

Program Announcement

Department of Defense (DOD) Congressionally Directed Medical Research Programs

Prostate Cancer Research Program (PCRP)

Laboratory-Clinical Transition Award: Stage I

Funding Opportunity Number: W81XWH-08-PCRP-LCTAI

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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/) (<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. Overview

The PCRCP Laboratory-Clinical Transition Award: Stage I mechanism was introduced in FY07. Since then, 17 proposals have been received and 3 have been recommended for funding.

The Laboratory-Clinical Transition Award: Stage I represents the first step of a three-step sequence to foster the bench-to-bedside transition of promising agents into the clinic to benefit prostate cancer patients. The Laboratory-Clinical Transition Award: Stage I supports *goal- and product-driven* preclinical studies of lead agents that have the potential to revolutionize the prevention, detection, or treatment of prostate cancer. The second step, the Laboratory-Clinical Transition Award: Stage II, will fund production and testing of current Good Manufacturing Practices (cGMP) agents before clinical trials. The Laboratory-Clinical Transition Award: Stage II, described briefly at the end of this section, will be offered in FY10 pending availability of funds. The third step, conduct of Phase I and Phase II clinical trials of the cGMP-produced agent, may be sponsored through the PCRCP Clinical Trial Award, which is anticipated to be offered yearly pending availability of funds, or similar award mechanisms from other funding sources.

2. Laboratory-Clinical Transition Award: Stage I

The Laboratory-Clinical Transition Award: Stage I is intended to fund PIs who lack support to conduct the preclinical studies needed to advance lead agents to human testing. The goal of this award is the generation of sufficient data to justify inclusion of lead agents into future clinical trials for the prevention, detection, or treatment of prostate cancer.

For the purposes of the Laboratory-Clinical Transition Award: Stage I, *lead agents are defined as biological or chemical therapeutics, imaging agents, or preventive agents that have potential clinical application to prostate cancer.* Examples of lead agents include but are not limited to: novel chemotherapeutics, antibodies, viral particles, and contrast agents. *PIs are expected to identify and have access to either one lead agent or a limited number of lead agents for optimization at the time of proposal submission.*

All Laboratory-Clinical Transition Award: Stage I proposals must include preliminary data relevant to the lead agent(s) under development. ***Preliminary data must provide information regarding target availability and distribution in human prostate cancer tissues and must support the relevance of the target for the prevention, detection, or treatment of human prostate cancer. Preliminary data must also support the efficacy of each agent in model systems.***

The National Cancer Institute has constructed developmental pathways for translational research (<http://www.cancer.gov/images/trwg/Developmental-Pathway-Agent-Drug-Biologics.pdf>) that may be useful for designing translational research studies for support under this mechanism. These pathways are comprehensive and span the entire translational research continuum from discovery of a target to clinical trials. Please be aware that the Laboratory-Clinical Transition Award: Stage I only supports research from the identification of a lead agent up to but not including cGMP production of the agent. ***This award may not be used to conduct clinical trials.***

Studies that may be funded under this award include, but are not limited to:

- Comparative activity/efficacy testing to define a single lead agent from a limited library of candidates. ***Such studies must be completed within 12 months of the start date of the award. If the studies are not completed within 12 months of award initiation, funding for the award may be terminated.***
- Toxicology screening
- Drug metabolism, biodistribution, and pharmacokinetic assays
- Pharmacodynamic studies
- Radiation dosimetry
- Development and validation of assays and reagents required to measure biological responses and molecular endpoints

Studies that may NOT be funded under this award include, but are not limited to:

- Target discovery
- Drug screening
- Development of devices
- Development of serum- or tissue-based biomarkers for the primary diagnosis of disease
- New combinations or formulations of conventional therapeutics

Preclinical studies involving human subjects or specimens will be supported only if they are exempt under Title 32 of the Code of Federal Regulations Section 219.101(b)(4)(32 CFR 219.101(b)(4)) or qualify for expedited review under 32 CFR 219.110 or 21 CFR 56.1102. Studies that do not qualify for exempt status or expedited review will be administratively withdrawn and will not be funded.

