gov: http://www07.grants.gov/applicants/applicants.jsp. If your organization is already registered in Grants.gov, 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 http://fedgov.dnb.com/webform/displayHomePage.do 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 www.sam.gov. 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).

IV.6.3. 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 Basic and Fundamental Research Community Portal (www.dtrasubmission.net/portal). 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.

IV.6.4. 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 the 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 pre-application 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.

IV.6.5. Pre-application white papers and invited proposals may be withdrawn by written notice received at any time before award. Withdrawals are effective upon receipt of notice by the Grants Officer via the e-mail address listed in Section VII.1.

V. APPLICATION REVIEW INFORMATION

V.1. Evaluation Criteria. The evaluation criteria to be used for review of applications are listed below. Only the first two (2) criteria will be used to evaluate pre-application white papers; all four (4) will be used to evaluate invited proposals.

1. Technical/Scientific Merit. This area addresses the technical approach and the contribution of the research to advancing the scientific body of knowledge. It evaluates what research will be performed and how it will be accomplished. Three (3) factors will be considered. The factors are listed in the order of importance.

- *Soundness of Approach.* This factor addresses whether the proposal clearly identifies and demonstrates an understanding of the scientific challenges and whether the project has a well-designed methodology, based on sound scientific principles, and how technical risks are addressed, mitigated, and managed.

- *Degree of Innovation.* This factor addresses the originality of the concept, its scientific merit, its creativity, and/or the novelty of the approach and the potential of the project to advance the scientific body of knowledge. The degree of innovation will be judged based on the innovation or originality that is appropriate to the proposed project.

- *Anticipated Scientific Impact.* This factor addresses the potential of the proposed work to provide greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts and the anticipated impact on the state of the science.

2. Responsiveness to Topic Area and Program. This area evaluates the extent to which the proposed research supports specific topic areas. It also considers the derivative benefit that may be realized by the performer and its organization through performance of the proposed research. The two (2) factors are weighted equal to each other.

    - *Responsiveness to Topic Area.* This factor addresses the responsiveness of the proposal to the objectives in the specific topic area and the contribution to the C-WMD science needs outlined in the topic.

    - *Derivative Benefit.* This factor considers training of students in science, engineering, and/or mathematics through the proposed research.

3. Program Capabilities. This area addresses key personnel, facilities, and major equipment required to accomplish the research. The two (2) factors are weighted equal to each other.

    - *Qualifications.* This factor will be scored based on the qualifications and availability of the proposed PI, co-PIs and other key personnel who are critical in achieving proposed objectives.

    - *Capabilities.* This factor considers the applicant's current or planned facilities and equipment that support achieving the proposed objectives. Capabilities evaluation will be based on the total capabilities of the assembled team that will be brought to bear as part of the proposed project.

4. Cost Realism and Reasonableness. This factor considers the adequacy and reasonableness of resources applied to each project task. This includes labor (in terms of time and mix), equipment, other direct costs, and indirect costs.

V.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 will be reviewed within the period to which it

was submitted.

Pre-application white paper (Phase I) evaluation will be based on two (2) equally weighted criteria described in Section V.1: (1) Technical/Scientific Merit and (2) Responsiveness to Topic Area and Program, which will each be scored as Green (acceptable), Yellow (acceptable with minor issues), or Red (unacceptable). The Government reserves the right to limit the number of Phase II invited proposals requested depending upon the volume of pre-application white papers submitted, the results of the Phase I evaluation, and the specific needs of the Agency.

Invited Proposal (Phase II) Evaluation will be based on the four (4) criteria described in Section V.1: Criteria (1) Technical/Scientific Merit and Criteria (2) Responsiveness to Topic Area and Program are equally weighted and are more important than Criteria (3) Program Capabilities which is more important than Criteria (4) Cost Realism and Reasonableness. All four (4) criteria receive a numerical score ranging from 1 (unacceptable) to 5 (outstanding).

Other factors that may be considered during the selection process are the possible duplication with other research currently funded by the Government, program balance across research topics, and budget limitations. 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. ***Preference will be given to university-led awards, single scope awards, and young investigator awards.***

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.

Additional details, including the due date for Phase II submissions, may be provided to applicants in the invitation email.

V.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 applicants:

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.

V.4. Technical and Administrative Support by Non-Government Personnel

It is the intent of DTRA to use non-government personnel to assist with the review and administration of submittals for this BAA.

All invited proposals will be reviewed by subject matter experts (peer reviewers) who are non-government personnel.

Participation in this BAA requires DTRA support contractors to have access to pre-application white paper and invited proposal information including information that may be considered proprietary. Existing DTRA contractors include but may not be limited to the following: Engility Corporation (advisory and assistance services) and their subcontractors, JAB Innovative Solutions (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.

All individuals having access to any proprietary data must sign a non-disclosure agreement that states the 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.

All applicants to this BAA consent to the disclosure of their information under these conditions.

VI. AWARD ADMINISTRATION INFORMATION

VI.1. Award Notices.

A detailed review timeline is available to all applicants at the DTRA Basic and Fundamental Research Community Portal (www.dtrasubmission.net/portal). Applicants are responsible for checking the timeline at the www.dtrasubmission.net/portal for changes and updates to the schedule.

Applicants of pre-application white papers that are not selected for invitation will be notified of the decision 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.

An invitation to submit a proposal will be extended to those applicants whose submissions were selected in Phase I. The invitation will be transmitted 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.

Applicants will be notified by DTRA of their selection/non-selection for award from the Phase II

invited proposals 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. Notification of proposal selection is not an authorization to begin work.

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 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.

A debrief summary will be provided as part of all notification e-mails.

All notifications will be made from notification@dtrasubmission.net. **E-mails to this e-mail address will not be answered or forwarded.**

The 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 will not further attempt to contact the applicants**.

VI.2. Administrative and National Policy Requirements. The DTRA Grant Terms and Conditions may be found online at the DTRA Basic and Fundamental Research Community Portal (www.dtrasubmission.net/portal). (Note: There are different versions for different recipients. As the Terms and Conditions are updated, they will be posted on the www.dtrasubmission.net/portal.) 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 Section IV.6.3 for the certification(s) required at the time of submission.

VI.2.1. SAM Registration. DTRA uses the SAM to exclude recipients ineligible to receive Federal awards. SAM can be accessed online at http://sam.gov (Reference 2 CFR 25.200).

- Be registered in the SAM prior to submitting an application (or plan);
- Maintain an active SAM registration with current information at all times during which it has an active Federal award or an application (or plan) under consideration by an agency; and
- Provide its DUNS number in each application (or plan) it submits to the agency.

VI.2.2. Protection of Human Subjects. It is not anticipated that human subjects would be involved in basic research. If the proposed research does involve human subjects or materials, applicants are asked to justify the use of human subjects and to address the following issues: outline the human use, to include the source of the human subjects or materials involved in the research. Further information may be required if the proposal is successful. The Common Federal Policy for the Protection of

Human Subjects, codified by the Department of Health and Human Services at 45 CFR 46 and implemented by the Department of Defense at 32 CFR 219.

The recipient shall adhere to DTRA local clause 252.223-9002. The full text of this clause is as follows:

All research under this grant involving human subjects must be conducted in accordance with 32 CFR 219, 10 USC 980, and DoDD 3216.02, as well as other applicable federal and state regulations. Grantees 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 USC 980). DTRA Directive 3216.01 establishes the DTRA Human Subjects Protection Program, sets forth the policies, defines the applicable terms, and delineates 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 new starts and to continuing research.

The DTRA directive requires that research using human subjects may not begin or continue until the Defense Threat Reduction Agency's Research Oversight Board (ROB) has reviewed and approved the proposed protocol. Grantees 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 Institutional Review Board (IRB) to include consent forms for any planned research using human subjects to the DTRA ROB for its review through the Grants Officer's representative (if assigned) or the Grants Officer. The ROB review is separate from, and in addition to, local IRB review.

Written approval to begin research or subcontract for the use of human subjects under the proposed protocol will be provided in writing from the DTRA ROB, through the Grants Officer. A copy of this approval shall be maintained by both the Grantee and the government. 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 PI
- 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
- changes in perceived or measured risks or benefits to volunteers that require changes to the study

Research pursuant to such modifications or amendments shall 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. ROB review and approval is required annually. The Grantee or subcontractor must provide documentation of continued IRB review of protocols for ROB review and approval in accordance with these Terms and Conditions. Research must not continue without renewed ROB approval unless necessary to eliminate apparent and immediate hazards to the subject(s).

