Program Announcement

Department of Defense (DOD) Congressionally Directed Medical Research Programs

Prostate Cancer Research Program (PCRP)

Clinical Consortium Award

Funding Opportunity Number: W81XWH-08-PCRP-CCA

Table of Contents

I. HELPFUL INFORMATION

A. Contacts

1. Program announcement, proposal format, or required documentation: To view all funding opportunities offered by the Congressionally Directed Medical Research Programs (CDMRP), perform a Grants.gov basic search using the CFDA Number 12.420. Submit questions as early as possible. Response times will vary depending upon the volume of inquiries. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079

Fax: 301-619-7792

Email: cdmrp.pa@amedd.army.mil

2. eReceipt system: Questions related to pre-application components through the CDMRP eReceipt system should be directed to the eReceipt help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern time.

Phone: 301-682-5507

Website: https://cdmrp.org

Email: help@cdmrp.org

3. Grants.gov contacts: Questions related to submitting applications through the Grants.gov (http://www.grants.gov/) portal should be directed to Grants.gov help desk. Deadlines for proposal submission are 11:59 p.m. Eastern time on the deadline date. Therefore, there is an approximate 3-hour period during which the Grants.gov help desk will NOT be available. Please plan ahead accordingly, as the CDMRP help desk is not able to answer questions about Grants.gov submissions.

Phone: 800-518-4726, Monday through Friday, 7:00 a.m. to 9:00 p.m. Eastern time

Email: support@grants.gov

Grants.gov will notify Principal Investigators (PIs) of changes made to this Program Announcement and/or Application Package ONLY if the PI clicks on the "send me change notification emails" link and subscribes to the mailing list on the Opportunity Synopsis Page for this announcement. If the PI does not subscribe and the Application Package is updated or changed, the original version of the Application Package may not be accepted.

B. National Technical Information Service

The technical reference facilities of the National Technical Information Service (www.ntis.gov) are available for the purpose of surveying existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. All other sources should also be consulted to the extent practical for the same purpose.

C. Commonly Made Mistakes

- Not obtaining or confirming the organization's DUNS number well before the proposal submission deadline.
- Not obtaining or confirming the organization's registration with the Central Contractor Registry well before the proposal submission deadline.
- Failing to request "send me change notification emails" from Grants.gov.
- Not contacting HELP DESKS until just before or after deadlines.
- Not completing the pre-application submission before the mandatory pre-application deadline (i.e., pre-application remains in draft status).
- Using an incorrect Grants.gov application package to submit a proposal through Grants.gov. Each Program Announcement/Funding Opportunity requires a specific application package.
- Uploading attachments into incorrect Grants.gov forms.
- Attaching files in the wrong location on Grants.gov forms.
- Submitting attachments that are not PDF documents, except for the R&R Subaward Budget Attachment(s) Form.
- Exceeding page limitations.
- Failing to submit a proposal 48-72 hours before the deadline so that Grants.gov can provide notification of errors and allow for resubmission of application package.
- Failing to submit proposal by submission deadline.

II. FUNDING OPPORTUNITY DESCRIPTION

A. Program History and Objectives

The PCRP was established in fiscal year 1997 (FY97) to promote innovative research focused on eradicating prostate cancer. Appropriations for the PCRP from FY97 through FY07 totaled $810 million (M). The FY08 appropriation is $80M.

The overall goal of the FY08 PCRP is to find and fund innovative, high-impact research relevant to the prevention, detection, diagnosis, and/or treatment of human prostate cancer. Specifically, the PCRP seeks to:

- Support innovative research by individual investigators in multiple disciplines;

- Sponsor multidisciplinary team science to bring together diverse expertise and approaches that will accelerate the conquest of prostate cancer;
- Fund translational research to promote the bench-to-bedside-to-bench transition between basic and clinical science;
- Foster the next generation of prostate cancer investigators through mentored research and training; and
- Promote research into prostate cancer health disparities, including, but not limited to, race and ethnicity, socioeconomic status, access to health care, insurance status, age, geography, and cultural beliefs.

B. Award Description

1. General Information: The PCRP Clinical Consortium Award mechanism was introduced in FY05. Since then, 19 proposals have been received and 11 have been recommended for funding. Of these, 2 proposals were for the Coordinating Center, with one being funded, and 17 were for Clinical Research Sites, with 10 being funded.

The Clinical Consortium Award ***does not provide funding for research***, but, rather, provides the support to develop the collaborations and resources necessary for the consortium to rapidly execute Phase II or Phase II-linked Phase I (Phase I/II) clinical trials of therapeutic agents or approaches for the management or treatment of prostate cancer. ***Trials that incorporate clinical validation of novel biomarkers for risk assessment, early detection, prediction of aggressiveness, and/or progression of prostate cancer are strongly encouraged. Accordingly, since biomarker validation studies are typically associated with Phase III clinical trials, consortium members are permitted and encouraged to accrue patients to these studies as part of their consortium activities.***

The overarching goal of the Clinical Consortium Award is to combine the efforts of leading investigators to bring to market novel therapeutic interventions that will ultimately decrease the overall impact of the disease. PIs from both US and international institutions may apply. Submissions from institutions with enhanced access to patients from disproportionately affected populations are encouraged.

It is expected that the consortium will achieve financial self-sufficiency during the award period such that consortium activities can continue after funding through this mechanism ends.

The consortium will consist of approximately 12 **Clinical Research Sites** and one **Coordinating Center**. These participants will be jointly responsible for proposing, selecting, and conducting Phase II and Phase I/II clinical trials focused on prostate cancer therapeutic interventions. The structure of the Consortium is depicted in Figure 1 and described in more detail below.

