Program Announcement

for the

Defense Health Program

Department of Defense

Congressionally Directed Medical Research Programs

Prostate Cancer Research Program

Biomarker Development Award

Funding Opportunity Number: W81XWH-14-PCRP-BDA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), June 18, 2014
- **Invitation to Submit an Application:** early August 2014
- **Application Submission Deadline:** 11:59 p.m. ET, September 24, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, September 29, 2014
- **Peer Review:** November 2014
- **Programmatic Review, Stage 1:** January 2015
- **Invitation for Oral Presentation:** January 2015
- **Programmatic Review, Stage 2:** February 2015

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

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

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

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

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

PCRP Overarching Challenges *(revised for FY14)*

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

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

PCRP Focus Areas

All applications for the FY14 Biomarker Development Award are required to address the following PCRP focus area:

- **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

To view the full list of FY14 PCRP focus areas, which includes other areas not applicable to the Biomarker Development Award, refer to the Program Announcement for the FY14 PCRP Idea Development Award.

B. Award Information

Many putative prostate cancer biomarkers have been discovered in recent decades. The vast majority of these biomarkers have not been validated or qualified for clinical use, or such studies have been conducted on only a very limited basis, e.g., within a single institution. Thus, the number of markers that have been translated to clinical practice is very small, despite the known limitations of the current standard of care using the biomarker prostate specific antigen (PSA).

The PCRP Biomarker Development Award was introduced in FY12 to fund near-term validation or qualification studies that will advance known prostate cancer biomarkers into the clinical setting. **Specifically, this award will support high-impact research aimed at multi-institutional validation and/or qualification of 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.** It is anticipated that studies supported through this award will produce clinically useful biomarkers that will provide improved specificity for detection of clinically relevant prostate cancer, as well as distinguish between aggressive and indolent disease, which will in turn reduce the burdens of prostate cancer overtreatment and improve the clinical management of this disease.

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 aimed at discovery of new biomarkers, studies using tissues or other samples to further investigate biomarker expression patterns prior to large-scale validation or qualification, or studies in model systems to improve or refine biomarkers are not consistent with the intent of this award mechanism and will not be supported.***

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 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, which involves determining the range of conditions under which the biomarker will give reproducible and accurate data.[2] Alternatively, **biomarker qualification** is defined as the evidentiary fit-for-purpose process of correlating a biomarker with biological processes and/or clinical endpoints.[3]

[1] Biomarkers Definitions Working Group. 2001. Biomarkers and surrogate endpoints: Preferred definitions and conceptual framework. *Clinical Pharmacology and Therapeutics* 69:89-95.

[2] Lee JW, Devanarayan V, Barrett YC, et al. 2006. Fit-for-purpose method development and validation for successful biomarker measurement. *Pharmaceutical Research* 23:312-328.

[3] 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.

The PCRP recognizes that, to move beyond current practice, a combination of biomarkers including those measured in biofluids (e.g., blood, urine), tissue-based biomarkers that provide optimal patient-centered treatment, and new imaging techniques, are needed. ***The emphasis for the Biomarker Development Award mechanism is on biomarkers that can be assessed through noninvasive methods;*** *however, other types of studies will be considered for funding.* Examples of biomarkers may include, but are not limited to:

- circulating tumor cells
- signatures of genetic or epigenetic changes
- specifically expressed genes, proteins, or metabolites, and
- molecular, physiological, and/or immunological imaging entities

In addition, the significant heterogeneity of prostate tumors should be well considered in any proposed biomarker project. The molecular, cellular, histopathologic, and clinical heterogeneity of prostate tumors presents challenges to the efficacy of many biomarkers. Therefore, PIs are strongly encouraged to address the complexities of intratumoral heterogeneity and how their validation or qualification efforts, and ultimately the biomarker's clinical application, may be impacted.

