Announcement of Federal Funding Opportunity

Summary

I. GENERAL INFORMATION

The fiscal year 2005 (FY05) Congressional appropriation to the Department of Defense's (DOD's) Prostate Cancer Research Program (PCRP) has not been signed at this time. Therefore, **funding for the Clinical Trial Award mechanism is subject to availability and passage of appropriate Congressional language.** Program announcement release and the evaluation and decision-making process for proposals submitted for this award mechanism may commence before the actual receipt of funding at this Command. However, based on this Command's knowledge of the appropriation history for these programs, it is believed that Congress will provide the funds for this project.

The FY05 Clinical Trial Award is open to all eligible applicants with clinical trials relevant to prostate cancer treatment, diagnosis, detection, or prevention. In addition, as stated in the FY04 Clinical Trial Development Award Program Announcement, recipients of the FY04 Clinical Trial Development Award are required to compete for the FY05 Clinical Trial Award. All applicants must submit proposals, clinical protocols, and other supporting clinical documents.

A. Title of Award: Clinical Trial Award.

B. Program Name: DOD FY05 PCRP.

C. Funding Opportunity Number: PC05-CTA.

D. Agency Name: US Army Medical Research and Materiel Command (USAMRMC), Office of the Congressionally Directed Medical Research Programs (CDMRP), 1077 Patchel Street, Fort Detrick, Maryland 21702-5024.

E. Agency Contact(s):

1. Questions related to the Program, proposal format, or required documentation may be addressed to the CDMRP at:

Phone: 301-619-7079
Fax: 301-619-7792
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
US Army Medical Research and Materiel Command
ATTN: MCMR-ZB-C (PC05-CTA)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

2. Questions related to electronic submission: The help line phone number is 301-682-5507 and is also provided on the web. Other help desk contact information is:

Website: https://cdmrp.org/proposals (the proposal submission website)
E-mail: help-proposals-cdmrp@cdmrp.org

F. Anticipated Instrument Type(s): Grants/Cooperative Agreements.

G. Catalog of Federal Domestic Assistance (CFDA) Number(s): 12.420; Military Medical Research and Development.

H. Website Address to Access Application Package: Proposals must be submitted electronically at https://cdmrp.org/proposals. The website contains all the information, forms, documents, and links you will need to apply.

I. Award/Regulatory Approval: Please note that each award mechanism has specific requirements regarding human subjects and animal use. Please see the full text of the Program Announcement for details pertaining to this award mechanism. Once an award is made, the applicant may not use, employ, or subcontract for the use of any human subjects, human anatomical substances, cadavers, and/or laboratory animals without express written permission from the applicable USAMRMC Regulatory Compliance and Quality (RCQ) office. USAMRMC RCQ will forward these express written approvals directly to the applicant with a copy furnished to the institution's Sponsored Programs Office (or equivalent).

Applicants who are approved for funding for the award mechanism under this Announcement will be required to attend a pre-award meeting and protocol workshop at Fort Detrick, Maryland.

II. FUNDING OPPORTUNITY DESCRIPTION

The intent of the Clinical Trial Award mechanism is to sponsor clinical research in a Phase I, Phase I/II, or Phase II clinical trial that has the potential to significantly impact the treatment, diagnosis, detection, or prevention of prostate cancer.

FY05 Clinical Trial Award proposals may be submitted without prior submission or receipt of a FY04 Clinical Trial Development Award.

III. AWARD INFORMATION

- Type of award: grant/cooperative agreement.
- The FY05 Clinical Trial Award mechanism is anticipated to fund approximately five awards for up to $750,000 per award in direct costs over a 3-year period of performance, plus indirect costs as appropriate.
- A total of approximately $5 million is anticipated for this award mechanism.

IV. ELIGIBILITY INFORMATION

A. Applicants: Applicants must be independent investigators at an eligible institution.

B. Institutions: Eligible institutions include for-profit, non-profit, public, and private organizations.

C. Cost Sharing: It is expected that institutions will cost share. Please see "Major Equipment/Intervention" located in Subsection V.G.2.c of the Full Text of Program Announcement for details.

D. Other Eligibility Criteria: Please see the Full Text of Program Announcement description for details regarding duplicate submissions, applications from Historically Black Colleges and Universities/Minority Institutions, and administrative compliance issues.

V. PROPOSAL PREPARATION AND SUBMISSION INFORMATION

A. Proposal Information: Applicants are required to submit the Proposal Information prior to upload of the proposal. Complete the Proposal Information as described at https://cdmrp.org/proposals.

B. Proposal Preparation: All proposals must be converted into an electronic PDF (Portable Document Format) file for electronic proposal submission. Please see the Full Text of Program Announcement for details.

C. Submission Dates and Times: Deadline Date: December 7, 2004. Proposals must be approved on the CDMRP eReceipt system by the Contract Representative at the applicant's institutional Sponsored Programs Office (or equivalent) by 5:00 p.m. (Eastern time).

D. Electronic Submission Requirements: Electronic submission is required. No paper copy submissions will be accepted. Proposals must be submitted electronically at https://cdmrp.org/proposals. Please see the Full Text of Program Announcement for details.

VI. PROPOSAL REVIEW INFORMATION

The CDMRP uses a two-tier review process for proposals: scientific peer review, followed by programmatic review. Details of both tiers of review can be found in Section VI of the Full Text of Program Announcement.

VII. AWARD ADMINISTRATION INFORMATION

A. Award Notices and Administrative Requirements: Details of award notification procedures, and administrative requirements including RCQ documents (Certificate of Environmental Compliance, Research Involving Human Subjects and/or Anatomical Substances, Research Involving Animals, and Safety Program Plan) can be found in Subsection VII.D of the Full Text of Program Announcement.

B. Reporting Requirements: Annual reporting requirements apply.

C. Reverse Site Visit: One reverse site visit per award is anticipated in the Baltimore-Washington, DC area during the period of performance.

Full Text of Program Announcement

I. GENERAL INFORMATION

A. Title of Award: Clinical Trial Award.

B. Program Name: Department of Defense (DOD) Fiscal Year 2005 (FY05) Prostate Cancer Research Program (PCRP).

C. Funding Opportunity Number: PC05-CTA.

D. Agency Name: US Army Medical Research and Materiel Command (USAMRMC), Office of the Congressionally Directed Medical Research Programs (CDMRP), 1077 Patchel Street, Fort Detrick, Maryland 21702-5024.

E. Agency Contact(s):

1. Questions related to the Program, proposal format, or required documentation: Applicants should submit questions as early as possible. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079
Fax: 301-619-7792
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
US Army Medical Research and Materiel Command
ATTN: MCMR-ZB-C (PC05-CTA)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

2. Questions related to electronic submission: Help lines will be available to answer specific questions regarding the preparation of proposals for electronic submission or the process of electronic submission. The help line phone number is 301-682-5507 and is also provided on the web. Other help desk contact information is:

Website: https://cdmrp.org/proposals (the proposal submission website)
E-mail: help-proposals-cdmrp@cdmrp.org

F. Anticipated Instrument Type(s): The USAMRMC implements its extramural research program predominantly through the award of grants and cooperative agreements. More information on these funding instruments may be obtained by request from:

Fax: 301-619-2937
E-mail: qa.baa@det.amedd.army.mil
Mail: Director
US Army Medical Research Acquisition Activity
ATTN: MCMR-ZB-A
820 Chandler Street
Fort Detrick, MD 21702-5014

G. Catalog of Federal Domestic Assistance (CFDA) Number 12.420: Military Medical Research and Development.

H. Website to Access Application Package: Proposals must be submitted electronically at https://cdmrp.org/proposals. This website will contain all the information, forms, documents, and links you will need to apply. If you experience difficulties in downloading documents, contact the CDMRP as indicated in Subsection E.1 above.

I. Award/Regulatory Approval: Please note that this award mechanism has specific requirements regarding human subjects and animal use.

Once an award is made, the applicant may not use, employ, or subcontract for the use of any human subjects, human anatomical substances, cadavers, and/or laboratory animals without express written permission from the applicable USAMRMC Regulatory Compliance and Quality (RCQ) office. USAMRMC RCQ will forward these express written approvals directly to the applicant with a copy furnished to the institution's Sponsored Programs Office (or equivalent).

Applicants who are approved for funding for the award mechanism under this Announcement will be required to attend a pre-award meeting and protocol workshop at Fort Detrick, Maryland.

II. FUNDING OPPORTUNITY DESCRIPTION

A. Program History: The Clinical Trial Award is part of the DOD PCRP, which was established in FY97 to promote uniquely innovative research directed toward eliminating prostate cancer. Appropriations for the PCRP from FY97 through FY03 total $480 million (M). For this period, 1,010 proposals were funded out of total of 4,267 proposals that were received. The FY04 appropriation was $85M.