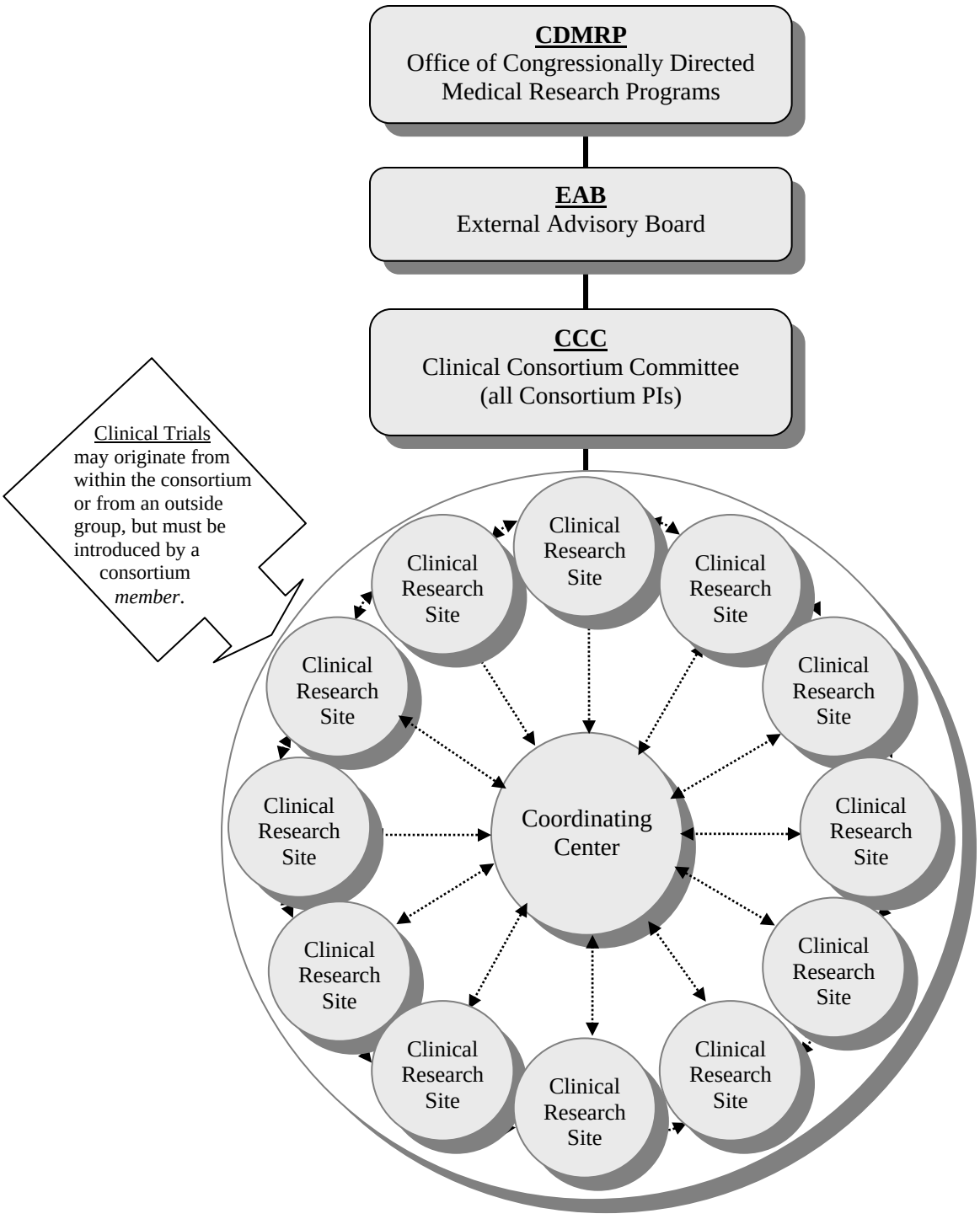

Figure 1. Clinical Consortium Organizational Structure

The Coordinating Center**,** in addition to functioning as a Clinical Research Site, will serve as the consortium information and planning nexus providing administrative, operational, and data management support services to participant Clinical Research Sites to implement consortium clinical trials in a timely manner. The Coordinating Center will have multidisciplinary expertise and extensive experience in developing and conducting multi-institutional clinical trials of innovative treatment approaches in support of prostate cancer research. Responsibilities of the Coordinating Center will include development of the clinical trial selection process, protocol coordination, regulatory coordination, study management and monitoring, data collection, management and statistics, and intellectual/material property coordination. The Coordinating Center also will be responsible for preparing two initial clinical trials for immediate consideration by the consortium within the first 3 months of the performance period. All sites (Clinical Research Sites and the Coordinating Center) will be required to participate in at least one of these two initial clinical trials.

After consideration of the initial clinical trials prepared by the Coordinating Center, a procedure will be established for the selection of clinical trials to be implemented within the consortium. All sites will be responsible for working collaboratively to identify new clinical trials for implementation by the consortium. Collectively, the consortium PIs will constitute the **Clinical Consortium Committee,** which will be responsible for selecting the clinical trials to be implemented by the consortium and for determining which consortium institutions will participate in each trial. A representative from US Army Medical Research and Materiel Command (USAMRMC) must be invited to these sessions as well as any other formal meetings of the consortium. Selected clinical trials will be maintained in a queue and prepared for implementation as resources become available. All sites may serve as entry points for clinical trials that originate from outside the consortium. The Coordinating Center will be responsible for facilitating this entire process. The consortium is strongly encouraged to (1) leverage the DOD investment whenever possible by implementing DOD-funded trials; and (2) implement trials that include clinical validation of novel biomarkers for risk assessment, early detection, prediction of aggressiveness, and/or progression of prostate cancer.

After the first 12 months of the performance period of the award, the consortium is expected to have 10 or more clinical trials open at any given time. In addition, each participant site is expected to present two or more clinical trials each year for the consortium's consideration and maintain accrual of 50 or more patients per year. In particular, all sites must provide plans for accruing patients from populations disproportionately affected by prostate cancer. At least 5% of all accrued patients at each site, independently or in partnership with other consortium or non-consortium institutions, must be from disproportionately affected populations.

