Program Announcement

Defense Health Program

Defense Medical Research and Development Program

Military Infectious Diseases Clinical Trial Award

Funding Opportunity Number: W81XWH-12-DMRDP-MID-CTA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-application Submission Deadline:** 5:00 p.m. Eastern time (ET), July 8, 2011
- **Invitation to Submit an Application:** July 2011
- **Application Submission Deadline:** 11:59 p.m. ET, September 7, 2011
- **Scientific Peer Review:** October 2011
- **Programmatic Review**: December 2011

New for FY11: The Grants.gov Research & Related Budget form is a mandatory component of all Grants.gov application packages.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

The Defense Medical Research and Development Program (DMRDP) was established in fiscal year 2010 (FY10) by the Defense Health Program in the Office of the Assistant Secretary of Defense for Health Affairs. The primary purpose of the DMRDP is to invest in research outcomes that will expedite translation of health care solutions toward advancement of the health and welfare of military personnel, families, and communities, by executing innovative approaches to basic and applied research. The objectives of the DMRDP are to discover and explore innovative approaches to protect, support, and advance the health and welfare of military personnel, families, and communities; to accelerate the transition of medical technologies into deployed products; and to accelerate the translation of advances in knowledge into new standards of care in multiple military-relevant areas.

B. Award Information

The Defense Health Program (Defense Medical Research and Development) has assigned funds to support clinical trials focused on combat-related infectious diseases. This Program Announcement/Funding Opportunity, DMRDP Military Infectious Diseases Clinical Trial Award (MID-CTA), is soliciting proposals focused on wound infection prevention and management as well as antimicrobial countermeasures. The FY12 MID-CTA seeks applications focused on reduction of morbidity and mortality of wound infections in wounded warriors and specifically seeks to accelerate transition of (1) medical technologies into deployed products and (2) advances in knowledge to improve clinical practices for use in the theater of war or in the clinical facilities of the Military Health System (MHS). The MID-CTA is intended to support early phase clinical trials/testing with the potential to have a major impact on treatment of combat-related wound infections. These studies must be responsive to the health care needs of military service members and veterans; however, the use of military populations in the clinical trial/testing is not a requirement. Proposed projects should be designed to demonstrate (1) the utility of a novel biomarker/assay, and/or (2) the safety and efficacy of novel therapies in human patients suffering from serious, debilitating wound infections due to trauma. The purpose of such demonstrations is to accelerate translation of greater medical capabilities to patients; ***this can range from proof of concept (i.e., first in human) trials through Phase II clinical trials, as well as Class I, II, or III medical device trials/testing. Neither Phase III trials for Food and Drug Administration (FDA) licensure of drugs, nor definitive testing for device or assay clearance by the FDA*** will be permitted under this Program Announcement/Funding Opportunity. Projects of interest are those focused on testing and translating investigational interventions/devices already proven in relevant definitive animal models, moving them into advanced clinical development.

Funding from this award mechanism must support a clinical trial/testing and cannot be used for preclinical research studies.

A clinical trial is defined as a prospective accrual of human subjects where 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 exploratory

information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. For this Program Announcement/Funding Opportunity the term "device" includes in diagnostics (e.g., in vivo, in vitro, and/or biomarkers). In vitro diagnostic products are those reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. For more information on clinical trials and phase/class of study, a Human Subject Resource Document is provided at https://cdmrp.org/Program_Announcements_and_Forms/.

All applications must address at least one of the following focus areas:

1. **Therapeutic clinical trials-preventative or directive.** Clinical trials to determine the optimum preventative or directive therapies for infections of trauma-induced wounds, using FDA-approved drugs, biologics, or devices, either alone or in combination. Preference will be given to studies that address infections with one or more multi drug-resistant organisms (MDROs) (particularly, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, extended-spectrum beta-lactamase producers, *Klebsiella*, and methicillin-resistant *Staphylococcus aureus*), and/or invasive, non-*Candida* fungal pathogens.

2. **Clinical trials for new indications of FDA-approved drugs.** Clinical trials to evaluate potential new indications of FDA-approved drugs or studies of Investigational New Drugs (INDs) targeting one or more MDROs (particularly, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, extended-spectrum beta-lactamase producers, *Klebsiella*, and methicillin-resistant *Staphylococcus aureus*), and/or invasive, non-*Candida* fungal pathogens, and/or pathogen biofilms.

3. **Therapeutic clinical trials.** Clinical trials to determine the optimum therapy for infections of trauma-induced wounds. Studies involving carbapenem-resistant organisms are particularly sought.

4. **Rapid detection of pathogens and/or microbial drug resistance markers.** Evaluation of a functional prototype device(s)/assay(s) (including in vitro or in vivo diagnostic assays) for the rapid detection of pathogens and/or microbial drug resistance markers in trauma-induced wounds. As appropriate for the device/assay, efforts shall include clinical laboratory evaluation and/or proof-of-concept clinical studies in order to confirm device/assay design, demonstrate safety, and collect preliminary effectiveness data. Deliverables shall include the documentation required to support follow-on development efforts for FDA clearance of the device/assay. This documentation shall include, but is not limited to, device/assay design, device/assay review, safety and preliminary effectiveness data, and quality control and quality assurance processes.

