Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Tick-Borne Disease Research Program

Investigator-Initiated Research Award

Funding Opportunity Number: W81XWH-16-TBDRP-IIRA

Catalog of Federal Domestic Assistance Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), August 3, 2016
- **Invitation to Submit an Application:** September 21, 2016
- **Application Submission Deadline:** 11:59 p.m. ET, November 16, 2016
- **End of Application Verification Period:** 5:00 p.m. ET, November 21, 2016
- **Peer Review:** January 2017
- **Programmatic Review:** February 2017

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

TABLE OF CONTENTS

I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2016 (FY16) Tick-Borne Disease Research Program (TBDRP) are being solicited for the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA). As directed by the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the DHA RDA Directorate manages the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. The managing agent for this Program Announcement/Funding Opportunity is the Congressionally Directed Medical Research Programs (CDMRP). The TBDRP was initiated in FY16 to support innovative and impactful research that addresses fundamental issues and gaps in knowledge of tick-borne diseases. The FY16 appropriation for the TBDRP is $5 million (M).

The TBDRP's vision is to prevent the occurrence, better diagnose, and resolve or minimize the impact of Lyme disease and other tick-borne illnesses. The TBDRP's mission is to support research to understand the pathogenesis of Lyme disease and other tick-borne illnesses and to deliver innovative solutions to prevent, better diagnose, and treat their manifestations for the benefit of U.S. Service members, Veterans, their families, and the American public.

B. FY16 TBDRP Focus Areas

To meet the intent of the award mechanism, applications submitted to the FY16 TBDRP *must* address at least one of the following specific Focus Areas in Lyme disease and other tick-borne diseases:

- **Pathogenesis**
  - Host-pathogen interactions
  - Human immune response
  - Mechanisms of persistence of Lyme disease
  - New research tools to support studies of pathogenesis

- **Prevention**
  - Interrupting the natural cycle of the disease
  - Personal protection measures
  - Targeted vaccines
  - Post-exposure prophylaxis

- **Diagnosis**
  - Direct detection of tick-borne pathogens or their products in humans
  - Biomarkers for diagnosis

- **Treatment**
  - Innovative approaches to treatment
  - Basic studies aimed at safe and effective treatments for the cause(s) of persistent symptoms in Lyme disease
  - Biomarkers of effective prognosis, therapy, and cure

Applications addressing persistence and direct detection of Lyme borreliae are highly encouraged.

C.   Award Information

The FY16 TBDRP Investigator-Initiated Research Award (IIRA) promotes a wide range of research from basic through translational, including preclinical studies in animal models or human subjects, as well as correlative studies associated with an existing clinical trial to establish proof-of-principle for further development in future studies. This award funds highly rigorous, high-impact studies that have the potential to make important contributions to Lyme disease and other tick-borne disease research, patient care, and/or quality of life. Applications should include a well-formulated, testable hypothesis based on strong scientific rationale that is established through logical reasoning, preliminary data, and critical review and analysis of the literature.

The following are important aspects of the FY16 TBDRP IIRA:

- **Impact:** Applications should articulate both the short- and long-term impact of the proposed research. High-impact research will, if successful, significantly advance Lyme disease and other tick-borne disease research, patient care, and/or quality of life.
- **Preliminary Data:** Unpublished data from the laboratory of the Principal Investigator (PI) or collaborators named on the application, and/or data from the published literature that are relevant to Lyme disease and other tick-borne diseases and support the proposed research project **are required**.