The PCRP Integration Panel (IP), Program Manager, and the CDMRP Grants Manager for the consortium will assume the role of an external advisory board (EAB) to the consortium. The EAB will provide scientific review, consortium oversight, and data and progress review. PIs must present written and oral semi-annual briefings to the EAB and USAMRMC staff at 1-day meetings, typically held in the Baltimore-Washington, DC area.

Based on these reports and presentations, USAMRMC staff, with recommendations from EAB members, will evaluate progress, provide feedback, and invoke modifications and terminations as needed to facilitate the success of the consortium. PIs also will be required to submit annual written progress reports and a final written comprehensive report.

Exercise of the options for continued performance of each participant site after the first year ***will be contingent upon*** meeting the following consortium requirements:

- A minimum number of 35 patients accrued per year; however, the expectation will be that accrual rates of 50 or more patients per year will be achieved. At least 5% of all accrued patients at each site, independently or in partnership with other consortium or non-consortium institutions, must be from disproportionately affected populations. Accrual credit will also be granted, as an additional metric for evaluation, for each patient accrued to a Phase III trial, providing that participation in the trial includes a validation study of novel biomarkers. However, this evaluative credit is not in lieu of credit for accrual to Phase II and Phase I/II trials, and one quarter of an accrual point (0.25) will be granted.
- Contribution of patients and/or other resources to clinical trials initiating from other sites, not solely the PI's site. Patient contribution to trials from other sites shall constitute at least 20% of the minimum number of patients (i.e. 35) that a site must accrue to all trials.
- The presentation of at least one clinical trial to the consortium per year; however, the expectation will be that two or more clinical trials per year will be proposed.
- Annual written progress reports, semi-annual written briefings and presentations (at meetings typically held in the Baltimore-Washington, DC area).
- Timely submission of quality data as outlined by the Coordinating Center.

To assess data collection and accuracy, at the discretion of the government, each participant site may be expected to participate in an on-site ***audit*** by the government or its designee.

Failure to achieve the minimum requirements above may result in the Government's decision to not exercise the options for continued performance.

The Clinical Consortium Award mechanism will be used to select and fund both the Coordinating Center and the Clinical Research Sites. PIs will be required to indicate whether the institution is applying as the Coordinating Center or as a Clinical Research Site. PIs applying as the Coordinating Center have the option to be considered as a Clinical Research Site if not chosen as the Coordinating Center.

2. Responsibilities of the Consortium Participants: Procedures for the consortium, while proposed by the Coordinating Center, will be fully developed and agreed upon by all participants working collaboratively at the Pre-Award Planning Meeting to be attended by representatives of the Coordinating Center, Clinical Research Sites, EAB, and USAMRMC.

a. Coordinating Center: Responsibilities specific to the Coordinating Center include:

- Adherence to the responsibilities delineated below for a Clinical Research Site.
- Coordination and facilitation of at least 10 clinical trials at any given time after the first 12 months of the performance period.
- Development and maintenance of the consortium organizational structure.
- Provision of at least two initial Phase II or Phase I/II clinical trial protocols that seek to determine baseline activity of a new drug, or a novel combination of existing drugs, for consideration by the consortium within the first 3 months of the performance period.
- Management of consortium-developed procedures for review, selection, and implementation of clinical trials proposed by or through consortium members.
- Establishment and management of procedures to ensure compliance with the local institutional review boards (IRBs) of all sites for the conduct of clinical trials and the protection of human subjects.
- Establishment and management of procedures for ensuring compliance with Food and Drug Administration (FDA) requirements for investigational agents, devices and procedures.
- Establishment and management of a communications plan and an ongoing communications system between the Coordinating Center and Clinical Research Sites.
- Management of consortium-developed quality assurance and quality control mechanisms for study monitoring, including:
    - On-site monitoring program.
    - Management plan for the handling, distribution, analysis, and banking of specimens and/or imaging products generated from consortium studies necessary for the conduct and analyses of clinical trials during the performance period of the award.
    - Registration, tracking, and reporting of participant accrual.
    - Timely medical review and assessment of participant data.
    - Rapid reporting and communication of adverse events.
    - Interim evaluation and consideration of measures of outcome.
- Management of consortium-developed comprehensive data collection and data management systems that address the needs of all sites in terms of access to data, data security, and data integrity measures.
- Development of statistical plans for all consortium clinical trials.
- Management of consortium-developed intellectual and material property issues among institutions participating in the consortium.
- Management of consortium-developed procedures for the timely publication of major findings and other public dissemination of data.

- Development of a plan for ensuring financial self-sufficiency of the consortium by the end of the award period.
- Development, organization, and submission of the written and oral semi-annual briefings to the EAB and USAMRMC staff at 1-day meetings typically held in the Baltimore-Washington, DC area.
- Development, organization, and submission of the annual written progress reports and a final written comprehensive report to the USAMRMC.

b. Clinical Research Sites: The responsibilities of each site include:

- Full participation in the consortium, including but not limited to clinical trial introduction and selection, patient accrual for consortium studies (to include accrual from disproportionately affected populations), data collection and timely submissions, meeting attendance, and adherence to the consortium's operating procedures.
- Presentation of at least one clinical trial for the consortium's consideration per year; however, the expectation is that two or more trials will be presented annually. ***For the Coordinating Center, this requirement is in addition to the initial two clinical trials required at the beginning of the award.***
- Meeting minimum accrual requirements of 35 patients per year; however, the expectation is that enrollment of 50 patients or more per year will be achieved annually. At least 5% of all accrued patients at each site, independently or in partnership with other consortium or non-consortium institutions, must be from disproportionately affected populations. Additional, separate, and partial (0.25) accrual credit will be granted for each patient accrued to a Phase III trial, providing that participation in the trial includes a validation study of novel biomarkers.
- Provision for a Clinical Research Coordinator who will interact with the Clinical Research Coordinators of other Clinical Research Sites and the Supervising Clinical Research Coordinator of the Coordinating Center to expedite and guide clinical protocols through the regulatory approval processes and to coordinate patient accrual and study activities across sites.
- Implementation of the consortium's core data collection methodology and strategies.
- Compliance with consortium-developed quality assurance and quality control procedures, as appropriate, including:
    - Participation in an on-site monitoring program to be managed by the Coordinating Center.
    - Implementation of the consortium-developed management plan for acquisition, delivery, and storage of biological samples and study data.
    - Submission of appropriate data and materials to allow for verification and review of protocol-related procedures, for example, pathology, imaging techniques, surgical methods, and therapeutic use.