Non-compliance with any provision of this clause may result in withholding of payments under the grant pursuant to the grant's payments clause(s) and/or grant termination pursuant to the grant'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.

VI.2.3. Animal Use. It is not anticipated that animal use would be involved in basic research. If the proposed research does involve animal use, however, applicants are asked to justify the use of animals and to address the following issues: any proposals that include animal studies or animal work must submit 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. Further information may be required if the proposal is successful.

The recipient shall adhere to DTRA local clause 252.235-9002 – Animal Use (Jul 2010). The full text of this clause is as follows:

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) are planned. This information, if applicable, must be included in the project narrative. 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 can be found on the ACURO website (https://mrmc-www.army.mil/index.cfm?pageid=Research_ Protections.acuro&rn=1). Allow 2 to 4 months for regulatory review and approval processes for animal studies. Offerors are to build this review time into their project schedules.

DoD Directive 3216.1, dated April 17, 1995, provides policy and requirements for the use of animals in DoD-funded research along with Army Regulation 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 Directive 3216.1 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.

VI.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: www.access.gpo.gov/nara/cfr/waisidx_99/32cfr626_99.html for a copy of 32 CFR 626.18, Biological Defense Safety Program.)

VI.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 [http://oba.od.nih.gov/biosecurity/news_events_oba.html#NSABB]. 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.

VI.2.6. Military Recruiting. This is to notify potential applicants that each grant awarded 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 cooperative agreements, 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 http://ecfr.gpoaccess.gov/. 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 grant awarded 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.

VI.2.7. 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).

VI.2.8. It is the policy of the DoD that the publication of products of basic research will remain unrestricted to the maximum extent possible. Pursuant to DoD policy, awardees are strongly encouraged to publish the results or findings of their research in peer-reviewed journals.

VI.2.9. 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)).

VI.2.10. 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).

VI.2.11. 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.

VI.3. Reporting. General requirements are provided below; however, each grantee should check the award agreement and its terms and conditions to determine the requirements for that specific award.

Annual Research Performance Progress Report(s): Annual progress reports will be due no later than 1 July of each year. Awards effective after 31 January will not require a progress report until 1 July of the following year.

Final Technical Reports: A comprehensive final technical report is required at the end of an effort, due on the date specified in the terms and conditions of the grant document. The purpose of the final report is to document the results of the effort. 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).

Federal Financial Reports (SF-425) are due annually by the date specified in the terms and conditions of the grant document. All reports shall be submitted to the Administrative Office identified in the Research Grant and as outlined in the Terms and Conditions of the award document.

VI.4. After-the-Award Requirements. 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).

VII. AGENCY CONTACTS

VII.1. All administrative and programmatic correspondence should be directed to: HDTRA1-BRCWMD-A@mail.mil.

Every effort will be made to provide a timely response to all inquiries; however, e-mails may not receive a response. Attachments will not be reviewed.

VII.2. Specific technical correspondence regarding the thrust areas as well as the topics may be directed to the following e-mail addresses:

Thrust Area 1: HDTRA1-BRCWMD-TA1@mail.mil

Thrust Area 2: HDTRA1-BRCWMD-TA2@mail.mil

Thrust Area 3: HDTRA1-BRCWMD-TA3@mail.mil

Thrust Area 3 (CB): HDTRA1-BRCWMD-TA3-CB@mail.mil

Thrust Area 4: HDTRA1-BRCWMD-TA4@mail.mil

Thrust Area 5: HDTRA1-BRCWMD-TA5@mail.mil

Please note that technical correspondence e-mails may or may not be reviewed and responded to; **attachments will not be reviewed**.

VII.2.1. Dialogue that assists the applicants in developing better pre-application white papers and invited proposals is encouraged.

VII.2.2. Questions regarding debriefing summaries for pre-application white papers that are invited to full proposals are encouraged.

VII.2.3. Requests to reconsider pre-application white papers and/or proposals, requests for additional information beyond the debriefing summaries for non-invites/non-selections, and rebuttals to the debriefing summary (e.g., additional data, further explanation, etc.) WILL NOT be considered under any circumstances.

VIII. OTHER INFORMATION – TOPICS

VIII.1. Topics for future periods with corresponding pre-application white paper due dates will be published via amendments to this BAA. 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.

VIII.2. This BAA, in addition to any amendments issued in conjunction with this BAA, will be posted to the Grants.gov Grant Opportunities Website (www.Grants.gov) and for informational purposes to the DTRA Basic and Fundamental Research Portal (www.dtrasubmission.net/portal).

Note: The DTRA Basic and Fundamental Research Portal (www.dtrasubmission.net/portal) is available to all applicants. Information available at the portal includes, but is not limited to, the following: a detailed timeline for this BAA, templates that may be used when preparing pre-application white papers and invited proposals, sign-in for applicants to view the status of their submission(s), and a list of previous awards made by the Basic Research for C-WMD Program.

DTRA Basic Research Needs

PerF-Topic 1: Plasma Chemistry for Nuclear Forensics (Thrust Area 1)

Average Award Amounts for PerF-Topic 1:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 1:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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: Immediately after a nuclear detonation, complex chemical and physical processes take place in the fireball. The material from the device and the surrounding area interact as plasma which eventually cools to produce a condensate of physical material as fallout debris. An in-depth understanding of the thermodynamics and kinetics within the fireball, including mixing of various materials present at a detonation site, and the resultant particle agglomeration, particle size distribution, chemical speciation, and other related phenomena of fallout formation at the extreme temperatures and pressures within and near the fireball at time scales extending from initiation to multiple seconds is needed.

The DoD provides the capability to collect and analyze post-detonation debris. DTRA is responsible for research and development that will enable this post-detonation forensics. Currently, models such as DELFIC and HYSPLIT exist but increased fidelity will enhance the speed of response both in terms of fallout modeling and useful/effective debris sample acquisition. Of interest are innovations that will help provide more robust and accurate information used to predict the resultant fallout debris field.

Disciplines which may advance the knowledge base for plasma chemistry for nuclear forensics include but are not limited to high temperature chemistry, physics, materials science, plasma physics, mathematics and statistics, computer science, and modeling and simulation.

Impact: An increased understanding of fireball plasma chemistry for nuclear forensics addresses DTRA's counter-WMD need to enable identification of those responsible for a nuclear attack, and improved response and recovery efforts. Such research has the potential to increase the accuracy of modeling and simulation for prediction of fallout plumes, leading to enhanced collection of debris for forensic analysis as well as protection of populated areas.

Objective: This topic seeks a greater understanding of the complex chemistry and physics taking place shortly after a nuclear detonation. Breakthrough methodologies are sought to enhance our understanding of plasma chemistry and related processes inherent in a nuclear event fireball, from blast to fallout (temperatures of 1 eV or lower). Specific interests include thermodynamics, kinetics, mixing of surface material, particle agglomeration, particle size distribution, plasma chemistry, dusty plasmas, and chemical speciation. White

papers proposing research on nuclear weapons effects, nuclear weapons environments, and/or radionuclide environmental fate and transport are not a primary focus of this topic. Proposals that engage government laboratory institutions are permitted and encouraged.

Research areas may include but are not limited to the following areas:

- Thermodynamic properties
    - Henry's law constant for noble gases in matrices
    - Gibbs free energy
- Chemical kinetic properties
    - Effects of temperature
    - Effects of pressure
- Methods to quantify amounts of specific material entrained in detonation fireball
- Methods to quantify particle agglomeration, including rates, sizes, etc. at the various temperatures and pressures within the fireball
- Determination of chemical speciation of fireball condensates (e.g. hydrides, oxides, nitrides) and their formation kinetics

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PerF-YIP-Topic 1: Plasma Chemistry for Nuclear Forensics (Thrust Area 1)

Average Award Amounts for PerF-YIP-Topic 1 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 1.

