

# Program Announcement

for the

Defense Health Program

Department of Defense

Congressionally Directed Medical Research Programs

## Prostate Cancer Research Program

### Clinical Exploration Award

Funding Opportunity Number: W81XWH-14-PCRP-CEA

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.***

## TABLE OF CONTENTS

<b>I. Funding Opportunity Description.....</b>	<b>3</b>
A. Program Description .....	3
B. Award Information.....	4
C. Eligibility Information .....	7
D. Funding .....	7
<b>II. Submission Information .....</b>	<b>8</b>
A. Where to Obtain the Application Package.....	9
B. Pre-Application Submission and Content Form .....	9
C. Application Submission Content and Forms .....	12
D. Verification of Grants.gov Application in eBRAP .....	18
E. Submission Dates and Times .....	18
F. Other Submission Requirements.....	18
<b>III. Application Review Information .....</b>	<b>19</b>
A. Application Review and Selection Process.....	19
B. Application Review Process .....	19
C. Recipient Qualification .....	22
D. Application Review Dates .....	22
E. Notification of Application Review Results .....	22
<b>IV. Administrative Actions.....</b>	<b>22</b>
A. Rejection .....	22
B. Modification.....	22
C. Withdrawal.....	23
D. Withhold .....	23
<b>V. Award Administration Information.....</b>	<b>24</b>
A. Award Notice .....	24
B. Administrative Requirements .....	24
C. National Policy Requirements .....	24
D. Reporting.....	24
E. Award Transfers.....	24
<b>VI. Agency Contacts.....</b>	<b>25</b>
A. CDMRP Help Desk.....	25
B. Grants.gov Contact Center.....	25
<b>VII. Application Submission Checklist.....</b>	<b>26</b>

## 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 Clinical Exploration Award mechanism was first offered in FY12. At that time, 18 applications were received, and 1 was recommended for funding. This award was not offered in FY13.

The Clinical Exploration Award supports early-phase, proof-of-principle clinical trials and correlative studies to investigate hypothesis-based, innovative interventions and/or avenues of research that have the potential to resolve current clinical barriers and result in a profound impact on the management of prostate cancer. While therapeutic approaches proposed for testing through the Clinical Exploration Award must represent novel, hypothesis-based, “outside-the-box” approaches for treating prostate cancer, they may include therapies already in clinical use, or undergoing clinical testing, for other diseases, provided that the proposed use for prostate cancer would lead to a major advancement for treating the disease. It is anticipated that outcomes from studies funded by this award will provide scientific rationale for subsequent development of larger, efficacy-based clinical trials of interventions that will transform prostate cancer clinical care.

**Clinical Trials:** The Clinical Exploration Award will support clinical trials encompassing Phase 0, Phase I, or pilot Phase II for drugs or drug combinations, Class II or III for devices, or other types of trials that conduct early clinical testing of innovative approaches for prostate cancer. 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. Principal Investigators (PIs) seeking funding for a preclinical research project should consider one of the other award mechanisms/funding opportunities being offered. 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. For more information, a Human Subject Resource Document is provided at <https://ebrap.org/eBRAP/public/Program>

**Correlative Studies:** The Clinical Exploration Award will also support innovative, hypothesis-based, correlative studies that derive from ongoing or completed clinical trials supported by other funding sources. These studies, if successful, will have the potential to significantly inform treatment strategies, identify subsets of patients for treatment with specific therapies, provide

increased understanding of biological changes resulting from the intervention in prostate cancer, or provide other insight that will significantly enhance clinical management of prostate cancer. Examples of correlative studies appropriate for submission to the Clinical Exploration Award may include, *but are not limited to*:

- Analyses of biomarkers for prognosis and/or prediction or assessment of therapeutic response or progression
- Investigations of the mechanism of action or the development of resistance to a drug
- Analyses of immune response or factors associated with progression
- Characterization of tumor antigens for the development of new or improved therapies