The preclinical drug development process may require resources beyond those available at a single laboratory or institution. As such, the PI must disclose any patents, issued or pending, and/or licenses, granted and/or pending, with respect to the lead agent(s) as well as any known patents that block the development of the lead agent(s). In the event that the project requires the use of a non-commercially available technology/material that is patented by a third party, the PI must provide documentation that the third party patent holder does not object to the PI's use of the patented technology/material.

Since the ultimate goal of translational research is to obtain Investigational New Drug (IND) approvals on lead agents, PIs are expected to abide by US Food and Drug Administration (FDA) proposed and existing regulations governing the conduct of preliminary studies and the collection of data in support of an IND application (refer to http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm). Please note that the focus of the Laboratory-Clinical Transition Award: Stage I is to support the optimization of an identified lead agent up to but not including cGMP production of the agent. ***Clinical trials are not acceptable under this mechanism. PIs wishing to apply for funding for a clinical trial should utilize the Clinical Trial Award mechanism.***

3. Laboratory-Clinical Transition Award: Stage II

The Laboratory-Clinical Transition Award: Stage II will facilitate and expedite the next stage of the bench-to-bedside transition of promising lead agents by funding:

- Full-scale cGMP production of the agent for clinical trials.
- Studies with the cGMP-produced agent (e.g., toxicology and pharmacology) to support an IND application (or equivalent) to the FDA or other regulatory agency.
- Development of a clinical protocol for submission to the PCRCP Clinical Trial Award or a clinical trial award mechanism from another funding source. Collaboration with the existing PCRCP Clinical Consortium for protocol development will be encouraged but not required.

All PIs funded by the Laboratory-Clinical Transition Award: Stage I who have viable lead agents are encouraged to compete for the Laboratory-Clinical Transition Award: Stage II, which is anticipated to be offered in FY10 pending receipt of appropriations. The Laboratory-Clinical Transition Award: Stage II will also be open to PIs who have not submitted to or been funded by the Laboratory-Clinical Transition Award: Stage I.

Full guidance regarding the format and content of the Laboratory-Clinical Transition Award: Stage II proposal will be provided in the Program Announcement for the Laboratory-Clinical Transition Award: Stage II.

Please note that there is no guarantee that funds will be available for the Laboratory-Clinical Transition Award: Stage II.

C. Eligibility

PIs at all academic levels (or equivalent) are eligible to submit proposals.

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

D. Funding

Funding for a Laboratory-Clinical Transition Award: Stage I can be requested for up to \$750,000 for direct costs for up to a 3-year performance period plus indirect costs as appropriate.

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

- Salary
- Research supplies
- Equipment
- Clinical costs
- Travel to scientific/technical meetings
- Travel between collaborating institutions

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).

The CDMRP expects to allot approximately \$5.4M of the \$80M FY08 PCRP appropriation to fund approximately four to five Laboratory-Clinical Transition Award: Stage I proposals, depending on the quality and number of proposals received. 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

A change in PI is not allowed for the Laboratory-Clinical Transition Award: Stage I 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 \(https://cdmrp.org/\)](https://cdmrp.org/) and (2) a proposal submission through [Grants.gov \(http://www.grants.gov/\)](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](https://cdmrp.org/) 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

- Attachment 1: Project Narrative (25-page limit)

The preclinical drug development process may require resources beyond those available at a single laboratory. Therefore, the Laboratory-Clinical Transition Award: Stage I is open to multi-laboratory and/or multi-institutional collaborations.

Describe the proposed project in detail using the outline below. *Preliminary data are required to demonstrate target availability in human prostate cancer tissues and support the relevance of the target for the prevention, detection, or treatment of human prostate cancer.*

The National Cancer Institute has constructed developmental pathways for translational research (http://www.cancer.gov/images/trwg/Developmental-Pathway-Agent-Drug_Biologics.pdf) that may be useful for designing translational research studies for support under this mechanism. These pathways are comprehensive and span the entire translational research continuum from discovery of a target to clinical trials. Please be aware that Laboratory-Clinical Transition Award: Stage I only supports research from the identification of a lead agent up to but not including cGMP production of the agent. *This award may not be used to conduct clinical trials.*

Background: Present the ideas and reasoning behind the proposed research; include relevant literature citations. Describe the preliminary data most pertinent to this proposal.