PerF-Topic 2: Basic Research on Prompt Diagnostic Signatures of Nuclear Detonations for Forensics (Thrust 1)

Average Award Amounts for PerF-Topic 2:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 2:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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: This topic explores research that may enable accurate knowledge of the specifics of a nuclear device (e.g., special nuclear material type and mass, device sophistication, etc.) after a detonation. Ideally this knowledge would be available in as short a time as possible with a high degree of confidence. The Defense

Threat Reduction Agency is responsible for research and development that will enable an improvement in post-detonation technical nuclear forensics capabilities. This topic investigates basic physical research on the prompt signatures of nuclear explosive events, such as novel methods for yield determination, device reaction history, or the radiation outputs of these nuclear explosions. Research could focus on the understanding of unique identifiers of these explosions, measurements of these identifiers, or other topics. In this context, prompt signatures indicate those which can be measured instantaneously to within a few hours after the event. These signatures are generally separate from radiochemical signatures that may require multiple days to collect and analyze.

Impact: Research into the prompt signatures will enable rapid technical nuclear forensics supporting attribution. Knowing the specifics of a nuclear device (e.g., special nuclear material type and mass, device sophistication, etc.) in as short a time as possible, with a high degree of confidence, is the ultimate goal of technical nuclear forensics. Shortening the timeline for when knowledge becomes available could have a revolutionary impact on the technical nuclear forensics timeline. A full exploitation of the prompt diagnostics of the nuclear event has the potential to greatly reduce the attribution timeline because of the immediate nature of these important signatures.

Objective: This topic explores novel methods and techniques in the measurement and analysis of the prompt diagnostic signatures of nuclear explosions for forensics purposes. A specific interest is the investigation of the prompt signatures of nuclear explosive events, such as novel methods for yield determination, device reaction history, or the radiation outputs of these nuclear explosions.

Research areas may include but are not limited to the following areas:

- Investigation of methods to fuse multi-modal data to determine the explosive yield and reaction history of a nuclear event.
- Investigate absorption and attenuation of Teller light in complex environments
- Exploration of methods to measure the gamma ray spectrum of a nuclear event.
    - Investigation of techniques to account for scattering effects of radiation transport
- Novel techniques for determining information about the nuclear explosion from radiofrequency (RF) measurements.
    - Exploration of the use of RF bands to determine turbulence
- Investigation of optical properties of air for signal propagation, exploring reflection and attenuation coefficients as a function of air composition and frequency

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PerF-YIP-Topic 2: Basic Research on Prompt Diagnostic Signatures of Nuclear Detonations for Forensics (Thrust 1)

Average Award Amounts for PerF-YIP-Topic 2 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 2.

PerF-Topic 3: Radiation Effects in Wide Bandgap Semiconductor Materials (Thrust Area 3)

Average Award Amounts for PerF-Topic 3:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 3:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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: Ultra-wide bandgap and wide bandgap materials (WBMs, where E_g >3 eV) possess many physical properties which are superior to those of silicon (Si, ~1.1 eV) and gallium arsenide (GaAs, ~1.4 eV) for electronics application that require fast switching or power handling, including breakdown electric field, electron or hole mobility, and thermal conductivity. These improvements in material properties should enable improvements in the radio frequency (RF) electronics and power systems which incorporate them – notably in breakdown voltage, switching frequency, power efficiency, current density, and operating temperature.

WBMs also possess two other improvements over Si and GaAs–increased threshold displacement energies and electron-hole pair formation energies – which should enable an essential property for DoD-critical RF and power systems: greater radiation insensitivity. Certain critical systems must be able to operate in challenging radiation environments (both natural and manmade), and this ability is normally achieved through some combination of component derating (which effects performance), hardening techniques (which may be a significant expense in terms of time, weight, and cost), and monitoring methods (which shut down devices before permanent damage can occur).

Silicon carbide (SiC) and gallium-facing gallium nitride (GaN) are two wide bandgap materials whose development have resulted in improvements to the RF and power systems essential to the DoD. However, various SiC and GaN devices have also exhibited problematic radiation effects. For example, GaN-based devices which use high mobility two-dimensional electron gases may encounter band bending and mobility degradation caused by interface strain, charge trapping, or Frenkel defect formation. Radiation effects observed in SiC power devices include increased leakage currents, anomalous charge amplification, or regenerative currents which lead to breakdown. The current understanding is that these are the result of ion-induced impact ionizations at high voltage or low-resistance paths caused by interactions between recoil-induced defects and as-grown defects.

Concurrent with the significant investments and advances made in GaN and SiC, intense research in a collection of other WBMs (AlN, N-polar GaN, n-type diamond, β-Ga_2O_3 and other oxides) has accumulated sufficient knowledge of the fundamental physics which govern these materials and their growth processes to enable the low-defect growth of these materials. These materials offer additional enhancements over SiC and Ga-facing GaN, such as: even wider bandgaps, further improvements in physical and electrical properties, simpler growth processes, integration with silicon processes, and greater anticipated radiation hardness.

With as-grown defects sufficiently minimized, radiation effects in test devices that incorporate these wide bandgap material systems may now be comprehensively examined and understood at the basic research level.

Impact: Understanding the effects of radiation in these alternate WBMs may enable the development of radiation-insensitive wide bandgap devices for critical power and RF applications with fewer hindrances to fabrication, integration, or performance than SiC and Ga-polar GaN. WBMs which offer inherent radiation

hardness from the start may mitigate the need for costly radiation hardening procedures later in the development cycle while enabling future devices to fully utilize the important improvements they offer over Si, GaAs, SiC, and GaN.

Objective: The objective of this topic is to understand the fundamental physics of radiation effects in wide bandgap and ultra-wide bandgap materials and devices with potential applications in RF generation and power switching. Total dose effects, displacement damage, and single event effects are of interest.

Possible wide bandgap and ultra-wide bandgap materials include, but are not limited to:

- N-face GaN
- β-Ga_2O_3
- c-Boron nitride
- Other wide bandgap oxides appropriate to RF and power devices
- Diamond
- AlN

This topic is **not** interested in materials or devices intended primarily for logic or memory applications. **Nor** is it focused on reducing the defects accrued during material growth.

Prospective investigators are encouraged to collaborate with NASA, DoD, DoE and other federally sponsored and overseas facilities in order to facilitate transition of the research to be performed to practice.

PerF-YIP-Topic 3: Radiation Effects in Wide Bandgap Semiconductor Materials (Thrust Area 3)

Average Award Amounts for PerF-YIP-Topic 3 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 3.

PerF-Topic 4: Radiation Effects in Non-Conventional Computing Approaches (Thrust Area 3)

Average Award Amounts for PerF-Topic 4:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 4:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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 and other critical DoD systems must operate in environments with high levels of natural radiation and survive the higher doses and dose rates of a manmade nuclear event. Traditionally the most vulnerable components, the digital computing microelectronics, have been protected by brute force hardening techniques. Digital computing, particularly using charge based devices in a traditional von Neumann architecture, is intrinsically susceptible to propagating errors and performance degradation caused by the effects of radiation. Traditional hardening of digital computing systems involves multiple hardening techniques including; material selection, process control, circuit design, layout optimization, triple redundancy, and software based error detection and correction. While these techniques have proven successful historically, they add cost, development time, complexity, and weight to critical systems. This traditional approach is further challenged by the availability of commercial rad-hard parts and the business trends in commercial semiconductor foundaries.

Several alternative computational approaches are in development that may be more intrinsically radiation resistant than the classic digital approach. Some of these alternate approaches, such as neuromorphic computing, quantum computing, and optical computing are being developed for their ability to address hard computational problems, such as image recognition and cryptography, faster and more efficiently. Neuromorphic computing seeks to emulate the low power, highly interconnected, and highly parallel computational processes used by neurons in the brains of living systems. This computational approach may be able to inherently correct upsets or transients caused by high energy particles and adapt to shifts in device performance caused by charge accumulation or displacement damage. Quantum and optical computing approaches are still in the early stages of development and it is difficult to predict the development timeline and what a final implementation might look like. However, as non-conventional computational approaches, they may also be intrinsically resistant to single event effects and significant work has already been done on error correcting in quantum computing.

Impact: Non-conventional computational approaches have the potential to offer orders of magnitude improvements in computational power and efficiency, especially for computationally hard problems such as pattern or image recognition. These non-conventional computing approaches also have the potential to operate reliably in high radiation environments due to an intrinsic system level radiation effects resistance rather than requiring extensive hardening.

Objective: Investigate the effects of radiation (gamma, neutron, proton, and heavy ion) on non-conventional computational approaches. Effects caused by single high energy particle strikes, as well the cumulative effects caused by total ionizing dose and displacement damage are of interest. This topic is interested in understanding the device level and computational level effects of radiation on non-conventional computation approaches through investigations of the fundamental physics of radiation interaction combined with theory, modeling, and simulation. This topic **not** interested in developing or fabricating unconventional computational devices. Some development and testing of devices and logical approaches or computational frameworks may be necessary to better understand potential radiation effects.

