DEFENSE THREAT REDUCTION AGENCY

BROAD AGENCY ANNOUNCEMENT

HDTRA1-11-16-BRCWMD-BAA

Amendment 2 (December 2012)

Research and Development Enterprise

Basic and Applied Sciences Directorate

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

March 2011

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OVERVIEW INFORMATION

1. Federal Agency Name:

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

2. Funding Opportunity Title:

   FY2011 – 2016 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 2016, 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:

   HDTRA1-11-16-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
1 March 2011	BAA announced on Grants.gov
Period A	
CLOSED	
~~2:00 PM EST,8 April 2011~~	~~Phase I pre-application white paper receipt deadline~~
~~2:00 PM EST, 27 June 2011~~	~~Phase II invitation-only proposal receipt deadline~~
January—March 2012	Period A Grants scheduled to be awarded
Period B	
~~1 December 2011~~	~~Amendment to the BAA announced on Grants.gov with Period B topics, application packages, and applicable deadlines~~
~~Midnight EST,~~ ~~13 January 2012~~	~~Phase I pre-application white paper receipt deadline~~
~~Midnight EST, Not prior to 2 April 2012, and not later than 20 April 2012 *~~	~~Phase II invitation-only proposal receipt deadline~~ ~~* The exact due date and time for the full proposals will be provided in the letters of invitation.~~
October—December 2012	Period B Grants scheduled to be awarded
Period C	
3 December 2012	Amendment to the BAA announced on Grants.gov with Period C topics, application packages, and applicable deadlines
Midnight (11:59PM) EST, 14 January 2013	Phase I pre-application white paper receipt deadline
Midnight EST, Not prior to	Phase II invitation-only proposal receipt deadline

5 April 2013, and not later than 3 May 2013 *	* The exact due date and time for the full proposals will be provided in the letters of invitation.
October—December 2013	Period C Grants scheduled to be awarded
Period D	
TBD	Amendment to the BAA announced on Grants.gov with Period D 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 D Grants scheduled to be awarded
Period E	
Period F	
Period G	
……	
Period 'n'	

Table 1: List of important dates

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)

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.

I.2.1. 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]

I.2.2. 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]

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

[1] DoDI 3210.1, September 16, 2005

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

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—Cognitive and Information Science:*** The basic science of cognitive and information 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 "PerC" are only valid for Period C of this BAA. Only pre-application white papers responsive to the topics posted for Period C and submitted by the Period C 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 Amendment 1 labeled "PerA" and "PerB" are NOT valid topics for "PerC". Pre-application white papers that address "PerA" and "PerB" 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.1.1. 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.4) 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.

II.1.2. The POP for the Seed Awards will be for one (1) year or less. Seed Awards may not include option years.

II.2. 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 expects to award 50-75 grants annually for a total grant value of approximately $66M.

II.3. 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.dtic.mil/whs/directives/corres/html/321006r.htm. See also 32 Code of Federal Regulations (CFR) 22, which can be accessed online at http://ecfr.gpoaccess.gov/.

II.4. 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 up to $500K per year for JSTO-CBD Program sponsored topics.

   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 up to $1M per year for JSTO-CBD Program sponsored topics.

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.

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.

II.5. 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.6. 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.7. Applications for renewal or supplementation of existing DTRA funded projects are not eligible to compete with applications for new awards.

II.8. The Government will not provide any hardware or software to execute the proposed research. Exceptions will not be made.

II.9. 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 Research and Applied Sciences Directorate, 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.

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.

III.4.2.1. Applicants (PI/Co-PIs) may submit pre-application white papers and invited proposals to one or more topics.

III.4.2.2. 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.

III.4.2.3. 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.

[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.

IV. APPLICATION AND SUBMISSION INFORMATION

IV.1. Address to Request Application Package.

IV.1.1. This announcement contains all information required to submit a pre-application white paper and invited proposal.

IV.1.2. 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.1.3. 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 must be used for submission of pre-application white papers.**

IV.1.4. 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 must be used for submission of invited proposals.** Application packages for Phase II submissions will be posted following the notification of invitation for proposals.

IV.1.5. Example application packages for both pre-application white papers and invited proposals are included with this posting. These example packages are for demonstration purposes only and must not be used to submit applications pursuant to this BAA. These packages are clearly noted with the Competition ID of "Example" and the Competition Title of "Phase I Example Pre-Application White Paper" and "Phase II Example Application," respectively.

IV.1.6. DTRA WILL NOT review any of 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.
- Application packages submitted using the Competition ID of "Example."

Exceptions WILL NOT be made under any circumstances.

IV.1.7. 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	Phase II Invited Proposal
SF-424 (R&R) Application for Federal Assistance Form	Required	Required
RR FedNonFed Budget Form	N/A	Required
R&R Subaward Budget (Fed/Non-Fed) 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.

IV.2.1. 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.

IV.2.2. 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.2.3. **Phase I Pre-Application White Paper Submission and Content.**

IV.2.3.1. 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.

IV.2.3.2. 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 (Section in the BAA)	Attachment	Action
SF-424 (R&R) Application for Federal	Up to four (4)	Enter the appropriate

Assistance Form (IV.2.4.2.1)	page white paper.	information in data fields

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

IV.2.3.2.1 Each Phase I application package contains the **SF 424 (R&R) Application for Federal Assistance**. To be considered a complete package, an up to four (4) page white paper is required to be uploaded as an attachment to the SF 424 (R&R) (Note: all other BAA guidelines must also be met to be considered a true complete package). 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.** Must be used to attach an up to four (4) page white paper. The white paper itself should provide sufficient information on the research being proposed (e.g., the hypothesis, theories, concepts, approaches, data measurements, and analysis, etc.) to allow for an assessment by a technical expert.

  Any pages submitted for the white paper that exceed the limit of four pages will not be read or evaluated. A page is defined as 8 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).
- 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.2.4. **Phase II - Invited Proposal Submission and Content.**

IV.2.4.1. 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.

IV.2.4.2. 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 (Section in the BAA)	Attachment	Action
SF-424 (R&R) Application for Federal Assistance Form (IV.2.4.2.1)		Enter the appropriate information in data fields
RR FedNonFed Budget Form (IV.2.4.2.2)	Budget Justification for entire performance period	Attach to Section K in budget period one
R&R Subaward Budget (Fed/Non-Fed) Attachment(s) Form *(if applicable)* (IV.2.4.2.3)	Individual subaward budgets	Attach a separate budget with justification for each subaward
Research & Related Senior/Key Person Profile Form (IV.2.4.2.4)	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 (IV.2.4.2.5)	Proposal Summary/ Abstract	Attach to Block 7 Project Summary/ Abstract
	Technical Proposal	Attach to Block 8 Project Narrative
Disclosure of Lobbying Activities (SF-LLL) (IV.2.4.2.6)	N/A	N/A
Attachments Form (IV.2.4.2.7)	Attachment 1 – SOW	Upload as Attachment 1
	Attachment 2 – Quad Chart	Upload as Attachment 2

Table 4: Phase II Proposal Package Chart.

IV.2.4.2.1 **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 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.***

IV.2.4.2.2 **RR FedNonFed Budget Form.** The Research and Related Budget (Total Fed + Non-Fed) 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 (Total Fed + Non-Fed) 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**.

IV.2.4.2.3 **R&R Subaward Budget (Fed/Non-Fed) 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.

IV.2.4.2.4 **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.

IV.2.4.2.5 **Research and Related Other Project Information Form.**

- **Block 7 – Project Summary/Abstract.** The uploaded project abstract should be concise (less than 250 words) and 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.

- **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.

IV.2.4.2.6 **Disclosure of Lobbying Activities (SF-LLL) Form.** The Disclosure of Lobbying Activities Standard Form-LLL, if applicable, should be completed.

IV.2.4.2.7 **Attachments Form.**

- **Attachment 1 – SOW.** The SOW does not have a page limit, but should be approximately 3-5 pages in length for incorporation into grant. 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 www.dtrasubmission.net/portal (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 www.dtrasubmission.net/portal (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.