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:

1. **Candidate Biomarker(s) and Evaluation:** Applications for this award must include clear descriptions of the candidate biomarker(s) for validation or qualification studies. ***Projects studying multiple biomarkers are highly encouraged.*** Applications must also include relevant preliminary data from previously completed testing that demonstrate the suitability of the biomarker(s) for further testing toward clinical application. Sufficient detail must be provided to demonstrate how the biomarker(s) will be validated or qualified, 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:

    - 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)[4] and, as applicable, be consistent with current U.S. Food and Drug Administration (FDA) guidance for biomarker validation or qualification. Useful information can be found at the following:

- FDA Biomarker Qualification Process:
  - FDA DDT Qualification Process
  - FDA Biomarker Qualification Program
  - FDA Guidance for Industry (Draft)

In addition, it is highly recommended that PIs demonstrate appropriate consideration of the literature on optimal design of marker studies.[5]

2. **Multi-institutional Approach:** Applications to the PCRP Biomarker Development Award are **required** to be multi-institutional in their approaches to large-scale biomarker validation or qualification. Importantly, inclusion of independent patient cohorts is an expectation for supported studies.

   In addition, due to the multi-institutional nature of this award mechanism, the award will accommodate up to three PIs, each of whom will receive a separate award. One partner is identified as the Initiating PI and additional PIs are identified as Partnering PIs. The Initiating and Partnering PIs have different application submission requirements; however, each PI should contribute to the preparation of each of the application components. The PIs may have expertise in similar or disparate scientific disciplines. It is the responsibility of the collaborating investigators to describe how their efforts will combine and synergize to maximize the project's outcomes.

3. **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 validated or qualified nor are they 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://ncla-pcap.org/index.php]), 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.

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[4] 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.

[5] For example, McShane LM, Altman DG, Sauerbrei W, et al.; Statistics Subcommittee of the NCI-EORTC Working Group on Cancer Diagnostics. 2005. Reporting recommendations for tumor marker prognostic studies (REMARK). *Journal of the National Cancer Institute* 97:1180-1184.

It is the responsibility of the PI(s) to explain how the proposed research leverages existing resources. 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.

4. **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. ***It is strongly encouraged that PIs begin discussions with the FDA early to determine FDA-driven milestones, which should be incorporated into the implementation plan.*** 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 appropriate, in proposed investigation(s).

5. **Research Team:** Applications should include a clear description of a consistent and coordinated research effort, with a robust communications plan, by all investigators involved in the project. The overall effort should be led by one or more experienced PIs with records 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 prostate cancer biomarkers to clinical practice. The inclusion of scientific advisors, external to the conduct of the research, is encouraged. ***The PCRP Science Officer assigned to any resulting award must be invited to participate in periodic research team meetings. The plan for such meetings should be noted in the application.***

Oral Presentation: An oral presentation to the PCRP Integration Panel (IP) is a requirement for application review as described below:

- ***Programmatic Review, Stage 2:*** An Initiating 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 National Capital Area in February 2015.

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 Institutional Review Board (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.

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

- Each PI (Initiating and Partnering) 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 **3** years.
- The maximum allowable combined 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 applicants may together 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(s) may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.
- A separate award will be made to each PI.

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:

Must be requested for:

- Travel for the PIs to attend a 1-day meeting to be held in the National Capital 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 each application's budget.

May be requested for (not all-inclusive):

- Salary
- Research supplies
- Equipment
- Research-related human subject costs
- Clinical research costs
- Purchases of datasets and/or databases
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year per person for three individuals among the PI(s) and the key personnel to attend scientific/technical meetings. ***The Government reserves the right to direct the selection of one of these meetings, should a PCRP-sponsored meeting be convened during the award period of performance.***

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

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from federal agencies submit applications, they must submit through Grants.gov. Therefore, federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

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

The CDMRP expects to allot approximately $3.6M of the $80M FY14 PCRP appropriation to fund approximately 1 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 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, provided there is no cause for administrative rejection of the application (see Section IV.A., Rejection).

The Biomarker Development Award mechanism is structured to accommodate up to three PIs. One partner will be identified as the Initiating PI and will be responsible for the majority of the administrative tasks associated with application submission. The other PI(s) will be identified as Partnering PI(s). Initiating and Partnering PIs each have different submission requirements; however, all PIs should contribute significantly to the development of the proposed research project including the Project Narrative, Statement of Work, and other required components. The Initiating PI must complete the pre-application submission process and submit the contact information for each Partnering PI. Each Partnering PI will then be notified of the pre-application submission separately by email. Each Partnering PI must follow the link in this email and register with eBRAP in order to associate his/her grant application package with that of the Initiating PI. If an application is invited, only the Initiating PI will receive notification of invitation via email from CDMRP. The letter will provide the information necessary to begin application submission through Grants.gov.