PerF-YIP-Topic 4: Radiation Effects in Non-Conventional Computing Approaches (Thrust Area 3)

Average Award Amounts for PerF-YIP-Topic 4 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 4.

PerF-Topic 5: Understanding Plasma Surface Discharges Generated by X-rays: Effects on Active Satellite Solar Arrays (Thrust Area 3)

Average Award Amounts for PerF-Topic 5:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 5:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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: Space systems are used to coordinate mission-critical information in all operational systems which impact the mission performance of the U.S. warfighter; policy, logistics, operations, reconnaissance, planning. Photovoltaic arrays are the components which power these systems in orbit around the Earth. To guarantee support when it is needed, these arrays and the systems they power must have very high reliability which includes robustness against prompt nuclear radiation doses, particularly x-rays.

Most modern satellites employ solar arrays that consist of multiple cells connected in series to form "strings" to achieve the desired voltage. The strings of cells are constructed in parallel connections to achieve the necessary current and the solar cells are typically protected by anti-reflective coated (e.g.: MgF2) insulating cover glasses and mounted on insulating composite substrates. The normal operating voltage of an array is typically less than 100 Volts and the potential gradients will not cause breakdowns of the dielectric supporting structure. The space radiation environment (high energy electrons, X-rays, gamma rays, etc.) can build up charges in the dielectric surfaces that can generate electric potentials large enough to cause a dielectric surface breakdown between cells or from a cell to a conducting satellite structure. If the breakdown is localized and only discharges the stored charges in the dielectric materials, the array typically is not significantly damaged. However, if once initiated, the breakdown results in an arc that is driven by a sustained current generated by the solar array, it can cause failures of the array panel.

How the prompt x-ray dose from a nuclear event in space produces surface plasma and its subsequent behavior to include arc formation in satellite solar arrays is currently 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 by the high dose-rates. The plasmas can span the dielectric surfaces and couple the biased solar cells to each other and to spacecraft structures. The subsequent potential to support breakdowns and arc formation in the presence of the plasma, the nature and temporal behavior of the plasma, and the effective conductivity across dielectric surfaces are not well understood or modeled.

As an 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. The Omega laser was used to drive an aerogel target to generate ~2 nanosecond long x-ray pulses. 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 ~1 keV ranged from 0.03 – 0.3 Joule/cm^2. 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. Comparable and lower fluence is also of interest,

Impact: Understanding the mechanisms which govern plasma discharge formation and its scaling with x-ray spectra, fluence and pulse width will direct future design efforts to manage these events and their consequences on space systems. The expectation is that this will eventually result in better, more cost-effective ways of designing future space system solar arrays that are not vulnerable to natural and nuclear radiation effects.

Objectives: The overall objective of this topic is to explore the fundamental physics of the generation and properties of the warm, dense plasma that can be generated by X-ray exposures and may lead to low voltage-drop discharges across typical solar array dielectric surfaces. Experimental, theoretical, modelling, and computational efforts that accurately describe, predict, and replicate the phenomenon are of interest to DTRA. All efforts should be focused on discovering the fundamental science that explains the formation and evolution of high conductivity discharge paths between two metallic electrodes and across an exposed dielectric surface in a nuclear-weapon-enhanced space radiation environment, not on engineering approaches that seek to develop new methods for mitigation or new solar array designs.

Research areas may include but are not limited to the following areas:

- The time-dependent interaction 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 of conductive paths across dielectric surfaces
- The nature of electrical conduction properties of the surface plasma generated in the aforementioned range for discharges driven by the voltages and currents typically generated by a solar array. Models should be validated with experiments using laser- or pulsed-power-driven x-ray sources

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PerF-YIP-Topic 5: Understanding Plasma Surface Discharges Generated by X-rays: Effects on Active Satellite Solar Arrays (Thrust Area 3)

Average Award Amounts for PerF-YIP-Topic 5 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 5.

PerF-Topic 6: Bridging the Gap: From In Vitro to In Vivo Studies for Radiogenic Disease Risk Estimation (Thrust Area 3)

Average Award Amounts for PerF-Topic 6:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 6:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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 U.S. military annually monitors 70,000 individuals, amounting to ~2% of its workforce, for occupational ionizing radiation exposure[1]. The DoD has the largest integrated radiation exposure of any federal agency (59% in 2006)[2] and has the potential for radiation exposure of its affiliated individuals during a nuclear or radiological event[3]. The U.S. military supports independent scientific studies to ascertain whether service members have experienced adverse health effects as a result of their radiation exposure[4], although determining the link between exposure events, cellular "initiating events", and development of latent disease states remains a challenge. In the absence of such knowledge, devising systematic approaches to prevent "after-battlefield" effects will be nontrivial. Gender-based differences compound the problem, as relative sensitivities to radiogenic disease development[5] may dictate use of more refined and individualized therapeutic approaches.

Current attempts to estimate radiogenic disease risks at doses between 0.1-1 Gy based upon epidemiological studies carry significant uncertainties, as demonstrated by the large standard errors associated with excess relative risk for virtually every exposure-correlated disease state[6]. The task of quantifying excess relative risk is problematic for many reasons related both to the general vagaries of properly parsing and interpreting epidemiological data and to the difficulties in determining the key cellular events that lead to adverse outcomes like radiocarcinogenesis[7,8]. The nature of the dose-response curve and defining thresholds at which deterministic versus stochastic events may predominate are hotly debated issues. Although increasingly more sophisticated approaches are being applied to the problem of epidemiological uncertainty, epidemiological studies alone are unlikely to yield desired information on cellular changes which probabilistically favor the development of radiogenic disease.

Instead, targeted research that evaluates informational content in existing studies and relevance of selected biological markers to disease initiation could be useful in teasing out causal relationships between cellular alterations resulting directly or indirectly from radiation exposure and whole animal responses. A wealth of *in vitro* and *in vivo* data is already available, thus it may be prudent to integrate and analyze those data before conducting additional laboratory studies, in order to make best use of available resources: "…circumstances require that we move away from an overdependence on in vivo testing and make greater use of computational…tools" in order to "minimize reliance on resource-intensive testing approaches[9]." Recent advances in the fields of bioinformatics and systems biology provide promise that computational approaches can be successfully applied to the present task.

Impact: Conducting the work described herein will help to identify initiation events and pathways for radiogenic disease at doses relevant to warfighter and C-WMD missions. The information can be used to make better use of available therapeutic interventions to combat latent diseases associated with radiation exposure and reduce "after battlefield" effects. As importantly, identification of trigger events characteristically associated with development of latent effects will enable likewise identification of targets for protection. Knowledge gained as a result of these studies can be applied to design of "smart" radioprotectants specifically tailored to prevent damage to identified cellular targets. The long-term benefit will manifest as reduced mortality and morbidity for the warfighter which will increase mission effectiveness as well as reduce long-term healthcare costs.

Objective: The overarching goal is to identify molecular targets whose perturbation acts as a primary initiating event for or significant contributing event to development of latent radiogenic disease. Moreover, synthesis of existent data is desirable in order to identify critical gaps in knowledge and provide an analytical framework to guide future studies. The present topic focuses in particular upon radiocarcinogenic phenomena and seeks

bioinformatics approaches which can convincingly reconcile data from *in vitro* and laboratory *in vivo* studies such that correlations between observed damage and response pathways in discrete cell lines and development of solid tumor cancers in [non-human] animal model systems can be elucidated. Proposed efforts should be purely computational and should make use of existent *in vitro* and *in vivo* datasets available in archives, literature, and unpublished studies where applicable. Studies designed to identify biomarkers or for development of radiobiology profiles to guide radiotherapy treatment regimens will not be considered.

The Life Span Study and others document the relative sensitivity differences between males and females with respect to development of bladder, lung, colon, stomach, and other solid tumor cancers, thus actuation pathways for such cancers are of particular interest. Applicants should focus on studies that evaluate effects of low-LET radiation doses within the range 0.1 – 1 Gy, where estimations of excess relative risk in exposed populations suggest linearity of the relationship between dose and response. Thyroid and blood cancers which deviate from the linear dose-response model, at least in the range indicated, are not desirable study endpoints for the work described herein. Consistency of dose rates among the studies evaluated should be sought, where possible. Proposals to interrogate biological effects outside of the specified dose range are not considered responsive.