- Implementation of procedures established by the Coordinating Center for ensuring compliance with FDA requirements for investigational agents, as appropriate.
- Implementation of procedures established by the Coordinating Center to meet the local IRB requirements for the conduct of clinical trials and the protection of human subjects.
- Serving as a resource for the conduct of protocol-specified laboratory projects (such as tumor biology studies).
- Participation in consortium-developed procedures for the timely publication of major findings.
- Participation in consortium-developed procedures for resolving intellectual and material property issues among institutions participating in the consortium.
- Implementation of the plan developed by the Coordinating Center for ensuring financial self-sufficiency of the consortium by the end of the award period.
- Attendance at a Pre-Award Planning Meeting with all consortium members to develop the operational features of the consortium, the requirements for progress and evaluation, and the award negotiations process.
- Presentation of written and oral semi-annual briefings to the EAB and USAMRMC staff at 1-day meetings typically held in the Baltimore-Washington, DC area.
- Submission of annual written progress reports and a final written comprehensive report.
- Preparing for the possibility of a site visit audit.
- Additional responsibilities based on recommendations and guidance from the consortium EAB and USAMRMC staff.

3. Clinical Consortium Award Proposal Requirements: All proposals for the PCRP Clinical Consortium Award must indicate if the application is being submitted for consideration as a:

- Clinical Research Site, or
- Coordinating Center, or
- Coordinating Center with the option to be considered as a Clinical Research Site if the proposal is not selected for award as the single Coordinating Center.

a. Coordinating Center: Proposals from Coordinating Center PIs must include all of the requirements noted in the Clinical Research Sites section below, in addition to the following:

- Evidence of institutional commitment to using facilities and resources in the conduct of consortium operations as required.

- Descriptions of the consortium organizational structure, an ongoing communications plan, and standard operating procedures for proposing and determining which studies the consortium will pursue. The organizational structure should include the following key features:
    - Coordinating Center for administration and day-to-day management of consortium operations; developing the clinical trial selection process; protocol coordination; regulatory coordination; study management and monitoring; data collection, management, and statistics; intellectual/material property coordination; and performance as a Clinical Research Site.
    - Clinical Research Sites for conceiving, developing, and conducting clinical trials in prostate cancer, as well as serving as entry points for clinical trials from outside the consortium.
    - Clinical Consortium Committee composed of the PIs from the Coordinating Center and Clinical Research Sites, for the clinical trial selection process and for the continual development and operation of the consortium. A representative from the USAMRMC is to be invited to all official meetings of the Clinical Consortium Committee.
    - An EAB composed of members of the PCRP IP, the PCRP Program Manager, and the CDMRP Grants Manager for scientific review, oversight, data monitoring, and evaluation.
- An intellectual and material property plan for all participating institutions.
- Descriptions of procedures for coordinating the development and regulatory approval of consortium clinical protocols and associated clinical documents in a timely manner.
- Description of the two clinical trials to be considered within the consortium within the first 3 months of the award period, including a brief description of clinical protocols and informed consent/assent form(s) that indicate the level of review achieved prior to submission of the Clinical Consortium Award.
- Descriptions of procedures for ensuring compliance with FDA requirements for investigational agents, as appropriate.
- A **named** Supervising Clinical Research Coordinator who will interact with and oversee all Clinical Research Coordinators to expedite and guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.
- Plans for ongoing communications among Clinical Research Sites and between Clinical Research Sites and the Coordinating Center; plans should address methods for information distribution within the consortium, how information technologies will be used to facilitate routine multi-institutional communication, and provide ongoing communication and data sharing.
- Descriptions of quality assurance, quality control, and study monitoring procedures.

- A comprehensive data management and statistical analysis plan including:
  - A discussion of the overall approach to data collection and management.
  - A statistical plan that includes sample size calculations, methods to monitor quality and consistency of data collection, and methods to measure outcomes.
  - A plan for ongoing data transfer.
  - Data security and integrity measures.
- Descriptions of methods for the handling, distribution, analysis, banking, and security of specimens and/or imaging products generated from consortium-sponsored studies, including a specimen handling and distribution plan for all institutions in the consortium.
- Plans for ensuring rapid publication and other public dissemination of data generated by consortium-sponsored studies that address all relevant privacy issues.
- Descriptions of how the PI intends to achieve financial self-sufficiency of the consortium after the performance period for the Clinical Consortium Award ends.

b. Clinical Research Sites: Proposals from each PI must include:

- Descriptions of the PI's commitment to and experience in prostate cancer clinical research.
- Description of the prostate cancer patient population and documentation of ability to enroll at least 35 evaluable individuals with prostate cancer per year into consortium-sponsored studies. Provide a plan for accruing patients from disproportionately affected populations.
- Evidence of multidisciplinary clinical and laboratory expertise **within the applicant institution** that could serve as the basis for the implementation of clinical protocols by the consortium.
- Demonstration of adequate resources and expertise for data management and maintenance of data security/confidentiality.
- Evidence of institutional commitment to using facilities and resources in the conduct of consortium operations as required.
- Documentation of willingness to resolve intellectual and material property issues.
- A **named** institutional Clinical Research Coordinator who will interact with the Clinical Research Coordinators at other Clinical Research Sites and the Supervising Clinical Research Coordinator at the Coordinating Center to guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.

- Descriptions of procedures for ensuring compliance with FDA requirements for investigational agents, as appropriate.