B. Program Objectives: The objectives of the FY05 PCRP are to (1) prevent prostate cancer, (2) detect prostate cancer in its earliest stages of development, (3) cure prostate cancer, and (4) improve the quality of life for individuals and their families living with prostate cancer.

C. Award Mechanism Description: The intent of the Clinical Trial Award is to provide for the rapid execution of novel patient-oriented research in a Phase I, Phase I/II, or Phase II clinical trial that has the potential to significantly impact the treatment, diagnosis, detection, or prevention of prostate cancer. Proposals should focus on new interventions (e.g., drugs, biologics, and devices.)

This award is intended to support both new and established scientists across a broad spectrum of disciplines. The FY05 Clinical Trial Award is open to all eligible applicants with clinical trials relevant to prostate cancer treatment, diagnosis, detection, or prevention. In addition, as stated in the FY04 Clinical Trial Development Award Program Announcement, recipients of the FY04 Clinical Trial Development Award are required to compete for the FY05 Clinical Trial Award. All applicants must submit proposals, clinical protocols, and other supporting clinical documents.

Applicants should clearly specify in the proposal which type of Clinical Trial Award is being requested (i.e., Phase I, Phase I/II, or Phase II).

Phase I Clinical Trials:

These trials should focus on determining the safety, toxicity, tolerability, and pharmacokinetics/ pharmacodynamics of new interventions or devices, or treatment schedules in humans. It is expected that this award will allow the recipient the opportunity to obtain the data and experience necessary to conduct a Phase II clinical trial, if appropriate. Applicants for Phase I trials must include a clear scientific rationale for the trial as well as adequate preclinical supplemental data to support the feasibility of their hypotheses and approaches. Applicants also must include a detailed plan for completing the Phase I trial during the award period and a clear experimental and appropriately powered statistical plan to perform the clinical trial. Phase I applicants are encouraged but not required to pursue correlative studies.

Phase II Clinical Trials:

These trials should focus on determining the efficacy of new interventions or devices. Applicants for Phase II clinical trials must include Phase I or pilot clinical trial data, adequate preclinical supplemental data to support the feasibility of their hypotheses and approaches, and a detailed plan for completion of the Phase II clinical trial during the award period. Applicants also must include a clear experimental and appropriately powered statistical plan to perform the Phase II clinical trial. Phase II applicants are encouraged but not required to pursue correlative studies.

Phase I/II Clinical Trials:

These trials must address all applicable requirements detailed above under Phase I and Phase II.

If the trial is multi-institutional, applicants should include in the appropriate sections of the main body of the proposal (Subsection V.E.6.e) plans for communication and real-time data transfer between the collaborating institutions, as well as how specimens and/or imaging products obtained during the study will be handled. An intellectual property plan agreed upon by all participating institutions is also required for multi-institutional clinical trials as a part of the administrative documentation of this proposal (see Subsection V.E.13).

Please note that all DOD-funded research involving human subjects, human anatomical substances, cadavers, and/or laboratory animals must be reviewed and approved by the Human Subjects Research Review Board (HSRRB) in addition to local Institutional Review Boards (IRBs). It is recommended that all protocols be prepared according to the guidelines provided in the document titled "Research Involving Human Subjects and/or Anatomical Substances," which can be found at https://cdmrp.org/programAnnouncements.cfm under "Regulatory Document Forms." An HSRRB-approved template for clinical protocols also can be found at this site.

All proposals for the Clinical Trial Award should include:

- The objective(s) and rationale of the proposed clinical trial, including any preclinical science and preliminary clinical research relevant to the trial to include data supporting the feasibility of the hypothesis and approaches;
- The relevance of the proposed clinical trial to prostate cancer treatment, diagnosis, detection, or prevention;
- A clear description of the particular target, pathway, molecule or device that is the focus of the clinical trial.
- The proposed intervention(s) to be tested in the clinical trial and a brief description, as appropriate, of its:

- Source,
- Investigational New Drug (IND) status,
- Evidence of the availability of the substance in sufficient quantity under current Good Manufacturing Practice (cGMP) production. If the substance is to be provided from industrial sources, evidence of a cost-sharing plan also must be provided,
- Dosing and toxicity,
- Mechanisms of action, and
- Preclinical/clinical evidence of efficacy.

- A named study coordinator who will guide the clinical protocol through the IRB, HSRRB, and other regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate patient accrual;
- The sample size for the clinical trial with appropriate statistical analyses presented to verify power for the sample size; a patient accrual/recruitment schedule including inclusion and exclusion criteria; and evidence of access to appropriate patient population(s) that support rapid execution of the Clinical Trial Award following receipt of funds;
- A clinical protocol, a Manual of Operations and Procedures (if available), and consent/assent form(s) that includes HSRRB-prescribed content;
- Internal scientific and local IRB review documents for the clinical protocol and consent forms that indicate the level of review achieved prior to submission to the Clinical Trial Award. Indicate the highest level possible of review within the participating institutions prior to submission of a proposal;
- A document addressing human subjects protection requirements as outlined by the HSRRB at https://cdmrp.org/programAnnouncements.cfm under "Regulatory Document Forms";
- A clinical trial management plan, including a plan for ensuring the standardization of procedures across sites and among staff;
- Evidence of institutional commitment(s) for the proposed clinical trial; and
- A description of the clinical trial team to include names, background, qualifications, time commitments, and contributions made to the trial.

III. AWARD INFORMATION

Please note that funding for the Clinical Trial Award mechanism is subject to availability and passage of appropriate Congressional language. However, based on this Command's knowledge of the appropriation history for these programs, it is believed that Congress will provide the funds for this project.

Approximately $5M is anticipated to be available for this award mechanism. It is anticipated that this award mechanism will fund approximately five awards for up to $750,000 each in direct costs over a 3-year period of performance, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, and travel to scientific meetings. The amount for travel to scientific meetings may not exceed $1,800 per year per investigator. Applicants should also budget for travel to a pre-award meeting and protocol workshop at Fort Detrick, Maryland and a reverse site visit in the Baltimore-Washington, DC area during the period of performance.

The FY05 Clinical Trial Award is open to all eligible applicants with clinical trials relevant to prostate cancer treatment, diagnosis, detection, or prevention. In addition, as stated in the FY04 Clinical Trial Development Award Program Announcement, recipients of the FY04 Clinical Trial Development Award are required to compete for the FY05 Clinical Trial Award. All applicants must submit proposals, clinical protocols, and other supporting clinical documents.

All applicants must provide evidence of sufficient institutional support and commitment for the proposed studies, such as the provision of access to adequate laboratory facilities and equipment. Consideration of cost sharing with other funding sources and multi-institutional/multidisciplinary research collaborations is encouraged. The nature of this award mechanism does not allow for renewal of grants or supplementation of existing grants with DOD funds.

IV. ELIGIBILITY INFORMATION

A. Applicants: Applicants must be independent investigators at an eligible institution.

B. Institutions: Eligible institutions include for-profit, non-profit, public, and private organizations. The USAMRMC is especially interested in receiving applications from Historically Black Colleges and Universities and Minority Institutions (HBCU/MI).

C. Cost Sharing: It is expected that institutions will cost share. Please see full details under "Major Equipment/Interventions" located in Subsection V.G.2.c.

D. Other Eligibility Criteria:

1. Duplicate Submissions: Submission of the same research project to the FY05 PCRP under different award mechanisms or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative proposals.

2. HBCU/MI: A goal of the DOD is to allocate funds for the CDMRP's peer reviewed research to fund proposals from HBCU/MI. This provision is based upon guidance from Executive Orders.[1] Proposals submitted to the DOD are assigned HBCU/MI status if the submitting institution is so designated by the Department of Education on the date that the program announcement is released. The Department of Education list is posted on the CDMRP website under Minority Institutions at http://cdmrp.army.mil/funding/pdf/mipcrp061104.pdf.

3. Administrative Compliance Issues: Compliance guidelines have been designed to ensure the presentation of all proposals in an organized and easy-to-follow manner. Peer reviewers expect to see a consistent, prescribed format for each proposal. Nonadherence to format requirements makes proposals difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in proposal rejection or a lower global priority score.

The following will result in administrative rejection of the entire proposal prior to peer review:

- Main body of proposal exceeds page limit (see Subsection V.E.6).
- Main body of proposal is missing.
- Clinical protocol is missing.

[1] Executive Orders 12876, 12900, and 13021

- Detailed cost estimate is missing.
- Proposal is incomplete after the deadline.
- Required administrative documentation is not included.

For any other sections of a proposal with a defined page limit, any pages over the specified limit will be removed from the proposal and not forwarded for peer review.

Unless specifically requested by the Government, any material submitted after the submission deadline will be considered late and will not be forwarded for peer review.

V. PROPOSAL PREPARATION AND SUBMISSION INFORMATION

A. Proposal Components Summary: This subsection is a summary of submission requirements. Details, URLs, and other links are provided in the appropriate subsections of this program announcement.