Applicants should delineate and justify assumptions, including those associated with hypothetical cause-and-effect relationships between proposed indicators and outcomes. Likewise, ample rationale should be provided for selection of data types (e.g., biomarkers versus bioindicators, -omics changes versus gene amplification, and so on) and choice of model systems. Proposals should clearly establish that model systems are appropriate surrogates for warfighter populations. Competitive proposals will incorporate sensitivity analysis and risk mitigation plans, especially for cases where small changes to assumptions may result in large changes to end-state predictions. Proposals should explain methods that will be used or developed to quantify uncertainties.

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PerF-YIP-Topic 6: Bridging the Gap: From In Vitro to In Vivo Studies for Radiogenic Disease Risk Estimation (Thrust Area 3)

Average Award Amounts for PerF-YIP-Topic 6 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 6.

PerF-Topic 7: Isotopic Discrimination using Biological Systems (Thrust Area 3)

Average Award Amounts for PerF-Topic 7:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 7:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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 is charged with providing for sustainment of operations in CBRNE environments. Detection of fissile material, which may be identified either directly or through characteristic fission products, is necessary to support this aim. Extant detection technologies require collection of material for off-site laboratory analysis, whereas on-site systems are relatively non-specific and require extensive logistical support. Biologically-based detection systems which can report the presence of specific isotopes characteristic of nuclear activity may provide an attractive alternative to conventional methods. Previous research has demonstrated the remarkable selectivity of biological systems for specific analytes at the exclusion or near-exclusion of others. Moreover, even when analyte is no longer present within the system, physiological changes resulting from exposure can persist and are detectable.

The present topic seeks novel solutions for detection and discrimination of signatures indicating proximity of nuclear processes, with a particular focus on use of indigenous biological systems for said purpose. Signatures are limited to isotopes indicative of nuclear fuel cycle or weapon development activity. The anticipated end-state capability is a reliable biosensor of radionuclide exposure or accumulation for use in environments characterized by low levels of contamination.

Exposure to ionizing radiation (IR) is characterized by genetic mutations, modifications to cellular pathways and associated –omics expression patterns[1,2], structural alterations[3,4], and organellular dysfunction[5,6]. Organismal response to low dose irradiation is different from that of high dose exposure, thus simple extrapolation from the well-defined effects consequential to high doses is not expected to be predictive of changes induced by low level exposures. Further, the quality or linear energy transfer (LET) of the radiation can alter the radiation response[7]. High-dose IR will, among other effects, damage DNA and elicit a damage response that activates repair[8]. Low dose radiation (LDR), defined here as < 0.1 Gy, will elicit responses such as an adaptive response (AR), genomic instability, hypersensitivity, and the bystander effect. Ultrastructural changes to organelles such as the

mitochondria[5] and lysosomes[6] may be correlated with observed effects and could prove useful as proxy indicators of exposure. However, the hypothetical mechanisms by which they contribute to cellular damage have yet to be experimentally validated. LDR responses have been shown to include phenotypic modifications driven by processes such as DNA methylation, histone modification, and expression of noncoding RNAs such as microRNAs (miRNAs) and ling noncoding RNAs (lncRNAs)[7,9]. Additionally, LDR has been shown to induce changes in DNA methylation that are tissue specific and exhibit dose and time dependence[8]. Such modifications may also result from exposure to other toxicants, such as heavy metals[10]. Recent work has demonstrated that microbial communities characteristically exhibit specific protein isoforms in the presence of Pb, as in uranium mine tailings[1], and preferentially produce certain types of porphyrins following UVB exposure[4], although dose- and isotopic-dependencies have not been further investigated for these markers.

Taken together, the aforementioned results suggest that identifying biological profiles indicative of internal or external exposure to a specific radionuclide or distinguishing among exposures to different isotopes of a particular element is possible. The research described herein is designed to establish, characterize, and determine the stability and consistency of profiles resulting from exposure to selected radionuclides of interest.

Impact: The fundamental knowledge generated as a result of these research efforts will be broadly applicable to core DTRA requirements for supporting the warfighter during CBRNE operations. In addition to addressing existent capability requirements, detailed characterization of radionuclide exposure profiles in organisms will provide the baseline understanding necessary to engineer field detection technologies in response to novel and emerging threats. Finally, the development of radionuclide detection technologies to address a number of diverse mission needs is of paramount interest to the DoD and is critical to maintaining technological advantage.

Objective: The overarching goal is to determine the feasibility of characterizing measurable biological responses that are specific to a mode and level of energy transfer to the cell (alpha, beta, gamma, and neutron) and can differentiate among elemental sources. Interrogation of micro- and macro-organisms is acceptable, provided the organisms are either ubiquitously distributed or, if indigenous, expected to be present in some abundance in ecosystems of interest. Geographical ranges for selected organisms should be limited and/or well-defined. Research efforts should focus on sentinel organisms for which a reasonable amount of biological information is available, and life cycles of either populations or individuals (dependent upon model system) should be compatible with periodicity of contamination events. Appropriate model systems are those which have a high likelihood of exposure to radiation as a result of their natural ecologies.

Both discriminatory power and persistence of biological signal should be evaluated. Biological signals are broadly described as "organismal responses" in the background section but may include others, provided there is literature precedent that provides reasonable expectation of utility for the present purpose. Proposed studies should include necessary controls to validate specificity of response to radiation as opposed to other toxicants (e.g., heavy metals) or endogenous / exogenous conditions that could instigate similar responses.

Relevant elements and isotopes, as well as environmental fates and chemistries which would dictate biological availability, should be established by reviewing standard nuclear engineering texts and other documents. Competitive submissions will demonstrate that both levels of exposure and forms of the elements and isotopes being investigated are reasonably anticipated to be correlated with likely releases and release amounts for nuclear processes of interest. Useful signatures are those uniquely relatable to processes of interest and for which little or no background signal is anticipated to be present. Preliminary research can establish proof-of-concept for biological response, but option year plans should propose means to establish that limits of detection are congruent with expected environmental level(s) for a given analyte.

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PerF-YIP-Topic 7: Isotopic Discrimination using Biological Systems (Thrust Area 3)

Average Award Amounts for PerF-YIP-Topic 7 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 7.

PerF-Topic 8: Dynamic Characterization of Post-Detonation Fireballs Involving Agent Defeat Additives and Agent Simulants (Thrust Area 4)

Average Award Amounts for PerF-Topic 8:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 8:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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: Prompt counter-WMD operations in non-permissive or access-denied environments often require energetics to effectively defeat a target (i.e., those containing WMD targets with biological and chemical agents). Destruction during the counter-WMD operation and post-operation neutralization by the environment need to be characterized and understood to evaluate the full effect of counter-WMD operations on targets containing chemical agents, simulants and precursors. Characterization capabilities are needed to assess the confidence in immediate lethality of a weapon formulation against an agent and potential longer term viability of the threat. There is a great need to develop next-generation diagnostic techniques to effectively characterize the physical and chemical processes occurring during rapid combustion in an expanding fireball, particularly those interacting with WMD agent. Challenges for rapid diagnosis include optical thickness of the associated fireball (approaching 5-6 logs) and harsh pressure and temperature environments that may damage equipment in or near the fireball.

New techniques utilizing both novel materials and sources for measuring interactions of weapons with WMD targets containing viable agents are highly desired. Both spatially resolved measurements and standoff measurements may offer additional insight into these interactions. Dynamic characterization will provide information for modeling and simulation efforts, from microseconds to seconds of the expanding fireball. Key parameters of interest include species concentrations, chemical identification and temperature field. Newly developed techniques would initially be applied to agent simulants. Innovative use of the combination of coherent or quasi-coherent photons, material science, and modeling may allow reconstruction of the spatiotemporal evolution of post blast field involving CWMD weapon additives and agent simulants.

Impact: The immediate potential payoff of these research efforts is expected to be the development of dynamic characterization techniques that will enable the ability to measure parameters such as agent species and concentration which will vastly improve blast and weapon modeling. The primary focus would be to extract the species and concentration data. Knowledge of species and concentrations as a function of space and time are critical for predicting a weapon's effectiveness and lethality against chemical-agent containing WMD targets. Other parameters such as localized time-dependent temperature inside the fireball may be simultaneously measurable using these new techniques. Previous investments in temperature sensors provided limited temporal information. With the new techniques being sought, more critical temporal data may be feasible. The optimization of these tools 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 chemical weapon agents, reduce or eliminate collateral effects and enhance post-strike assessments, in all attempts to successfully destroy WMD in hostile environments.

