# Appendix A
## Fiscal Year 2002 Prostate Cancer Research Program Announcement
## Electronic Letter of Intent

All applicants considering submission of a proposal in response to this program announcement are requested to submit an electronic Letter of Intent no later than 2 weeks prior to the award mechanism's receipt deadline. This form can be found on the Congressionally Directed Medical Research Programs web site at http://cdmrp.army.mil/funding/02pcrp1

# Appendix B

## Proposal Preparation

## Table of Contents

# Proposal Preparation

## 1. Who May Apply

Eligible institutions include for-profit, non-profit, public, and private organizations. Examples include universities, colleges, hospitals, laboratories, companies, and agencies of local, state, and federal governments. All individuals, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by, or affiliated with, an eligible institution. The U.S. Army Medical Research and Materiel Command (USAMRMC) is especially interested in receiving applications from Historically Black Colleges and Universities/Minority Institutions (HBCU/MI).

Please refer to sections on specific award mechanisms for additional eligibility criteria.

Investigators are cautioned that awards are made to institutions. Should the Principal Investigator (PI) of a funded project leave the recipient institution, both the PI and an official of the recipient institution should contact the U.S. Army Medical Research Acquisition Activity (USAMRAA) awarding office prior to the PI leaving the recipient institution to discuss options available for continued support of the research project.

**Historically Black Colleges and Universities/Minority Institutions**

A goal of the Department of Defense (DOD) is to allocate funds for the Congressionally Directed Medical Research Programs' (CDMRP's) peer reviewed research to fund proposals from HBCU/MI. This provision is based upon guidance from Executive Orders[1] and is intended to "advance the development of human potential, provide quality education, increase opportunities to participate in and benefit from Federal Programs and strengthen the capacity of targeted institutions." An institution's minority status is established by the Department of Education (DOEd). Proposals submitted to the DOD are assigned HBCU/MI status if they are so designated by the DOEd on the date that the program announcement is released. The DOEd list is posted on the CDMRP web site at http://cdmrp.army.mil/spp under Minority Institutions. Any individual, regardless of ethnicity, nationality, or citizenship status, may apply for funding as long as they are employed by, or affiliated with, an eligible institution.

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 when award recommendations are determined. Consistent with the CDMRP's goal, recommendations for funding HBCU/MI submissions will be based upon scientific excellence and program relevance.

[1] Executive Orders 12876, 12900, and 13021

## 2. Proposal Acceptance Criteria

Please follow the compliance guidelines listed below when preparing your proposal. **Note that all proposals must be converted into an electronic PDF (Portable Document Format) file for electronic submission. Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.**

Compliance guidelines have been designed to ensure the presentation of all proposals in an organized and easy-to-follow manner in order to assist scientific reviewers responsible for reviewing proposal merit. Scientific peer reviewers will expect to see a consistent, prescribed format for each proposal. Nonadherence to format requirements (such as font size, margins, line spacing, proposal components out of order) 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 poorer global priority score in scientific peer review. **Excess pages may result in administrative rejection prior to scientific peer review.**

For the preparation of proposals for PDF submission, it is required that the instructions in this section be followed carefully. The proposal must be clear and legible and conform to the following format, font size, spacing margin, and printing guidelines:

- Type Font: 12 point, 10 pitch.
- 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.
- Type Color: Black type for all graphs, diagrams, tables, and charts. The proposal should contain only material that can be photocopied. Investigators are cautioned that color graphs or photographs may not reproduce in subsequent photocopies. Therefore, submission of color figures, tables, graphs, or photographs is not recommended.
- 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. (Note to international applicants: The text of the proposal must not exceed 7.0 x 10.0 inches [approximately 19 cm x 25.5 cm].)

To assist applicants, the following example is included.

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## 3. Resubmissions and Duplicate Submissions

Resubmission of a proposal reviewed in a previous fiscal year is acceptable. For fiscal year 2002 (FY02), proposals that have been declined for funding in a previous year may be resubmitted to the PCRP through a new resubmission process that allows the applicant to directly address the peer and programmatic review critiques. Resubmitted/amended proposals should meet the requirements for the appropriate award category in this program announcement and adhere to this year's format guidelines. See Section 11 of this appendix for additional resubmission directions.

Despite these new measures, the applicant should be cautioned that the year-to-year status of funding for the Prostate Cancer Research Program (PCRP) does not permit the establishment of standing panels for scientific peer review. In addition, as described in the Overview (Section I), the programmatic focus of the Integration Panel and the PCRP may change from year to year. Therefore, the submission of a revised proposal does not guarantee any funding advantage or an improved global priority score.

**Submission of the same research project to the FY02 PCRP under different award mechanisms is not allowed, and all such duplicate submissions may be administratively withdrawn. This includes duplicate submissions under different award mechanisms by different PIs. The Government reserves the right to reject any proposal.**

## 4. Proposal Information

Please complete the Proposal Information as described at http://cdmrp.org/proposals. Instructions will be available through the web site by April 15, 2002. See Section 6, page iv of the Foreword or Part 22 of this Appendix (Proposal Submission) for more information regarding the complete electronic submission process.

## 5. Title/Referral Page – No page limit

Please complete the Title/Referral Page, which can be downloaded from the CDMRP web site at http://cdmrp.army.mil/funding/reposit Complete each section as described:

a. Proposal title (up to 160 characters).

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

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

d. Award mechanism.

e. 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. Also, list specific keywords and descriptive technical terms that would best describe the technical aspects of the project (e.g., cell signaling, apoptosis, angiogenesis, drug delivery systems, gene therapy, x-ray crystallography, genetic counseling, quality of life, nuclear medicine, immunology, clinical oncology, nutrition).

f. Conflicts of interest: Every effort is made to avoid real and apparent conflicts of interest during the peer review process. To assist the staff in this regard, list the names of all scientific participants in the proposal including the PI, co-investigators, research associates, research assistants, consultants, collaborators, and subcontractors. In addition, list the names of other researchers 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 role(s) on the proposed project or perceived conflicts of interest.

