Program Announcement

for the

Defense Health Program

Department of Defense
Congressionally Directed Medical Research Programs

Prostate Cancer Research Program

Laboratory - Clinical Transition Award

Funding Opportunity Number: W81XWH-14-PCRP-LCTA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), July 23, 2014
- **Invitation to Submit an Application:** late August 2014
- **Application Submission Deadline:** 11:59 p.m. ET, October 29, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, November 3, 2014
- **Peer Review:** December 2014
- **Programmatic Review:** February 2015

__Change for Fiscal Year 2014__: The CDMRP eReceipt System has been replaced with the Electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to the end of the application verification period.

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.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2014 (FY14) Prostate Cancer Research Program (PCRP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The PCRP was initiated in 1997 to promote innovative research focused on eradicating prostate cancer. Appropriations for the PCRP from FY97 through FY13 totaled $1.29 billion. The FY14 appropriation is $80 million (M).

The mission of the FY14 PCRP is to find and fund research that will lead to the elimination of death from prostate cancer and enhance the well-being of men experiencing the impact of the disease. Specifically, the PCRP seeks to promote highly innovative, groundbreaking research; high-impact research with near-term clinical relevance; multidisciplinary, synergistic research; translational studies to support the fluid transfer of knowledge between bedside and bench; research on patient survivorship and quality of life; the next generation of prostate cancer investigators through mentored research; and research on disparities in the incidence and mortality of prostate cancer.

PCRP Overarching Challenges *(revised for FY14)*

Consistent with the program's mission to eliminate death from prostate cancer and enhance the well-being of men experiencing the impact of the disease, including those from disproportionately affected populations, each PCRP funding opportunity either requires or encourages (see Section I.B., Award Information) applications to address one of the following four PCRP overarching challenges:

- Develop better tools for early detection of clinically relevant disease
- Distinguish aggressive from indolent disease in men newly diagnosed with prostate cancer
- Develop effective treatments and address mechanisms of resistance for men with high-risk or metastatic prostate cancer
- Develop strategies to optimize the physical and mental health of men with prostate cancer

PCRP Focus Areas

All applications for the FY14 PCRP funding opportunities are also expected to address at least one of the following PCRP focus areas:

- **Biomarker Development:** Validation and qualification of biomarkers for early detection of clinically relevant disease or for prognosis or prediction and assessment of response to therapies

- **Genetics:** Understanding host or tumor genetics and epigenetics responsible for susceptibility, disease progression, and treatment outcomes for clinically relevant prostate cancer

- **Imaging:** Development of new anatomic, functional, and molecular imaging approaches for the detection and management of clinically relevant prostate cancer

- **Mechanisms of Resistance:** Understanding primary and acquired resistance to therapy

- **Survivorship and Palliative Care:** Improving the quality of life and well-being of prostate cancer patients and their families

- **Therapy:** Identification of new targets, pathways, and therapeutic modalities

- **Tumor and Microenvironment Biology:** Understanding the intrinsic and extrinsic mechanisms contributing to tumor development and the progression of prostate cancer

B. Award Information

The PCRP Laboratory - Clinical Transition Award (LCTA) mechanism was introduced in FY07. Since then, 114 applications have been received, and 13 have been recommended for funding.

The Laboratory - Clinical Transition Award supports product-driven preclinical studies of promising lead agents or medical devices that have the potential to revolutionize prostate cancer clinical care.

Lead Agents: It is anticipated that lead agent development projects supported by this award will focus on generating pharmacology and toxicology data in preclinical studies for inclusion in a U.S. Food and Drug Administration (FDA) Investigational New Drug (IND) application and/or establishing agent production according to current Good Manufacturing Practice (cGMP). Applicants are expected to have a validated target and to have identified one lead agent (or a limited number of lead agents for optimization) before applying for this award. In addition, the PI should present data establishing the lead agent's mechanism of action and demonstrating reliability, reproducibility, effectiveness (including sensitivity and specificity), and target availability and distribution in relevant human tissues. In addition, the inclusion of substantive information from model systems that supports the potential efficacy of the lead agent in humans is highly recommended. ***Lead agents are defined as novel biological and molecular or chemical therapeutic or imaging agents having potential clinical application to prostate cancer.*** Examples of lead agents include, but are not limited to, novel chemotherapeutics, antibodies, nanoparticles, imaging contrast agents, and others.