The Principal Investigator (PI) is responsible for uploading the following information:

- **Proposal Information:** The Proposal Information consists of two parts, both of which are entered as data fields. A Letter of Intent is generated when Part 1 of the Proposal Information is saved.
- **Statement of Work (SOW) and Proposal Abstracts:** The SOW, Technical Abstract, and Public Abstract are each entered as a separate data field.
- **Proposal:** The proposal is uploaded as a PDF (Portable Document Format) file under the "Required Files" tab.
- **Clinical Protocol and Supporting Clinical Documents:** The clinical protocol and supporting clinical documents are uploaded as a PDF file under the "Required Files" tab.
- **Budget Information:** The budget information is uploaded as a PDF file under the "Required Files" tab.
- **Regulatory Documents:** The Certificate of Environmental Compliance and the Principal Investigator Safety Program Assurance form are each uploaded as separate PDF files under the "Required Files" tab.

The Contract Representative or institutional official responsible for sponsored program administration (or equivalent) from the applicant's institution is responsible for the following:

- **Information Profile:** The Contract Representative's contact and information profile must be completed prior to electronic approval of all proposal components.
- **US Army Medical Research Acquisition Activity (USAMRAA) Required Documents:** The institute's currently negotiated "Rate Agreement," "Certifications and Assurances for Assistance Agreements," and the "Representations for Assistance Agreements" are to be uploaded as separate PDF files under the Contract Representative's "My Profile" tab.
- **Approval:** The Contract Representative or institutional official responsible for sponsored program administration must provide electronic approval of all proposal components (Proposal Information, SOW, Abstracts, Proposal, Clinical Protocol and Supporting Clinical Documents, Budget Information, and Regulatory documents). Contract Representative approval must occur prior to the submission deadline of 5:00 p.m. (Eastern time) December 7, 2004. The eReceipt

system will **not** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time December 7, 2004 deadline.

B. Proposal Information: Applicants are required to submit the Proposal Information, Parts 1 and 2, prior to upload of the proposal and the budget information. Complete the Proposal Information as described in https://cdmrp.org/proposals. The Proposal Information must include the e-mail address of a representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate on behalf of the institution.

- **Letter of Intent:** An electronic Letter of Intent should be submitted by November 5, 2004. To accomplish this, the applicant should complete Part 1 of the Proposal Information section at https://cdmrp.org/proposals, then save the information by clicking on the "Save and Forward Letter of Intent" button. This information may be changed at any time until the applicant submits the final Proposal Information by clicking on the "Submit Final" button.

C. SOW – 11,400-character limit, including spaces (approximately two pages): The SOW is captured as a data field under the "SOW/Abstract" tab in the CDMRP eReceipt system. To submit the SOW, the applicant may either type in the SOW or "cut and paste" it from a word processing application into the data field. Sample SOWs can be found at https://cdmrp.org/samples.cfm.

The SOW is a concise restatement of the research proposal that outlines, step by step, how each of the major goals or objectives of the proposed research/services will be accomplished during the timeline for which the USAMRMC will provide financial support.

As appropriate, the SOW should:

- Describe the work to be accomplished as tasks (tasks may relate to specific aims),
- Identify the timeline and milestones for the work over the period of the proposed effort,
- Indicate the numbers of research subjects (animal or human) and/or anatomical samples projected or required for each task,
- Identify methods, and
- Identify outcomes, products, and deliverables for each phase of the project.

D. Proposal Abstracts – 5,700-character limit, including spaces (approximately one page), for each abstract: Both a structured technical abstract and a public (nontechnical) abstract are required. These abstracts are vitally important to both the peer and programmatic review process.

Programmatic review is based upon the Integration Panel's (IP's) review of these two abstracts as part of the peer review summary statements; therefore, it is paramount that the investigator submit abstracts that fully describe the proposed work.

Each abstract must contain the title of the proposal and the name of the PI. Each abstract must be submitted as a data field under the "SOW/Abstracts" tab of the CDMRP eReceipt system. Applicants can either type in their abstracts, or "cut and paste" them from a word processing application into the respective data fields. Do not include figures or tables in either abstract. Spell out all Greek or other non-English letters.

Abstracts of all funded proposals will be posted on the CDMRP website at http://cdmrp.army.mil. Thus, proprietary or confidential information should not be included in the abstracts.

1. Technical Abstract: Sample technical abstracts can be found at https://cdmrp.org/samples.cfm. The structured technical abstract should provide a clear and concise overview of the proposed work, including the background, objective or hypothesis and its supporting rationale, specific aims of the study, study design, and significance of the proposed work to the Program's goals.

Use the outline below for preparing the structured technical abstract.

- Background: Provide a brief statement of the ideas and reasoning behind the proposed clinical trial. Briefly describe the studies that led to the proposed clinical trial.
- Intervention: State the intervention or device to be tested. Provide evidence or rationale that supports the intervention or device.
- Trial Design: Briefly describe the proposed clinical trial, including proposed patient sample size, accrual, and outcome measures. Indicate the phase (I, I/II, or II) of the clinical trial.
- Relevance: Provide a brief statement explaining the relevance of the proposed clinical trial to prostate cancer treatment, diagnosis, detection, or prevention.

2. Public Abstract: Sample public abstracts can be found at https://cdmrp.org/samples.cfm. The public abstract is intended to communicate the purpose of, and rationale for, the study to non-scientific audiences. The public abstract is an important component of the proposal review process because consumer advocates, who are part of the review and funding decision process, use this abstract as a part of their review. It must be composed in a way to make the scientific objectives and rationale for the proposal understandable to non-scientifically trained readers. **The public abstract should not be a duplicate of the technical abstract**, but should describe the goals and objectives of the research project, and its relevance to the Program.

In addition to describing the project, the public abstract must answer the following questions:

(1) What are the ideas and reasoning behind the proposed clinical trial?

(2) What will be the ultimate applicability of the clinical trial to prostate cancer?

- What types of patients will it help and how?
- What are the potential clinical applications, benefits, and risks?
- What is the projected time it may take to achieve a consumer-related outcome?

E. Proposal:

1. Format: All proposals must be converted into an electronic PDF file for electronic submission. Proposals must be uploaded under the "Required Files" tab of the CDMRP eReceipt system. Applicants unfamiliar with the preparation of PDF files are encouraged to acquire appropriate software and learn the process before the submission deadline. To prepare proposals for PDF submission, the instructions in this subsection must be followed carefully.

The proposal must be clear and legible and conform to the following guidelines:

- Font Size: 12 point.
- Font Type: Times New Roman.
- Type Density: No more than 15 characters per inch. (For proportional spacing, the average for any representative section of text should not exceed either 15 characters per inch or 114 characters per line.)
- Spacing: Single-spaced between lines of text, no more than five lines of type within a vertical inch.
- Margins: Minimum of 0.5-inch top, bottom, right, and 1-inch left.
- Color, Resolution, and Multimedia Objects: Proposals may include color, high resolution, or multimedia objects (e.g., MPEG, WAV, or AVI files) embedded in the PDF files; however, these items must not exceed 15 seconds in length and a size of 10 megabytes (MB). Since some reviewers work from black and white printed copies, applicants may wish to include text in the proposal directing the reviewer to the electronic file for parts of the proposal that may be difficult to interpret when printed in black and white.
- Spell out all acronyms the first time they are used. One page following the proposal body is allocated to spell out acronyms, abbreviations, and symbols.
- Language: English.
- Print Area: 7.0 x 10.0 inches (approximately 18 cm x 25.5 cm).

2. Title/Referral Page: No page limit. Complete the Title/Referral Page, which can be downloaded at https://cdmrp.org/programAnnouncements.cfm?prg=PCRP&prg_fy=2005. Complete each section as described below:

a. Proposal title (up to 160 characters).

b. Proposal log number (this will be automatically provided when the Proposal Information is completed and saved).

c. PI's full name (first, middle initial, last).

d. Submitting institution.

e. Award mechanism: Type in "Clinical Trial Award." Indicate the clinical trial phase (Phase I, I/II, or II).

f. Keyword descriptive technical terms: To assist the staff in assigning proposals to the appropriate scientific peer review panel, please specify the subject area of the proposal and list specific keywords and descriptive technical terms that would best describe the technical aspects of the project.

g. Conflicts of interest: To avoid real or apparent conflicts of interest during the review process, list the names of all scientific participants in the proposal including consultants, collaborators, and subawardees. In addition, list the names of other individuals outside the scope of this proposal who may have a conflict of interest in review of this proposal. Provide the following information for each participant: name, institutional affiliation(s), and, if applicable, his or her role(s) on the proposed project.

3. Table of Contents/Checklist: Start section on a new page; two-page limit. Prepare a Table of Contents/Checklist, with page numbers. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page.