5. **Rapid detection of biomarkers.** Evaluation of a functional prototype device(s)/ assays(s) (including in vitro or in vivo diagnostic assays) for the rapid detection of novel and specific in vivo or in vitro biomarkers (from wound, serum, saliva, or urine) that predict development of infection or discriminate between infection and colonization. As appropriate for the device/assay, efforts shall include clinical laboratory evaluation and/or proof-of-

concept clinical studies to confirm device/assay design, demonstrate safety, and collect preliminary effectiveness data. Deliverables shall include the documentation required to support follow-on development efforts for FDA clearance of the device/assay. This documentation shall include, but is not limited to, device/assay design, device/assay review, safety and preliminary effectiveness data, and quality control and quality assurance processes.

The MID-CTA seeks applications for well-controlled clinical trials/testing that are responsive to at least one of the above focus areas. Each application should propose only one clinical trial with a distinct study design.

If the proposed trial involves the use of a drug that has not been approved by the FDA for its investigational use, an IND application to the FDA may be required and must be submitted to the FDA prior to the grant submission. If the proposed study involves an Investigational Device that has not been approved or cleared by FDA for its investigational clinical use, the study may be required to comply with the FDA Investigational Device Exemption (IDE) regulations. If applicable, the IDE application must be submitted prior to the grant submission. The Government reserves the right to withdraw funding if an IND or IDE required for conduct of the proposed research has not been obtained within 6 months of the award date.

All of the following are important aspects of submission for a clinical trial:

- The proposed clinical trial is expected to begin no later than 12 months after the award date.
- The inclusion of all preliminary data that are relevant to the proposed research is required; any unpublished preliminary data should originate from the laboratory of the Principal Investigator (PI), collaborator(s), or subawardee(s) named on this application.
- The proposed research project should be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature as documented in the application.
- The application should demonstrate and document availability of and access to the drug/ compound, device, and/or materials needed.
- Demonstrate availability of and access to a suitable human subject population that will support a meaningful outcome for the study. Discuss how accrual goals will be achieved, and how standards of care may impact the study population.
- Describe appropriate and clearly defined endpoints for the proposed clinical trial/testing.
- The application should include a clearly articulated statistical analysis plan, as well as appropriate statistical expertise and a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- Discuss the potential impact of the study results on prevention and/or treatment of combat-related wound infections.
- Include a study coordinator(s) who will guide the clinical trial protocol through the local Institutional Review Board (IRB) of record and other regulatory approval processes,

coordinate activities from all sites participating in the trial, and coordinate human subject accrual.

- Demonstrate institutional support.
- The application should include a Transition Plan that describes a clear path to further develop the trial product and how the project will continue to the next level after the end of the award period of performance.

Use of Human Subjects and Human Anatomical Substances: All Department of Defense (DOD)-funded research involving new and ongoing research with human subjects and human anatomical substances must be reviewed and approved by the US Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local IRB of record. Local IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DOD. These laws and directives are rigorous and detailed, and will require information in addition to that supplied to the local IRB. Allow a minimum of 4 months for regulatory review and approval processes. Refer to the General Application Instructions, Appendix 5, for more information. The term "human subjects" is used in this Program Announcement/Funding Opportunity to refer to individuals who will be recruited for or who will participate in the proposed clinical trial.

This Program Announcement/Funding Opportunity is intended only for extramural investigators or extramural investigators with one or more intramural collaborator(s). An ***intramural*** investigator is defined as a **DOD employee** working within a DOD laboratory or medical treatment facility (MTF), or a DOD activity embedded within a civilian medical center. An ***extramural*** investigator is defined as all those not included in the definition of intramural investigator **(including Department of Veterans Affairs [VA] and other Federal investigators).** Pre-applications submitted to this Program Announcement/Funding Opportunity by an intramural investigator will be administratively withdrawn. A separate Program Announcement/Funding Opportunity will be released exclusively for intramural applications.

DOD-Aligned Organizations: Relevance to the health care needs of the Armed Forces and/or the U.S. veteran population is a key feature of this award. Therefore, applications with collaborations partnering extramural academic industry and non-DOD federal investigators with intramural investigators (especially PIs at MTFs), are highly encouraged. For applications that include intramural collaborations, the extramural PI must provide more than a nominal contribution to the research project. ***Note: Intramural collaborators are not allowed to be subawardees to the extramural applicant, but must submit a separate budget that will be funded through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Details for funding of such collaborations can be found in Section I.D., Funding.*** Other Federal applicants, including VA or Health and Human Services/National Institutes of Health PIs may submit as PIs or be included as subawardees..

The following websites may be useful in identifying information about ongoing DOD areas of research interest pertinent to the MID-CTA focus areas:

Air Force Research Laboratory
http://www.wpafb.af.mil/afrl

Clinical and Rehabilitative Medicine Research Program
https://crmrp.amedd.army.mil/

Congressionally Directed Medical Research Programs
http://cdmrp.army.mil

Defense Advanced Research Projects Agency
http://www.darpa.mil/

Defense Technical Information Center
http://www.dtic.mil

Military Infectious Diseases Research Program (MIDRP)
https://mrmc.amedd.army.mil/index.cfm?pageid=medical_r_and_d.midrp.overview

Naval Health Research Center
http://www.med.navy.mil/sites/nhrc

Naval Medical Research Center
www.med.navy.mil/sites/nmrc

Navy and Marine Corps Public Health Center
http://www-nmcphc.med.navy.mil/

Office of Naval Research
http://www.med.navy.mil/

Office of the Under Secretary of Defense for Acquisition, Technology and Logistics
http://www.acq.osd.mil/