Objectives: The objective of this topic is to support basic research in characterizing the extreme environment of an emerging fireball containing agent defeat additives interacting with chemical agent simulants. There is a lot of interest in the ability to increase pulsed probing rates significantly beyond kHz (toward MHz). Primarily, interest is in tracking the evolution of key species and concentrations of weapon additives and simulants within the fireball; however, innovative approaches looking at regions slightly removed from the most optically dense region may also be considered.

Characterization capabilities may include, but are not limited to:

- Identify and measure species concentrations using absorbance beyond kHz repetition rates
- Photoacoustic techniques appropriate for highly transient environments
- Linear and nonlinear optical techniques appropriate for characterizing species and species concentrations within high optical thickness environments (approaching 5-6 logs signal reduction)
    - Enabling research on optical sources and transport materials for probing key spectral regimes (e.g. fingerprint region of simulants)
- Reconstruction of temporally resolved temperature fields in and around the blast of the energetic material and simulant
- Post-blast material analysis and model validation to support spatiotemporal fireball characterization

PerF-YIP-Topic 8: Dynamic Characterization of Post-Detonation Fireballs Involving Agent Defeat Additives and Agent Simulants (Thrust Area 4)

Average Award Amounts for PerF-YIP-Topic 8 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 8.

PerF-Topic 9: Photochemistry of Organohalides and Agent Simulants (Thrust Area 4)

Average Award Amounts for PerF-Topic 9:

- Single Scope Awards will average approximately $100,000 to $150,000 per year.
- Multidisciplinary Awards will average approximately $200,000 to $300,000 per year.

Award Structure for PerF-Topic 9:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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: Prompt defeat of agents relies heavily upon energetic systems creating conditions for thermal decomposition or chemically generated reaction pathways, both leading to defeat of the agent. This topic is intended to investigate mechanisms generated via controlled interaction between optical frequencies and energetic systems containing organohalide molecules and other additives (metals and oxides). The ability to control reactions involving organohalide molecules may lead to enhancements in desired performance for agent defeat.

Current laser technologies offer great potential for highly controllable optoelectronic interactions with molecules. Controllable laser parameters include wavelength, intensity, phase control, etc. Lasers offer the ability for controlled decomposition of organohalide molecules and chemical agent simulants. We desire to understand the limits of photo induced control for decomposition and reactions involving potential additives and agent simulants. Better understanding of these photo-controlled processes may lead to new understanding of potential reaction pathways and formation of possible toxic intermediates/products.

Impact: Prompt defeat of agents is typically carried out in access denied environments through traditional energetics and is challenging to control the reaction mechanisms and energy release rate. This work may demonstrate the viability of controllable mechanisms involving optical fields and small scale energetics and agents. This effort work may lead to knowledge resulting in increased lethality against viable agents.

Objectives: The objective of this topic is to support basic research using coherent photons to control the decomposition pathways of organohalide molecules and those interacting with organophosphorous agent simulants and coated spore simulants. We want to identify conditions for molecular decomposition of organophosphorous agent simulants. We are primarily interested in experimental efforts, but will consider complementary theoretical/computational efforts.

Research areas may include, but are not limited to the following:

- Photocontrol of reaction mechanisms for decomposition of organohalides
- Photo induced interactions of organohalides with organophosphorous simulants
- Optical interactions involving additives (such metals and oxides) with simulants
- Nonlinear optical interactions directly with agent simulants (i.e. organophosphorous molecules and coated spore simulants)

PerF-YIP-Topic 9: Photochemistry of Organohalides and Agent Simulants (Thrust Area 4)

Average Award Amounts for PerF-YIP-Topic 9 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 9.

PerF-Topic 10: Novel Signatures and Methodologies to Monitor Very Low Yield Explosions (Thrust Area 5)

Average Award Amounts for PerF-Topic 10:

- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerF-Topic 10:

- Will predominately be for a base period of three (3) years with up to two (2) additional years as possible options.
- 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. See Section II.1.1 for details on the possible structure of awards under this BAA.
- 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: Monitoring technologies are noted for their importance to support nuclear arms control and nonproliferation, and to assure compliance with current and future nuclear weapon related treaties/agreements. Countering future weapons proliferation should go beyond current treaty approaches to the problem. It is important to conduct basic research to significantly improve existing approaches, or to identify and understand novel approaches, in order to identify very low yield events that are difficult to observe under traditional international sensor networks. Recent events and historical trends serve to emphasize the continuing need for improvements in nuclear test monitoring because of continued nuclear testing. Seismic methods provide a major means of detecting and characterizing underground explosions. These methods can be augmented by other techniques; e.g., infrasound, hydroacoustic, or radionuclide networks. Sensing and characterization of

suspected nuclear events may involve additional signatures or approaches than those of traditional monitoring systems. For example, there may be environmental factors near an underground explosion that are disturbed. Alternatively, truly novel advances in seismic methods beyond traditional approaches may enable game changing capability in monitoring. Basic research into observable phenomena may yield novel means for understanding events that represent potential nuclear explosions.

Impact: Advancements in fundamental science may foster future technologies that extend both the lower limits and reliability of yield determination; help discriminate between nuclear and non-nuclear events that may be confused with nuclear explosions; and support countering proliferation of nuclear weapons capability. Success in this research will lead to ability to monitor explosions beyond the capability of the current international networks.

Objective: The objectives of this topic are to identify and explore novel approaches to explosion monitoring in order to observe event yields below 1 kiloton equivalent yield, and push the measurement as low as possible toward zero to better advance discrimination globally.

Research areas may include but are not limited to the following areas:

- Conducting theoretical, computational, or experimental studies to significantly improve understanding of geological factors that affect phenomena (i.e., non- seismic particle or energy transport as well as seismic propagation) near the energy source of an event.
- Advancing the body of basic knowledge of seismic signal generation or propagation in the source region of events for extending measurement to as low as possible in yield determination; and, quantitative predictions of transformation of signals from the source to far term propagation.
- Exploring non-seismic approaches to very low yield detection and measurement.

PerF-YIP-Topic 10: Novel Signatures and Methodologies to Monitor Very Low Yield Explosions (Thrust Area 5)

Average Award Amounts for PerF-YIP-Topic 10 will be approximately $100,000 per year.

For topic description and award structure see PerF-Topic 10.

JSTO-CBD Basic Research Needs

The Chemical / Biological Technologies Department basic research program targets strategic, mission-focused basic research investments with high potential impact for the US Chemical and Biological Defense Program (CBDP). Chem-Bio Basic Research is seeking new and innovative proposals for fundamental research in the following topics:

PerF-Topic 11: Rapid Identification and Design of Protective Epitopes for Vaccines (Thrust Area 3)

Average Award Amounts for PerF-Topic 11:

- Single Scope or Multidisciplinary Awards may be up to $500,000 per year. Further guidance on scope and cost may be provided in each full proposal invitation.

Award Structure for PerF-Topic 11:

- Will be for a base period of one (1) year with up to four (4) additional years as possible options.
- 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 goal of this topic is to solicit proposals focused on rapid identification and/or design of protective vaccine immunogens or epitopes that may naturally be masked by non-protective immunodominant epitopes. By doing so, it may be possible to optimize vaccine immunogen design to enhance protective responses to the immunorecessive epitopes of pathogens for which there are currently no prophylactic vaccines. There is an increasing body of evidence that viral and bacterial pathogens express immunodominant B-cell and T-cell epitopes that have evolved to act as decoys to mask or subvert potentially protective responses as a means of evading immune surveillance[1,2]. Such immunogenic but non-protective epitopes are often encoded in regions of the pathogen genome that are highly susceptible to mutation[3]. Furthermore, protective epitopes themselves are often encoded by regions of hypermutable sequence that allows the pathogen to escape a protective immune response[3,4]. Efforts to discover immunogenic epitopes for *Burkholderia mallei* and *Burkholderia pseudomallei* in particular has been stymied due to possible decoy antigens or motifs that misdirect or suppress host immune responses and thus serve as poor immunogens in vaccines. Discovering antigenic motifs that facilitate immune evasion, suppression or modulation by *B. mallei* and *B. pseudomallei* are also of interest in this topic. Selective design and presentation of immunogens and specific epitopes may be key in refocusing the immune response to what have thus far been vaccine-resistant pathogens.