Research involving human subjects and human anatomical substances is permitted; however, clinical trials are not allowed under this Program Announcement/Funding Opportunity. A clinical trial is defined as a prospective accrual of patients in which an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the subject of that intervention or interaction. For more information on clinical trials and clinical research overall, a Human Subject Resource Document is provided on the CDMRP electronic Biomedical Research Application Portal (eBRAP) system at https://ebrap.org/eBRAP/public/Program.htm.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All Department of Defense (DoD)-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO) prior to research implementation. This administrative review requirement is in addition

to the local Institutional Review Board (IRB) or Ethics Committee (EC) review. Local IRB/EC approval at the time of submission is *not* required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB/EC. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes***. Refer to the General Application Instructions, Appendix 6, and the Human Subject Resource Document available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

Rigor of Experimental Design: All projects should adhere to accepted standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. Core standards are described in Landis, S.C., et al., A call for transparent reporting to optimize the predictive value of preclinical research, *Nature* 2012, 490:187-191 (www.nature.com/nature/journal/v490/n7419/full/nature11556.html). While these standards were written for preclinical studies, the basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in research and should be applied consistently across basic and translational studies. Applicants should consult the ARRIVE (Animal Research: Reporting *In Vivo* Experiments) guidelines to ensure relevant aspects of rigorous animal research are adequately planned for and, ultimately, reported. The ARRIVE guidelines can be found at http://www.elsevier.com/__data/promis_misc/622936arrive_guidelines.pdf.

Research Involving Animals: All DoD-funded research involving new and ongoing research with animals must be reviewed and approved by the USAMRMC ORP Animal Care and Use Review Office (ACURO), in addition to the local Institutional Animal Care and Use Committee (IACUC) of record. IACUC approval at the time of submission is not required. Specific documents relating to the use of animals in the proposed research will be requested **if the application is selected for funding**. The ACURO must review and approve all animal use prior to the start of working with animals, including amendments to ongoing projects. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the animal use appendix titled "Research Involving Animals." ***Allow at least 2 to 3 months for ACURO regulatory review and approval processes for animal studies.*** Refer to General Application Instructions, Appendix 6, for additional information.

Use of Military and Department of Veterans Affairs (VA) Populations or Resources: If applicable, access to target military or VA patient population(s) or resources should be confirmed at the time of application submission. A letter of support, signed by the lowest ranking person with approval authority, should be included in Attachment 2 for studies involving active duty military, Veterans, military and/or VA-controlled study materials, and military and/or VA databases.

The CDMRP intends that information, data, and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section K.

D. Eligibility Information

- Independent Investigators at or above the level of Assistant Professor (or equivalent) are eligible to submit applications.

- Cost sharing/matching is not an eligibility requirement.

- Eligible investigators must apply through an organization. Organizations eligible to apply include Federal agencies, national, international, for-profit, nonprofit, public, and private organizations.

- An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Submissions from intramural (DoD) organizations are allowed and encouraged for this Program Announcement/Funding Opportunity. Applicants submitting through their intramural organizations are reminded to coordinate receipt and commitment of funds through their respective resource managers. ***If an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.***

- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **3** years.

- The anticipated direct costs budgeted for the entire period of performance will not exceed **$700,000**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$700,000** direct costs or using an indirect rate exceeding the organization's negotiated rate.

- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.

- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **3** years.

For this award mechanism, direct costs may be requested for:
- Salary
- Research supplies
- Equipment
- Research-related subject costs
- Clinical research costs

- Support for multidisciplinary collaborations, including travel
- Travel costs for up to one investigator to travel to one scientific/technical meeting per year.

Shall not be requested for:

- Clinical trial costs

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural (DoD) agencies and other Federal agencies may be managed through a direct funds transfer (e.g., the Military Interdepartmental Purchase Request [MIPR]; Funding Authorization Document [FAD] process; or DD Form 1144 Support Agreement). Direct transfer of funds from the recipient to a DoD agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. *For Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions*.

The CDMRP expects to allot approximately $3.36M of the $5M FY16 TBDRP appropriation to fund approximately three Investigator-Initiated Research Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II.   SUBMISSION INFORMATION

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application(s).

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/). Refer to the General Application Instructions, Section II.A., for registration and submission requirements for eBRAP and Grants.gov.