# Title/Referral Page
**No Page Limit**

a. Proposal title (up to 160 characters)

| |
|---|
| |

b. Proposal log number

| |
|---|
| |

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

| |
|---|
| |

d. Award mechanism

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| |

e. Keyword descriptive technical terms

| |
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| |

f. Conflicts of interest: Include the following information (no page limit)

| Name | Institutional Affiliation(s) | Role(s) on Proposed Project or Perceived Conflicts of Interest |
|---|---|---|
| | | |
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| | | |

## 6. Table of Contents – Start section on a new page – 1-page limit

Prepare a Table of Contents, with page numbers, using the outline provided in the Proposal Preparation section under each award mechanism. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI's name (last name, first name, middle initial) and proposal log number (this will be automatically provided when a draft of the electronic Proposal Information is saved).

## 7. Checklist for Proposal Submission (Instructions)

The Checklist for FY02 PCRP Proposal Submission found on page B-8 must be completed and submitted with the electronic version of your proposal. Place it immediately after the Table of Contents.

*Complete and place this form immediately after the Table of Contents to confirm that all components are included in your application.*

## Checklist for FY02 PCRP Proposal Submission

| Yes | No | |
|---|---|---|
| ☐ | ☐ | Proposal Information completed |
| ☐ | ☐ | Title/Referral Page |
| ☐ | ☐ | Table of Contents |
| ☐ | ☐ | Checklist for FY02 PCRP Proposal Submission |
| ☐ | ☐ | Structured Technical Abstract (1-page limit) |
| ☐ | ☐ | Lay Abstract (1-page limit) |
| ☐ | ☐ | Statement of Work (2-page limit) |
| ☐ | ☐ | Proposal Relevance Statement (1-page limit) |
| ☐ | ☐ | Proposal Resubmission (if applicable) |
| ☐ | ☐ | Proposal Resubmission Statement (2-page limit) |
| ☐ | ☐ | Previous Submission Summary Statement (no page limit) |
| ☐ | ☐ | Proposal Body **(adhere to page limits for the individual mechanism)** |
| ☐ | ☐ | Abbreviations (1-page limit) |
| ☐ | ☐ | References (no page limit) |
| ☐ | ☐ | Biographical Sketches (3-page limit per individual) |
| ☐ | ☐ | Principal Investigator |
| ☐ | ☐ | Collaborating investigators and other key personnel |
| ☐ | ☐ | Existing/Pending Support (no page limit) |
| ☐ | ☐ | Facilities/Equipment Description (no page limit) |
| | | *Administrative Documentation*: |
| ☐ | ☐ | List of items included in this section |
| ☐ | ☐ | Statement of Eligibility form (Postdoctoral Traineeship, Health Disparity Training-Prostate Scholar Award, and New Investigator only) |
| ☐ | ☐ | Letter of Eligibility (Health Disparity Research-Prostate Scholar Award only) |
| ☐ | ☐ | Letters of support from collaborating individuals and/or institutions (all awards) |
| ☐ | ☐ | Detailed Cost Estimate (no page limit) |
| ☐ | ☐ | Total cost estimate matches Proposal Information, item 4 |
| ☐ | ☐ | Instruments (no page limit) |
| ☐ | ☐ | List of documents included in Instruments Section (all awards) |
| ☐ | ☐ | Publications and/or Patent Abstracts (5-document limit) |

**NOTE: Exceeding page limits may result in proposal rejection prior to peer review. Submit only materials specifically requested or required in this program announcement. Submission of additional materials may be construed as an attempt to gain an unfair advantage.**

## 8. Proposal Abstracts – Start each abstract on a new page – 1 page each

Both a 1-page structured technical abstract and a 1-page lay (nontechnical) abstract are required. Each proposal abstract page should contain the title of the proposal and the name of the PI. Abstracts must be submitted as part of the proposal. **Do not include figures or tables in either abstract.**

These abstracts are vitally important to the review of the proposal. **Programmatic review is based upon the Integration Panel's review of these two abstracts as part of the peer review summary statements; therefore, it is paramount that the investigator submits abstracts that fully describe the proposed work.** Sample abstracts are included in Appendix D of this program announcement.

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, significance of the proposed work to the program's goals, specific aims of the study, and study design.

Please use the outline below for preparing the structured technical abstract.

a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work.

b. Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.

c. Specific Aims: State concisely the specific aims of the study.

d. Study Design: Briefly describe the study design.

e. Relevance: Provide a brief statement explaining the potential relevance of the proposed work to the program's goals. For example, how the study will prevent or improve the detection or treatment of the disease.

The lay abstract is intended to communicate the purpose of, and rationale for, the study to the non-scientific community. It should be composed in a way to make the scientific objectives and rationale for the proposal understandable to non-scientifically trained readers. The lay abstract should not duplicate the technical abstract.

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

## 9. Statement of Work – Start section on a new page – 2-page limit

The Statement of Work (SOW) is a concise restatement of the research proposal that outlines and establishes the PI performance expectations and timeline for which the USAMRMC will provide financial support. Although some allowance is made for problems encountered and uncertainties that are part of research, the PI is expected to meet the provisions and milestones in the SOW.

The SOW should be a series of relatively short statements that outline, step-by-step, how each of the major goals or objectives of the proposed research/services will be accomplished. As appropriate, the SOW should:

a. Describe the work to be accomplished as tasks (tasks may relate to specific aims),

b. Identify the timeline and milestones for the work over the period of the proposed effort,

c. Indicate the numbers of research subjects (animal or human) for each task,

d. Identify methods, and

e. Identify products/deliverables for each phase of the project.

The SOW must not exceed 2 pages of single-spaced typing. Several sample SOWs are included in Appendix D of this program announcement.

## 10. Proposal Relevance Statement – Start section on a new page – 1-page limit

In the Proposal Relevance Statement, the investigator should describe how the proposed research/services are pertinent to one or more critical issues of the disease.

## 11. Proposal Resubmission Statement – 2-page limit

Proposals that have been declined for funding in a previous year may be resubmitted to the PCRP. Resubmitted/amended proposals should meet the requirements for the appropriate award category in this program announcement and adhere to this year's format guidelines. Revised proposals to the PCRP in FY02 are allowed to address the issues identified in the previous summary statement of the unfunded application in a 2-page section. This section should be placed after the Proposal Relevance Statement and before the proposal body. The revision section should highlight and summarize all deletions, additions, and other changes, and be responsive to all aspects of the critique from the previous peer and programmatic reviews. Reference should be made to any new preliminary data included. Resubmissions that have not clearly taken into account the major comments or concerns resulting from the prior peer and programmatic reviews will be reviewed accordingly. A copy of the summary statement from the unfunded application should also be included following the resubmission statement.

