Program Announcement

Defense Health Program

Department of Defense

Congressionally Directed Medical Research Programs

Prostate Cancer Research Program

Biomarker Development Award

Funding Opportunity Number: W81XWH-12-PCRP-BDA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), May 3, 2012
- **Invitation to Submit an Application:** June 15, 2012
- **Application Submission Deadline:** 11:59 p.m. ET, August 23, 2012
- **Peer Review:** October 2012
- **Programmatic Review, Stage 1:** December 2012
- **Invitation for Oral Presentation:** December 2012
- **Programmatic Review, Stage 2:** January 2013

TABLE OF CONTENTS

I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

The Prostate Cancer Research Program (PCRP) was established in 1997 to promote innovative research focused on eradicating prostate cancer. Appropriations for the PCRP from FY97 through FY11 totaled $1.13 billion. The FY12 appropriation is $80 million (M).

The overall goal of the FY12 PCRP is to find and fund research that will lead to the elimination of death and suffering from prostate cancer. 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

Consistent with the program's overall goal, each PCRP funding opportunity either requires or encourages (see Award Information below) applications to address one of the following PCRP overarching challenges:

- Develop effective treatments for advanced prostate cancer (i.e., disease progression with no available curative therapy)
- Distinguish aggressive from indolent disease

PCRP Focus Areas *(revised for FY12)*

All applications for FY12 PCRP funding opportunities must also address at least one of the following PCRP focus areas:

Biomarker Development: Qualification or validation of biomarkers for detection of aggressive disease, prediction and assessment of response to therapies, and prognosis and progression. These include validation studies of circulating tumor cells. Biomarker studies may include discovery if accompanied by qualification or validation.

Genetics: Understanding host or tumor genetics and epigenetics responsible for susceptibility, disease progression, and treatment outcomes for aggressive prostate cancer.

Imaging: Development of new anatomic, functional, and molecular imaging approaches for the detection and management of aggressive 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 prognosis and progression of prostate cancer.

B. Award Information

The PCRP Biomarker Development Award mechanism is being offered for the first time in FY12.

The intent of the Biomarker Development Award is to support the near-term translation of prostate cancer biomarkers to clinical practice. Specifically, this award will support high-impact research aimed at qualifying or validating prostate cancer biomarkers for crucial decision-making in prostate cancer management, including detection of aggressive disease, prognosis and progression, and prediction and assessment of response to therapy. Proposed projects should demonstrate a high potential for commercialization and clinical use of the projects' outcomes. ***As such, the inclusion of clinical trials is allowed.*** It is the responsibility of the Principal Investigator (PI) to clearly articulate the potential near-term impact of the study on current clinical practice for prostate cancer management. ***Due to the expectation for near-term impact, studies toward discovery of new biomarkers or studies in model systems to improve or refine biomarkers are not consistent with the intent of this award mechanism.***

A ***biological marker,*** or ***biomarker,*** is defined as a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or biological responses to a therapeutic intervention[1]. For the purpose of this award, **biomarker qualification** is defined as the evidentiary fit-for-purpose process of correlating a biomarker with the effects of an agent on biological processes and clinical endpoints. Alternatively, **biomarker validation** refers to the process of ensuring that a biomarker or technology (e.g., imaging) will be accurately and reliably measured through the performance characteristics of a biomarker assay[2]. The PCRP strongly encourages the study of biomarkers that can be detected through minimally invasive procedures (e.g., blood, urine, serum, prostatic fluids, imaging, etc.). Examples of biomarkers may include circulating tumor cells, signatures of genetic or epigenetic changes, specifically expressed genes, proteins, or metabolites, and molecular, physiological, and/or immunological imaging entities, among others.

All projects proposed for the Biomarker Development Award must address one of the PCRP overarching challenges and the PCRP focus area of Biomarker Development.