Medical Devices: Medical device projects to be supported by this award will test medical devices in preclinical studies with the intent of achieving an FDA Investigational Device Exemption (IDE) application and/or cGMP production of the medical device. As appropriate, the PI should present preliminary data demonstrating reliability, reproducibility, and effectiveness (including sensitivity and specificity) for the medical device, as well as target availability and distribution in relevant human tissues. In addition, the inclusion of substantive information from model systems that supports the potential efficacy of medical device in humans is highly recommended. Examples of medical devices include, but are not limited to, diagnostic

or prognostic tests (e.g., microfluidic device, genomic and genetic microarray devices), imaging devices, and other medical technology.

Lead agents or medical devices supported by this award are expected to have high potential for commercial licensing for continued development and clinical use. The PI must provide a transition plan (including potential funding and resources) to describe how the product will progress to the next phase of development (e.g., clinical trials and/or delivery to market) after the completion of the PCRP award. ***The PCRP strongly encourages investigators to leverage existing resources with commercial partners to increase potential gains in translating preclinical research outcomes for continued development and clinical application. Applications that demonstrate cost-sharing with commercial partners are particularly encouraged.***

The National Cancer Institute has constructed developmental pathways for translational research that may be useful for designing translational research studies for support under the LCTA mechanism. These pathways are comprehensive and span the entire translational research continuum from discovery of a target to clinical trials (http://www.cancer.gov/PublishedContent/Files/images/trwg/agents_oct08.pdf).

PIs applying to the LCTA are expected to address at least one of the PCRP focus areas and are highly encouraged to address one of the PCRP overarching challenges. If the proposed project does not address any of the overarching challenges, the application should include a description to justify how the project will nevertheless address a critical need in the field of prostate cancer research and/or patient care.

Studies proposed under this award may include, but are not limited to:

- Comparative activity testing to optimize a lead agent and/or define a single lead agent from a limited library of candidates. ***Such studies must be completed within 12 months of the start date of the award. If the lead agent has not been finalized within 12 months of award initiation, funding restrictions may be imposed.***

- Toxicology screening

- Pharmacokinetic (e.g., absorption, distribution, metabolism, and excretion) studies

- Pharmacodynamic studies

- Radiation dosimetry

- Testing medical devices for safety or effectiveness in preclinical systems

- Development and validation of assays and reagents required to measure biological responses and molecular endpoints of the lead agent; ***such studies may only be proposed in conjunction with lead agent development***

- Combination of the lead agent with agents already in clinical testing or practice

- cGMP production of the lead agent or medical device

Studies proposed under this award should not include:

- Target discovery

- Drug screening

- Early development of medical devices

- New combinations, formulations, or modifications of agents already in clinical testing or practice (other than in combination with the lead agent)

- Mechanism of action studies

- Prevention agents

The preclinical drug or medical device development process may require resources beyond those available at a single laboratory or organization. As such, the PI must disclose within the application any patents issued or pending and/or licenses granted and/or pending, with respect to the lead agent or medical device as well as any known patents that may block the development of the lead agent or device. The PI must provide documentation, such as a Material Transfer Agreement and/or licensing agreement, of access to and permission to use all intellectual and material property. Participating organizations must be willing to resolve potential intellectual and material property issues and to remove organizational barriers that might interfere with the cooperation necessary to ensure that the proposed studies can be completed.

PIs are expected to abide by the existing and proposed FDA guidance governing the conduct of preliminary studies and the collection of data in support of an IND or IDE application. Websites with relevant information may include, but are not limited to:

- http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm,

- http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046706.htm, and

- http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/InvestigationalNewDrugINDorDeviceExemptionIDEProcess/ucm094309

It is strongly encouraged that PIs begin discussions with the FDA early to determine FDA-driven milestones, which should be incorporated into the Statement of Work for the application.