4. Proposal Relevance Statement: Start section on a new page; one-page limit. Applicants should state explicitly how the proposed clinical trial will have a major impact on the treatment, diagnosis, detection, and prevention of prostate cancer. If this proposal is duplicative of a proposal submitted to another FY05 CDMRP program announcement, provide a strong justification for submitting duplicate proposals and the proposal's relevance to prostate cancer.

5. Proposal Resubmission Statement: Not applicable for Clinical Trial Award submissions.

6. Main Body: Start section on a new page; 25-page limit (12 point, Times New Roman) inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other relevant information needed to judge the proposal. All Clinical Trial Award applicants must submit promising and well-founded preliminary data relevant to prostate cancer and the proposed project. In addition, the inclusion of Phase I or pilot clinical trial data is required for Phase II clinical trial applicants.

Describe the proposed project using the following general outline. The main body of the proposal will be reviewed as a stand-alone document. Therefore, include the appropriate information from the clinical protocol to discuss the topics listed below. Do not reference the clinical protocol.

a. Background: Describe the ideas and reasoning behind the proposed work and previous experience most pertinent to the proposal. Cite relevant literature references.

b. Rationale: State the purpose of the study and the expected results.

c. Objectives: State the specific aims of the study.

d. Preliminary Studies: Present the studies that led to the proposed clinical trial. In addition, Phase II clinical trial applicants must provide Phase I or pilot clinical trial data. State the relevance of the proposed clinical trial to prostate cancer treatment, diagnosis, detection, or prevention.

e. Methods and Data Analyses: Provide a brief discussion of the topics listed below.

- Include a named study coordinator who will be charged with guiding the protocol through the IRB, HSRRB, and other regulatory approval processes, coordinating activities from all sites participating in the trial, and coordinating patient accrual.
- Description of the intervention or device to be tested. Provide evidence that a sufficient quantity of the substance is available and is produced under cGMP conditions. Include a cost-sharing plan if the substance or device is to be provided from industrial sources.
- Study design for the intervention(s) to be used.
- Potential biases in the protocol and how they will be addressed.
- Clinical, behavioral, laboratory, and physiological tests and protocols.
- Patient recruitment, including (1) patient availability; (2) inclusion and exclusion criteria; (3) methods for recruiting, retention, and follow-up; (4) data to support recruitment/retention estimates; (5) patient assignment to experimental groups and methods of randomization (if any); and (6) study endpoints.

- Data management, including the (1) overall approach to data management; (2) a plan for real-time data transfer; (3) a statistical plan that includes sample size calculations and methods to monitor quality and consistency of the intervention(s) and data collection; and (4) data security measures. For multi-institutional trials, include plans for communication and real-time data transfer between the collaborating institutions.
- Methods for the handling, distribution, analysis, and security of specimens, and/or imaging products (primary and secondary endpoints should be clearly defined and related to the power calculation). For multi-institutional trials, include a specimen handling and distribution plan agreed upon by all collaborating institutions.
- Any issues that may lead to concern for the welfare of human subjects and confidentiality, including a plan for addressing human subject protection requirements as outlined by the HSRRB at https://cdmrp.org/programAnnouncements.cfm under "Regulatory Document Forms."
- Internal scientific and local IRB reviews for the clinical protocol and consent/assent form(s) at the highest possible level within the participating institutions, up to and including preliminary IRB approval if available at the institution(s).
- A study organization and management plan, including a plan for real-time communication among collaborating institutions, if appropriate; a plan for ensuring the standardization of procedures across sites and among staff; and an organizational chart and a timetable for completion of the clinical trial and publication.

f. Intellectual Property: Provide a brief description of an intellectual property plan agreed upon by all institutions involved in the clinical trial detailing how all involved are willing to resolve intellectual property issues.

Please note that the clinical protocol, Manual of Operations and Procedures (if available), consent forms, and other supporting clinical documents must be submitted in the appropriate section of the proposal (see Subsections V.F.1 and V.F.2). Ensure that the information describing the clinical protocol in the main body matches that in Subsections V.F.1 and V.F.2. In addition, any available IRB approvals for this work must be submitted as supporting clinical documents (see Subsection V.F.2).

7. Abbreviations: Start section on a new page; one-page limit. Provide a list of all acronyms, abbreviations, and symbols used.

8. References: Start section on a new page; no page limit. List all relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

9. Biographical Sketches: Three-page limit per individual. Biographical sketches should be included for each of the key personnel listed on the budget page, including collaborating investigators and support staff. These documents are a critical component of the review process. Incomplete or missing biographical sketches may result in lower priority scores. The Biographical Sketch form may be used. Use of this form is not mandatory, but the information requested shall be presented in a similar format.

10. Existing/Pending Support: Start section on a new page; no page limit. List on a separate page the titles, time commitments, supporting agencies, durations, and levels of funding for all existing and pending research projects involving the PI and key personnel. If no support exists, state

"none." Proposals submitted under this program announcement should not duplicate other funded research projects.

11. Facilities/Equipment Description: No page limit. Describe the facilities available for performance of the proposed research/services. Describe the institutional commitment, including any additional facilities or equipment proposed for purchase or available for use at no cost to the USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use.

12. Publications and/or Patent Abstracts: Five-document limit. Include up to five relevant publication reprints and/or patent abstracts. A patent abstract should provide a non-proprietary description of the patent application. If more than five such items are included in the submission, the extra items will not be peer reviewed.

13. Administrative Documentation: No page limit. Submit only material specifically requested or required in this program announcement. **This section is not for additional figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, or other relevant information needed to judge the proposal.** Unrequested material that is submitted may be construed as an attempt to gain a competitive advantage and will be removed; it may be grounds for administrative rejection of the proposal.

The first item in this section must be a list of all the items included in the Administrative Documentation section.

- Provide letters of support from any collaborating individuals or institutions in this section of the proposal.
- Provide letters of commitment from senior leaders at the institutions participating in the clinical trial.
- Provide documentation that the participating institutions have an intellectual property plan and are willing to resolve intellectual property issues.
- Provide documentation of the availability of the substance or device to be used in the clinical trial. If the substance or device is to be provided from industrial sources, provide documentation of a cost-sharing plan.

All administrative documentation must be incorporated into the electronic PDF version of your proposal. Support documentation will not be accepted separately from the electronic proposal submission. All documents or letters requiring signatures must be signed and then incorporated into the submitted proposal.

F. Clinical Protocol and Supporting Clinical Documents:

1. Clinical Protocol: No page limit. The clinical protocol is a required element for the Clinical Trial Award. The protocol must be prepared according to the HSRRB-approved template for clinical protocols, which is adapted below from the document titled "Research Involving Human Subjects and/or Anatomical Substances," which can be found at under "Regulatory Document Forms" at https://cdmrp.org/programAnnouncements.cfm.

It is critical that the information entered in the main body of the proposal matches the information contained within the clinical protocol.

Required elements for submission of a **clinical protocol** are:

a. Protocol Title: The protocol title must be the same as the proposal title unless multiple protocols are being submitted within one proposal. In a proposal with multiple protocols, the proposal title must be referenced consistently across all protocols.

b. Phase: Designate the protocol as Phase I, I/II, or II.

c. Principal Investigator: List the complete name, address, telephone and fax number, and e-mail address of the PI. List the names of all personnel who will have significant involvement in the research study; include their practice license (e.g., MD or RN), highest degree(s), job title, and employing institution. In addition, include the name of the Medical Monitor with his or her current curriculum vitae for Greater Than Minimal Risk Studies. (See part p of this section for details on the Medical Monitor requirement.)