4. Use of Funds: The purpose of the PCRP Clinical Consortium Award is to provide the funding to establish the necessary collaborations and resources to rapidly execute clinical trials by the consortium. This award will not fund research or development of clinical protocols.

a. Coordinating Center: In addition to the permitted use of funds for the Clinical Research Sites described below, the Coordinating Center may use funds from this award to:

- Furnish salary support for personnel needed to meet the goals of the consortium, such as the PI, Consortium Clinical Research Coordinator, Administrative Assistant(s), Research Nurse(s), Statistician(s), Database Manager, and Informatics Manager.
- Implement consortium-developed standardization plan, data management program, and ongoing communications system for the consortium.
- Support consortium-related meetings, teleconferences, and travel among participating investigators.
- Purchase computers, specialized software, and specialized software licenses pertinent to Coordinating Center-specific responsibilities for use at participating institutions.
- Coordinate preparation of informed consent/assent forms and other IRB-required materials among different institutions.
- Manage the resolution of intellectual property and material rights among institutions.
- Develop definitive statistical plans.
- Develop sources for intervention supply or availability.
- Other costs directly associated with planning and developing the consortium.

b. Clinical Research Sites: Funds from the Clinical Consortium Award may be used to:

- Attend and support consortium-related meetings.
- Purchase computers and general software required to participate in the consortium.
- Furnish salary support for personnel needed to meet the goals of the consortium such as the PI, Clinical Research Coordinator, Research Nurse, and Data/Informatics Coordinator.
- Support collaborations among Clinical Research Sites and the Coordinating Center to:
    - Implement data management, ongoing communication, and/or administration

plans for the consortium.

- Reimburse institutions for costs associated with conducting the IRB review of the clinical protocols and informed consent/assent forms.
- Provide other costs directly associated with planning, implementing, and supporting the consortium.

C. Eligibility

PIs must be independent investigators at the Assistant Professor level (or equivalent) or higher at an eligible institution. Current PCRP Clinical Consortium Award recipients are eligible to compete for this award.

Refer to the Application Instructions, Appendix 1, for general eligibility information.

D. Funding

The PCRP plans to invest $25M in the Clinical Consortium Award over a five year period. A total of $5M will be allocated from the FY08 budget to fund the first year of performance. Options will be included for continued performance in subsequent years with $5M expected from each of the FY09-FY12 budgets to fund the options. The initial performance period of the award and each option period will be for twelve months. ***Exercise of the options for continued performance is contingent on receipt of sufficient congressional appropriations to the PCRP in FY09-FY12 and acceptable performance by the awardee.***

1. Coordinating Center: Of the expected $25M total, funding for the Coordinating Center will be available for up to approximately $4.7M for direct costs for a 5-year performance period, plus indirect costs as appropriate. These funds are for all Coordinating Center functions, administrative and clinical, as described in this announcement.

Within the guidelines provided in the Application Instructions, funds for the Coordinating Center can cover:

- Administrative support including salary
- Consortium meetings and travel among participating investigators
- Database generation and software development
- Purchase of computers
- Design of websites
- Teleconferences
- Other costs directly associated with planning and developing the consortium collaborations and resources

2. Clinical Research Sites: Funding will be available for 12 Clinical Research Sites up to approximately $12M in direct costs for the 5-year period, plus indirect costs as appropriate.

Funding for each Clinical Research Site will be up to approximately $1M in direct costs over a 5-year performance period, plus indirect costs as appropriate.

Within the guidelines provided in the Application Instructions, funds for the Clinical Research Sites may cover:

- Administrative support including salary
- Consortium meetings and related travel among participating investigators.
- Teleconferences
- Other costs directly associated with planning and developing the consortium

Exercise of the options for continued performance for each Clinical Research Site after the first year will be contingent upon meeting the following consortium requirements:

- A minimum number of 35 patients accrued per year; however, the expectation will be that accrual rates of 50 or more patients per year will be achieved. At least 5% of all accrued patients at each site, independently or in partnership with other consortium or non-consortium institutions, must be from disproportionately affected populations. Additional, separate, and partial (0.25) accrual credit will be granted for each patient accrued to a Phase III trial, providing that participation in the trial includes a validation study of novel biomarkers.
- Contribution of patients and/or other resources to clinical trials initiating from other sites, not solely the PI's site.
- The presentation of at least one clinical trial to the consortium per year; however, the expectation will be that two or more clinical trials per year will be proposed.
- Annual written progress reports, semi-annual written briefings and presentations (at meetings typically held in the Baltimore-Washington, DC area).
- Timely submission of quality data as outlined by the Coordinating Center.

3. All Sites (Coordinating Center and Clinical Research Sites): All PIs must budget for travel to:

- A consortium Pre-Award Planning Meeting in the Baltimore-Washington, DC area to be held after notification of award status and prior to disbursement of funds.
- Semi-annual progress review meetings (typically held in the Baltimore-Washington, DC area).

In addition, funding must be requested for the PI to travel to the next PCRP IMPaCT (Innovative Minds in Prostate Cancer Today) Meeting (tentatively scheduled for 2010).

All PIs must provide evidence of sufficient institutional support and commitment for the proposed clinical trial. Consideration of cost sharing with other funding sources is encouraged.

Based on programmatic requirements, funding amounts may be tailored to produce the most efficient, cost-effective consortium possible; the PCRP IP reserves the right to recommend modifications to budgets to meet the needs of the consortium. Exercise of the options for continued performance past the first year is contingent on receipt of sufficient congressional appropriations to the PCRP in FY09-FY12 and acceptable performance by the recipient.

The CDMRP expects to allot approximately $5M of the $80M FY08 PCRP appropriation to fund the first year of performance of 1 Clinical Consortium-Coordinating Center and approximately12 Clinical Consortium – Clinical Research Site Award proposals, depending on the quality and number of proposals received. Options will be included for continued performance in subsequent years with $5M expected from each of the FY09-FY12 budgets to fund the options. Funding of proposals received in response to this Program Announcement/Funding Opportunity is contingent on the availability of Federal funds for this program.

E. Award Administration

Institution changes in the Coordinating Center or Clinical Research Sites will not be allowed for the Clinical Consortium Award mechanism.

Refer to the Application Instructions, Appendix 5, for general award administration information.