Clinical trials will not be supported by the LCTA. Other projects involving human subjects or human anatomical substances will be supported only if they are exempt from IRB review under Title 32 of the Code of Federal Regulations Section 219.101(b) (4) (32 CFR 219.101(b) (4)) or qualify for expedited review under 32 CFR 219.110 or 21 CFR 56.1102. ***Applications proposing studies that do not qualify for exempt or expedited review status will be administratively withdrawn.*** For definitions and other information on clinical trials and clinical research overall, the "Human Subject Resource Document" is provided at https://ebrap.org/eBRAP/public/Program

New for FY14

All projects should adhere to a core set of standards for rigorous study design and reporting to maximize the reproducibility and translational potential of preclinical research. The 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). The basic principles of randomization, blinding, sample-size estimation, and data handling derive from well-established best practices in clinical studies and should be well-considered in any project proposed for this award mechanism. Projects that include research on animal models are required to submit Attachment 8, Animal Research Plan, as part of the application package to describe how these standards will be addressed. 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.nc3rs.org.uk/page.asp?id=1357.

All investigators applying to the Laboratory - Clinical Transition Award are encouraged to include clinical collaborators in prostate cancer, if the PI is not a prostate cancer clinician.

All investigators applying to FY14 PCRP funding opportunities are encouraged to consider leveraging resources available through the PCRP-funded Prostate Cancer Biorepository Network (PCBN) (http://www.prostatebiorepository.org) and/or the North Carolina – Louisiana Prostate Cancer Project (PCaP) (http://www.ncla-pcap.org) if retrospectively collected human anatomical substances or correlated data are relevant to the proposed studies.

The Congressionally Directed Medical Research Programs (CDMRP) intends that 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 L.

C.   Eligibility Information

- The PI must be an independent investigator at or above the level of Assistant Professor (or equivalent).

- Cost sharing/matching is not an eligibility requirement.

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

- 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 direct costs for the entire period of performance are **$1,500,000** plus indirect costs.

- 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.

- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

For this award mechanism, direct costs may be requested for (not all-inclusive):

- Salary

- Research supplies

- Equipment

- Research-related subject costs (for studies with exempt or expedited review status only)

- Clinical research costs (clinical trials are not allowed)

- Support for collaborations

- Travel between collaborating organizations

- Travel costs of up to $1,800 per year per person for the PI and one member of the key personnel to attend scientific/technical meetings. ***The Government reserves the right to direct the selection of one of these meetings, should a PCRP-sponsored meeting be convened during the award period of performance.***

Intramural (DoD), other federal agency, and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. 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. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. ***In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.***

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from federal agencies submit applications, they must submit through Grants.gov. Therefore, 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.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other federal agencies will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Direct transfer of funds from the recipient to a federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.4. Research & Related Budget, for additional information on budget considerations for applications involving federal agencies.

The CDMRP expects to allot approximately $4.8M of the $80M FY14 PCRP appropriation to fund approximately 2 Laboratory - Clinical Transition 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 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/).

New for FY14: ***The CDMRP has replaced its eReceipt System with eBRAP.*** Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at *https://ebrap.org/eBRAP/public/UserGuide.pdf)*. Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon the registration and affiliation. ***Application viewing, modification, and verification in eBRAP is <u>strongly</u> recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.*** If verification is not completed by the end of the application verification period, the application will be reviewed as submitted through Grants.gov, provided there is no cause for administrative rejection of the application (see Section IV.A., Rejection).

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.

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-14-PCRP-LCTA.

B. Pre-Application Submission and Content Form

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 preapplication 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 preapplication, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507. A change in PI or organization after submission of the pre-application will be allowed only at the discretion of the US Army Medical Research Acquisition Activity (USAMRAA)
Contracting/Grants Officer.

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):

- **Application Information – Tab 1**

- **Application Contacts – Tab 2**
    - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.

- **Collaborators and Conflicts of Interest (COI) – Tab 3**

  FY14 PCRP Integration Panel (IP) members should not be involved in any preapplication or application. A list of FY14 PCRP IP members can be found at http://cdmrp.army.mil/pcrp/panels/panel14. For questions related to IP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the

- **Required Files – Tab 4**

  Notes: Upload document(s) 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, etc.) 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 describe the proposed project using the following outline:

  - **Background/Rationale:** Clearly present the ideas and reasoning behind the proposed research; include relevant literature citations. Clearly describe the target, lead agent or device, and mechanism of action in prostate cancer.