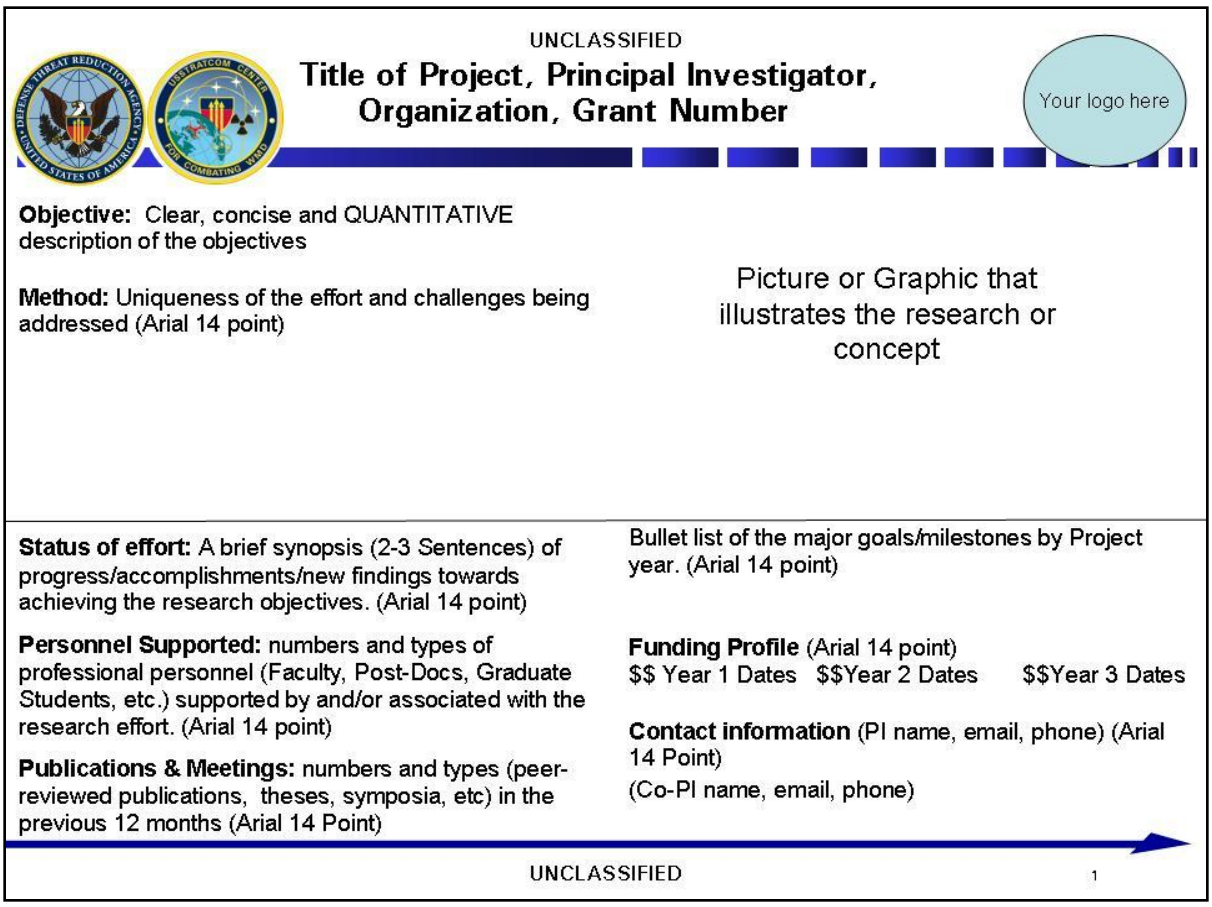


Figure 1: Sample Quad Chart.

IV.2.5. File Format.

IV.2.5.1. Perform a virus check before uploading any files to Grants.gov as part of your application package. If a virus is detected, it may cause rejection of the file.

IV.2.5.2. Do not lock or encrypt any files you upload to Grants.gov as part of your application package.

IV.2.5.3. Most documents should be uploaded as a Portable Document File (PDF) format. An exception to this is the quad chart (MS PowerPoint file compatible with the most recent version of MS PowerPoint) for the Phase II submission.

IV.2.5.4. Movie and sound file attachments will not be accepted.

IV.2.6. All submissions must be UNCLASSIFIED.

IV.3. Submission Dates and Times.

IV.3.1. 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 will not be reviewed if they are received after these deadlines. Exceptions will not be considered.

IV.3.1.1. 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.

IV.3.1.2. 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.

IV.3.1.3. 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.

IV.3.1.4. Please note 15 U.S.C. 260a establishes daylight saving time as the standard time during the daylight saving period.

IV.3.2. 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.

IV.3.3. 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	
CLOSED	
~~2:00 PM EST, 8 April 2011~~	~~Phase I pre-application white paper receipt deadline~~

~~2:00 PM EST, 27 June 2011~~	~~Phase II invitation-only proposal receipt deadline~~
January—March 2012	Period A Grants scheduled to be awarded
Period B	
CLOSED	
~~1 December 2011~~	~~Amendment to the BAA announced on Grants.gov with Period B topics, application packages, and applicable deadlines~~
~~Midnight EST,~~ ~~13 January 2012~~	~~Phase I pre-application white paper receipt deadline~~
~~Midnight EST, Not prior to 2 April 2012, and not later than 20 April 2012 *~~	~~Phase II invitation-only proposal receipt deadline~~ ~~* The exact due date and time for the full proposals will be provided in the letters of invitation~~
October—December 2012	Period B Grants scheduled to be awarded
Period C	
3 December 2012	Amendment to the BAA announced on Grants.gov with Period C topics, application packages, and applicable deadlines
Midnight (11:59 PM) EST, 14 January 2013	Phase I pre-application white paper receipt deadline
Midnight EST, Not prior to 5 April 2013, and not later than 3 May 2013 *	Phase II invitation-only proposal receipt deadline * The exact due date and time for the full proposals will be provided in the letters of invitation.
October—December 2013	Period C Grants scheduled to be awarded
Period D	
TBD	Amendment to the BAA announced on Grants.gov with Period D 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 D Grants scheduled to be awarded
Period E	
Period F	
……	

Period 'n'

Table 5: List of important dates. (Same as Table 1 located in the Overview Information)

IV.3.4. Late Submissions. 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" and will not be considered. Exceptions will not be considered.

IV.3.5. Interruption of Government Processes. 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. Indirect costs may be restricted to less than 35% of the total grant value regardless of previously negotiated rates with the cognizant agency. The 2008 DoD Appropriations Act (Public Law 110-116, Section 8115), 2009 DoD Appropriations Act (Public Law 110-329, Section 8109), and the 2010 DoD Appropriations Act (Public Law 111-118, Section 8101) applied this restriction to awards made using fiscal year 2008, 2009, and 2010 Basic Research funds. This restriction does not apply to awards made using fiscal year 2011 and 2012 Basic Research funds but **may** apply to future awards.

IV.6. Other Submission Requirements.

IV.6.1. Phase I and Phase II applications must be made through 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 is announced by the original posting of the BAA and the application packages are 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 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 Central Contractor Registration (CCR) by calling the CCR Assistance Center at 1-866-606-8220, or you may register online at http://www.ccr.gov. You will NOT be able to complete your CCR registration until CCR 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, see Section IV.2.4.2.6.

IV.6.4. Marking Guidance for Pre-Application White Paper and Invited Proposal and Disclosure of Proprietary Information other than to the Government.

IV.6.4.1. 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.

IV.6.4.2. 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.

IV.6.4.3. 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."

IV.6.4.4. The Government assumes no liability for disclosure or use of unmarked data and may use or disclose such data for any purpose.

IV.6.4.5. 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.

IV.6.4.6. 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.

V.2.1. 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.

V.2.2. Each pre-application white paper and invited proposal will be reviewed within the period to which it was submitted.

V.2.3. 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.

V.2.4. 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).

V.2.5. 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.

V.2.6. 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.

V.2.7. Additional details, including the due date for Phase II submissions, may be provided to applicants in the invitation email.

V.3. Technical and Administrative Support by Non-Government Personnel

V.3.1. It is the intent of DTRA to use non-government personnel to assist with the review and administration of submittals for this BAA.

V.3.2. All invited proposals will be reviewed by subject matter experts (peer reviewers) who are non-government personnel.

V.3.3. 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: TASC Inc. (advisory and assistance services) and their subcontractors, Suntiva Executive Consulting (contract specialist support) and their subcontractors, BRTRC Inc, SBG Technology Solutions, and Terremark Worldwide Inc. 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.

V.3.4. 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.

V.3.5. All applicants to this BAA consent to the disclosure of their information under these conditions.

VI. AWARD ADMINISTRATION INFORMATION

VI.1. Award Notices.

VI.1.1. 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.

VI.1.2. 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.

VI.1.3. 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.

VI.1.4. 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.

VI.1.4.1. 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.

VI.1.5. A debrief summary will be provided as part of all notification e-mails.

VI.1.6. All notifications will be made from notification@dtrasubmission.net. **E-mails to this e-mail address will not be answered or forwarded.**

VI.1.7. 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.

VI.1.8. 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.

VI.2.1. 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.)

VI.2.2. 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.2.3. CCR Registration. In accordance with 2 CFR 25.200(b), each entity applying to this BAA (that is not exempt under 2 CFR 25.110) is required to:

- Be registered in the CCR prior to submitting an application (or plan);
- Maintain an active CCR 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.2.4. Protection of Human Subjects.

VI.2.4.1. 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.

VI.2.4.1.1 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.

VI.2.4.1.2 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.2.5. Animal Use.

VI.2.5.1. 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.

VI.2.5.2. 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, offerors 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 Volume III, Supplemental Information, of the Phase II full proposal. 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.2.6. Biological Defense Research Program (BDRP) Requirements: BioSurety and Select Agent Use.

VI.2.6.1. 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.

VI.2.6.2. 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.2.7. 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.2.8. 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.2.9. 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.2.10 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.2.11 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.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.

VI.3.1. Annual Progress Reports: Annual progress reports will be due no later than 1 September of each year. Grants effective after 31 May will not require a progress report until 1 September of the following year.

VI.3.2. 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.

VI.3.2.1. The purpose of the final report is to document the results of the effort.

VI.3.2.2. 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).

VI.3.3. The Federal Financial Report, SF425 is due annually, no later than 90 days after the end of the reporting period for all grants. The reporting period shall be from 1 July–30 June. First year reports shall have a reporting period of the start date of the grant through 30 June. Final reports shall be submitted no later than 90 days after the project or grant period end date.

VI.3.4. 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 32.61 – 63 (For-Profit Organizations).

VII. AGENCY CONTACTS

VII.1. All administrative and programmatic correspondence should be directed to HDTRA1-BRCWMD-A@dtra.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: BRCWMD-TA1@dtra.mil

Thrust Area 2: BRCWMD-TA2@dtra.mil

Thrust Area 3: BRCWMD-TA3@dtra.mil

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

Thrust Area 4: BRCWMD-TA4@dtra.mil

Thrust Area 5: BRCWMD-TA5@dtra.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

PerC-Topic 1: Manipulating Multiple Domains of the Electromagnetic Spectrum for Sensing Nuclear Materials in Complex Environments (Thrust Area 1)

Average Award Amounts for PerC-Topic 1:
- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerC-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: Conventional methods for the detection of nuclear signatures are limited by many obstacles which ultimately reduce their effectiveness at large distances. This topic explores novel methods and advancements in the ability to remotely sense alternative signatures of nuclear materials. In particular, this topic promotes the necessity of understanding the interactions between alternate signatures associated with nuclear materials and the surrounding environment or emitting material. This may include interferences from shielding materials or from large background sources. Advances in research exploring these novel methods may lead to an ability of sensing nuclear material remotely, with high signal to noise ratios, and at longer ranges (>100 meters).