NOTE: Research investigators must complete appropriate institutional training before conducting human subjects research. Documentation of the most recent ethics training must be submitted for investigators of all protocols in the Supporting Clinical Documents section of the proposal (Subsection V.F.2). In addition, for all investigational drug and device protocols, documentation of successful completion of a course in the conduct of clinical research in accordance with Good Clinical Practices (GCP) must be submitted for all investigators. The most recent ethics training and GCP course must be successfully completed within 1 year of the planned initiation of the protocol.

d. Location of Study: List all centers, clinics, or laboratories where the study is to be conducted. Include the name, degree(s), title, employing institution, and complete address of the investigator(s) for each site.

e. Time Required to Complete the Study: State the month and year of expected start and completion times.

f. Background: Include a background section that describes the rationale for conducting the study as well as the study's relevance and applicability of findings. Include descriptions of any preliminary studies and findings that led up to the development of the protocol. If the protocol was initiated using other findings prior to obtaining funding managed by USAMRMC, explain the history and evolution of the protocol and declare the source of prior funding. HSRRB approval is required prior to continuing enrollment using USAMRMC managed funds.

g. Objectives: Provide a detailed description of the purpose and objectives of the study.

h. Study Population:

i. Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site (population from which the sample will be recruited/drawn).

ii. Describe the methods that will be used to obtain a sample of subjects from the accessible population (e.g., convenience, simple random, stratified random) together with the inclusion and exclusion criteria (include age, gender, and ethnicity).

i. Protocol Design: Describe the type of study to be performed (prospective, retrospective, randomized, controlled, etc.). Outline the proposed methodology in sufficient detail to show a

clear course of action. Technological reliability and validity of procedures should be indicated. Minimum guidance for the plan should include:

i. Subject Identification: Describe the code system to be used to maintain the confidentiality of subjects.

ii. Description of the Recruitment Process: Describe who will identify potential subjects, who will recruit them, and how they will be recruited. Provide copies of all recruitment and advertisement materials for review.

iii. Description of the Informed Consent Process: Specifically describe the plan for the informed consent process by stating who will perform the informed consent interview, when the interview will take place relative to the participant beginning study participation and in relation to any stressful situation (e.g., being informed he has cancer) or in relation to the administration of any mind-altering substances such as tranquilizers, conscious sedation, or anesthesia. Address how privacy and time for decision-making will be provided and whether or not the potential subject will be allowed to discuss the study with anyone before making a decision. Two copies of the consent form should be completed so that the subject can get an original copy and a copy can be kept for the PI's study records. A third copy may be needed for the patient's medical record; check with the participating site for specific study-site requirements.

iv. Subject Assignment: Describe the randomization process or other procedures used for subject group assignments.

v. Subject Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, history, and/or physical examination) that are required to determine eligibility/suitability for study participation. Please note that some screening procedures may need a separate consent or a two-stage consent process.

vi. Data Collection Procedures: Describe all data collection procedures to be used in conducting the study (e.g., laboratory evaluations, specimens to be collected, schedule and amounts, storage to include where and whether special conditions are required, labeling, and disposition). For studies using multiple measures or tests over time, it is helpful to display the data collection schedule in a spreadsheet or tabular format.

vii. Clinical Assessments: Provide a schedule of clinical evaluations and follow-up procedures. Provide any case report forms, data collection forms, questionnaires, rating scales, and/or interview guides that will be used in the study.

viii. Research Interventions: Describe the research intervention or activity that the subject will experience. Provide sufficient detail in chronological order for a person uninvolved in the research to understand what the subject will experience.

ix. Data Analysis: Describe the data analysis plan. The data analysis plan should be consistent with the study objectives.

j. Risks/Benefits Assessment:

i. Describe risks (physical [including pain and discomfort, disfigurement, infection, injury, death], psychological, social, economic, legal, and privacy/confidentiality risks]) associated with the research, measures to be taken to minimize and/or eliminate risks or to manage unpreventable risks and special medical or nursing care that will be needed prior to, during, or following participation.

ii. Describe benefits of the research to the subject. If there will be no benefits to the subjects, (other than knowing he has contributed to science), state this in the protocol and consent form.

iii. Payment or compensation for participation is not considered to be a benefit and must be addressed in a separate section.

k. Reporting of Serious or Unexpected Adverse Events:

i. Serious or unexpected adverse events can occur in any and all types of studies, not just experimental interventions or clinical trials.

ii. Include a definition of what constitutes an adverse event in the study.

(1) For IND or Investigational Device Exemption (IDE) research, include definitions as described in 21 CFR 312.32.[2]

(2) All IND protocols must address the following requirements.

"An adverse event temporally related to participation in the study should be documented whether or not considered to be related to the test article. This definition includes intercurrent illnesses and injuries and exacerbations of preexisting conditions. Include the following in all IND safety reports: Subject identification number and initials; associate investigator's name and name of medical treatment facility (MTF); subject's date of birth, gender, and ethnicity; test article and dates of administration; signs/symptoms and severity; date of onset; date of resolution or death; relationship to the study drug; action taken; concomitant medication(s) including dose, route, and duration of treatment, and date of last dose."

iii. Describe agencies or offices to be notified with point of contact information in the event of a serious and unexpected adverse event.

All protocols should contain the following language regarding the HSRRB reporting requirements for adverse events and unanticipated problems. (Note that unanticipated problems can occur in a study that does not require a research/clinical intervention.)

"Unanticipated problems involving risk to volunteers or others, serious adverse events related to participation in the study and all volunteer deaths should be promptly reported by phone (301-619-2165), by e-mail (hsrrb@det.amedd.army.mil), or by facsimile (301-619-7803) to the Army Surgeon General's Human Subjects Research Review Board. A complete written report should follow the initial telephone call. In addition to the methods above, the complete report can be sent to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-ZB-QH, 504 Scott Street, Fort Detrick, Maryland 21702-5012"

Refer to the "HSRRB Information Sheet for Investigators: Unanticipated Problems" for examples of unanticipated problems located on RCQ's website at https://mrmc.detrick.army.mil/index.asp?EntryURL=/crprcq.asp.

[2] Title 21, Code of Federal Regulations, Part 312.32; for more information, go to http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR=312.32.

For protocols that have a Medical Monitor assigned (see part p below), the following language should also be included.

> "The Medical Monitor is required to review all unanticipated problems involving risk to volunteers or others, serious adverse events and all volunteer deaths associated with the protocol and provide an unbiased written report of the event. At a minimum, the Medical Monitor should comment on the outcomes of the event or problem and in the case of a serious adverse event or death comment on the relationship to participation in the study. The Medical Monitor should also indicate whether he or she concurs with the details of the report provided by the study investigator. Reports for events determined by either the investigator or Medical Monitor to be possibly or definitely related to participation and reports of events resulting in death should be promptly forwarded to the HSRRB."

l. Description of Protocol Drugs or Devices: If the protocol uses an investigational drug or device, provide the following information:

i. IND/IDE number and name of sponsor, if the study is in support of an application to the Food and Drug Administration (FDA).

ii. Complete names and composition of all medication(s), device(s), or placebo(s).

iii. Source of medications, devices, or placebos.

iv. Location of storage for study medications.

v. Dose range, schedule, and administration of test articles.

vi. Washout period, if used, should be described in detail.

vii. Duration of drug or device treatment.

viii. Concomitant medications allowed.

ix. Antidotes and treatments available.

x. Disposition of unused drug.

xi. The procedure by which the IND sponsor will monitor the protocol in accordance with 21 CFR 312.[3]

xii. In addition to the above list of requirements to be included in the protocol, the following additional items need to be submitted:

(1) A copy of the Investigator's Brochure and/or device manual and associated case report/data collection forms. If the study involved the testing of an approved drug for a new indication, provide a copy of the package insert.

(2) A signed Form FDA 1572 for IND Applications filed with the FDA, including the following information. Also, for non-FDA new drug protocols, the following information should be included in the protocol:

(a) Name, address and a statement of the qualifications for each investigator and the name of each sub-investigator working under the PI.

[3] Investigational New Drug Application procedures and requirements; for more information, go to http://www.fda.gov/cber/ind/21cfr312.pdf.

(b) Names and addresses of facilities to be used.

(c) Name and address of each IRB reviewing the protocol.

(3) For investigational devices, include your local IRB's assessment of the risk (nonsignificant or significant) of the investigational device you plan to use in your study. If the device poses significant risk to research subjects, specify the IDE number obtained from the FDA, the name of the sponsor, and the procedure by which the sponsor will monitor the protocol in accordance with 21 CFR 812.[4]

m. Disposition of Data: Describe where data will be stored, who will keep the data, how the data will be stored and the length of time data will be stored. Note that records of IND studies must be kept until 2 years after a New Drug Application is approved/issued, or for 2 years after the IND is withdrawn. Records required for IDE studies should be retained for 2 years following the date that the investigation is terminated or completed or the date that the records are no longer required for support of the pre-market approval application, whichever is sooner.

n. Modification of the Protocol: Describe the procedures to be followed if the protocol is to be modified, amended, or terminated before completion. Note that any modification to the protocol, consent form, and/or questionnaires, including a change to the PI, must be submitted to the local IRB for review and approval and then the HSRRB for second level review and approval. Address this procedure even if you do not anticipate making any modifications.

o. Departure from the Protocol: Describe procedures and notifications to be made in the event of deviations from the approved protocol to include both the local IRB and the HSRRB.

p. Roles and Responsibilities of Study Personnel: Briefly describe the duties of all study personnel to include each of the persons listed as investigators, research staff, consultants, and the Medical Monitor. Describe their roles in the research effort (e.g., Research Coordinator, 80%, recruit and consent subjects, maintain study records, administer study drug, take and record vital signs, enter data into computer database). Duties of the Medical Monitor, as defined in HSRRB Clause 8.02, are as follows:

> "A Medical Monitor must be assigned to Greater Than Minimal Risk protocols. The name and curriculum vitae of the Medical Monitor, who is someone other than the PI, must be provided. This individual should be a qualified physician who is not associated with the protocol, able to provide medical care to research subjects for conditions that may arise during the conduct of the study, and able to monitor subjects during the conduct of the study. In some studies it may be acceptable to have a qualified health care provider other than a physician serve as Medical Monitor, depending upon the type of risk that might occur in the study (e.g., a clinical psychologist). The Medical Monitor is required to review all unanticipated problems involving risk to volunteers or others, serious adverse events, and all volunteer deaths associated with the protocol and to provide an unbiased written report of the event. At a minimum the Medical Monitor should comment on the outcomes of the adverse event and relationship of the event to the protocol or test article. The Medical Monitor should also indicate whether he or she concurs with the details of the report provided by the PI. Reports for events determined by either the investigator or Medical Monitor to be possibly or definitely related to participation and reports of events resulting in death should be promptly forwarded to the HSRRB."