U.S. Army Institute of Surgical Research (USAISR)
http://www.usaisr.amedd.army.mil/

U.S. Army Medical Research Acquisition Activity
http://www.usamraa.army.mil

U.S. Army Medical Research and Materiel Command
https://mrmc.amedd.army.mil

U.S. Army Research Laboratory
http://www.arl.army.mil

U.S. Department of Veterans Affairs, Office of Research and Development
www.research.va.gov

U.S. Naval Research Laboratory
www.nrl.navy.mil

Walter Reed Army Institute of Research (WRAIR)
http://wrair-www.army.mil/

Walter Reed Army Institute of Research, Multidrug-resistant Organism Repository and Surveillance Network (MRSN)
http://wrair-www.army.mil/index.php?view=MRSN

Use of Military and VA Populations or Resources: If applicable, access to target military or VA patient population(s) should be confirmed at the time of application submission. Studies involving active duty military, military-controlled study materials, and/or military databases must include a letter of support signed by the lowest ranking person with approval authority. Studies proposing to recruit subjects from VA Medical Centers or use VA-controlled materials or information from VA data systems must either include an investigator with a VA appointment as the primary PI or a collaborator, or include a letter from an appropriate authority providing access to veterans (as applicable), VA-controlled study materials, or VA data. Use Attachment 14 to provide this documentation.

C. Eligibility Information

- Independent investigators at any academic level (or equivalent) are eligible to submit applications.
- Cost sharing/matching is not an eligibility requirement.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

- The maximum period of performance is **3** years.
- The maximum allowable costs for the entire period of performance are **$2,500,000** including indirect costs.
- 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.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.
- All direct and indirect costs of any subaward (subgrant or subcontract) with a non-federal collaborator must be included in the total direct costs of the primary award.
- Funding for intramural collaborators will not be executed as subawards, but will be executed through the MIPR or FAD process. This process may include incremental funding; therefore, intramural collaborators are required to coordinate this process with their respective resource manager. For applications that include one or more intramural collaborators, these collaborator(s) must submit a separate budget form (in addition to the PI's budget) for their work on the project. Budget submission steps for intramural collaborators are detailed in Section II.B., Notification of Pre-Application Screening Results, and Section II.D., Budget Submission for Intramural Collaborators.
- Regardless of whether there is an intramural collaborator, total funding for the entire project, covering direct and indirect costs of extramural and intramural institutions, is $2,500,000 for the entire period of performance.

Refer to the General Application Instructions, Section II.C., for budget regulations and instructions for the Research and Related Budget form. In addition, for this award mechanism, direct costs:

Must be requested for:

- Travel costs for the PI to attend one DOD-specified meeting per year during the award period of performance. For planning purposes, it may be assumed that such meetings will be held in the Washington, DC-Baltimore, Maryland metropolitan area.

May be requested for (not all-inclusive):

- Salary, including salary for a Study Coordinator

- Research-related subject costs
- Clinical research costs
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs of up to $3,600 per year to attend scientific/technical meetings

The DMRDP expects to fund four FY12 MID-CTA applications, depending on the quality and number of applications received and the total cost of applications approved for funding. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this Program. Funding allotted for this Program Announcement/Funding Opportunity is approximate and subject to realignment. Currently $2.5M in FY12 funds are available and approximately $8M of FY11 funds may become available to fund additional awards. Intramural collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers.

II. SUBMISSION INFORMATION

Submission is a multi-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

Submission of the same research project to different funding opportunities within the same program and fiscal year is discouraged. The Government reserves the right to reject duplicative applications.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-12-DMRDP-MID-CTA.

B. Pre-Application Submission Content and Form

All pre-application components must be submitted by the PI through the CDMRP eReceipt System (https://cdmrp.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.

Changes in the PI or organization after the pre-application deadline are strongly discouraged. Requests for a change in PI or organization for a MID-CTA application will be reviewed on a case-by-case basis. If a change in PI or organization is necessary after submission of the pre-application, the PI must contact the Help Desk at help@cdmrp.org or 301-682-5507.

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

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
- **Collaborators and Conflicts of Interest (COI) – Tab 3**

  The PI must enter the contact information for any intramural collaborator(s) and/or subawardees in the Partnering PI section.

- **Required Files – Tab 4**

  Preproposal Narrative (three-page limit): The Preproposal Narrative page limit applies to text and any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons.

  The Preproposal Narrative should address the following:

  - **Research Plan:** State the ideas and reasoning on which the clinical trial is based. Clearly specify which type (e.g., drug, device, behavioral) of clinical trial/testing is being proposed, and indicate the phase of trial and/or class of device and regulatory status as appropriate. Concisely state the project's objectives and specific aims.
  - **Personnel:** Briefly state the qualifications of the PI and key personnel to perform the described research project.
  - **Impact:** State explicitly how the proposed work will have an impact on research and patient care related to combat-related wound infection. Describe how the study will accelerate promising treatments into clinical practice.
  - **Military Relevance:** Describe how the proposed work is applicable to the health care needs of military service members and U.S. veterans recovering from combat-related wound infection.
  - **Alignment with Focus Areas:** Explain how the proposed work addresses at least one of the FY12 DMRDP MID-CTA focus areas.