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-BDA.

B. Pre-Application Submission and Content Form

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

The Initiating PI is responsible for submission of all pre-application components.

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

  The Initiating PI must enter the contact information for each Partnering PI in the Partnering PI section. This Program Announcement/Funding Opportunity allows a ***maximum of two*** Partnering PIs.

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

The Preproposal Narrative should describe the proposed project using the outline below:

- **Background/Rationale:** Clearly present the ideas and reasoning behind the proposed research; include relevant literature citations and preliminary data. Describe how the validation or qualification of the proposed candidate biomarkers will address critical problems in prostate cancer clinical care and to what degree the biomarkers will be assessed through noninvasive or minimally invasive means. Address any challenges presented by prostate tumor heterogeneity. ***Studies proposed under this award should not include discovery of new biomarkers, studies using tissues or other samples to further investigate biomarker expression patterns prior to large-scale validation or qualification, or improving or refining biomarkers in model systems.***
- **Objective:** State the objective 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 multi-institutional 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 required, ***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 "Abbrev.pdf."

- PI and Key Personnel Biographical Sketches (four-page limit per individual). Upload all biosketches as a single, combined file with the file name "Biosketch_LastName.pdf."

- **Submit Pre-Application – Tab 5**

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

Pre-Application Screening

- **Pre-Application Screening Criteria**

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

  - **Intent of the Award Mechanism:** 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 based on a sound rationale, 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(s) 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, near-term impact on crucial decision-making points in prostate cancer management.

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

  Following the pre-application screening, Initiating 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 Initiating 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 and should be submitted as directed below.

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).***

The CDMRP requires separate Grants.gov application package submissions for the Initiating PI and each Partnering PI, even if the PIs are located within the same organization. Initiating and Partnering PIs will each be assigned unique log numbers by eBRAP. Each Grants.gov application package must be submitted using the unique log number. Note: All associated applications (Initiating and each Partnering PI) must be submitted by the Grants.gov deadline.

Application Components for the Initiating PI:

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 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.

     The Biomarker Development Award supports research focused on the validation or qualification of prostate cancer biomarkers and their translation into clinical use. ***Studies proposed under this award should not include discovery of new biomarkers, studies using tissues or other samples to further investigate biomarker expression patterns prior to large-scale validation or qualification, or improving or refining biomarkers in model systems.***

Describe the proposed project in detail using the outline below. The inclusion of preliminary data relevant to the potential of the candidate prostate cancer biomarkers for validation or qualification is required. Any preliminary data provided should be from the laboratory of the PI(s) or member(s) of the collaborating team.

- **Background:** Present the ideas and reasoning behind the proposed research; include relevant literature citations. Describe how the validation or qualification of the proposed candidate biomarkers will address critical problems in prostate cancer clinical care and to what degree the biomarkers will be assessed through noninvasive means. Address any challenges presented by prostate tumor heterogeneity. Describe the research team's 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:** 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 validating or qualifying 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 validation or qualification 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 validation or qualification. Include a robust data and statistical analysis plan where appropriate. ***The study design should demonstrate appropriate consideration of the literature on optimal design for biomarker validation or qualification efforts.***
  - 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. Address any potential ethical concerns.
- 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 research experience and leadership abilities of the PI(s) provide substantial qualifications 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 environments 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:** Describe how the proposed research is responsive to one of the PCRP overarching challenges.

- **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. ***A letter for each organization involved in the project should be provided.***
- Letters of Collaboration (if applicable): Provide a signed letter from each collaborating individual or organization that describes how he/she will support the project(s), to include:
  - Unique expertise
  - Availability and access to research resources, and/or
  - Availability of and access to appropriate populations (and/or access to available samples/data or database[s]) (if applicable). ***Note:*** It is strongly recommended that a collaborator be included to provide epidemiological evidence for population selection.
- 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. 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: Provide a plan for resolving intellectual and material property issues among participating organizations.

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

  The technical abstract is used by all reviewers. Of particular importance, programmatic reviewers rely on the technical abstract for appropriate description of the project's key aspects. Therefore, clarity and completeness within the space limits of the technical abstract are highly important.