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application

submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

The application title, eBRAP log number, and all information for the PI, Business Official(s), performing organization, and contracting organization must be consistent for the entire pre-application and application submission process. Inconsistencies may delay application processing and limit the ability to view, modify, and verify the application in eBRAP. If any changes need to be made, the applicant should contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application deadline.

Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. ***The Project Narrative and Budget cannot be changed after the application submission deadline.*** Prior to the full application deadline, a corrected or modified full application package may be submitted. Other application components may be changed until the end of the [application verification period](#). After the end of the application verification period, the full application cannot be modified.

A.   Where to Obtain the Grants.gov Application Package

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-16-TBDRP-IIRA in Grants.gov (http://www.grants.gov/).

B.   Pre-Application Submission Content

The pre-application process should be started early to avoid missing deadlines. There are no grace periods. During the pre-application process, each submission is assigned a unique log number by eBRAP. This unique eBRAP log number will be needed if invited for a full application submission via Grants.gov.

All pre-application components must be submitted by the PI through eBRAP (https://eBRAP.org/). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

The pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Tab 1 – Application Information**

- **Tab 2 – Application Contacts**
  - ○ Enter contact information for the PI. Enter the organization's Business Official responsible for sponsored program administration (the "person to be contacted on matters involving this application" in Block 5 of the Grants.gov SF424 (R&R) Form). The Business Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.
  - ○ Select the performing organization (site at which the PI will perform the proposed work) and the contracting organization (organization submitting on behalf of the PI, which corresponds to Block 5 on the Grants.gov SF424 (R&R) Form), and click on "*Add Organizations to this Pre-application.*" The organization(s) must either be selected from the eBRAP drop-down list or invited in order for the pre-application to be submitted.
  - ○ It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

- **Tab 3 – Collaborators and Key Personnel**
  - ○ Enter the name, organization, and role of all collaborators and key personnel associated with the application.
  - ○ FY16 TBDRP Programmatic Panel members should not be involved in any pre-application or application. *A list of the FY16 TBDRP Programmatic Panel members can be found at http://cdmrp.army.mil/tbdrp/panels/panels16.shtml.* For questions related to Panel members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.
  - ○ To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in application preparation, research, or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess.shtml). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage conflicts of interest (COIs) are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.

- **Tab 4 – Conflicts of Interest**
  - ○ List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship). Refer to Appendix 1, Section C, of the General Application Instructions for further information regarding COIs.

- **Tab 5 – Pre-Application Files**

  Note: Upload documents as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

  Preproposal Narrative (three-page limit): The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application.

  The Preproposal Narrative should include the following:

  - **Relevance:** Describe how the proposed research is relevant to at least one of the FY16 TBDRP Focus Areas.

  - **Background/Rationale:**
    - State the ideas and reasoning on which the proposed research project is based. Clearly demonstrate that there is sufficient rationale for the proposed research.
    - Clearly state the type of study proposed (e.g., development, animal validation, human validation), and demonstrate that there is sufficient scientific evidence to support moving into the stage of proposed research.
    - Briefly state the qualifications of the PI and key personnel to perform the described research project.

  - **Hypothesis, Specific Aims, and Approach:**
    - Concisely state the project's hypothesis, specific aims, and describe the scientific approach. Include a description of controls, as appropriate, and demonstrate that the work is appropriately powered.

  - **Impact:**
    - Describe the immediate and long-range outcomes of the proposed study and their impact on Lyme disease and other tick-borne disease research, patient care, and/or quality of life, including the impact on the FY16 TBDRP Focus Area(s) being addressed.

  Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application *must be uploaded as individual files* and are limited to:

  - References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

  - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.

- ○ Key Personnel Biographical Sketches (six-page limit per individual): ***All biographical sketches should be uploaded as a single combined file.*** Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

- **Tab 6 – Submit Pre-Application**
  - ○ This tab must be completed for the pre-application to be accepted and processed.