  - **Objective:** State the objective(s) to be reached.

  - **Research Approach:** State the project's specific aims and briefly describe the experimental approach to accomplishing the aims, including enabling and IND/IDE or cGMP production. ***This award cannot be used to conduct clinical trials.***

  - **Impact:** Describe the potential short-term and long-term impact of this study on prostate cancer research and patient care. Briefly describe how the proposed study is responsive to one of the PCRP overarching challenges or, alternatively, provide a description to justify how the project will nevertheless address a critical need in prostate cancer clinical care.

  Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application ***must be uploaded as individual documents*** 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). Upload as "References.pdf."

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

  - PI and Key Personnel Biographical Sketches (four-page limit per individual). Upload as "Biosketches.pdf."

- **Submit Pre-Application – Tab 5**

  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 PCRP, pre-applications will be screened by the PCRP IP based on the following criteria, which are of equal importance:

  ○ **Intent of the Award Mechanism:** To what degree the lead agent or medical device is sufficiently developed so that the award will effectively bring it toward IND or IDE application and /or cGMP production.

  ○ **Research Approach:** To what degree the experimental approach for accomplishing the specific aims is feasible and addresses the objective.

  ○ **Impact:** To what degree the lead agent or medical device is responsive to the PCRP overarching challenges, or is otherwise justified as significantly addressing another critical issue, and has the potential to revolutionize prostate cancer research and patient care.

- **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.

C. Application Submission Content and Forms

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

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 through the Grants.gov portal (http://www.grants.gov/).

New for FY14: *Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification.* The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: Changes to either the Project Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a "Changed/Corrected Application" with the Previous Grants.gov Tracking ID *prior to the application submission deadline (which occurs earlier than the end of the application verification period).*

Grants.gov application package components: For the Laboratory - Clinical Transition 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**

   - **Attachment 1: Project Narrative (25-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 will result in administrative withdrawal of the application.

     Describe the proposed project in detail using the outline below. ***The inclusion of preliminary data is required.*** Any preliminary data provided should be from the laboratory of the PI or member(s) of the collaborating team.

     ○ **Background:** Present the ideas and reasoning behind the proposed research; include relevant literature citations. Describe previous experience most pertinent to this application.

     ○ **Lead Agent or Device:** Describe the target, the lead agent or device and its clinical utility, and the mechanism of action. Indicate whether the lead agent or device is being developed in partnership with another organization, and the nature of the partnership.

     ○ **Objective:** State the 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.

     ○ **Research Strategy:** Describe the experimental design for preclinical validation of the lead agent or device under development. Describe in detail the methods and analyses, including appropriate controls, a timeline for the completion of each proposed task, and how the approaches are compliant with FDA guidance for IND or IDE application, if applicable. Address potential problems and present alternative methods and approaches. Clearly describe the statistical plan and the rationale for the statistical methodology as well as an appropriate power analysis, if applicable. If animal studies are proposed, briefly describe the key elements of the study/studies as they relate to the overall project; detailed information is required in Attachment 8, Animal Research Plan. If human subjects or human anatomical samples will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples. ***Projects involving human subjects or anatomical substances will be supported only if they are exempt or qualify for expedited review status; however, this award cannot be used to conduct clinical trials.***

○ **Overarching Challenges and Focus Areas:** Describe how the proposed research is relevant to at least one of the PCRP focus areas and responsive to one of the PCRP overarching challenges. If the proposed project does not address any of the overarching challenges, provide a description to justify how the project will nevertheless significantly address a critical need in the field of prostate cancer research and patient care.

- **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 may result in the removal of those items or 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 Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must 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 Collaboration (if applicable): 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. ***The inclusion of a clinical collaborator in prostate cancer is highly encouraged if the PI is not a prostate cancer clinician.***

  ○ Intellectual Property

    – Background and Proprietary Information (if applicable): All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations (DoDGAR) requirements. Provide a list of all background intellectual

property to be used in the project. Identify any proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the federal purpose license.

– Patents and Permissions (if applicable): Disclose any patents, issued or pending, and/or licenses, granted and/or pending, with respect to the lead agent or device as well as any known patents that may block the development of the lead agent or device. The PI must provide documentation of access to and permission to use all intellectual and material property.