  Describe the proposed research project including the following elements:

  - Background: Present the ideas and reasoning behind the proposed project.
  - Objective: State the objective to be reached. Provide evidence or rationale that supports the objective.
  - Specific Aims: State the specific aims of the study.
  - Study Design: Briefly describe the study design. 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.*** 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 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.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 Biomarker Development Award mechanism, use the SOW format example titled "SOW for Collaborative PI projects." The SOW must be in PDF format prior to attaching.

  Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI(s) should be noted for each task.

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

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

  Describe the near-term impact: Detail the anticipated 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 elimination of death from prostate cancer and enhance 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.

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

  Provide 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. *It is strongly encouraged that PIs begin discussions with the FDA early to determine FDA-driven milestones, which should be incorporated into the implementation plan.* 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 appropriate in proposed investigation(s).

- **Attachment 8: 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 9: Data- and Research Resource-Sharing Plan (one-page limit):** Upload as "Sharing.pdf."

  Describe how unique and/or final research data will be shared with the wider prostate cancer research community, 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 pre-existing 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.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."
        - ***Include biographical sketches for both the Initiating and Partnering PI(s).***
    - Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
        - ***Include previous/current/pending support for both the Initiating and Partnering PI(s).***

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."

    Initiating and Partnering PIs must each submit a budget and justification specific to their own portion of the efforts as part of their separate Grants.gov application packages. The Research & Related Budget for the Initiating PI should not include budget information for Partnering PI(s), even if they are located within the same organization. The combined total direct costs for the Initiating and Partnering PI(s)' budgets cannot exceed $2.25M.

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.

Additional Application Components: In addition to the complete Grants.gov application package of forms and attachments, Biomarker Development Award applications also require the following components:

Oral Presentation: Initiating 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 National Capital Area in February 2015. In the event a PI is invited to the Programmatic Review, Stage 2 (see Section III.B.2., Programmatic Review), but is unable to attend, CDMRP Staff and the Grants Officer will consider alternative arrangements on a case-by-case basis.

Each presentation will include a 10-minute talk by the Initiating PI, followed by a 20-minute question and answer session with IP members. 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 five-slide presentation that specifically addresses these questions:

- Without addressing the specific technical/scientific aspects of your project, what do you consider to be the most critical barriers to be overcome in biomarker development for prostate cancer clinical management, and how do the goals of your proposed effort relate to other current efforts to address these barriers?
- Without addressing the specific technical/scientific aspects of your project, how do you envision transitioning the results from your efforts into a near-term, major advancement from the current standard of care for the management of prostate cancer and, in addition, ultimately contribute significantly to the elimination of death from prostate cancer and enhancing the well-being of men experiencing the impact of the disease?
- Without addressing the specific technical/scientific aspects of your project, what leadership skills will you use in your research team's efforts to move the project quickly and effectively toward completion of the objectives?

Application Components for the Partnering PI(s):

Each Partnering PI MUST follow the link in the email from eBRAP and complete the registration process prior to the application submission deadline in order to associate his/her grant application package with that of the Initiating PI.

The application submission process for Partnering PI(s) uses an abbreviated application package of forms and attachments from Grants.gov that includes:

1. **SF 424 (R&R) Application for Federal Assistance Form**

2. **Attachments Form**

   - **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 information on completing the SOW. ***Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI(s) should be noted for each task.*** For the Biomarker Development Award mechanism, use the SOW format example titled "SOW for Collaborative PI projects" located at https://ebrap.org/eBRAP/public/Program

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

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

   Initiating and Partnering PIs must each submit a budget and justification specific to their own portion of the efforts as part of their separate Grants.gov application packages. The Research & Related Budget for the Partnering PI(s) should not include budget information for the Initiating PI, even if they are at the same

organization. The combined total direct costs for the Initiating and Partnering PIs' budgets cannot exceed $2.25M.

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

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

D. Verification of Grants.gov Application in eBRAP

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

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

E. Submission Dates and Times

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

F. Other Submission Requirements

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

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a Data Universal Numbering System (DUNS) number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the System for Award Management (SAM) with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, USAMRMC, based on (a) technical merit and (b) the relevance to the mission of the DHP and PCRP and to the specific intent of the award mechanism. The 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 Title 18 United States Code 1905.