III. TIMELINE FOR SUBMISSION AND REVIEW

Proposal submission is a two-step process consisting of (1) pre-application submission and (2) proposal submission. ***Pre-application submission is a required first step***.

- **Pre-application Submission Deadline: 5:00 p.m. Eastern time, June 11, 2008**
- **Proposal Submission Deadline: 11:59 p.m. Eastern time, July 2, 2008**
- **Peer Review: September 2008**
- **Programmatic Review: November 2008**

Awards will be made approximately 4 to 6 months after receiving the funding notification letter, but no later than September 30, 2009.

IV. SUBMISSION PROCESS

Proposal submission is a two-step process consisting of (1) a pre-application submission through the CDMRP eReceipt system (https://cdmrp.org/) and (2) a proposal submission through Grants.gov (http://www.grants.gov/).

Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative proposals.

A. Step 1 – Pre-Application Components and Submission

The pre-application consists of the components discussed below. All pre-application components must be submitted electronically through the CDMRP eReceipt system by ***5:00 p.m. Eastern time on the pre-application deadline***. Refer to the Application Instructions for detailed information.

1. Proposal Information
2. Proposal Contacts
3. Collaborators and Conflicts of Interest
4. Letter of Intent Narrative

B. Step 2 – Proposal Components and Submission

Proposal submission will not be accepted unless a pre-application was submitted by the pre-application deadline. Proposals must be submitted electronically by the Authorized Organizational Representative through Grants.gov (www.grants.gov). No paper copies will be accepted.

Each proposal submission must include the completed Grants.gov application package of forms and attachments identified in www.grants.gov for the US Army Medical Research Acquisition Activity program announcement. In addition to the specific instructions below, please refer to the Application Instructions for detailed requirements of each component.

The package includes:

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

2. Attachments Form

a. Attachment 1: Project Narrative (70-page limit for Coordinating Center, 30-page limit for each Clinical Research Site)

The Project Narrative is the main body of the proposal.

i. Coordinating Center: 40-page limit. It is the investigator's responsibility to clearly articulate the ability of his or her group to serve as the consortium Coordinating Center and support the design and conduct of consortium clinical trials. (Coordinating Center PIs must also provide the information outlined in the Award Description.)

Describe the qualifications of the group and plans for the development of key features of the consortium Coordinating Center using the following general outline:

(1) Commitment to and Experience in Multidisciplinary and Multi-Institutional Prostate Cancer Clinical Research: Describe previous experience

and accomplishments related to the design, administration, and fiscal management of multi-institutional prostate cancer clinical trials, with particular emphasis on Phase II clinical trials. Describe previous experience with establishing communications systems and data management resources for multi-institutional projects. Reference relevant publications and submit reprints with the proposal.

(2) Institutional Resources: Provide evidence of institutional commitment to provide the necessary resources needed to develop and support standardized data collection, data management and analysis, and data security and integrity for the consortium participants.

(3) Consortium Organizational Structure: Provide a detailed description of the overall consortium organization, plans for ongoing communications, procedures for transference of funds, and standardized operating procedures for selection and implementation of clinical trials. The organizational structure should include the following key features:

- Coordinating Center for administration and day-to-day management of consortium operations; developing the clinical trial selection process, protocol coordination; regulatory coordination; study management and monitoring; data collection, management, and statistics; intellectual/material property coordination; and performance as a Clinical Research Site.
- Clinical Research Sites for conceiving, developing, and conducting clinical trials in prostate cancer, as well as serving as entry points for clinical trials from outside the consortium.
- Clinical Consortium Committee composed of the PIs from the Coordinating Center and Clinical Research Sites, for the clinical trial selection process and for the continual development and operation of the consortium. A representative from the USAMRMC is to be invited to all official meetings for the Clinical Consortium Committee.
- An EAB composed of members of the PCRP IP, the PCRP Program Manager, and the CDMRP Grants Manager for scientific review, oversight, data monitoring, and evaluation.

(4) Clinical Trials Implementation: Describe plans for coordinating the submission, review, selection, and implementation of clinical trials within the consortium.

- Outline plans for coordinating IRB submissions and approvals at participating sites.
- Outline plans for developing procedures to ensure compliance with FDA requirements for investigational agents, as appropriate.

(5) Study Management and Monitoring: Describe plans for ongoing communication among all institutions participating in the consortium.

- Include a **named** Supervising Clinical Research Coordinator who will interact with and oversee the Clinical Research Site clinical coordinators to guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.
- Outline procedures for quality assurance, quality control, and study monitoring.
- Describe plans for the development of methods for the handling, distribution, analysis, banking, and security of specimens and/or imaging products generated from consortium-sponsored studies.

(6) Data Management: Outline a strategy for the development and implementation of a data management plan, including:

- Descriptions of the overall approach to data collection and management.
- A statistical plan that includes methods to monitor quality and consistency of data collection and methods to measure outcomes.
- A plan for ongoing data transfer.
- Data security and integrity measures.

(7) Publication and Data Dissemination: Describe plans for ensuring rapid publication and other public dissemination of data while maintaining participant privacy.

(8) Fiscal Administration: Describe previous experience with the financial management of multi-institutional clinical research studies. Outline a strategy for achieving financial self-sufficiency of the consortium after the performance period for the Clinical Consortium Award ends.

(9) Two Initial Clinical Trials: Start section on a new page; 10-page limit for this section. Provide brief descriptions of two currently funded Phase II or Phase I/II prostate cancer clinical trials proposed for immediate consideration by the consortium. It is expected that most, if not all, of the patients for these studies will be accrued from within the consortium. The proposed studies will be evaluated at both peer and programmatic reviews. Coordinating Center PIs also must provide the information outlined in the Award Description.