- **Pre-Application Supporting Documentation**
  - **Quad Chart:** This document must be submitted by the pre-application submission deadline. The Quad Chart is a PowerPoint file that must be downloaded from the CDMRP eReceipt System and saved using Adobe Acrobat Reader as a PDF file. The Quad Chart must include the following sections:
    - Focus Area – Include the MID-CTA focus area(s) as a subtitle on the Quad Chart.
    - Problem and Military Relevance – Provide a bulleted summary of the problem to be studied and its military relevance.
    - Proposed Solution – Provide a bulleted summary of the objectives of the work based on the Preproposal Narrative.
    - Picture – Insert a picture or other graphic that is representative of the work to be performed; this may, for example, show some aspect of the research to be

performed, the expected technology outcome of the work, or the military problem that is being addressed.

- Timeline and Cost – Identify the major planned activities or phases of the work and their duration on the chart provided, and provide the estimated direct costs by year.

- **Key Personnel Biographical Sketches** (four-page limit per individual)
- **References Cited** (one-page limit)

- **Submit Pre-application – Tab 5**
- **Other Documents Tab**

  No additional documents are required.

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and its relevance to the mission of the DOD, pre-applications will be screened by the Joint Program Committee for Military Infectious Diseases based on the following criteria:

  - **Research Plan:** How the proposed project addresses the intent of the award mechanism and the program. How well the rationale and specific aims support the research idea.
  - **Personnel:** How the qualifications and expertise of the PI and key personnel are appropriate to perform the proposed research project.
  - **Impact:** How well the study addresses an important problem relevant to combat-related wound infection prevention and management, and antimicrobial countermeasures. If successful, how the study will improve our capabilities to prevent and/or treat combat-related wound infections.
  - **Military Relevance:** How the proposed study will directly or indirectly benefit military service members and/or the U.S. veteran population.
  - **Alignment with Focus Areas:** How well the project addresses at least one FY12 DMRDP MID-CTA focus area.

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

  Following the pre-application screening:

  - PIs will be notified by email of whether or not they are invited to submit an application; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application. Intramural collaborators, if applicable, will also be notified by email whether or not the PI was invited to submit an application.
  - Intramural collaborators whose PI is invited to submit a full application must register with the CDMRP eReceipt System (http://cdmrp.org).

- Pre-application notification dates are indicated on the title page of this Program Announcement/Funding Opportunity.

C. Application Submission Content and Form

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

- If the PI was invited to submit an application, the intramural collaborator is required to download a Research and Related Budget form from Grants.gov and upload his/her individual budget in the CDMRP eReceipt System, as described in Section II.D.
- Intramural collaborators are required to ensure their budget forms are in compliance with MIPR and FAD policies.
- The PI is responsible for ensuring that the total budget (including any intramural collaborators and/or subawardees, if applicable) does not exceed the maximum allowed costs.
- Budgets for subawardees will be included in the PI's Research and Related Budget form submitted through Grants.gov.

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

Grants.gov application package components: For the MID-CTA 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. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

   Note: All essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6-8 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

   - **Attachment 1: Project Narrative (20-page limit):** Upload as "ProjectNarrative.pdf."

     Describe the proposed project in detail using the outline below.

- **Background:** Describe in detail the rationale for the study and include a literature review, preliminary studies, and/or preclinical data that led to the development of the proposed clinical trial/testing. The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.
- If the proposed clinical trial/testing was initiated using other funding prior to this application, explain the history and background of the clinical trial/testing and declare the source of prior funding. Specifically identify the portions of the study that will be supported with funds from this award.
- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/ hypotheses.
- **Study Design:** Describe the type of study to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action.
  - Identify the intervention to be tested and describe the projected outcomes.
  - Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
  - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
  - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
  - Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. Specify the approximate number of human subjects that will be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Describe the data analysis plan in a manner that is consistent with the study objectives.

- **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. ***Each component has no page limit unless otherwise noted.***
  - 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 USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present contract under which the facilities or equipment items are now accountable. There is no form for this information.
- Publications and/or Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then they must be included. Extra items will not be reviewed.
- Letters of Organizational Support (two-page limit per letter): Provide a letter (or letters if applicable), signed by the Department Chair or appropriate organization official, reflecting the laboratory space, equipment, and other resources available for the project.
- Letters of Collaboration (if applicable) (two-page limit per letter): 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 and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations. Disclose any patents, issued or pending, and/or licenses, granted and/or pending, with respect to the intervention/device. Discuss and document availability of and access to the intervention/device. Provide documentation of access to and permission to use all intellectual and material property, as applicable.
- 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, for more information about the CDMRP expectations for making data and research resources publically available.
- Current Quad Chart: Provide a current Quad Chart in the same format as in the pre-application. If no changes have been made to the project, the same Quad Chart submitted with the pre-application may be used.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  Technical abstracts should be written using the outline below. (Proprietary or confidential information should ***not*** be included.)

  - Background: Present the ideas and reasoning behind the proposed work.
  - Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.

- Specific Aims: State the specific aims of the study.
- Study Design: Briefly describe the study design including appropriate controls.
- Clinical Impact: Briefly describe how the proposed clinical trial/testing will have an impact on military infectious disease research or patient care.
- Military Relevance: Briefly describe how the proposed clinical trial/testing impacts the military population.

- **Attachment 4: Public Abstract (one-page limit):** Upload as "PublicAbs.pdf."

  Public abstracts should be written using the outline below.

  - Clearly describe, in a manner readily understood by lay persons, the rationale and objective for the proposed work.
    - Do not duplicate the technical abstract.
  - 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?

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C., for detailed information.