Key aspects of this award include:

Candidate Biomarker(s) and Evaluation: Applications for this award must include clear descriptions of the candidate biomarker(s) for qualification or validation studies. ***Projects studying multiple biomarkers are highly encouraged.*** Applications must also include relevant preliminary data from pilot testing that demonstrate the suitability of the biomarker(s) for further testing toward clinical application. Sufficient detail must be provided to demonstrate how the biomarkers will be qualified or validated, including the approaches that will be applied to establish feasibility, reliability, and reproducibility, and the criteria that will provide the evidence for evaluating the biomarkers. These criteria may include, but are not limited to:

[1] Biomarkers Definitions Working Group. 2001. Biomarkers and surrogate endpoints: Preferred definitions and conceptual framework. *Clinical Pharmacology and Therapeutics* 69:89-95.
[2] Sistare FD, Dieterle F, Troth S, et al. 2010. Towards consensus practices to qualify safety biomarkers for use in early drug development. *Nature Biotechnology* 28:446-454.

- Improved performance relative to current, clinically accepted biomarkers
- Availability of a robust analytical assay to reliably and reproducibly assess the validity of the biomarker's association with prostate cancer or clinical outcomes
- Biological association of the biomarker(s) with prostate cancer (e.g., disease stage/grade, distinguish aggressive/indolent)
- Strength of association of changes in biomarker levels with pathological/clinical outcomes
- Sufficient sensitivity and specificity to guarantee the biomarker(s) does not detect benign physiological processes of the prostate gland and other organs

In addition, applications must include, where appropriate, consideration of the Tumor Marker Utility Grading System (TMUGS)[3] and, as applicable, be consistent with current U.S. Food and Drug Administration (FDA) guidance for biomarker qualification or validation. Useful information can be found at the following:

- FDA Biomarker Qualification Process:
  - http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284621.htm
  - http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284076.htm
  - http://www.c-path.org/pdf/FDADraftDDTools.pdf
- FDA Office of In Vitro Diagnostic Device Evaluation and Safety:
  - http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHOffices/ucm115904.htm

Leveraging of Resources: The PCRP expects that PIs applying for the Biomarker Development Award will leverage existing prostate cancer resources to address high-impact research ideas. For example, many putative prostate cancer biomarkers have never been qualified or validated nor are readily available for study beyond the laboratories where they were first discovered. Because these biomarkers are not leveraged for study beyond the original source, other groups expend additional time and resources duplicating efforts. Therefore, this award strongly encourages evidence of leveraging biomarker development efforts. Additionally, this award seeks to leverage other resources, supported by the PCRP or other agencies, such as prostate cancer biorepositories (e.g., Prostate Cancer Biorepository Network [PCBN] [http://www.prostatebiorepository.org], North Carolina - Louisiana Prostate Cancer Project [PCaP] [http://www.ncla-pcap.org]), epidemiological resources, databases of clinical data and/or metadata, transcriptome or proteome datasets, or other existing resources. PIs should consider collaborations with personnel affiliated with established prostate cancer resources.

[3] Hayes DF, Bast RC, Desch CE, et al. 1996. Tumor marker utility grading system: A framework to evaluate clinical utility of tumor markers. *Journal of the National Cancer Institute* 88:1456-1466.

It is the responsibility of the PI to explain how the proposed research leverages existing resources and why the resource is uniquely suited to answer the research question and/or accomplish the goals of the project. Applications should also include evidence to support sufficient accessibility and availability of all materials and resources needed to conduct the study so that the project can commence immediately after an award is made.

Implementation Plan: The project(s) must be supported by a detailed plan that identifies critical milestones, outlines the knowledge, expertise, and technical innovations that the investigative team will utilize to achieve the milestones, and explains how the outcomes of the project(s) will be translated to patients in the near-term. The application must include information demonstrating accessibility and availability of human subjects, substances, data, and/or materials necessary for the study so that the project(s) can commence immediately after an award is made. A robust statistical plan and statistical expertise should be included where applicable in proposed investigation(s).

Research Team: Projects proposed under this award mechanism are strongly encouraged to be multi-institutional. Applications should include a clear description of a consistent and coordinated research effort by all investigators involved in the project. The overall effort should be led by an experienced PI with a record of successfully leading large, focused projects, and who will combine the resources and expertise of all investigators into a synergistic collaboration to achieve the goal of moving biomarkers to clinical practice.