For example, the advent of nonlinear optical science has made available a wealth of investigative techniques for various fields such as materials science and biological imaging, promising great capabilities in detection of alternative signatures. Even with this high-intensity laser technology, there are complexities that deter some techniques from being used in complex and dynamic environments. Long stand-off distances for source generation and detection, air breakdown, and direct line-of-sight place limits on detection capabilities of nuclear materials. In general, local factors, such as humidity and atmospheric absorption, may also hinder certain regions of the electromagnetic spectrum from being used.

Basic understanding of physical mechanisms to enhance the specific signatures in nuclear materials in complex environments is critical to advancing the current state of the art. Formation of short-lived optical components at long distances may create advances in spectral and spatial distribution for signal enhancement. Observing and manipulating the temporal domain of material response for signal enhancement of alternative signatures to nuclear components is of particular interest.

Impact: Truly novel methods of manipulating light interactions with matter may transform

detection techniques for nuclear materials and related secondary signatures. This topic is important to the counter-WMD mission of DTRA by addressing the need to extend detection of fissile materials and nuclear weapons to distances beyond current short-range capabilities. Developing novel detection methods could lead to the ability to sense shielded nuclear material.

Objective: Leveraging the entire electromagnetic spectrum (excluding γ's) and various time scales of nuclear and atomic processes may increase detection capabilities for the warfighter. Collaboration across multiple disciplines is strongly encouraged in order to successfully tackle some of the scientific challenges associated with this scale of work. Investigations may include, but shall not be solely limited to methods utilizing ionization mechanisms and fluorescence detection of the primary component of air (N_2). Limited consideration will be given to studies utilizing THz detection and filamentation, but must adequately address the unique challenges related to nuclear material detection.

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

- Investigate alternative signatures of nuclear and secondary materials in complex environments using the following examples of techniques or others not listed:
  - Laser matter interactions and/or detection mechanisms in or near nuclear environments
  - Ionized air molecules with a vetoed singlet-oxygen background
  - Cold-atom gravity gradiometry
- Exploration of one or more of the following aspects of alternate-signature detection methods:
  - Manipulate multiple domains (spatial, temporal and spectral) of an electromagnetic wave to probe the complex environment in close proximity to nuclear materials
  - Demonstrate understanding of mechanisms of light-matter interactions to enhance response of low level alternative signatures
  - Novel means for sensing air fluorescence from the interaction of radiation with the environment
  - Consider quantum effects including coherent control
  - Increase detection sensitivity via perturbation of local environments

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PerC-YIP-Topic 1: Manipulating Multiple Domains of the Electromagnetic Spectrum for Sensing Nuclear Materials in Complex Environments (Thrust Area 1)

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

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

PerC-Topic 2: Advancing Nuclear Forensic Methods for Collecting and Analyzing Post-Detonation Debris (Thrust Area 1)

Average Award Amounts for PerC-Topic 2:

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

Award Structure for PerC-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 ways to enable accurate post-detonation analysis of debris from a nuclear event on a short time scale. The Department of Defense provides the capability to collect and analyze post-detonation debris. DTRA is responsible for research and development that will enable this post-detonation forensics. The current methodology includes a radiochemical assay that requires time to obtain statistically accurate results. The advancement of analytical techniques could lead to the ability to accurately analyze debris on time scales shorter than this current methodology. Of interest are innovations that identify and quantify elemental and isotopic constituents of a fresh radioactive fallout debris sample. Of particular interest are accurate and timely measurements of major, minor, and trace constituents, including actinide species. Ideally, novel methodologies to perform these measurements would be field-adaptable and non-destructive, allowing for additional confirmation analysis on the same sample. Furthermore, improvement within the capability of sample collection is needed; novel methods are sought which have the potential for greater robustness under a wider variety of adverse conditions. Combining novel collection and analysis techniques is of interest where the analysis provides either identification or quantitative isotopic composition of the debris. Other areas of interest include understanding phenomenology that govern novel analysis methodologies, methodologies for compiling, assessing, and interpreting large sets of data, as well as understanding the treatment of data uncertainties. Disciplines which may advance the science for post-detonation nuclear forensics include but are not limited to chemistry, nuclear physics and engineering, materials science, instrument development, mathematics and statistics, computer science and modeling and simulation.

Impact: The development of advanced post detonation forensics addresses DTRA's counter WMD need to enable: prevention of future detonations, identification of those responsible, and improvement in response and recovery efforts. Such research has the potential to lead to a field deployable system with a real-time analysis capability.

Objective: This topic explores novel methods and advancements in the ability to collect samples of material, analyze radioactive debris, and identify signatures from debris analysis in a

post-detonation environment. Specific interests include the investigation of non-destructive analytical techniques, fundamental phenomenology of analytical measurements, and innovative data-set handling. Proposals that engage government laboratory institutions are also encouraged.

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

- Novel methods that enable rapid and cost-effective isotopic identification and measurement after a nuclear or radiological detonation
- Field-adaptable analytical techniques
  - Non-destructive methodologies are preferred
- Mathematical and statistical treatment methods of large, complex data sets relevant to radiological analyses
- Investigation of techniques with the potential to eliminate the need for time-consuming separative radiochemistry on a gross vs. net timeline
  - Techniques that reduce the overall timeline are preferred over techniques that have a short timeline but require multiple measurements, lengthy calibration procedures, etc.
- New scientific understanding of the phenomenology of techniques such as laser spectroscopy, mass spectrometry, and associated ionization methods
  - Insight via modeling or experimental methods into how the above techniques enhance counter-WMD science is encouraged over development of or improvements to instrumentation
- Investigations to improve databases of physical constants and their uncertainties
  - Constants such as cross sections, decay branching ratios, or nuclear energy levels relevant to nuclear forensic analysis
- Techniques or methodologies for repetitively validating and verifying measurements made on samples that have components inherently disappearing and changing with time.
- New methods for sample collection after a nuclear or radiological attack. Includes:
  - Airborne and ground collection methods
  - Combined collection and analysis methods
- Advanced methods of sample pre-concentration for higher signal output
- Exploration of methods with the potential to enable remote characterization and quantification of airborne debris

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PerC-YIP-Topic 2: Advancing Nuclear Forensic Methods for Collecting and Analyzing Post-Detonation Debris (Thrust Area 1)

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

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

PerC-Topic 3: Nanoscale Solutions for Radiation Sensing Systems (Thrust Area 1)

Average Award Amounts for PerC-Topic 3:

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

Award Structure for PerC-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: This topic seeks investigations which extend beyond the simple geometric scaling down of macroscale methods/materials by exploring nanoscale phenomenology and its potential impact upon an *entire system* for sensing and recognizing radiation from nuclear materials. Fundamental studies of the interaction of matter and mechanisms of transfer of energy are critical for successful development of nuclear sensing methodologies within the nanoscale regime as well as its viability as replacements for currently deployed technologies. Viability could be described to include the following: expense of nanomaterial, ease of mass production, ruggedness, "plug-and-play" functionality, etc. Highly viable nanomaterials would be those which have the potential to be mass-produced at a low cost for replacement of the more expensive materials presently used in radiation detectors, while maintaining or exceeding current detection capabilities (i.e. novel photodetectors as alternatives for the much older technology of photomultiplier tubes). Previous research in this topic area has shown that scintillators as well as semi-conductor sensors incorporating nanoparticles can lead to viable radiation detectors. Furthermore, previous research has shown that a detailed strategy for how to address the common problem of agglomeration of nanoparticles is essential for a successful project.

Impact: This topic is important to the counter-WMD mission of DTRA by revolutionizing point detection technology via the unique properties of nanomaterials that could provide unparalleled sensitivity and specificity.

Objective: Understanding nanoscale phenomenology is conducive to opening up new insight into possible applications for parts of the entire radiation sensing system, including novel sensor materials and alternative methods for photon or electron multiplication. It is desirable for the principal investigator(s) to form collaborations with experts in the areas of the interactions of radiation with matter or radiological and nuclear material sensing.