Lead Agent(s): Describe the lead agent(s) and their clinical utility. Explain the relevance of the target for the prevention, detection, or treatment of human prostate cancer. Indicate whether the lead agent or agents are being developed in partnership with another institution and the nature of this partnership. Describe access to the lead agent(s).

Objective: State the objective to be reached.

Specific Aims: Concisely explain the project's specific aims. If this proposal is part of a larger study, present only tasks that the DOD award would fund.

Research Strategy: Describe the experimental design for preclinical validation of the lead agent(s) under development. Please see the award description for examples of appropriate research. Describe in detail the methods and analyses, including appropriate controls and a timeline for the completion of each proposed task. Address potential problem areas and present alternative methods and approaches.

- Attachment 2: Supporting Documentation
 - References Cited
 - Acronyms and Symbol Definitions
 - Facilities & Other Resources
 - Description of Existing Equipment
 - Publications and/or Patent Abstracts (five-document limit)
 - Letters of Institutional Support
 - Letters of Collaboration (if applicable)
 - Patents and Permissions (if applicable; no page limit)

As appropriate, disclose any patents, issued or pending, and/or licenses, granted and/or pending, with respect to the lead agent(s) as well as any known patents that block the development of the lead agent(s). If the project requires the use of a non-commercially available technology/material that is patented by a third party, provide documentation that the third party patent holder does not object to the PI's use of the patented technology/material.

- Intellectual and Material Property Plan (if applicable)
- Attachment 3: Technical and Public Abstracts
- Attachment 4: Statement of Work
- Attachment 5: Impact Statement

State explicitly how the proposed work will, if successful, have an impact on human prostate cancer and how the expected results of the proposal will contribute to the goals of conquering prostate cancer and advancing research on the prevention, detection, or treatment of the disease. Explain the potential clinical applications, benefits, and risks.
- 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

4. Research & Related Budget Form

- Budget Justification

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

6. R&R Subaward Budget 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 of proposals against established criteria for determining scientific merit. The second tier is a programmatic 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/fundingprocess>

The peer review and program review processes are conducted confidentially and anonymously to maintain the integrity of the merit-based selection process. Each tier 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: All proposals will be evaluated according to the following criteria. Of these, Lead Agent(s), Research Strategy and Feasibility, and Clinical Impact are equally the most important, with the remaining criteria listed in decreasing order of importance.

- **Lead Agent(s)**
 - How the scientific rationale supports the feasibility and development of the lead agent(s) as demonstrated by a critical review and analysis of the literature, preliminary data, and logical reasoning.
 - To what extent the PI acknowledges and complies with relevant patents and permissions.
 - Whether the PI has demonstrated appropriate access to the lead agent(s).
- **Research Strategy and Feasibility**
 - To what extent the study has the potential of developing a viable lead agent that would be ready for cGMP production.

- How well the objectives, aims, experimental design, methods, and analyses are developed.
- How well the PI acknowledges potential problems and addresses alternative approaches.
- Whether the proposal includes a clear and appropriately powered statistical plan.
- How well the research strategy complies with FDA requirements for IND submissions.
- **Clinical Impact**
 - To what degree the target is relevant to the prevention, detection, or treatment of human prostate cancer.
 - To what degree the agent may have a major impact on prostate cancer clinical care.
- **Personnel**
 - How the research team's background and prostate cancer-related expertise are appropriate with respect to its ability to perform the proposed work. This includes any co-PIs (or collaborators).
 - To what degree the levels of effort are appropriate for successful development of the lead agent(s).
 - Whether letters of collaboration are provided for any proposed collaborative arrangements (as applicable).
- **Environment**
 - How the scientific environment(s) (as applicable) is appropriate for the proposed research.
 - Whether there is adequate support as demonstrated by the availability of and accessibility to facilities and resources (including collaborative arrangements).
 - How the quality and extent of institutional support are appropriate.
- **Budget**
 - How the budget is appropriate for the proposed research.

2. Programmatic Review: Criteria used by programmatic reviewers 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 Integration Panel (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 preapplication 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.