- **Either Attachment 6a: Human Subject Recruitment and Safety Procedures, or Attachment 6b: Human Sample Acquisition and Safety Procedures, must be submitted with a MID-CTA application. Select the appropriate document from the descriptions below.**

  Attachment 6a: Human Subject Recruitment and Safety Procedures (no page limit): Upload as "HumSubProc.pdf." The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  a. Study Population: Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site (population from which the sample will be recruited/drawn). ***Use of military populations is preferable but not required.*** Demonstrate that the research team has access to the proposed study population.

  Furthermore, discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided.

  b. Inclusion/Exclusion Criteria: List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report and congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the clinical trial.

c. Description of the Recruitment Process: Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification).

- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
- Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.
- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements, and should accurately reflect the study.

d. Description of the Informed Consent Process: Specifically describe the plan for obtaining informed consent from human subjects.

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent.
- Include information regarding the timing and location of the consent process.
- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.
- Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=browse_usc&docid=Cite:+10USC980). If

applicable, please refer to the General Application Instructions, Appendix 5, for more information.

- Provide a draft in English of the proposed Informed Consent Form. A plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial should be included.
- ***Assent.*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

e. Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. Please note that some screening procedures may require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.

f. Risks/Benefits Assessment:

- **Foreseeable risks:** Clearly identify all study risks. Study risks include any risks that the human subject is subjected to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.
- **Risk management and emergency response:**
  - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel, or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.
  - Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
  - Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
  - Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.

- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

Attachment 6b: Human Sample Acquisition and Safety Procedures (for in vitro devices/diagnostics, no page limit): Upload as "HumSubProc.pdf." The Human Sample Acquistion and Safety Procedures attachment should include the components listed below.

a. Study Design (for in vitro Devices and Diagnostics): Most in vitro devices are exempt from the medical device IDE regulations.

Studies required to demonstrate substantial equivalence include the following:

- In the majority of cases, analytical studies using clinical samples (sometimes supplemented by carefully selected artificial samples) will suffice.
- For some in vitro diagnostics, the link between analytical performance and clinical performance is not well defined. In these circumstances, clinical information may be required.
- FDA rarely requires prospective clinical studies for in vitro diagnostics, but regularly requests clinical samples with sufficient laboratory and/or clinical characterization to allow an assessment of the clinical validity of a new device. This is usually expressed in terms of clinical sensitivity and clinical specificity or agreement.

Note that the study design may include identification of surrogate endpoints to establish the device performance (clinical sensitivity and specificity or agreement) with relation to the identified endpoints in corollary studies using randomly collected clinical studies. ***Use of laboratory samples from military populations is preferable but not required.***

b. Inclusion/Exclusion Criteria: List the inclusion and exclusion criteria evaluation of samples for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report and congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if samples from women and/or minorities will be excluded from the clinical trial.

c. Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study inclusion and the diagnostic criteria for entry. Please note that some screening procedures may require a separate consent or waivers of consent. Informed consent or appropriate waives of consent must be obtained prior to initiation of any procedures for the purpose of determining

eligibility.

d. Laboratory Evaluations

- **Specimens to be collected, schedule, and amount:** All specimens that will be evaluated for study purposes must be clearly stated. The amount of material collected to be utilized for the study must also be clearly described.
- **Evaluations:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study.
- **Storage:** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
- **Laboratories performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

e. Description of the Informed Consent Process: In certain cases, federal regulations allow the IRB to approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or to waive the requirement to obtain any informed consent. Most complete waivers of consent involve studies in which there are minimal risks to subjects. Specifically describe the plan for obtaining informed consent or appropriate waivers of informed consent for clinical samples from human subjects.

- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent or appropriate informed consent waivers.
- Describe the biological origin of the samples to be tested (e.g., primary fibroblast cells from adults with and without disease).
- The narrative should also describe the sample source(s), such as purchased human samples obtained from a clinical repository, or previously collected as part of a research effort. If samples will be or have been collected as part of a research activity, the proposal should state whether donors provided consent for use of their samples in future research consistent with this proposed effort.
- Describe the plan, if appropriate, for obtaining waivers of informed consent or the informed consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study.
    - **Waiver of Informed Consent,** described in Federal regulation 45 CFR

46.116(d) Federal regulations at 45 CFR 46.116(d), establishes four criteria for waiving consent or altering the elements of consent in minimal risk studies. These four criteria must be addressed.

- **Waiver of Documentation of Consent,** described in Federal regulation 45 CFR 46.117(c), allows the IRB to waive the requirement for obtaining signed consent if it finds that either:

  (1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality (these criteria cannot be used for FDA-regulated studies), or

  (2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. This paragraph only also applies to FDA-regulated studies per 21 CFR 56.109(c)(1).

- State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=browse_usc&docid=Cite:+10USC980). If applicable, please refer to the General Application Instructions, Appendix 5, for more information.

g. Risks/Benefits Assessment:

- **Foreseeable risks:** Clearly identify all study risks. Study risks include any risks that the human subject is subjected to (including retroactively, as identified by the ORP and IRB) as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:** Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel, or to manage unpreventable risks.

- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

h. Quality Control: Quality control (QC) is a material or mechanism that, when used with or as part of a test system, monitors the analytical performance of that test system. It may monitor the entire test system or only one aspect of it. Note that the FDA regulates the *material or mechanism* **as a medical device**; it does not monitor how a QC component is used within a laboratory (i.e., how often other QC types should be run or whether the QC replaces other, more traditional external types of QC).