Some of the research areas may include (but are not limited to):

- Exploration of nanoscale and nanostructured phenomenology

- Interaction phenomena of primary and secondary radiations with nanomaterials resulting in conversion of radiation to observable signatures
- Assemblies of repetitive nanostructures for bulk detectors of penetrating radiation
- Properties of nanodevices and nanomaterials that enable micro-electromechanical systems for detection, characterization, and counting of radiation

- Nanostructured materials to be incorporated into room-temperature radiation sensors with excellent energy resolution
  - Innovative use of nanomaterials to provide novel mechanism of charge production transport and collection resulting from interaction with ionizing radiation
  - Novel detection of unique or ancillary signatures of fissile or radiological materials or the facilities in which they may be handled
- Investigation of compact, photosensitive solid-state sensors that may have the desirable properties of low-noise, fast response, and high quantum efficiency for the wavelengths that are commonly emitted by scintillators
- Flexible-nanostructured radiation sensors providing real-time dose reconstruction (nanomaterial dosimeter alternative)

PerC-YIP-Topic 3: Nanoscale Solutions for Radiation Sensing Systems (Thrust Area 1)

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

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

PerC-Topic 4: Understanding Multi-layer/Multi-dependent Network Responses to WMD Attacks and Developing Control Strategies for Cascading Failures (Thrust Area 2)

Average Award Amounts for PerC-Topic 4:
- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerC-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: In order to preserve essential military capabilities following an attack employing weapons of mass destruction (WMD), one must be able to predict the interdependent responses of the multiple interdependent military and national infrastructure networks that define the

military capability in response to damage and to changes in network demand that result from such an attack. These include military networks (US and coalition), like the defense strategic communications system, global information grid (GIG) and battlespace networks; non-military networks, the national power grid and transportation grids. Critical considerations in the face of WMD disruption are network availability, interoperability, robustness and recovery. The basic nature of a WMD attack is that multiple nodes will be compromised simultaneously to varying degrees through a multitude of failure mechanisms – some common mode, others implementation-specific, still others as a result of dependencies. The space- and time-correlated details of the damage and the specific nature of the faulty behavior are not known a priori. The WMD stressors to networks can include, for example, widely distributed failures of electronics from nuclear electromagnetic pulse or the long-term denial of network elements or segments due to WMD contamination from nuclear, biological, and chemical (NBC) material as well as direct physical damage. Many current management approaches and policies of network systems contain static assumptions about the structure of network, and they do not account for time dependent variation in traffic type, significant changes in the number of operating nodes, dynamic interdependencies on other networks, changing security conditions and user demands, including the potential need to prioritize network traffic. In order to understand the critical vulnerabilities and develop avoidance/recovery strategies of such diverse, yet interdependent networks to WMD attack, a fundamental understanding of the approaches which capture network dynamics is required. This effort is intended to answer questions such as: What are the essential elements of any network? How do different implementations impact on interoperability, vulnerability, survivability and recovery of networks in a WMD environment? What is the mix of implementations that optimize these measures? What data would be most valuable to collect from existing networks to supplement/validate the mathematical and statistical models that will be developed under this effort? What are adaptive network policies and optimization methods? What are routing approaches for networks with variable connectivity and information content? What policies are suitable for managing user demand in the event of major attacks? How do failures in one networks spread to dependent networks and how can this cascading failure be managed?

Impact: This research will advance theoretical understanding and methods necessary to improve multi-layer/multi-dependent network robustness, management and recovery, and resilience to cascading failures. Understanding the fundamental properties that contribute to the robustness of multi-layer networks will support system reliability, survivability and security. This research will identify methods to use indirect information (e.g. peacetime performance indicators or network outages from natural events) for determining what data and how much data are needed to adequately understand the impact of WMD stressors on complex multi-layer networks. This will impact many areas such as sensor networks, telecommunications, and systems of systems. Defense systems and operating procedures can be optimized to ensure the maintenance of capabilities rather than individual systems, reducing acquisition costs and increasing WMD survivability and operability.

Objective: A prime objective of this effort is to develop mathematical, statistical, and analytical techniques to understand and represent dynamics and responses of multi-layer/multi-dependent large geographic physical networks under Weapons of Mass Destruction (WMD) attacks such as how failures in one layer may cause cascading failures to the other layers; and develop strategies to prevent and control such cascading failures.

The main thrust of this topic is to extend prior research in networks from static to dynamical, from single layer to multi-layers, from currently existing to next generation network structures, from small/local to large/global multi-dependent physical networks, and particularly to measure/prevent/minimize/control the cascading failures that result from WMD attacks.

Some of the research areas may include (but are not limited to):

- ***Representing multi-layer/multi-dependent networks mathematically*** in large geographical scale under a WMD attack so that data analysis not only within one layer but also among different layers of entire multi-dependent networks is possible.
- ***Identifying responses of multi-layer/multi-dependent network outages*** under a single WMD attack to one layer and then multiple attacks to some of the layers of a multi-layer/multi-dependent network.
- ***Defining cascading failure survivability metric(s)*** that account for robustness, fragility, reconfigurability, and self-healing of the multi-dependent network.
- ***Modeling and analyzing dynamic information structure*** and exchange among different layers over large time régimes that cover both direct and cascading failures.
- ***Detecting, predicting and diagnosing rare WMD disruptions and cascading failures, quantifying the inter-dependency among various entities and layers,*** and developing innovative models and theories for capturing these inter-dependences.
- ***Developing algorithms and control techniques to prevent and minimize cascading failures*** such as through
  - Management algorithms for real time distribution and allocation of network resources with *minimum latency, overhead, and complexity*;
  - Adaptive control techniques and algorithms that include adaptive control methods which estimate failures and their effects at each time instance and can prioritize response via adaptive decision-making processes to stop the cascading failures.
  - Optimization techniques and algorithms developed from optimal control theory for multi-layer and multi-dependent network by minimizing certain cost functions under appropriately defined cascading-failure metrics.

High value is placed on innovative multi-layer network representations which capture essential dynamical features and interdependencies beyond static graphical representations; and control techniques for cascading failures which make networks robust to WMD stressors, speed up decision making processes and ultimately enable an automatic system responding and controlling cascading failures.

PerC-YIP-Topic 4: Understanding Multi-layer/Multi-dependent Network Responses to WMD Attacks and Developing Control Strategies for Cascading Failures (Thrust Area 2)

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

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

PerC-Topic 5: Radiation Effects in Advanced Gate Dielectrics and Channel Materials (Thrust Area 3)

Average Award Amounts for PerC-Topic 5:
- Single Scope Awards will average approximately $150,000 per year.
- Multidisciplinary Awards will average approximately $350,000 per year.

Award Structure for PerC-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: Recent significant materials and process developments, such as in atomic layer deposition, now appear to make the realization of high performance MISFET channel materials using compound semiconductors epitaxial films, germanium, or carbon based materials such as carbon nanotubes and graphene. These modified channel materials may have up to a 3-times improvement of the switching energy compared to the most advanced silicon devices. This is a result of the significantly higher intrinsic mobilities and lower effective carrier mass in these materials compared with silicon. Moreover, the continued improvement of high-K gate dielectrics, such as hafnium based layers, has allowed for order of magnitude reductions in gate leakage currents. While the development of high-K gate dielectrics is still in its infancy, it may enable the continued shrinking of silicon-based microelectronics and the extension of Moore's Law. These developments coupled with ultra-short gate lengths and semiconductor on insulator (SOI) technologies open up new vistas of advanced devices, such as gate-all-around devices, with ballistic electronic carrier transport far beyond the limitations of silicon-based technologies. These new technologies, when implemented, represent significant advancement of the current generation of microelectronics, extending the expectations of Moore's Law for at least a decade beyond the Si 5nm generations.

Currently, very little is understood with respect to radiation effects associated with these new CMOS device components (high-K gate dielectrics and advanced channel materials) including new challenges associated with length scales on the order of atomic dimensions, interfaces of complex compound materials, interfaces of non-silicon channel materials with surrounding materials, support layers dominating the physical structure, and myriad quantum effects. Nuclear radiation and particle effects, from both terrestrial and space radiation sources, have yet to be studied in any comprehensive manner.

Impact: As advanced devices and new materials are developed that will be incorporated into the next generation of microelectronics, it is essential to maintain an early understanding of the radiation effects and tolerances of these devices so they can be more readily adopted for use by

the Department of Defense (DoD). Incorporation of radiation effects mitigation procedures will be a critical technology consideration for DoD satellite assets and for any DoD system which may be subject to nuclear radiation bursts, high intensity EMP, microwave, or THz electromagnetic radiation.

Objective: The objectives of this topic are to conduct theoretical and/or experimental research to further the fundamental understanding of the radiation effects phenomena and the associated effects such as intense RF radiation mechanisms, transient effects, single event effect and total ionizing dose in advanced high-k dielectric gate stack structures, compound semiconductor interfaces, and in the interfaces of novel channel materials such as III-V compounds, graphene, germanium, etc. This research will determine the possible efficacy of these ballistic electronic carrier transport technologies for implementation in DoD systems, the development of performance restoration techniques and strategies, the development of circuit and layout design methodologies to mitigate these effects, and new utilization concepts and interactive testing to evaluate the possible use of these phenomena for DTRA mission focused activities. The approach will be based on a combination of theory, simulation, and basic research experiments.

The proposal must make the connection between the proposed basic physics research and countering chemical, biological, radiological, nuclear, or high explosive weapons or weapons effects. Submissions that focus on specific applications (not the basic enabling science), applied configuration research, or systems engineering are discouraged. Researchers are encouraged to gain an understanding of DTRA's core mission and propose novel research directions for radiation effects on advanced compound semiconductor channel materials and interfaces or high-k dielectric gates performance that further DTRA's counter-WMD mission.

PerC-YIP-Topic 5: Radiation Effects in Advanced Gate Dielectrics and Channel Materials (Thrust Area 3)

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

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

PerC-Topic 6: Kinetics and Turbulence in Chem/Bio Defeat (Thrust Area 4)

Average Award Amounts for PerC-Topic 6:

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

Award Structure for PerC-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: DTRA is interested in biological-agent and chemical-agent defeat weapons to deny enemy use of WMDs and WMD facilities. It is critically important that collateral effects associated with the destruction of WMD facilities be eliminated or vastly reduced when compared to current technology. Therefore, novel energetic materials with both thermal and chemical/catalytic chem/bio-agent kill mechanisms are being investigated for weapons development. Reducing collateral effects using these novel materials require accurate simulation of the chemical species and reactions (to estimate kill percent) followed by turbulent mixing with chem/bio-agents and plume spread (to estimate longer-time environment effects).