Oral Presentation: Due to the nature of the Biomarker Development Award, an oral presentation to the PCRP Integration Panel (IP) is a requirement for application review as described below:

- ***Programmatic Review, Stage 2:*** A PI whose application is selected for final consideration in Stage 2 of the Programmatic Review will be required to give an oral presentation that will be held in the Washington, DC area in January 2013.

Use of Human Subjects and Human Anatomical Substances: All Department of Defense (DoD)-funded research involving new and ongoing research with human subjects and human anatomical substances must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the IRB of record. IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DoD. These laws and directives will require information in addition to that supplied to the IRB. Allow a minimum of 2-3 months for regulatory review and approval processes. Refer to the General Application Instructions, Appendix 5, for more information.

The Congressionally Directed Medical Research Programs (CDMRP) intends that data and research resources generated by CDMRP-funded research activities be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section K.

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.
- 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 **$2,250,000** 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., for budget regulations and instructions for the Research & Related Budget. In addition, for this award mechanism, direct costs:

Must be requested for:

- Travel for the PI and up to two additional members of the research team to attend a 1-day meeting to be held in the Washington, DC area during the award period of performance. This meeting will be held to provide a presentation on progress. Costs associated with travel to this meeting, up to $1,800 per person, should be included in Year 2 of the budget.
- Travel for the PI and up to two additional members of the research team to attend one DoD PCRP Innovative Minds in Prostate Cancer Today (IMPaCT) meeting or other similar event as directed by the CDMRP, if the meeting occurs within the period of performance of the award. The IMPaCT meeting is held to disseminate the results of PCRP-sponsored research. Costs associated with travel to this meeting, up to $1,800 per person, should be included in Year 2 of the budget. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary
- Research supplies

- Equipment
- Research-related human subject costs
- Clinical research costs
- Purchase of datasets and/or databases
- Travel between collaborating organizations
- Travel costs of up to 5 individuals among the PI and the key personnel (maximum of $1,800 per year per person) to attend scientific/technical meetings

The CDMRP expects to allot approximately $3.6M of the $80M FY12 PCRP appropriation to fund approximately one Biomarker Development Award application, 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 multi-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

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

A. Where to Obtain the Application Package

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

B. Pre-Application Submission Content and Form

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

PIs and organizations identified in the application should be the same as those identified in the pre-application. If a change in PI or organization is necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@cdmrp.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 U.S. Army Medical Research Acquisition Activity (USAMRAA) Contracting/Grants Officer.

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

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

  FY12 PCRP IP members should not be involved in any pre-application or application. For questions related to IP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk (help@cdmrp.org or 1-301-682-5507).

- **Required Files – Tab 4**

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

  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 data. Describe how the qualification or validation of the proposed candidate biomarkers will address critical problems in prostate cancer clinical care. ***Studies proposed under this award should not include discovery of new biomarkers or improving or refining biomarkers in model systems.***
  - **Hypothesis or 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. Describe any existing prostate cancer resources that will be leveraged to conduct this research, and explain how the existing resource(s) is uniquely suited to support achieving the goals of the proposed project.
  - **Research Team:** Briefly describe the composition, expertise, and organization of the research team, each team member's role in the project, and how these features will facilitate the success of all aspects of the project.
  - **Impact:** Describe the potential near-term impact of the project on prostate cancer clinical care. Include comments on other benefits that will be realized beyond the required near-term impact. Briefly describe how the proposed study is responsive to one of the PCRP overarching challenges.

  Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application are limited to:

  - References Cited (one-page limit): List relevant references 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). The inclusion of Internet URLs to references is encouraged.

- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
- Biographical Sketches for the PI and Key Personnel (two-page limit per individual)

- **Submit Pre-Application – Tab 5**

  This tab must be completed for the pre-application to be accepted and processed by CDMRP.

- **Other Documents Tab**

  No additional documents are required**.**

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DoD and the PCRP, pre-applications will be screened by the PCRP IP based on the criteria shown below, which are of equal importance.