***Funding from the Clinical Exploration Award must support a clinical trial or correlative study associated with an ongoing or completed clinical trial and cannot be used for preclinical research studies.*** Because the Clinical Exploration Award seeks to support clinical trials and correlative studies that may deliver groundbreaking ideas, it is the responsibility of the PI to clearly articulate how the proposed study represents research that is beyond conventional therapeutic approaches for prostate cancer. Studies in a broad range of areas related to prostate cancer clinical management will be considered under the Clinical Exploration Award, including but not limited to evaluations of drugs, biologics, devices, surgical procedures, behavior modifications, or other types of therapeutic approaches. ***In addition, applicants 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 applicant should provide a description to justify how the project will nevertheless address a critical need in prostate cancer clinical management.

If the clinical trial involves the use of a drug that has not been approved by the U.S. Food and Drug Administration (FDA) for the proposed investigational use, evidence that an Investigational New Drug (IND) application that meets all requirements under the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312) has been submitted or will be submitted to the FDA ***within 60 days of award*** is required. If the investigational product is a device, evidence that an Investigational Device Exemption (IDE) application that meets all requirements under 21 CFR 812 has been submitted or will be submitted to the FDA ***within 60 days of award***, or that the device is exempt from an IDE, is required. The Government reserves the right to withdraw funding if the IND or IDE application has not been submitted to the FDA within 60 days of the Department of Defense (DoD) award date or if the documented status of the IND or IDE has not been obtained within 6 months of the award date.

The following are important aspects of submission for the Clinical Exploration Award:

- The application should clearly specify the type of clinical trial, including phase or class designation (if applicable), that is being proposed.
- ***The application must include documentation of application for an IND or IDE, if applicable.***
- The proposed intervention or correlative study must be based on sound scientific rationale that is established through logical reasoning, critical review and analysis of the literature, and preliminary data. ***The application should include data showing***

***strong statistical support from preclinical studies that substantiate the appropriateness of further clinical testing.***

- The application should demonstrate availability of, and access to, a suitable patient population that will support a meaningful outcome for the study. The PI should discuss how accrual goals will be achieved and how standards of care may impact the study population.
- The application should demonstrate documented availability of and access to the drug/compound, device, and/or other materials needed, as appropriate. The quality of the product should be commensurate with FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practices).
- The proposed clinical trial design should include clearly defined and appropriate endpoints, and follow Good Clinical Practice (GCP) guidelines.
- The application should include a clearly articulated statistical analysis plan, appropriate statistical expertise, and a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- The proposed clinical trial is expected to begin no later than 12 months after the award date.
- The application should include a Transition Plan (including potential funding and resources) showing how the product will progress to the next clinical trial phase.

**Use of Human Anatomical Substances, Human Subjects, or Human Cadavers:** All Department of Defense (DoD)-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), 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 requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB. Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes. Refer to the General Application Instructions, Appendix 6, for additional information.

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

- PIs must be independent investigators 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 **5** years.
- The maximum allowable direct costs for the entire period of performance are **\$450,000** 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 **5** 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
- Clinical research costs
- Travel between collaborating organizations
- Travel costs of up to \$1,800 per year 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.*

Shall not be requested for:

- Preclinical research studies

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 \$2.2M of the \$80M FY14 PCRP appropriation to fund approximately 3 Clinical Exploration 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 strongly 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 or may be subject to administrative rejection (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-CEA.

#### **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 pre-application is submitted.

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

- **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 (two-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 and preliminary studies that led to the development of the proposed clinical trial and/or correlative study. For a clinical trial, clearly describe the intervention and its target and mechanism of action in prostate cancer. If the proposed study is correlative to an ongoing or completed clinical trial, describe the relationship between the intervention and the question(s) to be studied.
- **Hypotheses or Objectives:** State the hypothesis(es) to be tested and/or the objective(s) to be reached.
- **Study Design:** Describe the design of the clinical trial or research approach for correlative studies. The description should include:
  - The type of study to be performed (e.g., phase/class, prospective, randomized, controlled, correlative, etc.) and proposed methodology.
  - The study variables and proposed measurement.
  - The research team’s capabilities in conducting clinical trials, including discussion of key coordinating activities.
  - The feasibility of initiating the clinical trial or correlative study within 12 months of the award date (*Note:* Invited applications must provide proof of *application for an IND or IDE*, if applicable).