Recent advances by researchers have developed simulation models to describe some of the mechanistic phenomena; however, there is still a lack of understanding across the field as to how agent-defeat materials perform in turbulent conditions with elevated temperature and/or pressure. Little attention has been paid to developing fluid dynamic models for clumped units of bacterial spores (micron-sized particles, similar to dust) in various turbulent flows, the differences in kill mechanisms for wet spores versus dry spores, and bio-agent heating/burning in the environmental conditions following detonation (humidity, temperature, and corrosive atmospheres). Basic knowledge of the response of chemical agents and agent simulants to blast loading and the high-temperature post-detonation environment are also inadequate.

Further, predicting where and when the fireball or detonation products are hot enough to neutralize agents, requires modeling the shock and detonation-induced instabilities leading to turbulent mixing. While mixing can be characterized on the macro scale (larger than the grid size), the micro scale (sub-grid size) still remains a challenge. Robust mixed-grid models, and in particular, uncertainty quantification in current models when various scales and grid sizes are combined, remains a challenge.

Impact: The immediate pay-off of these research efforts is: (1) a better understanding of multiphase reactive turbulent flow phenomenology and quantification of energy release; and (2) an understanding of how biological and chemical agents react to shock waves and subsequent hot corrosive environments. This understanding will improve weapon performance and optimize

tools for weapons-effects predictions.

The later impact of this research would be the capability to effectively defeat biological- and chemical-agent facilities by designing weapons to minimize collateral damage. Weapon modeling will be more accurate and validated by experimental results, enabling better damage estimates.

Objective: In order to eliminate undesired collateral effects of agent defeat weapons, the objective of this topic is to research experimentally validated equations and models for evaluating the probabilities of biological and chemical agents escaping from blast-damaged containers, getting intimately mixed with hot/corrosive detonation gases, interacting with fragments and dust, being distributed by turbulent instabilities, surviving and escaping to the environment.

Therefore, research in this topic belongs to two major categories:

- Turbulent Reactive Mixing: The objective is to gain an understanding of turbulent mixing and the instabilities of aerosolized biological and chemical agents in atmospheres of high temperature and corrosive/reactive gases. Research in computational fluid dynamics is needed to develop a novel approach to describe the mixing phenomena, especially when large higher density fragments are present along with small lower-density dust like particles. Investigation on functions that describe turbulence, and experiments on small scale mixing are needed in time scales of 10-5000 ms. Turbulence models with uncertainty quantification are desired, to assist in model efficacy and validation.
- Kinetics and mechanisms of Chemical-Agent and Biological-Agent Defeat: The objective is to gain an understanding of how spore-forming bacteria 'die' and how chemical agents are neutralized as a result of interactions with heat and reactive/corrosive gases that result from the detonation of a weapon. Research could focus on experiments to characterize heating and reactions of both wet and dry spore-forming biological agent simulants, in high temperature environments (30°C to 700°C) in contact with corrosive gases such as F_2, Cl_2, I_2, HF, HCl and HI, in an atmosphere of detonation product gases such as H_2O, NO_2, and CO. Research could also focus on neutralization or reactions of chemical agents or agent simulants at high temperatures (30°C to 700°C) and with gases such as F_2, Cl_2, I_2, HF, HCl and HI, in an atmosphere of detonation product gases such as H_2O, NO_2, and CO; and the reaction products resulting from these conditions.

PerC-YIP-Topic 6: Kinetics and Turbulence in Chem/Bio Defeat (Thrust Area 4)

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

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

PerC-Topic 7: Polymers and Binders for Chem/Bio Defeat Formulations (Thrust Area 4)

Average Award Amounts for PerC-Topic 7:

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

Award Structure for PerC-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 interested in biological- and chemical-agent defeat weapons to deny enemy use of WMD facilities. We are currently supporting many research projects looking for chemical and biological agent defeating explosive and reactive materials. Some of these projects are resulting in very effective bio- and chem-agent defeat explosives or reactive materials. Usually, the next step in weapon development is that such new explosive- or reactive- materials ingredients are formulated with binders and additives (though less than 20% of the mix), to be utilized in different weapon configurations or in different methods of weapon deployment.

Properties such as the malleability of an explosive, the ability to be poured and set, to be sprayed or pumped, adhered to a surface and then set, etc. are usually established by the polymers or binders or adhesives, which are incorporated with the reactive or energetic material, together with additives that allow setting or gluing, etc. Key characteristics of such binder systems would include viscosity, compressibility, and adhesion to a wide range of surfaces; in addition to compatibility with the explosive or reactive ingredients. One possible curing mechanism for binders for spray-slurry adhesive explosives may be an anaerobically stable polymeric binder that retains a low enough viscosity for spraying and then adheres and thickens (cures) in air, perhaps with prolonged evaporation of solvent.

Further, the most-effective chemical and biological defeating explosive and reactive materials being investigated are reactive with liquid water and water vapor (humidity), are reactive with oxygen (in air), and sometimes react with other ingredients in the formulation. These reactions or interactions with the environment cause breakdown of the biological/chemical-agent defeat properties of the explosive or reactive material during handling and storage. For example, metal fuel particles spontaneously oxidize when exposed to air; new halogen-oxidizers are so hydroscopic that they turn in to puddles with even a few minutes in high humidity. Such highly reactive yet most-effective explosive or reactive materials could only be utilized with the protection or passivation offered by a coating or binder system that would stabilize them in normal environments. For incorporation of these new chemical and biological defeating explosives and reactive materials into plastic-bonded explosives (PBXs), the characteristics of

the polymer, such as its mechanical properties, wetting of fill particles, crosslink density, glass transition temperature, ability to accept bonding agents, and cure at ambient temperature are important properties to consider. Some current binder systems in explosive formulations in wide use today are estane/BDNPA (PBX-9501), Kel-F (PBX-9502), and HTPB (PBXN-109).

Recent advances in block co-polymers, especially asymmetric co-polymers, polymers with hydrophilic or hydrophobic ends, polymers binding to nano-particles, etc. abound in scientific literature. Such new polymeric, organic and inorganic materials are reported to yield thermo-setting, air-setting, or water-setting abilities, and properties that form permeable or impermeable barriers as desired.

Impact: The pay-off of these research efforts is chemical and biological agent defeating explosive and reactive material formulations, which are formable, spray-able or pourable, with highly effective ingredients that are protected from possible water, air or other undesired interactions during handling and storage. The final impact of this research would be customized weapons to completely and effectively defeat and destroy biological- and chemical-agent facilities and prevent WMD use by adversaries, while minimizing collateral damage.

Objectives: Investigate polymers, binders or adhesives, and the appropriate additives, for agent-defeat energetic formulations; with ingredients (already being researched) that are made water-proof or air-proof, or other otherwise isolated from undesired interactions; and can be hand-formed to different shapes, poured, or sprayed, and adhere to different surfaces, as desired for particular deployment of counter-WMD weapons. The characteristics of the polymer, such as its mechanical properties, wetting of fill particles, crosslink density, glass transition temperature, ability to accept bonding agents, and cure at ambient temperature are important properties to address in the white paper. For basic research, initial work proposed may use sugar crystals as mock or simulant of energetic-material crystals.

One approach could be an anaerobically stable polymeric binder system that is impermeable to air, and retains a low enough viscosity for spraying and then adheres and thickens (cures) in air, perhaps with prolonged evaporation.

Another approach could be an amphiphilic coating that would protect air- and water-reactive energetics and then bonds with existing binders (such as those based on polybutadiene or fluoropolymers).

White papers with these or other novel and creative approaches are sought that yield the above objectives.

PerC-YIP-Topic 7: Polymers and Binders for Chem/Bio Defeat Formulations (Thrust Area 4)

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

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

PerC-Topic 8: Novel Physicochemical Signatures of Radiation Exposure History for Treaty Compliance (Thrust Area 5)

Average Award Amounts for PerC-Topic 8:

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

Award Structure for PerC-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: The physical inspection of elements dismantled from a state nuclear arsenal may be needed in future arms control treaty compliance and verification. Current treaties, such as New START, focus on strategic nuclear armaments and are enacted by limiting large scale elements of a nuclear arsenal such as individual warheads, bombers, missiles, and launchers. As future arms control treaties are developed the need to track and verify the history of individual components within a weapon system, such as a section of metal alloy, could arise. The development of basic research that can accurately describe the time-dependent radiation exposure history of these components could be extremely valuable in supporting such future treaties.

In order to verify treaty compliance but protect state secrets, rapid and reliable conclusions about the provenance of an item presented to an inspectorate must be produced. These methods must be scientifically sophisticated enough to conclusively identify the composition and time-dependent radiation exposure history of a component from a dismantled nuclear weapon system. As a complement to conventional nuclear detection techniques, unique physicochemical signatures may be a valuable way for the onsite inspection (OSI) team to determine if the object presented matches its declared use and history. Some challenges in this area of analysis include efficient identification of the material, verification of the materials history including time exposure data, and analysis in a small time interval with low measurement uncertainties. The development of techniques for this purpose will advance the capabilities of future OSI teams and their ability to assure state compliance with treaties in-force.

Impact: Research into the physicochemical signatures of time-dependent radiation exposure addresses DTRA's counter-WMD need by providing the scientific basis needed to develop equipment, analysis methods, and concept of operations to conduct a successful OSI for future treaties.

Objectives: The topic explores research into determining the unique physicochemical signatures needed to enable the proper identification of materials from a weapon system, including but not

limited to metals, alloys, paints, lubricants, and polymers. Signatures are desired that can be physically understood, modeled or simulated, and accurately predicted. Research areas should not focus on the development of new radiation sensitive detector materials but rather, on the radiation exposure history of existing materials. Specific interests include nondestructive determination of a material's exposure to radiation from a weapon, the time-dependent history of the exposure, and predictive models that support conclusive identification. Proposals investigating basic scientific phenomena of these non-nuclear signatures are preferred to proposals suggesting devices to accomplish the research. Proposals that engage government laboratory institutions are also encouraged.