[4] Investigational Device Exemptions; additional information can be found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812&showFR=1.

The Medical Monitor will forward reports to the US Army Medical Research and Materiel Command, ATTN: MCMR-ZB-QH, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

2. Supporting Clinical Documents: No page limit. Information on requirements for the following supporting clinical documents can be found in the document titled "Research Involving Human Subjects and/or Anatomical Substances," which can be found under "Regulatory Document Forms" at https://cdmrp.org/programAnnouncements.cfm.

The first item in this section must be a table of contents listing of all documents included in this section. Provide the following in this section of the proposal:

- Manual of Operations and Procedures (if available).
- Consent/assent forms.
- IRB approvals (if any).
- Questionnaires.
- Survey Instruments.
- Patient Recruitment Brochures.
- Case Report Forms.
- Investigator's Brochure for proposals with INDs.
- Documentation that an IND application has been submitted to the FDA. It is required that all IND approvals will be obtained prior to September 30, 2005. Please note that no award will be made until IND approval is obtained. If IND approval is not received by September 30, 2005, the Government reserves the right to not fund the award.
- A plan for the study investigators to successfully complete institutional ethics training and a course in the conduct of clinical research in accordance with GCP within 1 year of initiation of the protocol.

G. Budget Information: Budget Information includes the Detailed Cost Estimate forms and Budget Justification. Budget Information is uploaded under the "Required Files" tab of the CDMRP eReceipt system.

1. Funding Restrictions: Funding for the FY05 Clinical Trial Award is for up to $750,000 per award in direct costs for up to 3 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, and travel to scientific meetings. The amount for travel to scientific meetings may not exceed $1,800 per investigator. Travel costs should also be included for a pre-award meeting and protocol workshop at Fort Detrick, Maryland and a reverse site visit in the Baltimore-Washington, DC area during the period of performance.

2. Detailed Cost Estimate Forms and Justifications Instructions: Budget is an important consideration in both peer and programmatic review, and applicants are cautioned to use discretion when making budgetary requests. Budgets will also be reviewed during award negotiations. Complete justification must be provided for expenses in all categories. The Detailed Cost Estimate form and Justification for your proposal must be uploaded as a PDF file, separate from the proposal.

The following section provides instructions for preparing the Detailed Cost Estimate form. All amounts entered should be in U.S. dollars.

a. Personnel:

i. Name: Starting with the PI, list the names of all participants who will be involved in the project during the initial budget period, regardless of whether salaries are requested. Include all collaborating investigators, research associates, individuals in training, and support staff. Only **ONE** person may be identified as the PI of the proposal.

ii. Role on Project: Identify the role of each individual listed on the project. Describe his or her specific functions in the "Justification" section of the Detailed Cost Estimate form.

iii. Type of Appointment (Months): List the number of months per year reflected in an individual's contractual appointment with the applicant organization. The DOD staff assumes that appointments at the applicant organization are full time for each individual. If an appointment is less than full time, e.g., 50%, note this with an asterisk (*) and provide a full explanation in the "Justification" section of the Detailed Cost Estimate form. Individuals may have split appointments (e.g., for an academic period and a summer period). For each type of appointment, identify and enter the number of months on separate lines.

iv. Annual Base Salary: Enter the annual institutional base salary for each individual listed for the project.

v. Percentage of Effort on Project: The qualifications of the PI and the amount of time that he or she and other professional personnel will devote to the research are important factors in selecting research proposals for funding. For each key staff member identified on the budget form, list the percentage of each appointment to be spent on this project.

vi. Salaries Requested: Enter the salaries in whole dollar figures for each position for which funds are requested. The salary requested is calculated by multiplying an individual's institutional base salary by the percentage of effort on the project.

vii. Fringe Benefits: Fringe benefits may be requested in accordance with institutional guidelines for each position, provided the costs are treated consistently by the applicant organization for all sponsors. Documentation to support the fringe benefits should be provided.

viii. Totals: Calculate the totals for each position and enter these as subtotals in the columns indicated.

b. Consultant Costs: Regardless of whether funds are requested, provide the names and organizational affiliations of all consultants.

c. Major Equipment/Intervention: It is the policy of the DOD that all commercial and non-profit recipients provide the equipment needed to support proposed research. In those rare cases where specific additional equipment is approved for commercial and non-profit organizations, such approved cost elements shall be separately negotiated. Moreover, it is expected that institutions will share 50% of the cost of equipment purchased for this research proposal when individual equipment costs are equal to or exceed $5,000.

It is anticipated that the intervention or device will be provided at no cost to the clinical trial. However, if costs are incurred, state the source of the intervention and provide a cost-sharing plan.

d. Materials, Supplies, and Consumables: A general description and total estimated cost of expendable equipment and supplies are required. Itemize supplies in separate categories (e.g., glassware, chemicals, radioisotopes). Categories in amounts less than $1,000 do not need to be itemized. If animals are to be purchased, state the species, strain (if applicable), and the number to be used. If human cell lines are to be purchased, state the source and the description.

e. Travel Costs: Travel costs for scientific and technical meetings not to exceed $1,800 per investigator and additional travel costs for a pre-award meeting and protocol workshop at Fort Detrick, Maryland and a reverse site visit in the Baltimore-Washington, DC area during the period of performance.

f. Research-Related Subject Costs: Itemize costs of subject participation in the research study. These costs are strictly limited to expenses specifically associated with the proposed study. The USAMRMC will not provide funds for ongoing medical care costs that are not related to a subject's participation in the research study.

g. Other Expenses: Itemize other anticipated direct costs such as publication and report costs, rental for computers and other equipment (provide hours and rates), and communication costs. Unusual or expensive items should be fully explained and justified. Estimate the costs of publishing and reporting research results, including direct charges for clerical preparation, illustrations, reprints, and distribution.

h. Subaward Costs: A description of services or materials that are to be awarded by subcontract or subgrant is required. For awards totaling $10,000 or more, provide the following specific information:

- Identification of the type of award to be used (e.g., cost reimbursement, fixed price);
- Identification of the proposed subcontractor or subgrantee, if known, and an explanation of why and how the subcontractor or subgrantee was selected or will be selected;
- Whether the award will be competitive and, if noncompetitive, rationale to justify the absence of competition; and
- The proposed acquisition price.

i. Indirect Costs (overhead, general and administrative, and other): The most recent rates, dates of negotiation, base(s), and periods to which the rates apply should be disclosed along with a statement identifying whether the proposed rates are provisional or fixed.

j. Total Costs for the Entire Proposed Period of Support (second page of the Detailed Cost Estimate form): Enter the totals under each budget category for all additional years of support requested and itemize these totals in the "Justification" section of the Detailed Cost Estimate form. Note with an asterisk (*) and explain any significant increases or decreases from the initial year budget. All amounts should be in U.S. dollars. Total costs for the entire proposed period of support should equal the amount previously entered online in the Proposal Information https://cdmrp.org/proposals.

3. Justification (third page of the Detailed Cost Estimate form): Each item in the budget should be clearly justified under the "Justification" section of the Detailed Cost Estimate form.

H. Regulatory Requirements: Completed and signed copies of the "Certificate of Environmental Compliance" and "Principal Investigator Safety Program Assurance Form" must be uploaded under the "Required Files" tab of the CDMRP eReceipt system as separate PDF files.

In addition, Regulatory Documents pertaining to research involving human subjects and/or human anatomical substances or cadavers must be submitted within the Clinical Protocol and Supporting Clinical Documents section of the proposal (see Subsections V.F.1 and V.F.2) as a required file. Any other Regulatory Documents should not be submitted with the proposal. Instead, the applicant should provide these documents to the USAMRMC only upon request.

I. USAMRAA Required Documents: The most current version of the institution's negotiated "Rate Agreement," the "Certifications and Assurances for Assistance Agreements," and the "Representations for Assistance Agreements" must be uploaded by the Contract Representative from the Sponsored Programs Office (or equivalent). These documents must be uploaded as separate PDF files under the Contract Representative's "My Profile" tab of the CDMRP eReceipt system prior to negotiations.