- **Innovation:** Describe how the proposed study is an innovative, unconventional approach for the therapeutic management of prostate cancer.
- **Clinical Impact:** Describe how the proposed study, if successful, will have a major impact toward improving prostate cancer management and contribute to the elimination of death and suffering from prostate cancer. Briefly describe how the proposed study is responsive to one of the PCRCP overarching challenges or, alternatively, 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 PCRCP, pre-applications will be screened by the PCRCP IP based on the following criteria, which are of equal importance:

- **Intent of the Award Mechanism:** To what degree the proposed study includes a hypothesis-based, innovative intervention or avenues of research that has the potential to resolve current clinical barriers.
  - **Research Approach:** To what degree the experimental approach for accomplishing the specific aims is feasible and addresses the objectives.
  - **Clinical Impact:** To what degree the proposed study may lead to a profound impact on the clinical management of prostate cancer.
- **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 Clinical Exploration 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**

***The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) below.***

- Attachment 1: Project Narrative (15-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.

- **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. Include data showing strong statistical support from preclinical studies that substantiate the appropriateness of further clinical testing.

Provide a summary of relevant clinical trials and distinguish how the proposed study differs from other relevant or recently completed clinical trials. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). Clearly support the choice of study variables and explain the basis for the study questions and/or study hypotheses. Establish the relevance of the study and explain the applicability of the proposed findings.

If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source of prior funding. Specifically identify the portions of the study that will be supported with funds from this award.

If the proposed study is correlative to an ongoing or completed clinical trial, explain the history and background of the clinical trial and declare the source of funding.

***Clearly articulate how the proposed study represents research that is beyond conventional therapeutic approaches for prostate cancer.***

- **Objectives/Hypotheses:** State the hypotheses/study questions and overall objective(s) to be reached.
- **Specific Aims:** Concisely explain the project's specific aims. If this application is part of a larger study, present only tasks that this award would fund.
- **Study Design:** Describe the type of study to be performed (e.g., phase/class, prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate.
  - 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 study population, criteria for inclusion/exclusion, and the methods that will be used for recruitment/accrual of human subjects and/or samples (i.e., convenience, simple random, stratified random). Address any potential barriers to accrual and plans for addressing potential delays.
  - 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 discussion of risk/benefit considerations.

- Document the availability and accessibility of the drug/compound, device, or other materials needed.
- Describe in detail the laboratory evaluations (correlative studies) to be conducted.
- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study.
- **Study Personnel:** Identify the key members of the study team and describe their roles on the project. If applicable, a medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included.
- **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 clinical management.
- **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: 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. If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating availability of the product for the duration of the study, support for the proposed phase of research, and support for the indication to be tested.
- Intellectual Property
  - Background and Proprietary Information: 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 or provide a statement that none will be used. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the federal purpose license.
  - 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.

  - 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: Summarize the impact of the proposed research, if successful, on prostate cancer clinical management.

- **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 and impact 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 an impact on the standard of care for prostate cancer?
- What are the likely contributions of this study to advancing the field of prostate cancer research?

- **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 Clinical Exploration Award mechanism, use the SOW format example titled “SOW for Clinical 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:

- Identify the target population(s) that will participate in the proposed intervention, and describe the potential impact of the proposed clinical trial on the outcomes of individuals with prostate cancer.
- ***Describe the short-term impact:*** Detail the anticipated outcomes that will be directly attributed to the results of the proposed clinical trial. Explain how these results/outcome(s)/product(s) will have the potential to transform prostate cancer management and change clinical practice.
- ***Describe the long-term impact:*** Explain the anticipated long-term gains from the proposed research, including the long-term anticipated advantages that the new understanding may ultimately contribute to the 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. 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 prostate cancer clinical care.

- **Attachment 7: Innovation Statement (one-page limit).** Upload as “Innovation.pdf.”