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

- Determination of unique physicochemical signatures through advanced analysis techniques such as:
  - Mass spectrometry such as SIMS or GC-MS to look for changes in the elemental or molecular composition of the material
  - Microscopy techniques such as AFM or SEM to identify microstructural or morphological changes
  - Optical or surface spectroscopy such as Raman spectroscopy or ellipsometry to identify subtle chemical or physical property changes
  - Bulk measurement techniques such as nanoindentation or conductivity tests to quantify changes in hardness or charge mobility
  - Imaging techniques such as hydroacoustic imaging or x-ray to probe subsurface structural shifts or defects
- Novel methods to investigate both time-integrated and time-dependent radiation exposure history of a component
- Methods to distinguish between physicochemical signatures of operational radiation exposure and artificial aging of a component from a variety of radiation sources, both stockpile-relevant and other

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PerC-YIP-Topic 8: Novel Physicochemical Signatures of Radiation Exposure History for Treaty Compliance (Thrust Area 5)

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

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

JOINT DTRA and JSTO-CBD Basic Research Needs

PerC-Topic 9: Interaction of Substrate-Mediated Transport and Catalyst Kinetics in Multicatalyst Systems (Thrust Area 3)

Average Award Amounts for PerC-Topic 9:

- Single Scope Awards may average up to approximately $500,000 per year. Specific annual dollar value guidance will be provided in each full proposal invitation.
- Multidisciplinary Awards may average up to approximately $1,000,000 per year. Specific annual dollar value guidance will be provided in each full proposal invitation.

Award Structure for PerC-Topic 9:

- 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: Certain biological catalysts exhibit kinetics faster than the rate of substrate diffusion. This behavior has been variously attributed to, for example, (a) the ability of the catalyst scaffold to draw in and pre-orient substrate via dipolar electric fields or (b) for certain substrates (protons, electrons), quantum mechanical tunneling through the activation barrier to reaction.[5] It has also been suggested that the recently observed phenomenon of enzyme chemotaxis may play an underappreciated role in the activity of certain systems.[6] The ability of enzymes and scaffold components to respond to their environment by selectively directing mass transport is thought to play a fundamental role in the efficiency of biological catalytic cascades such as polymerases and many dehydrogenases.[7]

Scientists and engineers seeking to heterogenize homogeneous catalysts, for a wide variety of defense and industrial applications including those relevant to C-WMD, typically find a tradeoff between the desirable attributes of, on the one hand, the ability of the heterogeneous system to be compartmentalized and separated from the reaction mixture and, on the other hand, the more rapid rates of homogeneous catalysts. Mass transport limitations are thought to play a major role in diminishing the reactivity of heterogeneous catalysts, and today this is only partially mitigated by the use of highly porous scaffolds. [8] Strategies to introduce spatially anisotropic chemistry and topology into synthetic catalyst scaffolds have not been widely applied. However, the

[5] Doshi, U.; McGowan, L. C.; Ladani, S. T.; Hamelberg, D. Resolving the complex role of enzyme conformational dynamics in catalytic function. Proceedings of the National Academy of Sciences of the United States of America 109, 2012, 5699-5704.

[6] Muddana, H. S.; Sengupta, S.; Mallouk, T. E.; Sen, A.; Butler, P. J. Substrate Catalysis Enhances Single-Enzyme Diffusion. Journal of the American Chemical Society, 132, 2010, 2110-2111.

[7] Perham, R. N. Swinging Arms and Swinging Domains in Multifunctional Enzymes: Catalytic Machines for Multistep Reactions. Annual Review of Biochemistry 69, 2000, 961-1004.

[8] Li, B.; Guan, Z.; Wang, W.; Yang, X.; Hu, J.; Tan, B.; Li, T. Highly Dispersed Pd Catalyst Locked in Knitting Aryl Network Polymers for Suzuki-Miyaura Coupling Reactions of Aryl Chlorides in Aqueous Media. Advanced Materials 24, 2012, 3390-3395.

technology for tuning materials in this manner is increasingly refined,[9,10,11] and we believe that its convergence with the biological community will prove to be a fruitful pathway to both (a) better understand the role of substrate-mediated transport in biological multicatalyst systems and (b) develop the fundamental understanding needed to design disruptive materials for sensing, diagnostics, medical intervention, and protection. The fabrication of model synthetic systems and re-engineered natural ones as tools in elucidating the role of substrate-mediated mass transport provides a focus to this convergence.

Impact: By means of accomplishing the objective articulated below, this research topic seeks to establish structure/property relationships that enable (a) design and tailoring of materials incorporating functionalities necessary for meeting DTRA C-WMD challenges; (b) understanding the response of natural and synthetic multicatalyst systems to relevant environmental variables; and (c) development of targeted effectors that alter the function of multicatalyst systems. Therefore, the knowledge generated as a result of conducting the research will be broadly applicable to core DTRA mission requirements for sensing and recognition, personnel protection, medical countermeasures, and treaty monitoring/verification. In addition, the research will support larger DoD goals for engineering of novel multifunctional materials to address a variety of critical mission needs.[12,13]

Objective: Elucidate the role of substrate-mediated mass transport in the kinetics of multicatalyst systems by developing the predictive understanding required to couple new paradigms of directed molecular transport with the activity of supported catalysts.

The most competitive responses will, as tools to accomplishing this objective, develop and interrogate relevant multicatalyst model systems (here defined as heterogenous systems composed of two or more catalysts) or re-engineered natural systems that can: (1) rapidly separate components in a heterogeneous mixture, (2) selectively funnel individual components to and from specific catalytic centers, and (3) employ low-energy transport processes, ideally those relying only on ambient thermal energy and physicochemical interaction of the substrate with the scaffold and catalysts. Biotic, abiotic, or hybrid catalytic systems will be considered relevant to the goals of this research topic.

Competitive responses will likewise present a strategy that combines a theoretical approach, driven by a series of testable hypotheses, with material fabrication and evaluation; in particular, application of combinatorial design and computational learning algorithms is encouraged, as is modeling of substrate/scaffold/catalyst interactions, as framed within a careful design of experiments.

While the intent is to develop basic understanding, specific explored model systems must be

[9] Genzer, J.; Bhat, R. R. Surface-Bound Soft Matter Gradients. Langmuir 24, 2008, 2294-2317.
[10] Yonet-Tanyeri, N.; Evans, R. C.; Tu, H.; Braun, P. V. Molecular Transport Directed via Patterned Functionalized Surfaces. Advanced Materials 23, 2011, 1739-1743.
[11] Perl, A.; Gomez-Casado, A.; Thompson, D.; Dam, H. H.; Jonkheijm, P.; Reinhoudt, D. N.; Huskens, J. Gradient-driven motion of multivalent ligand molecules along a surface functionalized with multiple receptors. Nature Chemistry 3, 2011, 317-322.
[12] Committee on Materials Research for Defense After Next National Materials Advisory Board. Materials Research to Meet 21st-Century Defense Needs. The National Academies Press, Washington, D.C., U.S.A., 2003.
[13] Department of Defense Research and Engineering. Strategic Basic Research Plan, 2008, 13-15.

shown to be relevant to countering the threat posed by weapons of mass destruction. For example, long-term relevance to one of the following could be established:

- Active and selective self-reporting catalytic systems for sensing and degradation of a nerve agent or biological toxin to innocuous products via e.g. oxidation or hydrolysis, where the threat molecule is present in a complex mixture of closely related synthesis byproducts and potential environmental foulants
- Multicatalyst systems able to actively and selectively catalyze the binding and signal amplification of a toxicity biomarker, including those induced by exposure to chemical, biological, radiological, or nuclear agents, present in a complex biological fluid
- Multicatalyst systems able to actively and selectively catalyze the binding and signal amplification of radioactive residues or non-radioactive environmental indicators of WMD materials production, reprocessing, manufacturing, and storage
- Ability to mimic, sense and alter transport processes of biological catalytic cascades for diagnostic or therapeutic purposes directly relevant to C-WMD

PerC-YIP- Topic 9: Interaction of Substrate-Mediated Transport and Catalyst Kinetics in Multicatalyst Systems (Thrust Area 3)

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

Award Structure for PerC-YIP-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: Certain biological catalysts exhibit kinetics faster than the rate of substrate diffusion. This behavior has been variously attributed to, for example, (a) the ability of the catalyst scaffold to draw in and pre-orient substrate via dipolar electric fields or (b) for certain substrates (protons, electrons), quantum mechanical tunneling through the activation barrier to reaction.[14] It has also been suggested that the recently observed phenomenon of enzyme chemotaxis may play an underappreciated role in the activity of certain systems.[15] The ability of enzymes and scaffold components to respond to their environment by selectively directing mass transport is thought to play a fundamental role in the efficiency of biological catalytic cascades

[14] Doshi, U.; McGowan, L. C.; Ladani, S. T.; Hamelberg, D. Resolving the complex role of enzyme conformational dynamics in catalytic function. Proceedings of the National Academy of Sciences of the United States of America 109, 2012, 5699-5704.