J. Submission Dates and Times: Proposals must be approved on the CDMRP eReceipt system by the Contract Representative at the applicant's institutional Sponsored Programs Office (or equivalent) by the deadline. If your proposal is either incomplete or not approved electronically before the deadline, it will not be considered for review. The eReceipt system will **not** accept data entry, file uploads, or approvals submitted after the **5:00 p.m. Eastern time December 7, 2004 deadline**.

The timeline for Clinical Trial Awards is:

Online Letter of Intent:	Expected by **November 5, 2004**
Online Proposal Information:	Prior to proposal submission
Proposal Submission/Approval Deadline:	**5:00 p.m. Eastern time December 7, 2004**
Peer Review:	January 2005
Programmatic Review:	March 2005
Request for Additional Documents:	As early as 2 weeks after the completion of programmatic review
Notification Letter:	April 2005
Pre-Award Meeting:	As early as May 2005
IND Approval:	Required before award start, but no later than September 30, 2005
Award Start Date:	Between May 2005 and September 2006

K. Electronic Submission Requirements: Electronic submission is required. Proposals will be accepted only as PDF files submitted through the CDMRP eReceipt system at https://cdmrp.org/proposals.

Several steps are critical to successful proposal submission:

- The Proposal Information must be submitted prior to submission of the proposal. Applicants are encouraged to begin this part of the submission process early.

- The e-mail address of a Contract Representative from the Sponsored Programs Office (or equivalent) must be included.
- Applicants are encouraged to coordinate early with their Sponsored Programs Office.
- The Contract Representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate on behalf of the institution is required to provide final electronic approval in order for the proposal to be complete and eligible for review.
- The eReceipt system will **not** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time December 7, 2004 deadline.
- Any supporting documentation that the applicant includes with the proposal must be incorporated into the PDF file prior to upload.
- Some items to be included in the proposal will need to be scanned. These items might include figures, tables, letters, or publications. All scanned documents, including figures, tables, and graphs, should be scanned at a resolution of 300-400 dpi or less.
- Budget Information includes the Detailed Cost Estimate form and the Budget Justification form. Budget Information must be uploaded under the "Required Files" tab of the CDMRP eReceipt system.
- The Regulatory Documents required at submission include a completed, signed Certificate of Environmental Compliance and a completed, signed Principal Investigator Safety Program Assurance form. These must be uploaded under the "Required Files" tab of the CDMRP eReceipt system. Please refer to Subsection VII.D for information regarding the submission of other Regulatory Documents required for this award.

VI. PROPOSAL REVIEW INFORMATION

A. Proposal Review and Selection Overview:

1. Process: The CDMRP uses a two-tier review process for proposal evaluation. The two tiers are fundamentally different. The first tier is a scientific peer review of proposals and clinical protocols against established criteria for determination of scientific merit. The second tier is a programmatic review of proposals that compares submissions to each other and recommends proposals for funding based on scientific merit as well as overall program goals.

2. Peer Review: Peer review is conducted by panels organized according to scientific discipline or specialty area. The primary responsibility of the peer review panels is to provide unbiased, expert advice on the scientific/technical merit and relevance of proposals and clinical protocols, based upon the review criteria published for each award mechanism.

Peer review panels are composed of a chair, scientific reviewers, consumer reviewers, and a nonvoting scientific review administrator. Scientific reviewers are selected based on their expertise and their experience with scientific peer review. Consumer reviewers are nominated by an advocacy or support organization and are selected on the basis of their leadership skills, commitment to advocacy, and interest in science. Consumers augment the peer review by bringing the patient perspective to the assessment of science and to the relevance of research.

The peer review summary statement is a product of scientific peer review. Each summary statement includes the peer review scores and an evaluation of the project and clinical protocols

as assessed by the peer reviewers according to the evaluation criteria published in this program announcement.

3. Programmatic Review: The second tier is programmatic review. Programmatic review is accomplished by the IP, which is composed of scientists, clinicians, and consumer advocates. The scientific members of the IP represent diverse disciplines and specialty areas, and the consumer members represent national advocacy constituencies. Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool. IP members primarily use the peer review summary statements and the proposal abstracts at programmatic review. SOWs may also be reviewed. Full proposals are not forwarded to programmatic review.

HBCU/MI proposals will be reviewed concurrently with all others in the same research area during scientific peer review, but may be evaluated separately during programmatic review. Consistent with the CDMRP's goal, recommendations for funding HBCU/MI submissions will be based upon scientific excellence and program relevance.

B. Review Criteria:

1. Peer Review:

a. Proposal: Clinical Trial Award proposals will be evaluated according to the following criteria:

- **Trial Design:** Are the conceptual framework, design, methods, and analyses adequately developed and well integrated? Is there adequate laboratory and other preclinical evidence to support the clinical feasibility and promise of the approach? Does the applicant provide the background and a clear scientific rationale for the trial? Have the logistical aspects of the proposed clinical trial been appropriately addressed (e.g., plans for communication, real-time data transfer, and standardization of procedures among collaborating institutions, as appropriate)? Is there sufficient availability of subjects for the clinical trial, and are the prospect of their participation and the likelihood of subject attrition addressed? Is the recruitment schedule reasonable?
- **Clinical Relevance:** Does the study address an important problem(s) related to the treatment, diagnosis, detection, or prevention of prostate cancer? If the aims of the proposal are achieved, are they likely to have a substantial clinical impact on prostate cancer treatment, diagnosis, detection, or prevention?
- **Intervention or Device:** Is the proposed intervention or device to be tested in the clinical trial adequately described and available? Is the intervention or device novel? Has the applicant provided evidence of the availability and purity of the substance to be used in the clinical trial? Are there assurances that interventions to be used are available? If a drug, biologic, or device has been budgeted, is there a cost-sharing plan?
- **Statistical Plan:** Is a clear statistical plan, including sample size projections and power analysis, outlined in the proposal? Is the appropriate statistical expertise represented on the research team?
- **Principal Investigator and Personnel:** Does the PI have expertise in prostate cancer and experience in clinical trials? Is the PI appropriately trained to carry out this work? Are the other scientific personnel well qualified to participate in the project and do they complement the experience of the PI? Is there representation from all the areas of expertise needed to conduct the clinical trial successfully?

- **Environment:** Is there evidence for an appropriate clinical setting and the availability of institutional resources to support the study at each participating center? Are letters of institutional commitment included from each participating institution? Is there an intellectual property plan that is agreed upon by all participating centers?
- **Budget:** Is the budget appropriate for the research proposed? Is there evidence of adequate funding from this funding agency and other funding agencies, as appropriate, to support completion of this clinical trial?

b. Protocols: Clinical Trial Award protocols will be evaluated according to the following criteria:

- **Protocol Preparation:** Are the key elements of the clinical protocol (specific aims, methods, analyses, sample size, etc.) consistent with the information provided in the main body of the proposal?
- **Research Question:** Is the literature review thorough and up-to-date? Are the aims of the study clear and concise? Is the conceptual framework of the project adequately developed and well integrated with the project's design, methods, and analyses?
- **Protocol Design:** Is the proposed methodology described in sufficient detail? Are the recruitment, informed consent, subject screening, and subject randomization processes appropriate and adequately described? Is the research the research intervention or activity that the patient will experience fully described? If the proposal uses an IND or IDE, is it fully described?
- **Feasibility:** Is there adequate evidence to support the clinical feasibility and promise of the approach? Have the availability of subjects for the clinical trial, the prospect of their participation, and the likelihood of subject attrition been addressed? Is the recruitment schedule reasonable? Has the applicant provided evidence of the availability and quality of the substance to be used in the clinical trial? Have preliminary institutional IRB approval(s) for the clinical protocol and consent form been obtained at the highest level possible? If applicable, has an IND been submitted for the intervention? Have the FDA regulatory components of an IND trial been adequately addressed?
- **Personnel and Environment:** Do the personnel described as having significant involvement in the research study match those listed in the proposal? Are the roles and responsibilities of all study personnel clearly described? Are the clinical team, laboratories, and setting appropriate and adequate to support the trial?
- **Statistical Plan:** Is a clear statistical plan, including sample size projections and power analysis, provided? Are all data collection procedures to be used in conducting the study adequately described and appropriate? Is the data analysis plan consistent with the study objectives?
- **Ethics and/or Regulatory Issues:** Are ethical considerations and information privacy appropriately addressed? Is there an adequate assessment of the risks and benefits of participation in the clinical trial? Is there a plan for the study investigators to complete an ethics training program and a course in the conduct of clinical research in accordance with GCP within 1 year of protocol initiation? Have potential adverse events been defined for the intervention, and are there named agencies or offices to be notified in this event? Is there a plan for data disposition during and after the clinical trial? Are procedures in place for protocol modifications during the course of the study? If a Medical Monitor is required, is he or she appropriately qualified?