Describe the QC to be employed for the study and/or device and, as appropriate, include:

- Procedures that will be employed to monitor QC (i.e., how often other QC types should be run or whether the QC replaces other, more traditional external types of QC).
- Review of sample labeling for accuracy,
- Determination/inclusion of manufacture protocols and protocols to ensure stability.

- **Attachment 7: Intervention or Device (no page limit):** Upload as "Intervention.pdf." The Intervention attachment should include the components listed below.

a. Description of the Intervention/Device: As applicable, the description of the intervention/device should include the following components: source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions/devices should be fully described.

b. Study Procedures: Describe the interaction with the human subject to include the study intervention/device that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures.

- **Attachment 8: Data Management (no page limit):** Upload as "Data_Manage.pdf." The Data Management attachment should include the components listed below.

a. Data Management: Describe all methods used for data collection to include the following:

- **Identifiers:** Describe the unique identifiers or specific code system to be

used to identify human subjects, if applicable.

- **Confidentiality:**
  - Explain measures taken to protect the privacy of study human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
  - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of USAMRMC are eligible to review study records.
  - Address requirements for reporting sensitive information to state or local authorities.
- **Disposition of data:** Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, and the length of time data will be stored.
- **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study.

b. Laboratory Evaluations

- **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.
- **Evaluations:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).
- **Storage:** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
- **Laboratories performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Attachment 9: Study Personnel and Organization (no page limit):** Upload as "Personnel.pdf." The Study Personnel and Organization attachment should include the components listed below.

a. **Principal Investigator/Study Staff:** Provide an organizational chart identifying key members of the study team including institution/center/ department. Briefly describe their roles on the project. A medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included.

b. **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial/testing is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, should be included. Provide a plan for real-time communication among collaborating institutions (if applicable).

- **Attachment 10: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit):** Upload as "Surveys.pdf." The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study.
- **Attachment 11: Impact Statement (one-page limit).** Upload as "Impact.pdf."
  - Identify the volunteer population(s) that will participate in the proposed intervention, and describe the potential impact of the proposed clinical trial/testing on treatment of combat-related wound infections.
  - Describe the short-term impact: Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial/testing.
  - Describe the long-term impact: Explain the long-range vision for implementation of the intervention in the clinic or field and describe the anticipated long-term benefits for the targeted population.
  - Compare the proposed intervention to pharmacologic agents, devices, and/or clinical guidance currently available, if applicable.
- **Attachment 12: Transition Plan (one-page limit).** Upload as "Transition.pdf." Provide information on the methods and strategies proposed to move the product to the next phase of clinical trials/testing and/or delivery to the military or civilian market after successful completion of the award. The transition plan should include the components listed below.
  - Provide details of the funding strategy that will be used to bring the outcomes to the next level of clinical trials/testing and/or delivery to the military or civilian market (e.g., specific potential industry partners, specific funding opportunities to be applied for).
  - A description of collaborations and other resources that will be used to provide continuity of development. For any industry partner(s), include a description of their product development and/or marketing experience.
  - A brief schedule and milestones for bringing the outcome(s) to the next phase of

clinical trials/testing and/or delivery to the military or civilian market.

- A risk analysis for cost, schedule, manufacturability, and sustainability.
- A description of relevant product patents and intellectual property ownership, and their potential impact on product development and the Government's ability to access any technology or products supported with this award.

- **Attachment 13: Military Relevance Statement (one-page limit):** Upload as "MilRel.pdf."

  Describe how the proposed study is responsive to the treatment of combat-related wound infections. Provide information about the incidence and/or prevalence of the disease or condition in military service members and/or veterans, if appropriate and available. Identify the MID-CTA focus area(s) aligned with the proposed project. Show how the proposed study complements ongoing DOD and VA areas of research interest.

  If active duty military and/or veteran population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed study, and the feasibility of accessing the population. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., military service members or veterans).

- **Attachment 14: Letters Confirming Access to Target Military or VA Patient Population(s), if applicable:** Upload as "Access.pdf."

  If applicable, provide a letter signed by the lowest ranking person with approval authority for studies involving active duty military, military-controlled study materials, and/or military databases. If applicable, provide a letter from an appropriate authority providing access to veterans, VA-controlled study materials, or VA data (unless a VA investigator with appropriate access is a PI or collaborator on the application).

- **Attachment 15: IND/IDE Documentation Form (if applicable):** Upload as "IND.IDE.pdf."

  Complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page for this Program Announcement/Funding Opportunity on Grants.gov.

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

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
   - Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
   - Key Personnel Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

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

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."
   - The PI is responsible for ensuring that the total budget (including any intramural collaborators and/or subawardees, if applicable) does not exceed the maximum allowed costs. Further details about intramural and extramural collaborators can be found in Section I.D., Funding, on p.8.