  - **Intent of the Award Mechanism:** Whether the candidate biomarker(s) is(are) ready for near-term translation to clinical practice and demonstrate a high potential for commercialization.
  - **Research Approach:** To what degree the experimental approach for accomplishing the specific aims is feasible, addresses the objectives, and appropriately leverages existing resources, if applicable.
  - **Research Team:** To what degree the combined expertise and proposed interactions of the PI and key personnel have a high likelihood of facilitating the project's success.
  - **Impact:** To what degree the candidate biomarkers are responsive to the PCRP overarching challenges and have the potential for major impact on crucial decision-making points in prostate cancer management.

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

C. Application Submission Content and Form

Applications will not be accepted unless the PI has received 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/). For the Biomarker Development Award, additional application components are also required.

Grants.gov application package components: For the Biomarker Development 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 Biomarker Development Award supports research focused on the qualification or validation of human prostate cancer biomarkers and their translation into clinical use. ***This award mechanism does not support projects focused on biomarker discovery.***

      Describe the proposed project in detail using the outline below. The inclusion of preliminary data relevant to pilot testing of candidate prostate cancer biomarkers 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 how the qualification or validation of the proposed candidate biomarkers will address critical problems in prostate cancer clinical care. Describe previous experience most pertinent to this application.
        - **Candidate Biomarker(s):** Describe the candidate biomarker(s), including relevant studies to date and the projected clinical utility.
        - **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 and Feasibility:** Describe the experimental design for qualifying or validating the candidate biomarkers.
            - Describe any existing prostate cancer resources that will be leveraged to conduct the research. Clearly articulate the availability and accessibility of the existing resource as well as any potential obstacles that might be encountered. Explain how the existing resource(s) is(are) uniquely suited to support achieving the goals of the proposed project. Explain how the outcomes of this research effort will be shared with the prostate cancer community to maximize leveraging of the shared existing resources, making this research effort more productive toward the qualification or validation of additional prostate cancer biomarkers for use in the clinic.

- Describe in detail the methods and analyses, including appropriate controls; a timeline for the completion of each proposed task; and how the approaches are consistent with current FDA guidance for biomarker qualification or validation.
- Address potential problems and present alternative methods and approaches.
- As appropriate, clearly outline the level(s) of evidence of validation based on the TMUGS.
- If human subjects or human anatomical samples will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples.
- Describe how and/or provide evidence that the research can be initiated without delay once the award is made.

○ **Research Team and Environment:** Describe how the PI's research experience and leadership abilities make him/her well qualified to coordinate this effort. Discuss the qualifications of the research team, each individual's specific contributions to the project, and how the appropriate expertise is incorporated to address the research question and enable the success of the proposed project. Describe the research environment(s) and how the facilities and resources will support the research requirements and the project. Present a plan to facilitate consistent and intensive interactions by all team members, including, where applicable, plans for biospecimen and data sharing, assay development, adherence to regulatory requirements, administrative support, and other components to accelerate translation of the project's outcomes.

○ **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 either 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/or 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 component unless otherwise noted. Include only those components described below; inclusion of items not requested may result in administrative rejection 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 if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present 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, ensuring the laboratory space, equipment, and other resources available for the project.
- Letters of Collaboration (if applicable) (2-page limit per letter recommended): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
- Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations. Include material transfer agreements (MTAs) or MTA requests, if applicable.

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

  The technical abstract is used by all reviewers; however, programmatic reviewers do not have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects.

  - 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. Comment on resources being leveraged to accomplish the objective of the project.
  - Impact: Summarize the near-term impact of the proposed project on prostate cancer clinical care.

- **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.*** The lay abstract is used by consumer reviewers along with other components of the application package.

  - 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 near-term 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., for detailed information.
- **Attachment 6: Impact Statement (one-page limit):** Upload as "Impact.pdf."

  Explain in detail how the proposed research project is important, as follows:

  Describe the near-term impact: Detail the anticipated results/outcome(s)/ product(s) that will be directly attributed to the results of the proposed research. Explain how these results/outcome(s)/ product(s) will improve prostate cancer management and/or change clinical practice. Describe the benefits and how rapidly they will be successfully translated to prostate cancer patients.