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the TBDRP, pre-applications will be screened based on the following criteria:

  - ○ **Relevance:** To what degree the proposed project is relevant to at least one of the FY16 TBDRP Focus Areas.

  - ○ **Background/Rationale:** How well the described research demonstrates scientific rationale and provides sufficient evidence that the research is ready to move into the stage of proposed research (e.g., development, animal validation, human validation). How appropriate personnel background and expertise are to accomplish the proposed research.

  - ○ **Hypothesis, Specific Aims, and Approach:** How well a clear hypothesis is stated and supported through scientific rationale, preliminary data, and referenced literature. How well the specific aims and approach will address the hypothesis. If applicable, whether the proposed study includes appropriate controls and is adequately powered.

  - ○ **Impact:** The extent to which the anticipated research outcomes, both short- and long-term, will contribute to significant advances in knowledge, improved patient care, and/or quality of life for individuals with Lyme disease and other tick-borne diseases, including the impact on the FY16 TBDRP Focus Area(s) being addressed.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity. Invitations to submit a full application are based on the Pre-Application Screening Criteria as published above.

C.   Full Application Submission Content

The application process should be started early on Grants.gov to avoid missing deadlines. There are no grace periods. Verify the status of the applicant's organization's Entity registration in the SAM well in advance of the application submission deadline. Allow 3 to 4 weeks to complete

the entire SAM registration process. Refer to the General Application Instructions, Section II, for additional information.

Applications will not be accepted unless the PI has received notification of invitation.

All contributors and administrators to the application must use matching compatible versions of Adobe software when editing and preparing application components. The use of different software versions will result in corruption of the submitted file. See Section II.C. of the General Application Instructions for details on compatible Adobe software.

The CDMRP cannot make allowances/exceptions to its policies for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.

Each application submission must include the completed Grants.gov application package for this Program Announcement/Funding Opportunity. The Grants.gov application package is submitted by the Authorized Organizational Representative through the Grants.gov portal (http://www.grants.gov/).

Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline.

If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID *prior to the application submission deadline*.

The Grants.gov application package must be submitted using the unique eBRAP log number to avoid delays in application processing.

Grants.gov application package components: For the Investigator-Initiated Research Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

    Each attachment to the Grants.gov application forms must be uploaded as an individual PDF file in accordance with the formatting guidelines listed in Appendix 2 of the General Application Instructions. For all attachments, ensure that the file names are consistent with the guidance. Grants.gov will reject attachments with file names longer than 50 characters or incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, Grants.gov has file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire Grants.gov application package may not exceed 200 MB.

- **Attachment 1: Project Narrative (12-page limit): Upload as "ProjectNarrative.pdf."** The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

  Describe the proposed project in detail using the outline below.

  - **Background/Rationale:** Present the ideas and rationale for the proposed research and include relevant literature citations. Clearly demonstrate that there is sufficient scientific evidence to support moving into the proposed stage of research. *Include preliminary data that are relevant to Lyme disease and other tick-borne diseases and the proposed project.*

  - **Hypotheses/Objectives:** State the hypotheses/study questions and overall objective(s) to be reached.

  - **Specific Aims:** Concisely explain the project's specific aims. If this application is part of a larger study, present only tasks that this award would fund.

  - **Focus Areas:** Describe how the proposed research is relevant to at least one of the FY16 TBDRP Focus Areas.

  - **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate randomization, blinding, sample-size estimation, and controls, in sufficient detail for evaluation. Clearly describe how data will be collected, handled, and analyzed in a manner that is consistent with the study objectives.

    – As applicable to the proposed research, provide a statistical plan and sample size estimate for each study arm and the method by which it was derived, including power analysis calculations to demonstrate that the sample size is appropriate to meet the objectives of the study.

    – Address potential problem areas and present alternative methods and approaches.

    – If cell lines or animals are to be used, justify why the proposed cell line(s) or animal model(s) were chosen. If animals studies are proposed, describe how they will be conducted in accordance with the ARRIVE guidelines (https://www.elsevier.com/__data/promis_misc/622936arrive_guidelines.pdf).