Impact: Identification and presentation of protective B and T cell epitopes of significant biothreat pathogens for which there are no or limited prophylactic medical countermeasures is of interest. These epitopes are often immunorecessive or masked by immunodominant responses that are not protective. Selective expression or redesign of these immunogens/epitopes is a key step in the path to rapid development of vaccines to protect the U.S. warfighter.

Objective: The goal of this topic is to solicit proposals focused on the rapid identification and/or design of protective vaccine antigens. Additionally, identification and optimization of the expression of immunorecessive vaccine immunogens or epitopes to overcome the effects of non-protective immunodominance in biothreat pathogens is of interest. This topic will likely involve both *in silico* and *in vivo* analysis, and selection and modification or design of immunogens. Key to this effort will be the validation of immunogens/epitopes of interest in relevant *in vivo* or *ex vivo* models of immunogenicity. Proposals that aim to identify conserved protective epitopes across multiple biothreat agents are also of interest. Pathogens of prioritized interest are as follows:

1. *Burkholderia pseudomallei* and *Burkholderia mallei*
2. *Coxiella burnetii*
3. *Francisella tularensis*
4. Western, Eastern and Venezuelan equine encephalitis viruses
5. Filoviruses (Ebola and Marburg species)

References:

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Avoids Deceptive Imprinting and Broadens the Immune Response to Foot-and-Mouth Disease Virus" Clin Vaccine Immunol. 2012 Apr;19(4):461-7

PerF-Topic 12: Predictive Computational Modeling of the Immune System to Bridge Animal and Human Immune Responses to Vaccines (Thrust Area 3)

Average Award Amounts for PerF-Topic 12:

- Single Scope or Multidisciplinary Awards may be up to $400,000 per year. Further guidance on scope and cost may be provided in each full proposal invitation.

Award Structure for PerF-Topic 12:

- Will be for a base period of one (1) year with up to four (4) additional years as possible options.
- 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 goal of this topic is to develop, refine and validate computational models of immune responses in humans based on those observed in animal models resulting from vaccination or challenge. There are numerous algorithms available for the prediction of T cell epitopes by MHC and supertype as well as both linear and non-linear B cell epitopes[1-3]. Additionally, software such as Rosetta Antibody has made it possible to predict the structure of an antibody variable region[4]. Beyond the prediction of T- and B-cell epitopes and antibody structure, there is a clear need to develop the capability to predict human cellular and humoral immune responses based on those observed in animal models. While computational epitope prediction is extremely valuable in vaccine development, it does not routinely address the full breadth of functions in the development of any particular immune response. Issues of B cell maturation and somatic mutation, T cell activation and differentiation, host-pathogen interactions, the development of immune memory and cross-species differences in these functions are examples of key gaps that prevent the accurate predictive bridging of immune responses in animals to humans.

Mitigating the absence of predictive immunological bridging across species leads to significant loss of time and efficiency in the process of Animal Rule-based licensure of prophylactic products for emerging infectious diseases and biothreat agents. Applying immunoinformatics, systems biology, genomic and proteomic databases, and computational modeling capabilities currently available should permit the development of sufficient computational tools to bridge animal and human immunologic data to reduce the uncertainty and burden in designing and selecting vaccine modalities, animal studies and human clinical sample analyses in support of FDA licensure. Ideally, this model could also be validated and applicable to lead vaccine selection and optimization.

Impact: Despite the existence of the FDA's Animal Rule licensure pathway for well over a decade, there has not yet been a vaccine licensed under this mechanism. A major hurdle in this pathway lies in bridging animal and human immune data with sufficient confidence to derive a correlate or surrogate of protection. Further upstream, the computational ability to precisely predict human immune responses based on animal data could also generate a substantial gain in lead selection and optimization time.

Objective: The goal of this topic is to solicit proposals focused on the development of *in silico* computational methods for predicting and/or bridging complex human immune responses, including humoral and cellular immunity, to immunogens/vaccination based on those observed in animal models. Modeling of immune

responses to vaccination will likely require, but is not limited to, use of genomic and proteomic databases, immunoinformatics, and systems biology to bridge animal and human immune responses. To establish some degree of reliability, a plan to gather and model animal and human data from FDA licensed vaccines that have an established correlate/surrogate of protection will be imperative. Future plans to model established animal data and DTRA-funded or non DTRA-funded human vaccine trial data may also be included. These aspects may provide some foundations and reliable modeling tools to predict the full breadth of immune responses to vaccine candidates that have not been tested in humans as of yet. The following immunological parameters, albeit additional parameters can be included in proposals, are of interest:

- B and T cell epitope recognition
- Antigen presenting cell profiles
- B cell and T cell profiles including characterization of the BCR and TCR, cellular maturation and differentiation, somatic mutation, and cytokine/chemokine profiles
- Immunological memory, including memory T cell and long-lived plasma cell profiles, and antibody repertoire

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PerF-Topic 13: Relationship of soil environmental "interactomics" and environmental triggers that result in increase in disease incidents for biothreat pathogens (Thrust Area 3)

Average Award Amounts for PerF-Topic 13:

- Single Scope Awards may be up to $500,000 per year. Further guidance on scope and cost may be provided in each full proposal invitation.
- Multidisciplinary Awards may be up to $1,000,000 per year. Further guidance on scope and cost may be provided in each full proposal invitation.

Award Structure for PerF-Topic 13:

- Will be for a base period of two (2) years with up to one (1) additional year as a possible option.
- 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: Due to Next Gen Sequencing (NGS), genomes from virtually all of the bio- and emerging threat bacterial pathogens as well as important near-neighbors, commensal, symbiotic and environmental organisms have now been sequenced. Cladistics analysis of these genomes continues to reveal the relationship and complex ancestral structure of pathogen phylogenetics. The finding that horizontal gene transfer and core and accessory genome recombination and re-assortment have key roles in the fitness of bacterial pathogens has been particularly surprising, even in some organisms previously thought to be "clonal". Many pathogen near-neighbors turn out also to be phylogenetically diverse. Thus, the concepts of pathogen and virulence factor

require contextual views. Recent work on Metagenomics methods, bioinformatics and quality control procedures have steadily improved and can now be employed to explore microbiome and outcomes.

The goal of this topic is two-fold: 1) to identify and characterize relationships, interactions, and dependencies of environmentally-derived bio-threat pathogens with other soil ecosystem and biome elements; and 2) to explore how environmental factors or the reservoir relationships can influence an increase in incidence of disease. Pathogens of specific concern are *Francisella tularensis* and *Burkholderia pseudomallei*. *Francisella tularensis* and *Burkholderia pseudomallei* are highly infectious, aerosolizable pathogens that could potentially pose a threat as biological weapons. Both microbes occur naturally in the environment and are known to cause natural disease incidents in humans and animals.

a) This topic seeks proposals to develop meta-genomic/proteomic approaches and workflows and provide foundational data and insights into whether factors derived from interactions with specific amoeboid, nematode, fungal, or insect predators create or modulate selective pressures that could result in effects on human virulence. Likewise, proposals should aim to shed light on the relationship between these interactions, the relative fitness measurements, and phenotypic expression of known and novel virulence factors, including multidrug resistance. Little is known about the life cycle of *B. pseudomallei*. Limited study with other soil-dwelling biothreats have shown some unexpected interactions in soil (*e.g. B. anthracis* and *F. tularensis* multiply in the phagocytic amoeba Acanthamoeba); but what fitness advantages are gained and how this relates to unique genomic plasticity is unknown. The identification of environmental factors that correlate with presence or absence of these threats and their virulence are needed.

b) This topic also seeks proposals that will explore how naturally occurring disease foci are correlated to large scale environmental factors that could trigger an increase in disease clusters and transmission. *Francisella tularensis*, the source of recent multiple Tularermia incidents, is known to be present in water ways, soil, arthropods and soil dwelling organisms[1,5]. The pathognomic correlates of these disease clusters and mechanisms by which the bacteria were distributed over large distances is still largely unknown. *Burkholderia pseudomallei*, the source of the disease Melioidosis, is also found in water and soil, but other reservoirs and environmental factors could be contributing to its virulence and increases in disease incidents as well. There is some evidence that soil with specific characteristics such as a specific soil texture or organic matter content may influence the persistence of *Burkholderia pseudomallei* [4]. Additional research linking the natural reservoirs, including data from meta-genomic/proteomic portion of the study and the literature, with environmental disease causing triggers would give the biosurvellience community an additional set of parameters to help with predicting future outbreaks. Environmental triggers could include enviro-climate data, arthropod growth cycles and data on complex soil relationships

Objectives: Proposals are sought to provide a basic scientific understanding of:

- The experimental identification and characterization of the relationships, interactions, and dependencies of environmentally-derived bio-threat pathogens with other soil ecosystem and biome neighbors.
- The development and utilization of "interactomic" tools to characterize microbiome interactions
- Determination of relationship of "interactome" constituents to virulence, antibiotic resistance, other phenotypic properties
- Identification of the nature of interaction with ecosystem/biome: host, reservoir, co-factor, *etc.* and what factors enhance risks of ecosystem changes (OneHealth approach).
- Identify the environmental reservoir and triggers that could be leading to increased disease incidents for bacteria of concern to the DoD, specifically *F. tularensis* or *B. pseudomallei*. The goal is to obtain relevant data that would inform predictive outbreak models.