  Describe the long-term impact: Although the expectation is that projects supported by the Biomarker Development Award will result in near-term benefits for patients, additional/ongoing benefits over time are also expected. Explain the anticipated long-term gains from the proposed research, including how the outcomes or products will ultimately contribute to eliminating death and suffering from prostate cancer.

  PCRP Overarching Challenges: Summarize how the proposed project addresses one of the PCRP overarching challenges.

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

  Provide information on the methods and strategies proposed to move the biomarker(s) to clinical use. 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, measurable, and should include a definition of the end user.
  - Details of the funding strategy that will be used to bring the outcomes to delivery to market (e.g., specific potential industry 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 delivery to market.

- **Attachment 8: Data- and Research Resource-Sharing Plan (one-page limit):** Upload as "Sharing.pdf."

  Describe how unique and/or final research data will be shared, along with any resulting research resources. This includes cases where pre-existing data or research resources will be utilized and/or modified during the course of the proposed project. If there are limitations associated with a preexisting agreement for the original data or research resources that preclude subsequent sharing, the applicant should explain this in the data- and/or research resource-sharing plan.

  Refer to the General Application Instructions, Appendix 4, Section K, for additional information.

  In preparing requested budgets, applicants may include anticipated costs associated with data- and research resource-sharing (i.e., making a large dataset available to the public or developing an important resource for the scientific community).

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C., for detailed information.
   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
   - Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
   - Key Personnel Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

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

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

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

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

Additional Application Components: In addition to the completed Grants.gov application package of forms, Biomarker Development Award applications also require the following component:

Oral Presentation: PIs whose applications are selected during Programmatic Review, Stage 1, for final consideration in Programmatic Review, Stage 2, will be required to give an oral presentation that will be held in the Washington, DC area in January 2013.

Each presentation will include a 10-minute talk by the PI, followed by a 20-minute question and answer session with IP members. Time limits will be strictly enforced. The oral presentation should not be used to reiterate the technical/scientific details of the project already described in

the written application. Rather, the following questions will be the topics for discussion during the PI's talk and the question and answer session. A PI who is invited must prepare a presentation that specifically addresses these questions:

- How were the biomarkers for your project selected, and how will their qualification or validation address a critical barrier that you consider to be the most urgent to overcome in prostate cancer clinical management?
- How will your project have a near-term, major impact on the management of prostate cancer and, in addition, ultimately contribute significantly to the elimination of death and suffering from prostate cancer?
- How will you, as the leader of the project, move the project quickly and effectively toward outcomes that can be rapidly and successfully translated to the clinic?

D. Submission Dates and Times

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

E. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines. All applications must be submitted through Grants.gov. Organizations are required to provide a Data Universal Numbering System (DUNS) number and register with the Central Contractor Registry (CCR) to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

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

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each level of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other corrective actions. Organizational personnel and PIs are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence

the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panelists or PIs that compromise the confidentiality of the review process may also result in suspension or debarment of their employing organizations from Federal awards. Furthermore, 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 Criteria

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

   - **Candidate Biomarkers**
     - To what degree the selected biomarkers are clearly justified as having high relevance to prostate cancer clinical management, e.g., presence of aggressive disease, prognosis, or response to therapy.
     - To what degree the biomarkers can be reliably detected through minimally invasive procedures.
     - To what degree the PI has maximized the potential outcome of the project, e.g., scope and/or ease of biomarker use, etc.
     - How well the rationale and preliminary data support the suitability of the biomarkers.
     - How well the PI has made appropriate plans to implement the leveraging of existing resources, where possible.
   - **Research Strategy and Feasibility**
     - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed.
     - How well the PI addresses the feasibility of the research strategy, including acknowledging potential problems and addressing alternative approaches.
     - To what degree the strategies are appropriately designed to foster confidence in the reliability and reproducibility of the biomarker study.
     - To what degree the proposed strategies are consistent with current FDA guidance for biomarker qualification or validation.
     - To what degree the Tumor Marker Utility Grading System (TMUGS) has been appropriately considered.
     - Whether plans for human subject recruitment or other acquisition of human samples are appropriate.
     - Whether the PI has demonstrated that the proposed research can be initiated without delay once the award is made.