Despite these new measures, the applicant should be cautioned that the year-to-year status of funding for the PCRP does not permit the establishment of standing panels for scientific peer review. Therefore, the submission of a revised proposal does not guarantee any funding advantage or an improved global priority score

## 12. Proposal Body – Start section on a new page

Each award mechanism has specific instructions for the description of the project and page limits. Investigators should refer to the specific evaluation criteria listed under the award mechanism to which they are applying to ensure that the necessary information is included.

## 13. Abbreviations – Start section on a new page – 1-page limit

Provide a glossary of all acronyms, abbreviations, and symbols used.

## 14. 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).

## 15. Biographical Sketches – 3-page limit per investigator

Biographical sketches should be included for each of the key personnel listed on the budget page, including collaborating investigators and support staff. Each biographical sketch must not exceed 3 pages. The Biographical Sketch form can be found in Appendix E or downloaded from the CDMRP web site at http://cdmrp.army.mil/funding/default

## 16. Existing/Pending Support – 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. Proposals submitted under this program announcement should not duplicate other funded research projects. If no support exists, state "none."

## 17. 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 acquisition or available for use at no cost to the USAMRMC. Indicate if government-owned facilities or equipment are proposed for use.

## 18. Administrative Documentation – No page limit

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

Provide letter(s) from proposed collaborating individuals or institutions confirming collaborative efforts that are necessary for the project's success. Other support documentation also may be required within specific award categories. Please follow specific instructions in each award mechanism.

**Note: This section is not for additional data, figures, or other similar information.** Support documentation **will not** be accepted separately from the electronic proposal submission.

**All administrative documentation must be incorporated into the electronic PDF version of your proposal.** All documents or letters requiring signatures must be signed and then scanned into the submitted proposal. Help lines will be available by April 15, 2002 to answer specific questions regarding the preparation of proposals for electronic submission, or the process of electronic submission. The help line phone numbers will be provided on two web sites: the CDMRP web site (http://cdmrp.army.mil) and the proposal submission web site (http://cdmrp.org/proposals). Alternately, help can be obtained by email, at help-proposals-cdmrp@cdmrp.org

## 19. Detailed Cost Estimate – No page limit

Budget is a key consideration in both scientific peer and programmatic review; applicants are cautioned to use discretion in budget requests. In addition, budgets will also be reviewed during award negotiations. Use the Detailed Cost Estimate form to prepare a detailed cost estimate of the proposed research/services. This form can be found in Appendix F or downloaded from the CDMRP web site at http://cdmrp.army.mil/funding/default. The cost of preparing proposals in response to this program announcement is not considered an allowable direct charge to any resultant award.

**For all DOD-funded research involving human subjects, medical care for research-related injuries must be provided at no cost to the subject.** Many institutions and states provide for this medical care as part of their liability insurance. If not, investigators should plan on budgeting for such costs. The institution business office can assist applicants with budgeting for this requirement. See part 7 of Appendix F (Detailed Cost Estimate) for more details.

## 20. Instruments – No page limit

Include an appropriately titled page listing the documents you have in this section. Questionnaires, survey instruments, or clinical protocols that apply to the proposal should be included in this section.

## 21. Publications and/or Patent Abstracts – 5-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. Submit only material specifically requested or required in this program announcement. Submission of unrequested material may be construed as an attempt to gain a competitive advantage and will be removed.**

**These documents must be incorporated into the electronic PDF version of your proposal**
Help lines will be available by April 15, 2002 to answer specific questions regarding the preparation of proposals for electronic submission, or the process of electronic submission. The help line phone numbers will be provided on two web sites: the CDMRP web site (http://cdmrp.army.mil) and the proposal submission web site (http://cdmrp.org/proposals). Alternately, help can be obtained by email, at help-proposals-cdmrp@cdmrp.org

## 22. Proposal Submission

**Electronic submission is required.** No paper copy submissions will be accepted.

Proposals will be submitted electronically at http://cdmrp.org/proposals. The web site will be available for proposal submission by April 15, 2002. One electronic PDF version of the proposal is required and will count as the official proposal submission. The electronic PDF version must be uploaded/submitted through the Internet by an authorized Administrative Representative from the Sponsored Programs Office (or equivalent) of your organization **no later than 11:59 p.m. (applicant's local time)** on either **May 14** or **May 16, 2002** and must be accompanied by the Proposal Information, as described below. Consult the timelines located in the Foreword (page iii) or specific award mechanism sections for the exact deadline date of electronic proposal submission.

Several steps are critical for successful electronic submission of your proposal.

1. The applicant is required to submit Proposal Information (referred to in previous years as "Proposal Cover Booklet") online at http://cdmrp.org/proposals, to include the e-mail address of an Administrative Representative from the Sponsored Programs Office who is authorized to conduct negotiations on the applicant's behalf. **The Proposal Information must be submitted prior to submission of the proposal. We encourage applicants to begin this part of the submission process early.**

2. Once the applicant has submitted the Proposal Information, the Administrative Representative from the Sponsored Programs Office will receive an e-mail notification that the Proposal Information is ready for his or her review.

3. Applicants will need to provide the Administrative Representative with an electronic copy of the proposal. Applicants are encouraged to coordinate early with their Sponsored Programs Office.
4. The Administrative Representative is required to provide final approval of the Proposal

Information and then to upload/submit the proposal file in PDF. Please note that the website does not allow applicants to upload/submit their proposals directly. **Proposals may ONLY be uploaded/submitted by the Administrative Representative from the Sponsored Programs Office and this can be done ONLY after he or she has approved the Proposal Information.**

Please note that all proposals must be submitted electronically to this program; printed supplemental materials will not be accepted. Any supporting documentation that the applicant wishes to include with the proposal must be scanned and incorporated into the PDF file prior to upload/submission. Proposal Information must be completed online and the PDF version of the proposal uploaded/submitted through the CDMRP web site no later than **11:59 p.m. (applicant's local time) on the due dates specified on page iii for the specific mechanism for which you are applying.** Detailed instructions for electronic submissions will be available by April 15, 2002 at http://cdmrp.org/proposals.