[15] Muddana, H. S.; Sengupta, S.; Mallouk, T. E.; Sen, A.; Butler, P. J. Substrate Catalysis Enhances Single-Enzyme Diffusion. Journal of the American Chemical Society, 132, 2010, 2110-2111.

such as polymerases and many dehydrogenases.[16]

Scientists and engineers seeking to heterogenize homogeneous catalysts, for a wide variety of defense and industrial applications including those relevant to C-WMD, typically find a tradeoff between the desirable attributes of, on the one hand, the ability of the heterogeneous system to be compartmentalized and separated from the reaction mixture and, on the other hand, the more rapid rates of homogeneous catalysts. Mass transport limitations are thought to play a major role in diminishing the reactivity of heterogeneous catalysts, and today this is only partially mitigated by the use of highly porous scaffolds. [17] Strategies to introduce spatially anisotropic chemistry and topology into synthetic catalyst scaffolds have not been widely applied. However, the technology for tuning materials in this manner is increasingly refined,[18,19,20] and we believe that its convergence with the biological community will prove to be a fruitful pathway to both (a) better understand the role of substrate-mediated transport in biological multicatalyst systems and (b) develop the fundamental understanding needed to design disruptive materials for sensing, diagnostics, medical intervention, and protection. The fabrication of model synthetic systems and re-engineered natural ones as tools in elucidating the role of substrate-mediated mass transport provides a focus to this convergence.

Impact: By means of accomplishing the objective articulated below, this research topic seeks to establish structure/property relationships that enable (a) design and tailoring of materials incorporating functionalities necessary for meeting DTRA C-WMD challenges; (b) understanding the response of natural and synthetic multicatalyst systems to relevant environmental variables; and (c) development of targeted effectors that alter the function of multicatalyst systems. Therefore, the knowledge generated as a result of conducting the research will be broadly applicable to core DTRA mission requirements for sensing and recognition, personnel protection, medical countermeasures, and treaty monitoring/verification. In addition, the research will support larger DoD goals for engineering of novel multifunctional materials to address a variety of critical mission needs.[21,22]

Objective: Elucidate the role of substrate-mediated mass transport in the kinetics of multicatalyst systems by developing the predictive understanding required to couple new paradigms of directed molecular transport with the activity of supported catalysts.

The most competitive responses will, as tools to accomplishing this objective, develop and

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[16] Perham, R. N. Swinging Arms and Swinging Domains in Multifunctional Enzymes: Catalytic Machines for Multistep Reactions. Annual Review of Biochemistry 69, 2000, 961-1004.
[17] Li, B.; Guan, Z.; Wang, W.; Yang, X.; Hu, J.; Tan, B.; Li, T. Highly Dispersed Pd Catalyst Locked in Knitting Aryl Network Polymers for Suzuki-Miyaura Coupling Reactions of Aryl Chlorides in Aqueous Media. Advanced Materials 24, 2012, 3390-3395.
[18] Genzer, J.; Bhat, R. R. Surface-Bound Soft Matter Gradients. Langmuir 24, 2008, 2294-2317.
[19] Yonet-Tanyeri, N.; Evans, R. C.; Tu, H.; Braun, P. V. Molecular Transport Directed via Patterned Functionalized Surfaces. Advanced Materials 23, 2011, 1739-1743.
[20] Perl, A.; Gomez-Casado, A.; Thompson, D.; Dam, H. H.; Jonkheijm, P.; Reinhoudt, D. N.; Huskens, J. Gradient-driven motion of multivalent ligand molecules along a surface functionalized with multiple receptors. Nature Chemistry 3, 2011, 317-322.
[21] Committee on Materials Research for Defense After Next National Materials Advisory Board. Materials Research to Meet 21st-Century Defense Needs. The National Academies Press, Washington, D.C., U.S.A., 2003.
[22] Department of Defense Research and Engineering. Strategic Basic Research Plan, 2008, 13-15.

interrogate relevant multicatalyst model systems (here defined as heterogenous systems composed of two or more catalysts) or re-engineered natural systems that can: (1) rapidly separate components in a heterogeneous mixture, (2) selectively funnel individual components to and from specific catalytic centers, and (3) employ low-energy transport processes, ideally those relying only on ambient thermal energy and physicochemical interaction of the substrate with the scaffold and catalysts. Biotic, abiotic, or hybrid catalytic systems will be considered relevant to the goals of this research topic.

Competitive responses will likewise present a strategy that combines a theoretical approach, driven by a series of testable hypotheses, with material fabrication and evaluation; in particular, application of combinatorial design and computational learning algorithms is encouraged, as is modeling of substrate/scaffold/catalyst interactions, as framed within a careful design of experiments.

While the intent is to develop basic understanding, specific explored model systems must be shown to be relevant to countering the threat posed by weapons of mass destruction. For example, long-term relevance to one of the following could be established:

- Multicatalyst systems able to actively and selectively catalyze the binding and signal amplification of radioactive residues or non-radioactive environmental indicators of WMD materials production, reprocessing, manufacturing, and storage

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JSTO-CBD Basic Research Needs

PerC-Topic 10: Comparative Immunology of Reservoir Hosts (Thrust Area 3)

Average Award Amounts for PerC-Topic 10:
- Single Scope Awards will average up to approximately $500,000 per year.
- Multidisciplinary Awards will average up to approximately $1,000,000 per year.

Award Structure for PerC-Topic 10:
- 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: Reservoir hosts play a key role in the circulation and population dynamics of zoonotic pathogens and some of these hosts have been identified for emerging viral threats that are of interest to the biodefense community. For example, bats have been shown to be a potential reservoir for both Ebola virus[23] and Hendra virus[24]. While these viruses represent

[23] E. M. Leroy, et.al. (2005) Fruit bats as reservoirs of Ebola virus. *Nature.* 438: 575-576.
[24] K. Halpin, et.al. (2000) Isolation of Hendra virus from pteropid bats: a natural reservoir of Hendra virus. *J Gen Virol*. 81(8): 1927-1932.

highly virulent pathogens in cases in which humans become infected, they appear to cause asymptomatic infections in bats. Given that both humans and bats are able to be infected by these viruses, understanding the differences in the immune responses to infection may shed light on key immunological factors that could confer protection against emerging viral threats.

Impact: This topic will support CBD Program goals by providing an understanding of an immune response that protects against severe disease caused by pathogens that are otherwise highly virulent in human hosts. This will generate a fundamental knowledge explaining how bats are able to serve as reservoir hosts for emerging viral threats. Furthermore, research in this area could provide insight in novel strategies for vaccines or therapeutics targeted against these viruses.

Objectives: The overall objective of this topic would be to characterize the immunological differences between reservoir hosts and humans that enable the reservoir to be infected by emerging viral threats asymptomatically. Proposals emphasizing comparative immunology between bats and humans will be given the highest priority. Also, proposals emphasizing reservoir hosts that harbor asymptomatic infections by Select Agent viruses will be given a higher priority. Research in this area may include the following:

- Production of whole genome sequences for key reservoir species to enable microarray and RNA-sequence-based analyses of the immune response
- Development of immunological reagents for the species in question for comparative analyses
- Comparative approaches to characterize differences between reservoir host and human immune responses to filoviruses and other emerging viral threats
- Confirmation of the impact of specific immunological factors on virulence phenotypes and/or protection

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PerC-Topic 11: Persisters: Antimicrobial Tolerance in Recurring Infections (Thrust Area 3)

Average Award Amounts for PerC-Topic 11:
- Single Scope Awards will average up to approximately $500,000 per year.
- Multidisciplinary Awards will average up to approximately $1,000,000 per year.

Award Structure for PerC-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: Antimicrobial tolerance, the ability of a microorganism to resist killing by antibiotics or other antimicrobials, is mechanistically distinct from multidrug resistance; it is not caused by mutation, rather, it is a result of non-heritable phenotypic variation. Tolerance is mediated by a small subpopulation of microbial cells, persisters, that exist in a transient,

dormant, non-dividing state.[25] Because of their non-dividing, metabolically in- or under-active physiological state, persister cells are insensitive to antibiotic treatment. Persister cells are associated with biofilms but are implicated in chronic and/or recurring infections and may be utilized by a pathogen population to counter the innate immune response, as well as antibiotic insult.[26] Although recognized for nearly 60 years, the molecular events through which persistence is established are poorly understood.

Impact: This topic will support CBD Program goals by contributing to the understanding of mechanisms by which pathogens survive under adverse conditions. This will generate fundamental knowledge, explaining the means by which pathogens evade antibiotic treatment and establish chronic and recurring infections. Furthermore, understanding the biology of persistence has potential downstream application to achieving more effective antibiotic treatment strategies.

Objectives: Proposals are invited that explore the significance and mechanism of persister phenotypes in the establishment of chronic and/or recurring bacterial infections. Proposals responsive to this topic will conform to the requirements of a short duration effort (one year) to explore innovative new ideas and proofs-of-concept that may be leveraged to develop larger programs. At a minimum, a successful proposal will describe a program that, within the first year, demonstrates the phenomenon of persistence in a previously uncharacterized (with regard to persistence) pathogen. Primary evaluation may include surrogate species, followed by confirmation in fully pathogenic strains. Characterization will include incidence of persistence under varying conditions, *e.g.* culture medium, temperature, antibiotic insult, multiple species or strains. Option year will include the determination of the significance of the persistent phenotype in the reoccurrence/relapse of infection *in vivo*, in particular following antibiotic treatment. Significant preference will be given to those proposals addressing biothreat agents, in particular *Burkholderia* spp. Additional project aims may include, but are not limited to the following:

- Discovery and deconvolution of molecular mechanisms by which the persistent phenotype is established
- Exploration of host factors that stimulate the persistent phenotype
- Demonstration of conservation of persistence mechanisms across divergent bacterial species
- Demonstration of the ability to subvert the mechanisms by which persistence is established or maintained

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PerC-Topic 12: Rules Governing Gram Negative Cell Wall Permeability to Molecules (Thrust Area 3)

Average Award Amounts for PerC-Topic 12:

- Single Scope Awards will average up to approximately $500,000 per year.
- Multidisciplinary Awards will average up to approximately $1,000,000 per year.