- **Impact**
    - To what degree the proposed study could make a near-term, significant impact on prostate cancer research and/or patient care, and ultimately contribute to the elimination of death and suffering from prostate cancer.
    - How well the proposed research addresses one of the PCRP overarching challenges.
    - Whether the transition plan is appropriately and sufficiently developed to enable rapid translation of the project outcomes to patients.
- **Research Team**
    - To what degree the PI is experienced in successfully leading large, focused efforts and therefore well-positioned to lead the research team in accomplishing the aims of the proposed project.
    - To what degree the PI has assembled an appropriately robust research team, including combined backgrounds and prostate cancer-related expertise to enable successful conduct of the project and the likelihood of achieving a near-term product.
    - Whether letters of collaboration provide appropriate support for the project.
    - Whether a robust plan to facilitate consistent and intensive interactions among all team members has been presented.
    - To what degree the levels of effort are appropriate for successful conduct of the proposed work.

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

- **Environment**
    - 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 influenced the review.

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

- **Stage 1:** During the first stage of programmatic review, applications will be selected for the second stage using the following criteria:
    - Adherence to the intent of the award mechanism
    - Programmatic relevance in relation to the PCRP overarching challenges and focus areas
    - Ratings and evaluations of the peer reviewers
    - Relative impact
    - Program portfolio composition
- **Stage 2:** During the second stage of programmatic review, the following criteria will be used:
    - Understanding of critical issues in prostate cancer management such that biomarkers have been selected for maximum benefit to patients;
    - Appropriate approach to achieve a biomarker qualification or validation outcome that will be readily translatable into clinical practice; and
    - Leadership capability to synergize the expertise and efforts of a large research team to effectively accomplish the aims of the project.

C. Recipient Qualification

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

D. Application Review Dates

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

E. Notification of Application Review Results

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

IV. ADMINISTRATIVE ACTIONS

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

A. Rejection

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

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

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

C. Withdrawal

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

- A FY12 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 document. A list of the FY12 PCRP IP members can be found at http://cdmrp.army.mil/pcrp/panels/panel12.
- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- 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.
- The PI does not meet the eligibility criteria as described in this Program Announcement/Funding Opportunity.

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 U.S. Army Medical Research Acquisition Activity (USAMRAA) Contracting/Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2013. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

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

C. Reporting

Attendance is required at a 1-day meeting to be held in the Washington, DC area for the purpose of reporting on progress.

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 E, for general information on reporting requirements.

D. 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 transfer of an award will not be allowed for any institution that includes a clinical trial at its location. Approval of a transfer request from an institution that does not include a clinical trial at its location will be at the discretion of the Grants Officer.

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

E. Pre-Award Meeting

At the Government's discretion, the PI and key personnel may be requested to participate in a pre-award meeting at the Government's expense.

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 the CDMRP eReceipt System should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 1-301-682-5507

Email: help@cdmrp.org

B. Grants.gov Contact Center

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

Phone: 1-800-518-4726

Email: support@grants.gov

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

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed.	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1.	
	Upload Supporting Documentation (Support.pdf) as Attachment 2.	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3.	
	Upload Lay Abstract (LayAbs.pdf) as Attachment 4.	
	Upload Statement of Work (SOW.pdf) as Attachment 5.	
	Upload Impact Statement (Impact.pdf) as Attachment 6.	
	Upload Transition Plan (Transition.pdf) as Attachment 7.	
	Upload Data- and Research Resource-Sharing Plan (Sharing.pdf) as Attachment 8.	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Current & Pending Support (Support_LastName.pdf) to the appropriate field.	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
	Attach Current & Pending Support (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete 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.	
Additional Application Components	**Action**	**Completed**
Oral Presentation	Confirm availability to give an oral presentation in the Washington, DC area in January 2013 (if selected for Programmatic Review, Stage 2).	