## 23. Submission Deadlines

**The submission deadline for all proposals requested in this program announcement is 11:59 p.m. (applicant's local time) on either May 14 or May 16, 2002; please check the Foreword (page iii) or the specific award mechanism for the exact date of submission. The electronic PDF version of your proposal must be sent through the Internet by the sponsored programs office (or equivalent) of your organization by that time.**

If your proposal is submitted electronically after 11:59 p.m. (applicant's local time) on the deadline date listed for the mechanism to which it was submitted, it may not be considered for review.

## 24. Regulatory Compliance and Quality Requirements

RCQ documents (Certificate of Environmental Compliance, Research Involving Human Subjects and/or Anatomical Substances, Research Involving Animals, and Safety Program Plan) should not be included with the submitted proposal; instead, these documents should only be provided by the PI to the USAMRMC upon request.

Institutional Review Board (IRB) documentation should be submitted and pending approval from the applicant's local IRB before the programmatic review of proposals is conducted.

All documents related to RCQ should be available on the CDMRP web site by April 2002.

# Appendix C

## Proposal Information

The Proposal Information and instructions for completing it will be available at the Congressionally Directed Medical Research Programs-related web site http://cdmrp.org/proposals. The web site will be available for proposal submission by April 15, 2002. One electronic PDF version of the proposal is required and will count as the official proposal submission. Applicants should refer to sections on individual award mechanisms and Appendix B for appropriate submission requirements.

Several steps are critical for successful electronic submission of your proposal.

1. The applicant is required to submit Proposal Information (referred to in previous years as "Proposal Cover Booklet") online at http://cdmrp.org/proposals, to include the email address of an Administrative Representative from the Sponsored Programs Office who is authorized to conduct negotiations on the applicant's behalf. **The Proposal Information must be submitted prior to submission of the proposal. We encourage applicants to begin this part of the submission process early.**

2. Once the applicant has submitted the Proposal Information, the Administrative Representative from the Sponsored Programs Office will receive an email notification that the Proposal Information is ready for his or her review.

3. Applicants will need to provide the Administrative Representative with an electronic copy of the proposal. Applicants are encouraged to coordinate early with their Sponsored Programs Office.

4. The Administrative Representative is required to provide final approval of the Proposal Information and then to upload/submit the proposal file in PDF. Please note that the web site does not allow applicants to upload/submit their proposals directly. **Proposals may ONLY be uploaded/submitted by the Administrative Representative from the Sponsored Programs Office and this can be done ONLY after he or she has approved the Proposal Information.**

Please note that all proposals must be submitted electronically to this program; printed supplemental materials will not be accepted. Any supporting documentation that the applicant wishes to include with the proposal must be scanned and incorporated into the PDF file prior to upload/submission. Proposal Information must be completed online and the PDF version of the proposal uploaded/submitted through the web site (http://cdmrp.org/proposals) no later than **11:59 p.m. (applicant's local time) on the due dates specified on page iii of the Foreword for the specific mechanism for which you are applying.** Detailed instructions for electronic submissions will be available at http://cdmrp.org/proposals.

Help lines will be available by April 15, 2002 to answer specific questions regarding Proposal Information and the preparation of proposals for electronic submission, or the process of

electronic submission. The help line phone numbers will be provided on two web sites: the CDMRP web site (http://cdmrp.army.mil) and the proposal submission web site (http://cdmrp.org/proposals). Alternately, help can be obtained by email, at help-proposals-cdmrp@cdmrp.org

# Appendix D

## Sample Abstracts and Statements of Work

## TECHNICAL ABSTRACT

Targeting the Target of Rapamycin for Prostate Cancer Therapy
Robert T. Abraham, Ph.D.

**Background:** Rapamycin is a clinically useful immunosuppressive agent that also displays potent but highly cell type-specific, antiproliferative activities against certain types of tumors, most notably prostate cancer (PCa). A rapamycin analog, CCI-779 (Wyeth-Ayerst), has successfully completed Phase I clinical cancer trials and will soon move into Phase II trials with PCa a priority disease target. The cellular effects of rapamycin are mediated through a unique pharmacological mechanism that results in the specific inhibition of a novel signaling kinase, which we have named the mammalian target of rapamycin (mTOR). The clinical application of rapamycin greatly increases the importance of understanding the regulation and function of mTOR as rapamycin/CCI-779 moves forward in clinical cancer trials. Accumulating evidence indicates that the phosphoinositide 3-kinase (PI3K)-dependent signaling pathway plays a central role as an upstream regulator of mTOR function in mitogen-stimulated cells. The linkage between the PI3K pathway and PCa has become compelling, as these cancers frequently acquire mutations that result in deregulated signaling through PI3K and/or its downstream protein kinase, AKT. The known functions of mTOR are consistent with the prediction that this protein plays a key role in coupling AKT activation to PCa cell growth, survival, and resistance of late-stage PCa cells to environmental stresses, including hypoxia and reduced nutrient supply.

**Objective/Hypothesis:** The underlying hypothesis driving this project is that constitutive activation of the PI3K–AKT–mTOR pathway plays important roles in the growth, proliferation, apoptotic resistance, and metabolic adaptation of PCa cells.

**Specific Aims:** The specific aims of this project are to examine (1) the role of mTOR in PCa cell growth and survival and the impact of rapamycin on these functions, (2) the role of mTOR in hypoxia-induced factor-1 dependent gene expression in PCa cells, and (3) the role of the PI3K–AKT–mTOR pathway in prostate cancer development and progression.

**Study Design:** The proposed studies (Aims 1 and 2) will use pharmacological and genetic approaches to examine the contribution of mTOR and the impact of the mTOR inhibitor rapamycin on the growth, survival, and metabolic stress resistance of established PCa cell lines. The third aim will focus on the use of nontransformed prostate epithelial cells as model systems for elucidation of the role of the PI3K–AKT–mTOR pathway in prostate tumorigenesis.