Describe how the proposed work is innovative, representing a novel, hypothesis-based, “outside-the-box” approach for treating prostate cancer. Research that represents an incremental advancement on published data is not considered innovative.

- **Attachment 8: Transition Plan (one-page limit).** Upload as “Transition.pdf.” Provide information on the methods and strategies proposed to move the product or knowledge outcomes to the next phase of clinical research or use after successful completion of the award. The transition plan should include the components listed below.
  - Details of the funding strategy that will be used to bring the outcomes to the next level of clinical trial (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.
- **Attachment 9: IND/IDE Documentation Form.** Upload as “IND-IDE.pdf.”
  - Complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page under this funding opportunity on Grants.gov. *All applications must include this form, regardless of whether or not an IND or IDE is required for the study.*

**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 DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an “Active” status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, 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, USAMRMC, based on (a) technical merit and (b) the relevance to the mission of the DHP and PCRCP and to 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 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 18 USC 1905.

#### **B. Application Review Process**

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

- **Clinical Impact**
  - Whether the appropriateness of further clinical testing has been substantiated by data showing strong statistical support from preclinical studies.
  - To what degree the proposed study could ultimately transform prostate cancer clinical management (e.g., detection, diagnosis, treatment, management, and/or quality of life), far beyond current clinical practice, including its potential contribution to the elimination of death and suffering from prostate cancer and enhancing the well-being of men experiencing the impact of the disease.
  - How well the sample population represents the targeted patient population that might benefit from the proposed or potential intervention.
  - How well the proposed research addresses at least one of the PCRCP focus areas and one of the PCRCP overarching challenges or is otherwise justified as significantly addressing another critical issue in prostate cancer.

- To what degree an appropriate plan for transitioning the study outcomes into further development is present, including:
  - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
  - Whether the funding strategy described to bring the outcome(s) to clinical testing or the next level of clinical trial is appropriate.
- **Innovation**
  - How well the research proposes to use a new intervention and/or existing intervention in a unique or creative way (e.g., first in prostate cancer, new and unconventional therapeutic approach, etc.).
  - To what degree the concept or research question is groundbreaking.
  - Whether the proposed research represents more than an incremental advance upon published data.
- **Research Strategy/Study Design**
  - How well the scientific rationale is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/preclinical evidence.
  - How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to answer clearly the clinical objective.
  - To what degree the statistical plan, including sample size projections and power analysis, as applicable, is appropriate and adequate for the study and all proposed correlative studies.
  - ***For applications proposing clinical trials:***
    - How well the inclusion, exclusion, and randomization criteria meet the needs of the proposed clinical trial, and how well the level of risk to human subjects is minimized.
    - To what degree the intervention addresses the clinical need(s) described.
    - Whether there is evidence to support availability and accessibility of the intervention, and to what degree the plans for application of the intervention are appropriate.
    - Whether a member of the study team holds the IND/IDE for the indication proposed, or whether the timeline proposed for obtaining the IND/IDE is appropriate (if applicable).
- **Recruitment, Accrual, and Feasibility**
  - How well the PI addresses the availability, accessibility, and interest of human subjects for the clinical trial, or how well the PI has justified the availability and accessibility of human samples for correlative studies.
  - How well the recruitment processes for human subjects, or the collection processes for human samples, are designed to meet the needs of the proposed study.

- How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.
- **Personnel**
  - 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.

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

- **Environment**
  - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial/study 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/study.
- **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 and innovation
  - 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 PCRIP 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 PCRIP 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 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**

For all awards including prospective accrual of human subjects, quarterly technical progress reports will be required.

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

### **E. Award Transfers**

Changes in PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer.

The institutional transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer.

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](mailto: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](mailto: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."	
	Innovation Statement: Upload as Attachment 7 with file name "Innovation.pdf."	
	Transition Plan: Upload as Attachment 8 with file name "Transition.pdf."	
	IND/IDE Documentation Form: Upload as Attachment 9 with file name "IND-IDE.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.	