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

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

D. Budget Submission for Intramural Collaborators (via CDMRP eReceipt System):

- Intramural collaborators are required to submit an independent Research and Related Budget form through the CDMRP eReceipt System (not Grants.gov). This budget form will include a Budget Justification statement, and detail only the intramural collaborator's contribution to the project. Intramural collaborators are reminded that they must consult their respective resource manager to validate whether incremental funding is being utilized and the proper procedures for executing those funds. The Research and Related Budget form (OMB No. 4040-0001) is accessible through Grants.gov using the following steps:

  1) From the Grants.gov Basic Search page, search this Funding Opportunity Number, W81XWH-12-DMRDP-MID-CTA.
  2) Within the DOD Military Infectious Diseases Clinical Trial Award page, click on "Application" at the top, and then download the Instructions and Application Package from the bottom of the page.
  3) Within the first page of the Grant Application Package is a block of Mandatory Documents. Highlight and select the Research and Related Budget form from this block and click the arrow in the center of the page to "Move Form to Complete." This will move the form into the Mandatory Documents for Submission block. Select the Research and Related Budget form from this block and click "Open Form" to open the file. You can now fill out the Research and Related Budget form, *save it to your computer*, and then upload it into the CDMRP eReceipt System (this will require eReceipt registration), under the "Other Documents" tab.
  4) When filling out the form, enter your own organization name and ***the PI's*** CDMRP Log Number in the Organization block of the Research and Related Budget form. Intramural collaborators should not enter an Organizational DUNS and should not indicate a Budget Type. Note: Intramural collaborators are also required to provide a Budget Justification (no page limit, block K in the Research and Related Budget form). Refer to the General Application Instructions, Section 4 for details on content and format.

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 any one of the deadlines shall result in application rejection.

F. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Organizations are required to provide a Data Universal Number System (DUNS) number and register with the Central Contractor Registry (CCR) to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists and clinicians using a two-tier review process. The first tier is a peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Commanding General for concurrence, and then to the Office of the Assistance Secretary of Defense for Health Affairs for final approval, based on technical merit, the relevance to the mission of the DOD and DMRDP, and the specific intent of the award mechanism. The highest scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier review process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each level of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other corrective actions. Organizational personnel and PIs 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 panelists or PIs that compromise the confidentiality of the review process may also result in suspension or debarment of their employing organizations from Federal awards. Furthermore, it is a crime for Federal officials to disclose confidential information of one party to another third party (Title 18 United States Code 1905).

B. Application Review Criteria

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

- How the results of the proposed clinical trial/testing will affect the scope of treatment of combat-related wound infections.
- How relevant the anticipated outcomes of the proposed clinical trial/testing are to addressing wound infection prevention and management, and antimicrobial countermeasures.
- How well the sample population represents the targeted patient population that might benefit from the proposed intervention or device.
- How the potential outcomes of the proposed clinical trial/testing or incremental progress will provide/improve the short-term benefits for individuals.
- How significantly the long-term benefits for implementation of the intervention may impact patient care and/or quality of life.

- **Ethical Considerations**
  - How the level of risk to human subjects is minimized.
  - How well the evidence shows that the procedures are consistent with sound study design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.
  - To what degree privacy issues are appropriately considered.
  - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.
- **Intervention (non-device trial)**
  - Whether there is evidence to support availability of the intervention, if applicable, for the proposed clinical trial.
  - To what degree the intervention addresses the clinical need(s) described.
  - How the intervention advances patient care beyond the currently available interventions.
  - Whether a member of the study team holds the IND and whether the timeline proposed for IND application is appropriate (if applicable).
  - For investigator-sponsored INDs, whether there is institutional support to serve as a sponsor and whether they are equipped to assume the monitoring required by the FDA.
  - To what degree the data collection instruments (e.g., surveys, questionnaires, etc.), if applicable, are appropriate to the proposed study.
- **Device Trial/Testing**
  - Whether there is evidence to support availability of the device, if applicable, for the proposed clinical trial/testing.
  - To what degree the device addresses the clinical need(s) described.
  - How the device advances patient care beyond the currently available devices.

- Whether a member of the study team holds the IDE and whether the timeline proposed for IDE application is appropriate (if applicable).
- For investigator-sponsored IDEs, whether there is institutional support to serve as a sponsor and whether they are equipped to assume the monitoring required by the FDA.
- To what degree the data collection instruments (e.g., surveys, questionnaires, etc.), if applicable, are appropriate to the proposed study.

- **Recruitment, Accrual, and Feasibility**
  - How well the PI addresses the availability of human subjects for the clinical trial/testing and the prospect of their participation and/or samples for clinical study.
  - Whether the PI has demonstrated access to the proposed clinical samples or human subjects population.
  - How the recruitment, informed consent, screening, and retention processes for human subjects/samples will be conducted to meet the needs of the proposed clinical trial/testing.
  - How well the application identifies possible delays and evidence of an adequate contingency plan to resolve potential delays (e.g., slow accrual, attrition).
  - To what extent the PI has adequately considered how the proposed clinical trial/testing will affect the daily lives of individual human subjects participating in the study and has developed mitigation plans for any effects of the intervention or device (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial/testing? Are human subjects required to stay overnight in a hospital?).
- **Research Strategy**
  - How well the scientific rationale for testing the intervention is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory and/or preclinical evidence.
  - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to clearly answer the clinical objective.
  - How well the inclusion criteria meet the needs of the testing phase or proposed clinical trial.
  - How well the exclusion criteria are justified.
- **Statistical Plan (as appropriate for the proposed clinical trial/testing)**
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.

- **Transition Plan**
  - Whether the funding strategy described to bring the outcome(s) to the next level of clinical trial/testing and/or delivery to the military or civilian market is appropriate.
  - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
  - How the schedule and milestones for bringing the outcome(s) to clinical trial/testing and/or delivery to the military or civilian market is appropriate.
  - How well the potential risk analysis for cost, schedule, manufacturability, and sustainability is developed.
  - How well the application identifies intellectual property ownership and addresses any impact of intellectual property issues on product development and subsequent government access to products supported by this Program Announcement/Funding Opportunity.