**Relevance of the Proposed Work to the Prostate Cancer Program Goals:** The outcomes of this project have near-term translational potential as a specific mTOR inhibitor, rapamycin/CCI-779, is moving into Phase II cancer trials, with PCa a priority disease target for these trials. Our results should help to identify those PCa patients who are most likely to benefit from rapamycin/CCI-779 therapy. Second, the proposed studies will fill important gaps in our understanding of the etiology and progression of PCa.

## LAY ABSTRACT

Targeting the Target of Rapamycin for Prostate Cancer Therapy
Robert T. Abraham, Ph.D.

In normal tissues, cells communicate extensively with their local environment, which instructs them to initiate or cease proliferation, to mature, or, in some cases, to commit suicide, thereby eliminating "marked" cells from the tissue. These complex responses to environmental cues are orchestrated by the activation or inhibition of signal transduction pathways that translate stimuli impinging on the outside of the cells into a form that can be interpreted by the response machinery located in the cell cytoplasm and nucleus. In most tissues, intracellular signaling serves to maintain a balance between cell growth and cell death such that the tissue maintains its normal size and architecture. However, this balance between "positive" and "negative" signaling is disrupted in cancer—cancer cells inevitably escape the controls that limit the growth, lifespan, and migratory abilities of normal cells. We now realize that cancer is, in part, a disease caused by disordered intracellular signaling, with the inescapable outcome being inappropriate cell growth and resistance to the environmental signals that effectively restrain the proliferation and movement of normal cells. Prostate cancer is no exception, and it is clear that the progression of this disease from the early stage to a more advanced, aggressive form of the disease is accompanied by characteristic alterations in intracellular signaling that allow these malignant cells to proliferate and migrate under conditions that would be incompatible with normal cell viability. It follows that drugs targeted against components of the deranged signaling pathways found in advanced prostate tumors might have significant therapeutic benefit against a type of cancer that has proven largely refractory to conventional chemotherapeutic strategies.

A potential candidate for such a signaling-targeted drug is a natural product (produced by a strain of bacteria) termed rapamycin. This drug has recently received clinical approval for use in organ transplant patients, and, hence, already has an established clinical history of use in humans. It turns out that rapamycin is an exquisitely specific inhibitor of a signaling molecule found in both normal and cancer cells. We identified this molecule and named it the mammalian target of rapamycin (mTOR). Subsequently, we and others have discovered that certain types of cancer cells are strongly growth-inhibited and even killed by exposure to rapamycin. Prostate cancer cells proved to be among the most sensitive to rapamycin. As a result of the preclinical studies on cancer cells, a rapamycin analog was placed into Phase I clinical cancer trials. The success of these studies prompted the design of Phase II trials slated to begin in late 2000, and prostate cancer is one of the top disease targets for this next phase of clinical testing.

Given the near-term clinical application of rapamycin in prostate cancer patients, it becomes imperative to understand the mechanism underlying the particular sensitivity of prostate cancer cells to this drug. We hypothesize that many prostate cancer cells exhibit deregulated signaling through a pathway that includes the rapamycin target protein mTOR as a key component. As such, we believe that the rapamycin sensitivity of prostate cancer cells to rapamycin reflects the fact that these cells are "hardwired" through mTOR for growth, survival, and resistance to environmental stress. The major goals of this project are to determine whether deregulated signaling through mTOR plays a major role in prostate cancer development and to examine in detail the impact of rapamycin on hallmark abnormalities of prostate cancer cells, including deregulated growth and resistance to stress-induced cell suicide. The results of these studies will greatly facilitate the selection of those patients who are most likely to benefit from rapamycin therapy. Over the longer term, this project will significantly increase our understanding of the processes that underlie prostate cancer development and progression in human males.

## TECHNICAL ABSTRACT

Comprehensive Development Program of Hunter-Killer Peptides for Prostate Cancer
Howard M. Ellerby

**Background:** The prostate gland is a relatively small organ but the incidence of cancer at this site is higher than in any other site in the human body. Current therapies for prostate cancer are mainly limited to treatments such as radical prostatectomy or radiotherapy for localized prostate tumors, and there is no cure once the disease has spread beyond the gland. Cytotoxic chemotherapy is the common systemic treatment of disseminated malignant tumors, and yet current chemotherapeutic agents have the narrowest therapeutic indices in all of medicine. A more specific and less toxic treatment is needed.

Tumor cell survival, growth, and metastasis require persistent new blood vessel growth (angiogenesis). A tumor cannot grow beyond the size of about 1mm in diameter without acquiring new blood vessels to nurture it. Consequently, a strategy has emerged to treat cancer by inhibiting angiogenesis.

We have designed short hunter-killer peptides (HKPs) (21-26 residues) that are composed of two functional domains. The first domain is a targeting sequence, designed to guide and internalize the HKP into angiogenic endothelial cells. The second domain is an anti-mitochondrial peptide, designed to be nontoxic when outside cells but pro-apoptotic when internalized into targeted cells by the disruption of mitochondrial membranes. When nude mice bearing human tumor xenografts derived from either prostate or breast tumor cell lines received HKP treatment, they outlived their untreated counterparts by several months, indicating that both primary tumor growth and metastasis were inhibited. Moreover, their tumor volumes were an order of magnitude smaller (on average) than that of control mice.

**Objective/Hypothesis:** Although our treatment was successful, we cannot proceed to clinical trials because the prototype HKPs are still too toxic. The overall objective of the proposed research is to produce HKPs that can be applied clinically in the fight against prostate cancer.

**Specific Aims:** (1) Optimize the dose of current HKPs in the TRAMP C model. (2) Design new HKPs with improved therapeutic indices. (3) Evaluate in vitro efficacy and toxicity of new HKPs. (4) Evaluate in vivo efficacy of new HKPs in the TRAMP model of prostate cancer. (5) Determine in vivo pharmacokinetics of HKPs in the TRAMP model of prostate cancer.