– 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 L 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. Of particular importance, programmatic reviewers typically rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

Describe the proposed research project including the following elements:

○ Background: Present the ideas and reasoning behind the proposed project.

○ Objective: State the objective to be reached. Provide evidence or rationale that supports the objective.

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

○ Study Design: Briefly describe the study design.

○ Impact: Summarize the impact of the proposed research, if successful, on the PCRP overarching challenges or other critical issues in prostate cancer.

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

Lay abstracts should be written using the outline below. ***Do not duplicate the technical abstract.*** Minimize 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 advocate community.

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

- ○ 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?

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

  The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Program Announcement and Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Laboratory - Clinical Transition Award mechanism, use the SOW format example titled "SOW for Advanced Tech Development Research." The SOW must be in PDF format prior to attaching.

- **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 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 how the new product may ultimately contribute to the goal of elimination of death from prostate cancer and enhancing the well-being of men experiencing the impact of the disease.

  PCRP overarching challenges: Summarize how the proposed project addresses one of the PCRP overarching challenges or another critical issue in prostate cancer research and/or patient care. State explicitly how the proposed work and the lead agent or medical device to be developed will, if successful, have an impact on prostate cancer research and clinical care.

- **Attachment 7: Transition Plan (one-page limit):** Upload as "Transition.pdf."

  Provide information on the methods and strategies proposed to move the product to clinical trial and/or delivery to market upon successful completion of the award. The transition plan should include the components listed below.

    - ○ A description of the expected outcome(s) that will result after completion of the proposed research project. Outcomes should be specific and measurable.

    - ○ Details of the funding strategy that will be used to bring the outcomes to clinical trial and/or delivery to market (e.g., specific potential commercial partners, specific funding opportunities to be applied for, etc.).

    - ○ A description of collaborations and other resources that will be used to provide continuity of development.

- ○ A brief schedule and milestones for bringing the outcome(s) to clinical trial and/or delivery to market.

  - ○ A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 8: Animal Research Plan (five-page limit):** Upload as "AnimalPlan.pdf."

  When the proposed study involves animals, the applicant is required to submit a summary describing the animal research that will be conducted. Applicants should not submit a verbatim replica of the protocol(s) to be submitted to the Institutional Animal Care and Use Committee (IACUC) as the Animal Research Plan. The Animal Research Plan should address the following points for each proposed animal study:

  - ○ Briefly describe the research objective(s) of the animal study. Explain how and why the animal species, strain, and model(s) being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.

  - ○ Summarize the procedures to be conducted. Describe how the study will be controlled.

  - ○ Describe the randomization and blinding procedures for the study, and any other measures to be taken to minimize the effects of subjective bias during animal treatment and assessment of results. If randomization and/or blinding will not be utilized, provide justification.

  - ○ Provide a sample size estimate for each study arm and the method by which it was derived, including power analysis calculations.

  - ○ Describe how data will be handled, including rules for stopping data collection, criteria for inclusion and exclusion of data, how outliers will be defined and handled, statistical methods for data analysis, and identification of the primary endpoint(s).

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.3., for detailed information. ***Note: Some of the items in this attachment may be made available for programmatic review***.

   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."

   - PI Previous/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 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."

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.

D.   Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. *The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.*

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 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. Applicant organizations and all subrecipient organizations must have a Data Universal Numbering System (DUNS) number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the System for Award Management (SAM) with an "Active" status 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 applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, U.S. Army Medical Research and Materiel Command (USAMRMC), based on (a) technical merit and (b) the relevance to the mission of the DHP and PCRP and to the specific intent of the award mechanism. The highestscoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier 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. Panel members sign a non-disclosure 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; of these, Lead Agent/Device, Research Strategy and Feasibility, and Impact are equally the most important, with the remaining criteria listed in decreasing order of importance:

   - **Lead Agent/Device**
     - Whether the PI has identified a well-defined target, and how well the preliminary data support the validity of the target for prostate cancer.
     - To what extent the development of the lead agent or device is justified by a sound scientific rationale that is supported by a critical analysis of the relevant literature, preliminary data, and logical reasoning.
     - To what extent there is potential for commercialization of the lead agent or device.
     - How the PI has clearly documented, with supporting preliminary and/or published data, that the mechanism of action of the lead agent or device on the target has been established.