B. Application Review Process

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

    - **Candidate Biomarker(s)**
        - How the selected biomarker(s) 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 biomarker(s) can be reliably detected through noninvasive procedures, if applicable.
        - To what degree the potential outcome of the project, e.g., scope and/or ease of biomarker use, etc., has been maximized.
        - How well the issue of tumor heterogeneity has been addressed in the proposed project.
        - How the rationale and preliminary data support the suitability of the biomarker(s).
        - How well the appropriate plans to implement the leveraging of existing resources, where possible, have been made.

- **Research Strategy and Feasibility**
    - How well the hypotheses or objectives, aims, experimental design, methods, and analyses are developed.
    - How well the feasibility of the research strategy has been addressed, including acknowledging potential problems and providing alternative approaches.
    - To what degree the strategies are appropriately designed to foster confidence in the reliability and reproducibility of the biomarker study, including the existence of an appropriate plan for data and statistical analyses.
    - To what degree the proposed strategies are consistent with current FDA guidance for biomarker validation or qualification.
    - To what degree the TMUGS has been appropriately considered.
    - If applicable, whether plans for human subject recruitment or other acquisition of human samples are appropriate, including ethical considerations.
    - Whether it is clear 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 clinical management and ultimately contribute to the elimination of death from prostate cancer and enhancing the well-being of men experiencing the impact of the disease.
    - 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.
- **Implementation Plan**
    - How well the proposed project(s) is(are) supported by a detailed plan that identifies critical milestones and explains how these milestones will be achieved.
    - To what degree the proposed plan is appropriate with respect to plans for decision making, allocation of resources, consistent interaction and coordination of personnel and collaborations, including regulatory approval processes, and conflict resolution among all participating PIs and institutions.
- **Research Team**
    - To what degree the PIs are 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 PIs have assembled an appropriate and 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 assurances of appropriate support for the project.
- How well the plan to facilitate consistent and intensive interactions among all team members is developed.
- 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.
  - If applicable, to what degree the intellectual and material property plan is appropriate.
- **Data and Resource Sharing**
  - To what degree the plan for sharing of project data and research resources is appropriate and reasonable to facilitate use by the wider prostate cancer research and consumer communities.
- **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:

   - **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 area

- 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 biomarker development toward a major improvement in prostate cancer clinical management
  - Articulation of a vision for achieving a biomarker validation or qualification outcome that will be readily translatable into clinical practice
  - Capability to lead and synergize the research team's efforts to effectively accomplish the aims of the project

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.
- All associated (Initiating and Partnering PI) applications are not submitted by the deadline.
- Project Narrative exceeds page limit.
- Project Narrative is missing.

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

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Preproposal Narrative and Project Narrative.
- Documents not requested will be removed.
- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

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

- A FY14 PCRP Integration Panel (IP) member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. A list of the FY14 PCRP IP members can be found at http://cdmrp.army.mil/pcrp/panels/panel14.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The Initiating PI and Partnering PI(s) do not meet the eligibility criteria as described in this Program Announcement/Funding Opportunity.
- The proposed project does not address one of the PCRP overarching challenges.
- 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

Attendance is required at a 1-day meeting to be held in the National Capital Area for the purpose of reporting on progress.

For the Biomarker Development Award, each PI, whether Initiating or Partnering, must submit individual progress reports as required by his or her individual assistance agreement; however, PIs are expected to work together in preparing the reports.

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 institution 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.

F. Pre-Award Meeting

At the Government's discretion, the PIs 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 eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

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

Phone: 800-518-4726

Email: support@grants.gov

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

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Initiating PI Completed	Partnering PI 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."		
	Implementation Plan: Upload as Attachment 7 with file name "Implementation.pdf."		
	Transition Plan: Upload as Attachment 8 with file name "Transition.pdf."		
	Data- and Research Resource-Sharing Plan: Upload as Attachment 9 with file name "Sharing.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 form as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.		
Project/Performance Site Location(s) Form	Complete form as instructed.		
R & R Subaward Budget Attachment(s) Form	Complete form as instructed.		
Oral Presentation	Confirm availability to give an oral presentation in the National Capital Area in February 2015 (if selected for Programmatic Review, Stage 2)		