2. Programmatic Review: The ratings and evaluations of scientific peer review panels are primary factors in programmatic review. The IP also considers other criteria to structure the PCRP's broad portfolio. The criteria the IP uses to make funding recommendations are:

- Ratings and evaluations of the scientific peer review panels,
- Programmatic relevance,
- Relative innovation,
- Program portfolio balance, and
- Budget.

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

VII. AWARD ADMINISTRATION INFORMATION

A. Award Notices: After the two-tier evaluation process is completed, every applicant will receive notification of the award status of his or her proposal and a copy of the peer review summary statement. Applicants can expect to be notified of the agency's decision by April 2005.

B. Administrative Requirements: All awards are made to organizations, not individuals. A PI should submit a proposal through, and be employed by or affiliated with, a university, college, non-profit research institute, commercial firm, or government agency (including military laboratories) in order to receive support. To be eligible for award, a prospective recipient should meet certain minimum standards pertaining to institutional support, financial resources, prior record of performance, integrity, organization, experience, operational controls, facilities, and conformance with safety and environmental statutes and regulations (Office of Management and Budget Circular A-110 and DOD Grant and Agreement Regulations). Any organization requesting receipt of an award from this announcement must be registered in the Central Contractor Registration (CCR) database. Access to the CCR online registration is through the CCR homepage at http://www.ccr.gov.

Transferring the grant from the original institution will not be permitted for the Clinical Trial Award. PI relocations may be permitted under certain conditions; the PI must inform USAMRAA of the pending relocation to discuss available options.

C. Award Negotiation: Award negotiation consists of discussions, reviews, and justifications of critical issues involving USAMRAA. A representative from USAMRAA will contact the Contract Representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate contracts and grants at the applicant's institution. As part of the negotiation process, additional documentation and justifications related to the proposed SOW and associated budgets may be required.

Note that the award start date will be determined during the negotiation process.

For Clinical Trial Award recipients, IND approval must be received before an award can be made. If IND approval is not received by September 30, 2005, the Government reserves the right to not fund the award.

D. Regulatory Review:

1. Overview: Concurrent with the USAMRAA negotiations, the Office of Surety, Safety and Environmental will review the Certificate of Environmental Compliance, and Principal Investigator Safety Program Assurance form submitted with the proposal. The USAMRMC RCQ office will review documents related to research involving animal use, research involving human subjects/anatomical substance use, and cadaver use submitted upon request to ensure that Army regulations are met. Applicants who are approved for funding will be required to attend a pre-award meeting and protocol workshop at Fort Detrick, Maryland.

2. Certificate of Environmental Compliance: The Certificate of Environmental Compliance must be submitted with the proposal. If multiple research sites/institutions are funded in your proposal, then a Certificate of Environmental Compliance for each site will be requested at a later date.

3. Safety Program Documents: The Principal Investigator Safety Program Assurance form must be submitted with the proposal.

A Facility Safety Plan is also required and will be requested at a later date. However, your institution may already have an approved Facility Safety Plan. To determine the status of approval, check the USAMRMC website at https://mrmc-www.army.mil/index.asp?EntryURL=/crprcqsohdfsplan.asp. If your institution is not listed on the aforementioned website, contact your Facility Safety Director/Manager to initiate completion of the institution-based Facility Safety Plan. Specific requirements for the Safety Program Plan can be found at https://mrmc-www.army.mil/docs/rcq/FY02FSPAppendix.doc.

If multiple research sites/institutions are funded in your proposal, then a Facility Safety Plan for each site/institution not listed in the aforementioned website will be requested at a later date.

4. Research Involving Animal Use: Animal use documents should not be submitted with the proposal and will be requested at a later date. Specific requirements for research involving animals can be found at https://mrmc-www.army.mil/docs/rcq/FY02AnimalAppendix.doc.

5. Research Involving Human Subjects/Anatomical Substances/Cadavers: (See Subsections V.H and V.I for information pertaining to the submission of human subjects and/or human anatomical substances documents or cadavers.) In addition to local IRB approval to conduct research involving human subjects and/or anatomical substances or cadavers, a second tier of IRB review and approval is also required by the DOD. This second review is conducted by the HSRRB, which is administered by the USAMRMC RCQ office. The HSRRB is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed and will require information in addition to that supplied to the local review board. For example:

- Intent to Benefit. In the development of a research protocol for submission to the DOD, the applicant must specifically address, if applicable, the Intent to Benefit. An individual not legally competent to consent (e.g., minors) may not be enrolled in DOD-sponsored research unless the research is intended to benefit each and every subject enrolled in the study. Applicants should be aware that this law makes placebo-controlled clinical trials problematic because of the 'intent to benefit' requirement whenever participation is sought of subjects from whom consent must be obtained by the legally authorized representative.

- The DOD considers cell lines of human origin to be human anatomical substances. Use of these cell lines is subject to HSRRB review and approval.

Specific requirements for research involving human subjects, human anatomical substances, and/or cadavers can be found at https://mrmc-www.army.mil/docs/rcq/HSAppendix19Feb02.pdf. An informed consent form template can be located at https://mrmc-www.army.mil/docs/rcq/consentform_template.pdf.

6. Award/Regulatory Approval: Please note that each award mechanism has specific requirements regarding human subjects and animal use.

Once an award is made, the applicant may not use, employ, or subcontract for the use of any human subjects, human anatomical substances, cadavers, or use of laboratory animals without express written approval from the applicable USAMRMC RCQ office. USAMRMC RCQ will forward these express written approvals directly to the applicant with a copy furnished to the institution's Sponsored Programs Office (or equivalent).

E. Reporting: All research awards will require the timely delivery of several reports during the research effort. Reporting requirements consist of an annual report (for each year of research except the final year) that presents a detailed summary of scientific issues and accomplishments and a final report (submitted in the last year of the award period) that details the findings and issues for the entire project.

VIII. OTHER INFORMATION

A. Disclosure of Proprietary Information outside the Government: By submission of a proposal, the applicant understands that proprietary information may be disclosed outside the Government for the sole purpose of technical evaluation. The USAMRMC will obtain a written agreement from the evaluator that proprietary information in the proposal will only be used for evaluation purposes and will not be further disclosed or utilized. Funded proposals may be subject to public release under the Freedom of Information Act; proposals that are not selected for funding will not be subject to public release.

B. Government Obligation: Applicants are cautioned that only an appointed Contracting/Grants Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government to fund preparation of a proposal or to support research should be inferred from discussions with a technical project officer. Applicants who, or organizations that, make financial or other commitments for a research effort in the absence of an actual legal obligation signed by the USAMRAA Contracting/Grants Officer do so at their own risk.

C. Information Service: Offerors may use the technical reference facilities of the National Technical Information Service, 5285 Port Royal Road, Springfield, Virginia, 22161, for the purpose of surveying existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. To the extent practical, all other sources should also be consulted for the same purpose.

D. Inquiry Review Panel: Applicants can submit a letter of inquiry to the USAMRMC in response to funding decisions made for a given proposal. Members of the CDMRP staff, USAMRMC Judge Advocate General staff, and USAMRAA Grants Officers constitute an Inquiry Review Panel and review each inquiry to determine whether factual or procedural errors in either peer or programmatic review have occurred, and if so, what action should be taken.

E. Title to Inventions and Patents: In accordance with the Bayh-Dole Act (35 USC 200 et seq.[5]), title to inventions and patents resulting from such federally funded research may be held by the grantee or its collaborator, but the U.S. Government shall, at a minimum, retain nonexclusive rights for the use of such inventions. An investigator must follow the instructions in the assistance agreement concerning license agreements and patents.

F. J-1 Visa Waiver: It is the responsibility of the awardee to ensure that the research staff is able to complete the work without intercession by the DOD for a J-1 Visa Waiver on behalf of a foreign national in the United States under a J-1 Visa.

[5]Title 35, United States Code, Section 200 et seq.

IX. ACRONYM LIST

AVI	Audio Video Interleave
CCR	Central Contractor Registration
CDMRP	Congressionally Directed Medical Research Programs
CFDA	Catalog of Federal Domestic Assistance
cGMP	Current Good Manufacturing Practice
DOD	Department of Defense
FDA	Food and Drug Administration
FY	Fiscal Year
GCP	Good Clinical Practices
HBCU/MI	Historically Black Colleges and Universities/Minority Institutions
HSRRB	Human Subjects Research Review Board
IDE	Investigational Device Exemption
IND	Investigational New Drug
IP	Integration Panel
IRB	Institutional Review Board
M	Million
MB	Megabyte
MPEG	Moving Picture Experts Group
PCRP	Prostate Cancer Research Program
PDF	Portable Document Format
PI	Principal Investigator
RCQ	Regulatory Compliance and Quality
SOW	Statement of Work
USAMRAA	US Army Medical Research Acquisition Activity
USAMRMC	US Army Medical Research and Materiel Command
USC	United States Code
WAV	Wave