- **Research Strategy and Feasibility**
  - To what extent the study has the potential of developing a viable lead agent or device that would be ready for cGMP production.
  - If applicable, whether the PI has presented a clear and feasible plan to narrow a small library of potential lead agents to one lead agent within the first 12 months after award initiation.
  - How well the objectives, aims, experimental design, methods, and analyses are developed.
  - How well the PI acknowledges potential problems and addresses alternative approaches.
  - Whether the proposal includes a clear and appropriately powered statistical plan, if applicable.
  - How well the research strategy complies with FDA recommendations for studies in support of IND or IDE applications, if applicable.
  - If applicable, how well the animal study (or studies) is designed to achieve the objectives, including the choice of model and endpoints/outcome measures to be used.
  - If applicable, how well the study (or studies) is designed to achieve reproducible and rigorous results, including controls, sample size estimation, blinding, randomization, and data handling.
  - If applicable, whether the PI has presented an Intellectual and Material Property Plan sufficient to resolve potential issues among participating organizations, including the acknowledgement of and compliance with relevant patents and permissions.
- **Impact**
  - To what extent the lead agent or device, if successfully developed, will have a major impact on prostate cancer clinical care and, ultimately, the elimination of death from prostate cancer and enhancing the well-being of men experiencing the impact of the disease.
  - How the proposed research addresses at least one of the PCRP focus areas and one of the PCRP overarching challenges or is otherwise justified as significantly addressing another critical issue in prostate cancer research and patient care.
- **Transition Plan**
  - Whether the plan for bringing the product to clinical trials or delivery to market, including potential funding strategies, is well developed and feasible.
  - To what extent the expected outcome(s) that will result after completion of the proposed research project are specific and measurable.
  - Whether plans for appropriate collaborations and other resources for providing continuity of development are well described.

- To what extent the schedule and milestones for bringing the outcome(s) to clinical trial and/or delivery to market are appropriate.
- Whether an appropriately developed potential risk analysis for cost, schedule, manufacturability, and sustainability is provided.

- **Personnel**
  - To what degree the research team's background and prostate cancer-related expertise are appropriate with respect to its ability to perform the proposed work.
  - Whether there is appropriate inclusion of clinical expertise in prostate cancer.
  - To what degree the levels of effort are appropriate for successful development of the lead agent or device.
  - Whether letters of collaboration are provided for any proposed collaborative arrangements (if applicable).

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

- **Environment**
  - To what degree the scientific environment is appropriate for the proposed research.
  - How well the research requirements are supported by the availability of and accessibility to facilities and resources (including collaborative arrangements).
  - To what degree the quality and extent of organizational support are appropriate.

- **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 influence the review.

2. **Programmatic Review:** To make funding recommendations, the following equally considered criteria are used by programmatic reviewers:

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

   b. **Relevance to the mission of the DHP and FY14 PCRP, as evidenced by the following:**
   - Adherence to the intent of the award mechanism
   - Programmatic relevance in relation to the PCRP overarching challenges and focus areas
   - Relative impact
   - Program portfolio composition

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.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

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

- A FY14 PCRP IP 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 FY14 PCRP IP members can be found at http://cdmrp.army.mil/pcrp/panels/panel14.

- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.

- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.

- 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).

- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., 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.

- The proposed research is, or requests funding for, a clinical trial.

- The application includes human subject or human anatomical substances studies that do not qualify for exempt or expedited review status.

- The PI does not meet the eligibility criteria as described in this Program Announcement/Funding Opportunity.

- The invited application does not propose the same research project described in the pre-application.

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 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, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

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

Reporting requirements, specific to each award, will be established during award negotiations. Well-defined milestones will be incorporated into the assistance agreement. The government reserves the right to terminate awards that do not achieve the established milestones.

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

E. Award Transfers

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

VI. AGENCY CONTACTS

A. 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

B.   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

      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 application package. If the 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	Action	Completed
SF-424 (R&R) Application for Federal Assistance	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	Transition Plan: Upload as Attachment 7 with file name "Transition.pdf."	
	Animal Research Plan: Upload as Attachment 8 with file name "AnimalPlan.pdf."	
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.	