    – If human subjects or human biological samples will be used, describe the study population and include a detailed plan for the recruitment of subjects or the acquisition of samples. *This award cannot be used to conduct clinical trials.*

- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are

scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in the removal of those items or may result in administrative withdrawal of the application.***

○ References Cited: List the references cited (including URLs, if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

○ List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.

○ Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.

○ Publications and/or Patents: Include a list of relevant publication URLs and/or patent abstracts. If publications are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.

○ Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the Program Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.

○ Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.

○ Intellectual Property

– Intangible property acquired, created or developed under this award will be subject to all rights and responsibilities established at 2 CFR 200.315. Should the applicant intend to use, in the performance of this program, pre-existing, legally protected and perfected intangible property and for which no Federal funds had been used in the development of said property, the applicant must:

▪ Clearly identify all such property;

▪ Identify the cost to the Federal Government for use or license of such property, if applicable; or

- Provide a statement that no property meeting this definition will be used on this project.
    - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.
  - Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, Section K, for more information about the CDMRP expectations for making data and research resources publicly available.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf."** The technical abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  - Relevance: State the FY16 TBDRP Focus Area(s) that the project addresses.

  - Background: Present the ideas and reasoning behind the proposed work.

  - Hypothesis/Objective: State the hypothesis to be tested or the objective to be reached. Provide evidence or rationale that supports the hypothesis/objective.

  - Specific Aims: State the specific aims of the study.

  - Study Design: Briefly describe the study design including appropriate controls.

  - Impact: Summarize the potential impact of the proposed project on the prevention, diagnosis, and treatment of Lyme disease and other tick-borne diseases, including the impact on one or more of the FY16 TBDRP Focus Areas being addressed. Describe the study's potential impact on the health and welfare of U.S. Service members, Veterans, their families, and the American public.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf."** The lay abstract is used by all reviewers. Abstracts of all funded research projects will be posted publicly. ***Do not include proprietary or confidential information.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Do not duplicate the technical abstract. Minimize the use of acronyms and abbreviations, where appropriate. The lay abstract is an important component of the application review process because it addresses issues of particular interest to the consumer community. Lay abstracts should be written using the outline below.

  - Describe the rationale, scientific objective, and aims for the proposed project in a manner that will be readily understood by readers without a background in science or medicine.

- State the FY16 TBDRP Focus Area(s) the project addresses.
  - What is the potential impact of the proposed research on the health and welfare of U.S. Service members, Veterans, their families and the American public?
- Describe the ultimate applicability of the research.
  - What types of patients will it help, and how will it help them?
  - What are the potential clinical applications, benefits, and risks?
  - What is the projected time it may take to achieve a patient-related outcome?
  - If the research is too basic for immediate clinical applicability, describe the interim outcomes.
  - What are the likely contributions of the study to advancing the field of Lyme disease and other tick-borne disease research?

- **Attachment 5: Statement of Work (SOW) (three-page limit): Upload as "SOW.pdf."** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Investigator-Initiated Research Award mechanism, use the SOW format example titled "SOW Generic Format." The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

- **Attachment 6: Impact Statement (one-page limit): Upload as "Impact.pdf."**

  Explain in detail why the proposed research project is important as follows:
  - *Describe the short-term impact:* Detail the anticipated short-term outcome(s)/product(s) that will be directly attributed to the results of the proposed research.
  - *Describe the long-term impact:* Explain the anticipated long-term gains from the proposed research, including the long-term anticipated advantages that the new understanding may ultimately contribute to the field of Lyme disease and other tick-borne disease research, patient care, and/or quality of life.