**Study Design:** We have created a comprehensive design and evaluation program to develop the next generation of less toxic/more effective HKPs. Such improvements are possible because HKPs can be optimized rationally with established principles of antimitochondrial peptide chemistry. Characteristics such as peptide length, hydrophobicity, etc., can be manipulated to reduce toxicity and increase efficacy. The specific aims are directed to optimize the dosing of current HKPs, design and test new less toxic HKPs in models of prostate cancer, determine HKP toxicity, and gain further insight into how HKPs exert their anticancer activity. We hope to produce a safer and more effective treatment of prostate cancer that can be brought to the stage of clinical relevancy. Our study design includes the use of magnetic resonance imaging (MRI) to accurately determine tumor volumes, the spread of metastases, and the real-time destruction of tumor vasculature using gadolinium contrast.

**Relevance:** Our HKPs have shown strong antitumor activity in mouse models of human prostate and breast cancer. However, the prototype HKPs are still too toxic for clinical use. Fortunately, the plasticity of the HKP concept allows us to create new, less toxic HKPs, which we have done in a pilot study. The relevance of the proposed work is that these studies should allow us to create HKPs that can be used clinically in the fight against human prostate cancer.

## LAY ABSTRACT

Comprehensive Development Program of Hunter-Killer Peptides for Prostate Cancer
Howard M. Ellerby

Although the prostate gland is a relatively small organ, the incidence of cancer found at this site is higher than any other site in the human body. Prostate cancer is now the most common cancer, the most common malignancy, and the second most common cause of death from cancer, among men in the United States. Furthermore, the incidence and mortality of prostate cancer are increasing at an alarming rate. Clinically, prostate tumors follow widely varying courses of progression, with a subset of tumors showing little or no advancement and rarely causing death, in contrast to aggressive adenocarcinomas that metastasize to bone, lymph nodes, or other sites and kill the patient.

Current therapies for prostate cancer are mainly limited to treatments such as radical prostatectomy or radiotherapy for tumors localized within the prostate. There is no cure for prostate cancer once the disease has spread beyond the gland. However, a large percentage of patients have advanced disease at the time of diagnosis, so it is imperative to find new approaches to the treatment of early and advanced prostate cancer. Cytotoxic chemotherapy is the basis of the systemic treatment of disseminated malignant tumors. However, a major limitation of the currently used chemotherapeutic agents is that these are the drugs with the narrowest therapeutic index in all of medicine. Thus, an effective dose of a wide variety of anticancer agents is restricted by their nonselective, highly toxic effect on normal tissues. What is required is a treatment that is both more specific and less toxic.

Tumor cell survival, growth, and metastasis require persistent new blood vessel growth. A tumor cannot grow beyond the size of about 1mm in diameter without acquiring new blood vessels to nurture it. Thus, a strategy has emerged to treat cancer by destroying a tumor's blood vessels, thereby starving the tumor to death. Indeed, this is our approach to prostate cancer.

At the heart of our approach is the design and synthesis of novel dual-purpose hunter-killer peptides (HKPs) that are composed of two parts. The first part is a peptide (the hunter) that guides the HKP to tumor blood vessels. The second is a peptide (killer) designed to be nontoxic to normal blood vessels but deadly to tumor blood vessels. Our prototype peptides had strong antitumor activity in models of both breast and prostate cancer. Indeed, HKPs doubled survival time, reduced tumor volumes by 5-10 fold, and retarded metastasis. However, the current peptides remain too toxic to proceed to clinical trials. The power of our approach is that we can use simple principles of peptide chemistry to design less toxic peptides. The proposed research is intended to optimize the dosing of current HKPs; design and test new, less toxic HKPs in a mouse model of prostate cancer; determine the toxicity of the peptides; and gain further insight into how the HKPs exert their anticancer activity. The significance of our innovation is that we invent a new class of anticancer peptides and apply them to the difficult problem of providing a safer and more effective treatment for both early and advanced prostate cancer.

**JONES, REBECCA E.**

## Statement of Work

## Development of Peptide Inhibitors of the "Cancer" Receptor (CR)

*Task 1.* To identify the minimal region of the CR polypeptide able to inhibit intact CR when co-expressed in cultured cells (Months 1-18):

a. Develop a series of plasmids for expressing the CR open reading frame (Months 1-7).
b. Perform assays to ascertain which fragments of CR block DNA-binding (Months 7-18).
c. Confirm that fragments of the CR open reading frame that block DNA-binding activity also inhibit CR function *in vivo* (Months 18-24).

*Task 2.* To identify short peptides modeled after the receptor that act as inhibitors of DNA binding and subunit association (Months 18-36):

a. Obtain synthetic CR peptides (Months 18-21).
b. Test the effect of synthetic peptides on the DNA-binding activity of CR (Months 20-24).
c. Characterize the inhibitory potency of active peptides and attempt to optimize the effect by testing additional overlapping peptides (Months 21-36).
d. Perform feasibility experiments to assess the ability of selected peptides to inhibit CR function in cultured cells (Months 20-36).

**WILSON, JOHN R**.

## Statement of Work

## Ultrasound Imaging

*Task 1*. Modification of ultrasound imaging gantry, Months 1-12:

a. Modify imaging gantry to permit measurements of the optics.
b. Perform measurements using a multi-modal scanning configuration.
c. Design of final optics.

*Task 2*. Extensive evaluation of ultrasound imaging gantry with the final optics, Months 13-36:

a. Repeat measurements using the final optics.
b. Measure the contrast improvement provided by the new detector configuration relative to conventional detector configuration.
c. Conduct specimen experiments to evaluate the increase in resolution provided by the magnification.
d. Investigate the extent of artifacts in fixed and scanning modes.
e. Participate in design of a clinical evaluation study comparing modified ultrasound mammography with conventional mammography.

**YOUNG, SUSAN D.**

**Statement of Work**

**Follow-up Care for Men and Women with Cancer**

*Task 1.* Develop Plan for Follow-up Patient Interviews, Months 1-3:

a. The tracking system shell from the previous cancer project will be modified to track patient recruitment and contact process.
b. The follow-up patient interview will be pre-screened with cancer patients from our hospital who are not enrolled in our study and modifications will be incorporated.
c. The environmental process interview (EPI) used for the baseline interview will be adapted for the follow-up interview.
d. Institutional Review Board approval will be obtained from all hospital sites.
e. The patient interviewer will be trained in medical terminology, measures of the interview, and use of the modified EPI system.