Include the following information for each of the two proposed clinical trials:

- Clinical trial title: Provide the title of each clinical trial.
- Phase: Designate the clinical trial as Phase I/II or II.
- Personnel: List the names of all personnel (including the PI) who will have significant involvement in the clinical trials; include their practice license (e.g., M.D. or R.N.), highest degree(s), job title, and employing institution;

- Location of study: List all centers, clinics, or laboratories where the studies are to be conducted; include details as to how consortium Clinical Research Sites will be integrated into these trials.
- Background: Describe the rationale for conducting the study, as well as the study's relevance and applicability of findings; include descriptions of preliminary studies, Phase I results, or other findings.
- Objectives: Describe the purpose, goals, and endpoint of the study.
- Drug or device: Describe the drugs or devices to be used in the studies; include Investigational New Drug (IND)/Investigational Device Exemption (IDE) numbers, sponsors, and sources, if applicable.
- Study population: Describe the target population and the proposed sample size and provide patient accrual rate requirements.
- Protocol design: Describe the type of study to be performed (prospective, retrospective, randomized, controlled, etc.) and outline the proposed methodology.
- Funding and IRB approval status: Provide evidence of funding status of the initial clinical trial(s); describe the status of IRB approval for the initial clinical trial(s).

ii. All Sites (Coordinating Center and Clinical Research Sites): 30-page limit. It is the responsibility of the PI to clearly articulate the qualifications of the research team and institution to participate as a Clinical Research Site in the consortium.

Provide evidence that the research team and institution fulfill each of the following criteria for participation in the consortium:

(1) Commitment to and Experience in Prostate Cancer Clinical Research

- Describe commitment to prostate cancer clinical research, which may include levels of effort, funding, and interactions with consumer advocacy groups.
- Describe experience in conducting multi-institutional clinical trials that demonstrate willingness and ability to function in the consortium.
- Describe specific areas of clinical research interest, such as novel drugs, combinatorial therapy schedules, surgical interventions, imaging techniques and immunotherapies. Include overall scope of program and demonstration of integration of basic and/or correlative science into the program.
- Provide details of ongoing or completed prostate cancer relevant clinical trials, particularly Phase II clinical trials, with an emphasis on clinical trials that might be brought into the consortium. Reference relevant publications and submit reprints with the proposal.
- Describe procedures for ensuring compliance with FDA requirements for investigational agents.

(2) Consortium Resources

- Include a **named** institutional Clinical Research Coordinator, who will interact with the Clinical Research Coordinators at other consortium Clinical Research Sites and the Supervising Clinical Research Coordinator at the Coordinating Center, to guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites.
- Describe the prostate cancer population (including size, age range, and clinical manifestations) and provide evidence of ability to enroll at least 35 evaluable individuals with prostate cancer per year into consortium-sponsored studies. Include documentation of access to and ability to recruit patients from disproportionately affected populations.
- Provide evidence of successful multi-center clinical trial collaborations.

(3) Institutional Resources

- Provide evidence of expertise in clinical trials within the applicant institution and describe experience in the development and conduct of prostate cancer clinical trials; as appropriate, describe any additional multidisciplinary clinical and/or laboratory expertise that could serve as the basis for the development of clinical trials by the consortium.
- Describe the resources and expertise available for the collection and processing of specimens from consortium-sponsored studies.
- Describe the resources and expertise for data management and maintenance of data security/confidentiality.
- Provide evidence of institutional commitment to providing facilities and resources in the conduct of consortium operations.

b. Attachment 2: Supporting Documentation

- References Cited
- Acronyms and Symbol Definitions
- Facilities & Other Resources
- Description of Existing Equipment
- Publications and/or Patent Abstracts (5-document limit for Clinical Research Site PIs, 10 for Coordinating Center PIs)
- Letters of Institutional Support
- Letters of Collaboration (if applicable)
- Intellectual and Material Property Plan (if applicable)
- Clinical Trial Funding and Approval Documentation (Coordinating Center PIs only). **No page limit.** Provide documentation of funding and IRB approval status for the two initial clinical trials.

c. Attachment 3: Technical and Public Abstracts

The Public Abstract is required for Coordinating Center PIs only.

d. Attachment 4: Statement of Work

e. Attachment 5: Impact Statement

Describe how the PI and other personnel will contribute to the productive preparation of the consortium and have an impact on the prevention, detection, diagnosis, or treatment of prostate cancer.

f. Attachment 6: Federal Agency Financial Plan (if applicable)

3. Research & Related Senior/Key Person Profile (Expanded)

- PI Biographical Sketch
- PI Current/Pending Support
- Key Personnel Biographical Sketches
- Key Personnel Current/Pending Support
- Budget Justification

4. Research & Related Budget Form

5. Research & Related Project/Performance Site Location(s) Form

R&R Subaward Budget

6. Attachment(s) Form (if applicable)

V. INFORMATION FOR PROPOSAL REVIEW

A. Proposal Review and Selection Overview

All proposals are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a scientific peer review that compares submissions to each other and recommends proposals for funding based on scientific merit and overall goals of the program. Additional information about the two-tier review process used by the CDMRP may be found at http://cdmrp.army.mil/funding/process.shtml.

The peer review and program review processes are conducted confidentially and anonymously to maintain the integrity of the merit-based selection process. Each tier of review requires panelists to sign a non-disclosure statement attesting that proposal 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 correcting actions. Correspondingly, institutional personnel and PIs are prohibited from contacting persons involved in the proposal review process to gain protected evaluation information or to influence the evaluation process. Violations of this prohibition will result in the administrative withdrawal of the institution's proposal. Violations

by panelists or PIs that compromise the confidentiality or anonymity of the peer review and program review processes may also result in suspension or debarment of their employing institutions from Federal awards.

The Government reserves the right to review all proposals based on one or more of the required attachments or supporting documentation (e.g., Impact Statement).

B. Review Criteria

1. Peer Review

a. Coordinating Center (to be reviewed in addition to the All Sites criteria below): All Coordinating Center proposals will be evaluated according to the following criteria. Of these, Personnel, Consortium Components, and Study and Data Management are equally the most important, with the remaining criteria listed in decreasing order of importance.