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

- **Personnel and Communication**
  - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
  - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
  - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial/testing.
  - To what degree the logistical aspects of the proposed clinical trial/testing (e.g., communication plan, data transfer, standardization of procedures) are adequate.
- **Environment**
  - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial/testing at each participating center or institution (including collaborative arrangements).
  - Whether there is evidence for appropriate institutional commitment from each participating institution.
  - If applicable, how the intellectual and material property plan that is agreed upon by each participating institution is appropriate for the proposed clinical trial/testing.

- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influenced the review.

2. **Programmatic Review:** To determine the application's relevance to the mission of the DOD and MIDRP, as well as to make funding recommendations, the following equally considered criteria are used by programmatic reviewers:

- Ratings and evaluations of the peer reviewers
- Military relevance
- Relative impact
- Program portfolio balance
- Adherence to the intent of the award mechanism
- Responsiveness to at least one of the MID-CTA focus areas

C. Recipient Qualification

Refer to the General Application Instructions, Appendix 1, for additional information on organization and Government agency requirements.

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 notification of the funding recommendation. PIs will receive a scientific peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eReceipt 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.
- Preproposal is submitted by an intramural investigator as defined in Section I.B. The

following will result in administrative rejection of the application:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing (PI or intramural collaborator).
- Human Subject Recruitment and Safety Procedures (Attachment 6a) *or* Human Sample Acquisition and Safety Procedures (Attachment 6b), as appropriate, is missing.
- Intervention/Device description (Attachment 7) is missing.
- Data Management (Attachment 8) is missing.
- Submission of an application for which a letter of invitation was not received.

B. Modification

- Pages exceeding the specified limits will be removed prior to review for all documents other than the Project Narrative and Preproposal Narrative.
- Documents not requested will be removed.
- Following the pre-application or application deadline, the PI or intramural collaborator, if applicable, may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed in Section IV.A., Rejection). The missing documents must be provided by 5:00 p.m. ET on the second full business day following the date the email was sent. Otherwise, the application will be reviewed as submitted.

C. Withdrawal

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

- FY11/12 MIDRP Joint Program Committee (JPC) member is found to be involved in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document. A list of the FY11/12 MIDRP JPC members may be found at http://cdmrp.army.mil/dmrdp/jpc/11jpc_2.

- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- Total costs as shown on the Research and Related Budget form exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs with the exception of links to published references.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- If applicable, IND/IDE has not been submitted and/or approved.
- The PI does not meet the eligibility criteria. Refer to the General Application Instructions, Appendix 1, for general eligibility information.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/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, 2013. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

Refer to the General Application Instructions, Appendix 4, Section C, for general information regarding administrative and national policy requirements.

C. Reporting

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

Quarterly technical progress reports will be required.

D. Award Transfers

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

The transfer of an award to another institution is strongly discouraged. A transfer will not be allowed for any institution that includes a study site/clinical trial at its location. Approval of a transfer request from an institution that does not include a study site at its location will be at the discretion of the USAMRAA Contracting/Grants Officer.

E. Pre-Award Meeting

At the Government's discretion, the PI and Clinical Study Coordinator may be requested to participate in a pre-award meeting. PIs recommended for funding will be notified during the award negotiation process whether a pre-award meeting will be required. In the event a pre-award meeting is required, the PI will be required to budget for travel expenses at that time.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements and questions related to the submission of the pre-application through the CDMRP eReceipt System 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: 1-301-682-5507

Email: help@cdmrp.org

B. Grants.gov Contact Center

Questions related to application submission through the 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: 1-800-518-4726

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. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. PI APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed.	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1.	
	Upload Supporting Documentation (Support.pdf) as Attachment 2.	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3.	
	Upload Public Abstract (PublicAbs.pdf) as Attachment 4.	
	Upload Statement of Work (SOW.pdf) as Attachment 5.	
	Upload Human Subject Recruitment and Safety Procedures (Attachment 6a) or Human Sample Acquisition and Safety Procedures (Attachment 6b) as HumSubProc.pdf, as appropriate.	
	Upload Intervention (Intervention.pdf) as Attachment 7.	
	Upload Data Management (Data_Manage.pdf) as Attachment 8.	
	Upload Study Personnel and Organization (Personnel.pdf) as Attachment 9.	
	Upload Surveys, Questionnaires, and Other Data Collection Instruments (Surveys.pdf), if applicable, as Attachment 10.	
	Upload Impact Statement (Impact.pdf) as Attachment 11.	
	Upload Transition Plan (Transition.pdf) as Attachment 12.	
	Upload Military Relevance Statement (MilRel.pdf) as Attachment 13.	
	Upload Letters Confirming Access to Target Military or VA Patient Population(s) (Access.pdf) as Attachment 14, as applicable.	
	Upload IND/IDE Documentation Form, if applicable, (IND.IDE.pdf) as Attachment 15.	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI 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 Current & Pending Support (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete form 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.	

VIII. INTRAMURAL COLLABORATOR CHECKLIST

Submission Requirements	Action	Completed
eReceipt Registration	Intramural collaborators must register with the CDMRP eReceipt System.	
Research & Related Budget	Download the Research and related Budget form from Grants.gov. Complete form as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field. Upload the form into the CDMRP eReceipt System, under the "Other Documents" tab.	