*Task 2.* Preparation for Medical Record Abstractions, Months 3-9:

a. The Medical Record Abstract form will be finalized and the investigator trained to perform patient data reviews using the instrument.
b. The Medical Record Abstract form will be revised for direct computer data entry.

*Task 3.* Subject Recruitment and Data Collection, Months 9-20:

a. Patients enrolled in our previous study will be recruited for the proposed follow-up study.
b. Interviews subsequent to the first follow-up will be modified as necessary to reflect issues relevant to patients beyond the period of adjuvant therapy.
c. Surveys will be sent to and data collected from enrolled patients every 6 months.

*Task 4.* Abstraction of Medical Records, Months 12-24:

a. Medical record abstractions will be performed for surviving enrolled patients annually.
b. Data entry and quality control measures will be ongoing.
c. Follow-up interviews will be conducted once annually with surviving enrolled patients over the 4-year study period.

*Task 5.* Interim Analyses, Months 24-44:

a. Interim statistical analyses of data obtained from interviews and medical record abstractions will be performed periodically.
b. Annual reports will be written.

*Task 6.* Final Analyses and Report Writing, Months 44-48:

a. Final analyses of data from interviews and medical record abstractions will be performed.
b. A final report and initial manuscripts will be prepared.

# Appendix E

## Biographical Sketches

Provide the following information for the key personnel listed on page 1 of the Detailed Cost Estimate form (see Appendix F) for the initial budget period.

| NAME | POSITION TITLE |
|---|---|
| | |

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

| INSTITUTION AND LOCATION | DEGREE (IF APPLICABLE) | YEAR(S) | FIELD OF STUDY |
|---|---|---|---|
| | | | |

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and representative earlier publications pertinent to this application. PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

# Appendix F

## Detailed Cost Estimate Form Instructions

The following sections describe the categories of costs that should be recorded on the Detailed Cost Estimate form. All amounts entered should be in U.S. dollars.

## Table of Contents

## 1. Personnel

- **Name:** Starting with the Principal Investigator (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.

- **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.

- **Type of Appointment (Months):** List the number of months per year reflected in an individual's contractual appointment with the offering organization. The Department of Defense (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 percent, 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.

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

- **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.

- **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.

- **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 as a direct cost to all sponsors. A copy of the rate agreement or other documentation to support the fringe benefits should be provided.

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

## 2. Consultant Costs

Regardless of whether funds are requested, provide the names and organizational affiliations of all consultants, other than those involved in consortium arrangements.

## 3. Major Equipment

It is the policy of the DOD that all commercial and nonprofit 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.

## 4. 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, and 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.

## 5. Travel Costs

Travel costs are allotted as a flat rate that varies depending on award mechanism. Please consult the appropriate award mechanism section of this program announcement and enter the amount specified for travel in the Detailed Cost Estimate form.

## 6. 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 U.S. Army Medical Research and Materiel Command will not provide funds for ongoing medical care costs that are not related to a subject's participation in the research study.

## 7. Research-Related Injury Medical Costs

Indicate costs for medical care for research-related injuries, should an injury to the subject occur as a result of the subject's participation in the proposed research. If the institution or state provides for this medical care as part of their existing liability insurance, annotate a cost of $0.00 and indicate in the "Justification" section of the Detailed Cost Estimate form that medical care for research-related injuries will be covered by existing institution/state insurance. If additional funds are needed to either supplement an existing policy or purchase a separate insurance policy to meet this requirement, annotate the budget requested and indicate in the "Justification" section of the Detailed Cost Estimate form how medical care for research-related injuries will be covered, and whether the cost is charged as direct or indirect costs. The institution business office can assist applicants with budgeting for this requirement. Subject costs are strictly limited to expenses specifically associated with the proposed study. The U.S. Army Medical Research and Materiel Command will not provide funds for ongoing medical care costs that are not related to a subject's participation in the research study.

## 8. Other Expenses

Itemize other anticipated direct costs such as publication and report costs, rental for computers and other equipment (giving 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.

## 9. Consortium 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:

a. The identification of the type of award to be used (e.g., cost reimbursement, fixed price);

b. The 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;

c. Whether the award will be competitive and, if noncompetitive, rationale to justify the absence of competition; and

d. The proposed acquisition price.

## 10. 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. A copy of the negotiation memorandum should be provided.

Training awards frequently have a different institutional overhead charge. All training investigators are encouraged to check with their institution concerning overhead costs.

## 11. 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. Also, explain any escalations of the budget from the initial to the future year(s) of support.** All amounts should be in U.S. dollars. Total costs for the entire proposed period of support should agree with the amount entered in item 4 of the Proposal Information (see Appendix C).

## 12. 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.

## 13. Relocation of Principal Investigator

Awards are made to institutions. If the PI leaves the recipient institution, both the PI and an official of the recipient institution should notify the U.S. Army Medical Research Acquisition Activity before the PI leaves to discuss options for continued support of the research project.

# Detailed Cost Estimate Form

**Name of Principal Investigator *(last, first, middle)***

| DETAILED BUDGET | | | | | FROM | THROUGH |
|---|---|---|---|---|---|---|
| PERSONNEL | | TYPE APPT. (MONTHS) | ANNUAL BASE SALARY | % EFFORT ON PROJECT | DOLLAR AMOUNT REQUESTED (OMIT CENTS) | | |
| NAME | ROLE ON PROJECT | | | | SALARY REQUESTED | FRINGE BENEFITS | TOTALS |
| | Principal Investigator | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| SUBTOTALS →→→→→ | | | | | | | $ |
| CONSULTANT COSTS | | | | | | | |
| MAJOR EQUIPMENT (ITEMIZE) | | | | | | | |
| MATERIALS, SUPPLIES, AND CONSUMABLES (ITEMIZE BY CATEGORY) | | | | | | | |
| TRAVEL COSTS | | | | | | | |
| SUBJECT-RELATED COSTS | | | | | | | |
| RESEARCH-RELATED INJURY MEDICAL COSTS | | | | | | | |
| OTHER EXPENSES (ITEMIZE BY CATEGORY) | | | | | | | |
| SUBTOTAL OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD →→→→→ | | | | | | | $ |
| CONSORTIUM COSTS | DIRECT COST | | | | | | |
| | INDIRECT COST | | | | | | |
| TOTAL PERSONNEL AND OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD | | | | | | | $ |
| TOTAL INDIRECT COSTS FOR INITIAL BUDGET PERIOD | | | | | | | $ |
| TOTAL COSTS FOR INITIAL BUDGET PERIOD | | | | | | | $ |