- **Personnel**
  - How well PI or other key personnel have demonstrated appropriate expertise in prostate cancer and in the design and administration of multi-institutional prostate cancer clinical trials.
  - Whether the PI and key personnel have previous success in acquiring funding for clinical trials.
  - Whether the Supervising Clinical Research Coordinator, who will interact with all Clinical Research Coordinators, possesses the appropriate expertise to coordinate regulatory approvals and consortium activities.
- **Consortium Components**
  - Whether the proposal includes all required consortium components (e.g., EAB, Clinical Consortium Committee, Coordinating Center, and Clinical Research Sites).
  - How clearly the PI outlined how each component will function as an integrated unit.
- **Study and Data Management**
  - How the strategies for the development and implementation of data management and statistical plans will provide access to data, data security, and data integrity.
  - Whether there is an outline of an appropriate study management plan, including plans for ongoing communication, quality control, and quality assurance.
  - Whether there are appropriate plans for the development of specimen handling, distribution, analysis, and banking methods.

- Whether there are appropriate plans for rapid publication and other public dissemination of data generated by the consortium.
- Whether all relevant privacy issues have been addressed appropriately.

- **Financial Management**
  - Whether the PI and/or other key personnel have appropriate experience and expertise in fiscal administration of multisite studies, including the distribution and management of funds.
  - How well the PI demonstrates commitment to achieving financial self-sufficiency of the consortium by the end of the award period.

- **Coordinating Center Two Initial Clinical Trials**

- **Personnel (applicable if a clinical trial(s) originates from outside the consortium and key personnel have not been previously listed)**
  - Whether the PI and other key personnel in the clinical trial have been named and whether they have the appropriate expertise in prostate cancer.
  - Whether the PI has a proven record of success in completing clinical trials.

- **Study Design**
  - Whether the trials are focused on therapeutic interventions.
  - Whether the study population has been adequately described.
  - Whether the investigational drugs or devices have been adequately described.
  - If from outside the consortium, whether the initiating institution(s) possess the appropriate qualifications.
  - Whether the proposed timelines indicate increased efficiency as a result of consortium participation.

- **Regulatory Process**
  - Whether there are appropriate plans for the coordination of IRB submissions and approvals at participating sites.
  - Whether there is an appropriate plan for developing procedures to ensure compliance with FDA regulations for investigational agents.
  - Whether the appropriate IND/IDE numbers been provided.

- **Impact**
  - Whether the trials address an important problem in prostate cancer.
  - To what extent the intervention or device to be tested, if the study is successful, will have a significant impact on prostate cancer.
  - Whether the types of studies proposed are appropriate.

b. All Sites (Clinical Research Sites and Coordinating Center): All proposals will be evaluated according to the following criteria. Of these, Personnel, Institutional Resources and Commitment, and Participant Recruitment are equally the most important, with the remaining criteria listed in decreasing order of importance.

- **Personnel**
  - Whether the PI meets the eligibility requirements.
  - How the research team's background and expertise are appropriate with respect to its ability to perform multi-institutional prostate cancer clinical research.
  - To what extent the research team has the ability and experience to contribute substantially to the design and conduct of consortium clinical trials.
  - Whether the named institutional Clinical Research Coordinator has the appropriate experience in guiding clinical protocols through the regulatory approval processes and the ability to foster communication with other consortium Clinical Research Coordinators.
  - Whether there are appropriate levels of effort for successful conduct of the proposed work.

- **Institutional Resources and Commitment**
  - Whether the institution has demonstrated appropriate commitment to working with the consortium.
  - How the PI is supported by the availability of and accessibility to facilities and resources, especially in regard to specimen collection and processing.
  - Whether the institution possesses appropriate resources and expertise for data management and maintaining security and confidentiality.
  - How well the institution has demonstrated its willingness and ability to resolve intellectual and material property issues with other institutions in the consortium.
  - Whether the institution has unique resources that may be of benefit to the consortium.

- **Participant Recruitment**
  - Whether the PI has demonstrated sufficient access to the appropriate prostate cancer patient population.
  - Whether the PI has provided sufficient evidence of access to and ability to recruit patients from disproportionately affected populations.
  - Whether the institution has proven success in recruiting patients for clinical trials.

- **Collaborations**
  - Whether the PI has demonstrated appropriate background, expertise, and success in collaborative prostate cancer clinical research.
  - How well the PI will integrate into the consortium and be a contributing member.
  - How well the PI's institution has facilitated the PI's collaborations.
- **Budget**
  - How the budget is appropriate for the proposed program.

2. Programmatic Review: Criteria used by the IP to make funding recommendations that maintain the program's broad portfolio include:

- Ratings and evaluations of the peer reviewers,
- Programmatic relevance,
- Relative impact,
- Program portfolio balance, and
- Adherence to the intent of the award mechanism.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be identified by IP members and recommended for funding to the Commanding General, USAMRMC.

VI. COMPLIANCE GUIDELINES

Compliance guidelines have been designed to ensure the presentation of all pre-applications and proposals in an organized and easy-to-follow manner. Peer reviewers expect to see a consistent, prescribed format. Failure to adhere to formatting guidelines makes documents difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in pre-application or proposal rejection. **Pre-applications or proposals missing required components as specified in the Program Announcement/Funding Opportunity may be administratively rejected.**

The following will result in administrative rejection of the entire proposal:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Margins are less than specified in the formatting guidelines.
- Print Area exceeds that specified in the formatting guidelines.
- Spacing is less than specified in the formatting guidelines.
- Budget and/or budget justification are missing.

- FY08 IP members are included in any capacity in the pre-application process, the proposal, budgets, and any supporting document. A list of the FY08 IP members may be found at http://cdmrp.army.mil/research

For any other sections of the pre-application or proposal with a defined page limit, pages exceeding the specified limit will be removed and not forwarded for peer review.

Material submitted after the submission deadline, unless specifically requested by the Government, will not be forwarded for peer review.

Proposals that appear to include plagiarized information will be administratively withheld from further consideration pending institutional investigation. The institution will be requested to perform the investigation and provide those findings to the Grants Officer for a determination of the final disposition of the application.