[25] Lewis, K. (2010). Persister cells. Annu Rev Microbiol. 64:357-72.
[26] Wu Y, Vulic M, Keren I, Lewis K. (2012). Role of oxidative stress in persister tolerance. Antimicrob Agents Chemother. 56(9):4922-6.

Award Structure for PerC-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: Gram-negative bacteria cause a number of significant human diseases, and certain members of this group are classified as biothreat agents, including species of *Brucella*, *Burkholderia*, *Francisella* and *Yersinia*. However, many common Gram-negative pathogens are increasingly resistant to available antibiotics. This situation is exemplified by a recent hospital outbreak of drug resistant *Klebsiella pneumonia*[27] and many wound infections with *Acinetobacter baumannii* seen in deployed military personnel. Such common infections, as well as potential casualties from biothreats agents, can cause long duration hospital stays and significant mortality. The antibiotic options available for Gram-negative infections are limited largely because these organisms possess an outer cell membrane that prevents entry into the bacterial cell of many categories of small molecules, including antibiotics[28] and disinfectants. In addition several of these organisms possess powerful molecular efflux pumps that clear antibiotics from the cell. Because of a lack of comprehensive knowledge of guiding physical properties, discovery of new antibacterial drugs able to effectively penetrate into Gram-negative pathogens that are not susceptible to efflux pumps is limited to a trial and error approach.

Impact: This topic will support CBD Program goals by providing a fundamental understanding of Gram-negative bacteria cell permeability. This knowledge will ultimately allow for more rapid design of effective antibacterials and disinfectants with increased likelihood of success in penetrating the into the cell to kill pathogens of interest to the DoD.

Objectives: The objective of this topic is to increase basic understanding of Gram negative cell permeability and develop a set of rules governing the penetration of small molecules into Gram-negative bacterial cells, particularly biothreats organisms of interest to DTRA. Research in this area may include the following:

- Experimental permeability testing of a selected diversity of molecules through both inner and outer membranes of Gram-negative organisms
- *In silico* modeling of molecules known to permeate and those that cannot permeate the cell wall and membranes
- Cell-free models of Gram-negative membranes that may be used as tools to define the rules of permeation
- Rational design strategies applied to molecules unable to permeate the outer and/or inner membranes of Gram negative organisms to increase the ability to permeate

[27] Snitkin et al (2012) Tracking a Hospital Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* with Whole-Genome Sequencing. Sci Transl Med 4(148):148.

[28] Delcour, Anne. (2009) Outer Membrane Permeability and Antibiotic Resistance. Biochim Biophys Acta. 1794(5): 808–816.

- Fundamental exploration of the molecular characteristics of substances that are transported via influx and efflux pumps/ transporters of Gram-negative bacteria

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PerC-Topic 13: Synthetic Biology for Therapeutics (SynBioTx) (Thrust Area 3)

Average Award Amounts for PerC-Topic 13:
- Single Scope Awards will average up to approximately $500,000 per year.
- Multidisciplinary Awards will average up to approximately $1,000,000 per year.

Award Structure for PerC-Topic 13:
- 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: Recently scientists reported successful use of modified commensal organism to sense and kill pathogens. They rewired *E. coli* circuitry in one case to affect *P. aeruginosa* biofilm formation[29], whereas in another case they were able to prevent *Vibrio cholera* infections in mice[30]. Also, traditional genetic engineering techniques have been effectively used to mass-produce monoclonal antibodies, human growth hormones, insulin, human albumin, antihemophilic factors, antibiotics, vaccines and many other medicines and materials[31]. And more recently, scientists successfully targeted and altered species-specific communication networks of multispecies microbial systems[32]. These and other advances in both systems biology and synthetic biology have set the stage to develop autonomous threat recognition and defeat systems. These "smart" bioactive systems would be able to sense and respond to a threat agent, with autonomously produced antimicrobial activity.

Impact: This topic addresses a very important area of countering WMD mission of DTRA by addressing novel capabilities for defeating biothreat agents without significant negative impact on the host. If successful, the capability developed will be broadly applicable in both military and civilian efforts to treat a range of diseases.

Objective: The immediate goal of this topic is to combine systems biology and synthetic biology to create custom designed synthetic biology-based systems (e.g., modified probiotics)

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[29] Saeidi N, Wong CK, Lo TM, Nguyen HX, Ling H, Leong SS, Poh CL, Chang MW (2011) Engineering microbes to sense and eradicate *Pseudomonas aeruginosa*, a human pathogen. Mol Syst Biol. 16 Aug 2011; 7:521. doi: 10.1038/msb.2011.55.

[30] Duan F, March JC (2010) Engineered bacterial communication prevents *Vibrio cholerae* virulence in an infant mouse model. Proc Natl Acad Sci U S A. 22 Jun 2010; 107(25):11260-4.

[31] John C. Avise (2004). The hope, hype & reality of genetic engineering: remarkable stories from agriculture, industry, medicine, and the environment. Oxford University Press US. p. 22. ISBN 978-0-19-516950-8.

[32] Gamby S, Roy V, Guo M, Smith JA, Wang J, Stewart JE, Wang X, Bentley WE, Sintim HO (2012) Altering the communication networks of multispecies microbial systems using a diverse toolbox of AI-2 analogues ACS Chem Biol. 15 Jun 2012; 7(6):1023-30.

that are capable of recognizing and defeating biothreat agents. The ultimate objective is the development of "smart" bioactive systems that would have additional capabilities, such as, an ability to migrate to and home to the target, evaluating the threat, and responding accordingly with the antimicrobial remedies.

Areas of research encompass all efforts that would significantly enhance the likelihood to accomplish the objective including, but not limited to:

- Design and implementation of genetic control networks that enable threat identification and directed motility
  - Elucidating threat markers and means of their recognition by bacteria
  - Elucidating regulatory pathways that with minimal perturbation, can be rewired to control essential bacterial systems
- Analyses of key antimicrobial pathways that could be utilized in a synthetic biology-based therapeutics, such as the following:
  - Elucidating and engineering critical cell-to-cell communication pathways
  - Elucidating and engineering novel antimicrobial production pathways
  - Elucidating and engineering contact-dependent inhibition pathways
- Incorporation of appropriate pathways from the above in the bioactive platform to demonstrate antimicrobial activity

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PerC-Topic 14: Human Antibody Responses to DoD Priority Biological Agents (Thrust Area 3)

Average Award Amounts for PerC-Topic 14:
- Single Scope Awards will average up to approximately $500,000 per year.
- Multidisciplinary Awards will average up to approximately $1,000,000 per year.

Award Structure for PerC-Topic 14:
- 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: Military personnel are at risk for natural or bioterrorist/biowarfare exposure to DoD priority biological agents. Little is known about the naturally occurring human immune response to such biological agents. This topic seeks to advance the knowledge of the molecular basis for recognition of DoD priority biological agents, and the genetic and structural basis for induction of broadly reactive antibodies that neutralize all antigenic variants of these biological agents. Previous studies have focused on polyclonal serum samples and techniques, which are limited in their capacity to define neutralization mechanisms. Studies using antibody or B cell clones and atomic level structures are desirable. Conventional studies are typically limited to strain- or type-specific responses, but broadly cross-reactive recognition is needed.

Understanding the molecular basis for broad neutralization of DoD priority biological agents by naturally occurring human monoclonal antibodies would provide a major leap forward for the basic science of immunity and could form the rational basis for new vaccine design. Recently, scientists elucidated the mechanism of human immune system interaction with influenza virus – "chasing" it as it mutates,[33] discovered a conserved epitope on the globular head of hemagglutinin and developed human hybridoma technology for human monoclonal antibody production.[34] These and other advances in immunology enable to tackle DoD priority biological agents.

Impact: This topic is important to the counter-WMD mission of DTRA by addressing the need to define the molecular basis for neutralization of viruses beyond the polyclonal antibody studies that are the current state-of-the-art. Developing robust methods for isolation and study of human broadly neutralizing antibodies from humans following natural infection could lead to the ability to design optimal antigens for use in biosensors and for vaccine design. The broadest impact area could be identification of broadly reactive antibodies (or antigens that induce them), pointing the way toward universal detection or vaccination strategies that apply to all strains of a particular pathogen or even an entire class of pathogen.

Objective: This topic explores novel methods and advancements in the ability to isolate human monoclonal antibodies and study their interaction with DoD priority biological agents at the molecular level, with an emphasis on discovering broadly cross-reactive responses.

Areas of research encompass all efforts that would significantly enhance the likelihood to accomplish the objective including, but not limited to:

- New methods for isolation of human monoclonal antibodies to DoD priority biological agents
- Structural studies of antibody-antigen complexes by cryo-EM, crystallography and other high-resolution techniques
- Biological characterization of the mechanism of neutralization of new human monoclonal antibodies to DoD priority biological agents
- Defining broadly cross-reactive protective epitopes and antigens that are relevant to all strains of a pathogen ("universal" antigens), instead of more conventional strain- or type-specific epitopes.

[33] Epitope-specific human antibody repertoires diversify by B cell intraclonal sequence divergence and interclonal convergence (2011) Krause JC, Tsibane T, Tumpey TM, Huffman CJ, Briney BS, Smith SA, Basler CF, Crowe JE Jr. *J. Immunol*. **187**(7):3704-11.

[34] A broadly neutralizing human monoclonal antibody that recognizes a conserved, novel epitope on the globular head of influenza H1N1 virus hemagglutinin (2011) Krause JC, Tsibane T, Tumpey TM, Huffman CJ, Basler CF, Crowe JE Jr. *J Virol*. **85**(20):10905-8.