- **Attachment 7: Relevance Statement (one-page limit): Upload as "Relevance.pdf."**
  - Focus Areas: Describe how the proposed research is relevant to at least one of the FY16 TBDRP Focus Areas in a way that is consistent with the program's goals.
  - Military Relevance: Describe how the proposed research is relevant to the healthcare needs and welfare of U.S. Service members, Veterans, and their families in a way that is consistent with the program's goals.

- **Attachment 8: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as "MFBudget.pdf."** If a Military Facility (military health system facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form, available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm), including a budget justification, for each Military Facility as instructed. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information**.**

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., for detailed information.

   - PI Biographical Sketch (six-page limit): Upload as "Biosketch_LastName.pdf." The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The five-page National Institutes of Health Biographical Sketch may also be used. All biographical sketches should be submitted in the portable document format (pdf) that is not editable.

      Biographical Sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished.

   - PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

   - Key Personnel Biographical Sketches (six-page limit each): Upload as "Biosketch_LastName.pdf."

   - Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., for detailed information.

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf." The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1.

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.5., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

   Collaborating DoD Military Facilities Form: A Military Facility collaborating in the performance of the project should be treated as a subaward for budget purposes. However, do not complete the Grants.Gov R & R Subaward Budget Attachment Form;

instead, complete the Collaborating DoD Military Facility Budget Form (use Attachment 8, Collaborating DoD Military Facility Budget Form) to show all direct and indirect costs. The costs per year should be included on the Grants.gov Research and Related Budget form under subaward costs. Refer to the General Application Instructions, Section II.C.7., for detailed information.

D. Applicant Verification of Grants.gov Submission in eBRAP

Prior to the end of the application verification period, PIs and organizational representatives can review and modify in eBRAP certain components of an application submitted to Grants.gov. Following retrieval and processing of the Grants.gov application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the Grants.gov application submission. eBRAP will validate retrieved files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in both the email and in the Full Application Files tab in eBRAP. eBRAP does not confirm the accuracy of file content. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the Program Announcement/Funding Opportunity. *If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID prior to the application submission deadline.* The Project Narrative and Budget Form cannot be changed after the application submission deadline.

E. Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in submission rejection.

F. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All extramural applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Section II.A., for information on Grants.gov registration requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. Each application is evaluated for its own merit, independent of other

applications. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the OASD(HA), based on technical merit, the relevance to the mission of the DHP and TBDRP, the specific intent of the award mechanism, and to other specified evaluation criteria in the Program Announcement/Funding Opportunity. Programmatic review is a comparison-based process in which applications with scientific and technical merit compete in a common pool. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in [Section III.B.2., Programmatic Review](#).*** Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.shtml.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from Federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are of equal importance:

- **Impact**
  - To what extent the anticipated research outcomes, either short- or long-term, will contribute to significant advances in knowledge, improved patient care, and/or quality of life for individuals with Lyme disease and other tick-borne diseases.
  - To what extent the proposed project will impact the prevention, diagnosis, and treatment of Lyme disease and other tick-borne diseases in U.S. Service members, Veterans, their families, and the American public.

- **Research Strategy and Feasibility**
  - How well the scientific rationale supports the project and its feasibility as demonstrated by a critical review and analysis of the literature, relevant preliminary data, and logical reasoning.
  - How well the hypotheses or objectives, aims, experimental design, methods, and analyses (and, if applicable, the statistical plan, rationale for the statistical methodology, and power analysis) are developed.
  - How well studies are designed to achieve reproducible and rigorous results, including the choice of model and the endpoints/outcomes to be measured.

- If human subjects or human anatomical samples will be used, how well the plan for the recruitment of subjects or the acquisition of samples is justified and appropriate to accomplish the proposed work.
- How well the PI acknowledges potential problems and addresses alternative approaches.

- **Relevance**
  - How well the proposed research addresses at least one of the FY16 TBDRP Focus Areas.
  - How well the proposed research addresses the healthcare needs and welfare of U.S. Service members, Veterans, and the American public.