- Explore models and strategies for identifying environmental "hot zones" rapidly, that would inform operations

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PerF-Topic 14: Feasibility of Interstitial Fluid for Biomarker Analysis and Threat Exposure Monitoring (Thrust Area 3)

Average Award Amounts for PerF-Topic 14:

- Single Scope Awards may be up to $350,000 per year. Further guidance on scope and cost may be provided in each full proposal invitation.
- Multidisciplinary Awards may be up to $700,000 per year. Further guidance on scope and cost may be provided in each full proposal invitation.

Award Structure for PerF-Topic 14:

- Will be for a base period of two (2) years with up to one (1) additional year as a possible option.
- 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: Traditional blood-based analytical methods have many drawbacks, such as the requirement of trained personnel for sample collection, as well as the inability of real-time measurements. Skin patches of microneedle arrays were initially developed for vaccine and drug delivery in the 1990s. These arrays inject products into the dermis or epidermis, depending on the length of the needles. Similar skin patches are now under study as a pain-free means to collect biofluids for analysis. However, it is currently unknown how dermal interstitial space analytes will compare to traditional biological fluids.

Impact: To ensure mission success, warfighters need to remain healthy. Early warning of a possible infection or chemical exposure could allow for a more timely treatment regimen which may increase the ability of warfighters to perform their missions. DTRA/CBA continues its efforts to characterize and develop multiplex biomarker panels on classifiers of human (and animal model) early exposure to biological and chemical agents via differential transcriptomic, regulatory, and proteomic expression methods.

Objective: Proposals are sought to explore interstitial fluid as a sample for chemical and biological agent diagnostics and exposure awareness. Attractive proposals will expand the understanding of the interstitial space and how interstitial fluid samples might compare to the host immuno/exposure profile developed from other biological fluids from animal exposure models, with a focus on host-based markers of insult or infection. Work should not be limited to specific microbial or chemical detection, but should provide a broader inventory of all components that might be informative for chemical or biological exposure awareness. This might include cytokines, mRNAs, small RNAs, antibodies, signaling proteins, inflammation markers, small molecule byproducts, etc., to include kinetics and persistence of such markers.

PerF-Topic 15: Influence of Respiratory Tract Components and Particle Dispersity in Aerosol Pathogenesis (Thrust Area 3)

Average Award Amounts for PerF-Topic 15:

- Single Scope Awards may be up to $350,000 per year. Further guidance on scope and cost may be provided in each full proposal invitation.
- Multidisciplinary Awards may be up to $700,000 per year. Further guidance on scope and cost may be provided in each full proposal invitation.

Award Structure for PerF-Topic 15:

- Will be for a base period of two (2) years with up to three (3) additional years as possible options.
- 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 goal of this topic is two-fold. The primary goal is to develop improved predictive understanding of the pathogenesis of toxic particulates, namely aerosolized toxic chemicals and peptide/protein toxins, as a function of (a) modulated molecular and cellular populations of the olfactory, respiratory tract and alveoli as well as (b) aerosol particle characteristics including, *e.g.*, composition, topology, and size distribution spanning a range including but also extending beyond 1-10 microns. The secondary goal is to employ this new understanding to enable novel strategies to prototype respiratory pretreatments and drug delivery methods.

Of particular interest is the role within aerosol pathogenesis of phenotype variation among the populations of alveolar macrophages, mucins, and the respiratory microbial ecosystem, as mediated in part by interactions with the alveolar epithelial cells and immune cells within the olfactory, bronchioles and interstitial space between the alveoli and blood vessels. Changes to these respiratory molecular and cellular components is a major determinant in reaction to toxic smokes and toxicant-induced susceptibility to infection [1,2], but is not well understood within the context of chemical and biological warfare agents. The highly adaptive nature of the alveolar macrophages[3] and their pivotal role in regulation of local immunological homeostasis as well as toxicant scavenging at the primary human/environmental chemical interface makes them a critical node for improved predictive toxicology and development of future medical countermeasures to inhaled chemical and biological threats[4-6].

Within the olfactory and bronchioles, mucus is the major ecological niche for the human microbiota, accommodating microbial densities of 10^{11}–10^{12} cells/mL, a record for any microbial ecosystem documented thus far. The matrix of constituent mucin glycoproteins provides a geometric and diffusive constraint to the distribution of nutrients, toxins, and oxygen[7]. Moreover, recent work has demonstrated the role of particular

mucin components in airway defense[8]. An improved understanding of how the respiratory mucus interacts with and regulates the respiratory microbial ecosystem as well as toxic particulates could therefore lead to improved risk assessments as well as radically new strategies for countering aerosolized threats at their primary initial site of intersection with humans.

Currently, inhalational exposure, infection and toxicology parameters are based on data from animal models, often under specific and limited experimental conditions. Generally, experimental conditions employ aerosol particles in the 1-3 µm range, or more broadly in the 1-10 µm range[9]. However, aerosols or airborne droplets can and do cover a wider size range. Few experiments have examined the role of aerosol particle size in pathogenesis, and those experiments have been restricted to a small number of agents of bioterrorism concern. There is growing evidence that particle size plays an important role not only in toxic dose, but also in pathogenesis and related kinetics.

Aerosols are a major focus of the Chemical and Biological Defense Program due to their role within weaponized chemical and biological agents as well as within potential delivery platforms for medical countermeasures to these threats[10,11]. The mechanisms of action of aerosolized toxicants are diverse, ranging from selective blockage of specific molecular reactions or binding to specific receptors, to those acting at multiple sites or levels[12]. Developing toxicant-specific medical countermeasures for all classes of potential toxicants would be prohibitively expensive. Therefore, pre-treatment strategies for broad-spectrum neutralization of diverse toxicants are of interest to the DoD, including those that are in an early stage of development.

Impact: This topic supports Chemical and Biological Defense Program goals by providing insights into inhaled chemical particulates and toxicants of diverse origins and by providing strategies and platforms for medical countermeasure discovery and development. This information will directly inform the advancement of appropriate chemical medical countermeasures, some of which may rely upon an understanding of aerosol-pulmonary interactions, as well as improved risk assessment capabilities.

Objective: The goal of this topic is to solicit proposals aimed at developing improved predictive understanding of the toxicokinetics and pathogenesis of aerosolized toxicants, with a specific focus on (a) modulated molecular and cellular populations of the olfactory, respiratory tract and alveoli as well as (b) aerosol particle characteristics spanning an extended range. The identification of early-stage strategies and platforms for medical countermeasure discovery and development is also encouraged. Proposals that address any or all of the following will be considered:

- Impact of modulated olfactory, respiratory, and alveolar molecular and cell genotypic and phenotypic variation on cellular penetration of inhaled particulates as well as progression of toxicological and pathogenic effects;
- Development of improved predictive *in silico*, *in vitro*, and low-cost *in vivo* assays and correlations between these models, to enable more accurate and rapid screening of acute pulmonary toxicity and partitioning into systemic circulation, as well as improved mechanistic understanding;
- Structure-property relationships correlating particle size, morphology, and physicochemistry with immunogenic and other interactions at the olfactory and epithelial cells of the alveoli and bronchioles.

Proposals that would support or enable development of strategies and platforms for medical pretreatments or countermeasures against multiple aerosolized threats having similar mechanisms of action will receive priority consideration for funding over those that deal with specific threat molecules.

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