**Name of Principal Investigator *(last, first, middle)***

| BUDGET FOR ENTIRE PROPOSED PERIOD OF SUPPORT | | | | | | | |
|---|---|---|---|---|---|---|---|
| BUDGET CATEGORY TOTALS[1] | | INITIAL BUDGET PERIOD (FROM FORM PAGE 1) | ADDITIONAL YEARS OF SUPPORT REQUESTED | | | | TOTAL |
| | | | 2nd | 3rd | 4th | 5th | |
| PERSONNEL | | | | | | | |
| FRINGE BENEFITS | | | | | | | |
| CONSULTANT COSTS | | | | | | | |
| MAJOR EQUIPMENT | | | | | | | |
| MATERIALS, SUPPLIES, AND CONSUMABLES | | | | | | | |
| TRAVEL COSTS | | | | | | | |
| SUBJECT-RELATED COSTS | | | | | | | |
| RESEARCH-RELATED INJURY MEDICAL COSTS | | | | | | | |
| OTHER EXPENSES | | | | | | | |
| **SUBTOTAL DIRECT COSTS** | | | | | | | |
| **CONSORTIUM COSTS** | **DIRECT** | | | | | | |
| | **INDIRECT** | | | | | | |
| **TOTAL DIRECT COSTS** | | | | | | | |
| **TOTAL INDIRECT COSTS** | | | | | | | |
| **TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PERIOD OF SUPPORT** | | | | | **$** | | |
| **TOTAL INDIRECT COSTS FOR ENTIRE PROPOSED PERIOD OF SUPPORT** | | | | | **$** | | |
| **TOTAL COSTS FOR THE ENTIRE PROPOSED PERIOD OF SUPPORT THIS AMOUNT SHOULD AGREE WITH THAT ENTERED ON THE PROPOSAL COVER BOOKLET, ITEM 4** | | | | | **$** | | |

[1] Itemize all budget categories for additional years on the Justification page that follows.

**JUSTIFICATION: FOLLOW THE BUDGET JUSTIFICATION INSTRUCTIONS EXACTLY. USE CONTINUATION PAGES AS NEEDED.**

# Appendix G

## General Information

Appendix G of this program announcement contains general information relating to U.S. Army Medical Research and Materiel Command (USAMRMC) policies and procedures.

## Table of Contents

# General Information

## 1. U.S. Army Medical Research and Materiel Command Award

The USAMRMC implements its extramural research program predominantly through the award of grants and cooperative agreements. Proposals selected for funding are processed by the U.S. Army Medical Research Acquisition Activity (USAMRAA).

All awards are made to organizations, not individuals. A Principal Investigator (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.

## 2. Disclosure of Information outside the Government

By submission of an application, the applicant understands that disclosure of information outside the Government shall be for the sole purpose of technical evaluation. The USAMRMC will obtain a written agreement from the evaluator that information in the proposal will only be used for evaluation purposes and will not be further disclosed or utilized. Funded projects 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.

## 3. Award Eligibility

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).

## 4. Government Obligation

PIs 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. PIs 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.

## 5. 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.

## 6. Funding Instrument

All awards under this program announcement are anticipated to be grants or cooperative agreements.

More information on these funding instruments may be obtained by request from:

**Fax:** 301-619-2937
**E-mail:** q&a.baa@det.amedd.army.mil
**Mail:** Director
U.S. Army Medical Research Acquisition Activity
ATTN: MCMR-AAA
820 Chandler Street
Fort Detrick, MD 21702-5014

## 7. 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 Congressionally Directed Medical Research Programs 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.

## 8. Equipment/Property

It is the policy of the Department of Defense that all commercial and non-profit recipients possess the equipment and facilities needed to support proposed research. In those rare cases when additional specific equipment is approved for commercial and non-profit organizations, such approved cost elements shall be separately negotiated.

Title to equipment or other tangible property purchased with grant or cooperative agreement funds may be vested in non-profit institutions of higher education or with non-profit organizations whose primary purpose is the conduct of scientific research. Normally, title will vest with the recipient organization if vesting will facilitate scientific research performed by the institution or organization for the Government.

# Appendix H

## Acronym List

| | |
|---|---|
| AAALAC | Association for Assessment and Accreditation of Laboratory Animal Care International |
| ACS | American Cancer Society |
| ALT | Applicant's Local Time |
| AR | Army Regulation |
| CDMRP | Congressionally Directed Medical Research Programs |
| CEQ | Council on Environmental Quality |
| CFR | Code of Federal Regulations |
| CV | Curriculum Vitae |
| DHHS | Department of Health and Human Services |
| DOD | Department of Defense |
| DOEd | Department of Education |
| FY | Fiscal Year |
| HBCU | Historically Black Colleges and Universities |
| HBCU/MI | Historically Black Colleges and Universities/Minority Institutions |
| HDR-PSA | Health Disparity Research-Prostate Scholar Award |
| HDT-PSA | Health Disparity Training-Prostate Scholar Award |
| HSRRB | Human Subjects Research Review Board |
| IACUC | Institutional Animal Care and Use Committee(s) |
| IDE | Investigational Device Exemption |
| IND | Investigational New Drug |
| IP | Integration Panel |
| IRB | Institutional Review Board |
| MPA | Multiple Project Assurance |
| NIA | New Investigator Award |
| NIH | National Institutes of Health |
| NSF | National Science Foundation |
| PCRP | Prostate Cancer Research Program |
| PDF | Portable Document Format |
| PI | Principal Investigator |
| RCQ | Regulatory Compliance and Quality |
| SBIR | Small Business Innovation Research |
| TSG | The Surgeon General |
| USAMRAA | U.S. Army Medical Research Acquisition Activity |
| USAMRMC | U.S. Army Medical Research and Materiel Command |
| USC | United States Code |
| USDA | U.S. Department of Agriculture |