- **Personnel**
  - To what degree the research team's background is appropriate with respect to its ability to perform the proposed work, including whether there is evidence of sufficient clinical and/or statistical expertise (as applicable).
  - To what degree the levels of effort by the PI and other key personnel are appropriate for successful conduct of the proposed work.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Budget**
  - Whether the **direct** maximum costs are equal to or less than the allowable direct maximum costs as published in the Program Announcement/Funding Opportunity.
  - Whether the budget is appropriate for the proposed research.

- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.

- **Environment**
  - To what extent the scientific environment is appropriate for the proposed research project.
  - How well the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
  - To what extent the quality and level of institutional support are appropriate for the proposed research project.
  - If applicable, to what degree the intellectual and material property plan is appropriate.

2. **Programmatic Review:** To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following criteria are used by programmatic reviewers:

    a. **Ratings and evaluations of the peer reviewers**

    b. **Relevance to the mission of the DHP and the FY16 TBDRP, as evidenced by the following:**

- Adherence to the intent of the award mechanism
- Programmatic relevance in relation to the FY16 TBDRP Focus Areas
- Program portfolio balance
- Relative impact

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eBRAP or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the pre-application:

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.

- Budget is missing.
- Submission of the same research project to different Funding Opportunities within the same program and fiscal year.

B.   Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Preproposal Narrative and Project Narrative.
- Documents not requested will be removed.

C.   Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- An FY16 TBDRP Programmatic Panel member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. *A list of the FY16 TBDRP Programmatic Panel members can be found at http://cdmrp.army.mil/tbdrp/panels/panels16.shtml.*
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages inclusion of any employee of its review contractors having any role in the preparation, research or other duties for submitted applications. For FY16, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (http://cdmrp.army.mil/about/2tierRevProcess.shtml). Applications that include names of personnel from either of these companies will be administratively withdrawn unless plans to manage COIs are provided and deemed appropriate by the Government. Refer to the General Application Instructions, Appendix 1, for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- A clinical trial is proposed.
- The PI does not meet the eligibility criteria.

D.   Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization will be required to

provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2017. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

Any assistance instrument awarded under this Program Announcement/Funding Opportunity will be governed by the award terms and conditions, which conform to DoD's implementation of the Office of Management and Budget (OMB) circulars applicable to financial assistance. Terms and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in the Code of Federal Regulations, Title 2, Part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards" (2 CFR part 200).

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 4 for general information regarding administrative requirements.

C. National Policy Requirements

Refer to the General Application Instructions, Appendix 5 for general information regarding national policy requirements.

D. Reporting

Refer to the General Application Instructions, Appendix 4, Section H, for general information on reporting requirements.

E. Award Transfers

Approval of an organizational or PI transfer request will be on a case-by-case basis at the discretion of the Grants Officer. An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

Refer to the General Application Instructions, Appendix 4, Section L, for general information on organization or PI changes.

VI. VERSION CODES AND AGENCY CONTACTS

A. Program Announcement/Funding Opportunity and General Application Instructions Version

Questions related to this Program Announcement/Funding Opportunity should refer to the Program name, the Program Announcement/Funding Opportunity name, and the Program Announcement/Funding Opportunity version code 20160210j. The Program Announcement/Funding Opportunity numeric version code will match the General Applications Instructions version code 20160210.

B. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

    Phone: 301-682-5507

    Email: help@eBRAP.org

C. Grants.gov Contact Center

Questions related to application submission through Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. Federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

    Phone: 800-518-4726; International 1-606-545-5035

    Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity or by responding to the prompt provided by Grants.gov when first downloading the Grants.gov application package. If the Grants.gov application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	7	Relevance Statement: Upload as Attachment 7 with file name "Relevance.pdf."	
	8	Collaborating DoD Military Facility Budget Form(s): Upload as Attachment 8 with file name "MFBudget.pdf," if applicable.	
Research & Related Senior/Key Person Profile (Expanded)		Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
		Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
		Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
		Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form		Complete form as instructed.	