DEPARTMENT OF DEFENSE

FISCAL YEAR 2002
CHRONIC MYELOGENOUS LEUKEMIA RESEARCH PROGRAM
PROGRAM ANNOUNCEMENT

June 11, 2002

Headquarters, U.S. Army Medical Research and Materiel Command
MCMR-PLF, 1077 Patchel Street
Fort Detrick, Maryland 21702-5024

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Foreword

The U.S. Army Medical Research and Materiel Command (USAMRMC) has been directed to establish the Department of Defense (DOD) Chronic Myelogenous Leukemia Research Program (CMLRP). The deadline, format, and other criteria specified for proposals in this DOD Fiscal Year 2002 (FY02) CMLRP Program Announcement are based on program objectives, public needs, and regulatory guidance.

Specific information on the USAMRMC, U.S. Army Medical Research Acquisition Activity the Congressionally Directed Medical Research Programs (CDMRP), and the DOD CMLRP can be obtained from the CDMRP web site at http://cdmrp.army.mil. A copy of this program announcement and associated forms also can be downloaded from the CDMRP web site; hard copies of the program announcement will not be provided (for information on completing the Proposal Information, see Section 5, page ii of this Foreword).

1. Who May Apply

Individuals, regardless of ethnicity, nationality, or citizenship status, may apply through an eligible institution. 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. Please refer to Section III for additional eligibility criteria.

2. Submission Deadline

An electronic PDF (Portable Document Format) version of your proposal, which will serve as the official proposal submission, must be uploaded/submitted through the Internet by an authorized Administrative Representative of the Sponsored Programs Office (or equivalent) of your organization no later than **11:59 p.m. (applicant's local time) September 18, 2002**. See Appendix B, part 20, and Appendix C for additional details.

Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

3. Timeline

Letter of Intent:	As soon as possible but no later than September 4, 2002
Proposal Receipt Deadline:	**One electronic PDF version** of the proposal must be sent through the Internet no later than **11:59 p.m. (applicant's local time) September 18, 2002**
Peer Review:	November 2002
Request for RCQ[1] Documents:	As early as November 2002
Programmatic Review:	January 2003
Notification:	Approximately 2 weeks after programmatic review
Award Date:	**Between February 2003 and September 2003**

4. Inquiries

Questions concerning the **proposal format or required documentation** can be addressed to the CDMRP at:

Phone: 301-619-7079
Fax: 301-619-7792
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (CMLRP02-Program Announcement)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

Applicants should submit questions regarding this program as early as possible. Every effort will be made to answer questions within 5 working days.

Help lines are also available to answer specific questions regarding the preparation of proposals for **electronic submission or the electronic submission process**. The help line phone number is 301-466-6495. Help can also be obtained by e-mail at help-proposals-cdmrp@cdmrp.org.

5. Proposal Submission

Applicants should refer to Section III and Appendix B for appropriate submission requirements.

Proposals will be submitted electronically at http://cdmrp.org/proposals. An authorized Administrative Representative from the Sponsored Programs Office of the applicant's organization must upload/submit

[1] Regulatory Compliance and Quality

one electronic PDF version of the applicant's proposal, which will count as the official proposal submission.
Several steps are critical for successful electronic submission of the applicant's proposal.

1. The applicant is required to submit Proposal Information 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 (see Appendix C). **The Proposal Information must be submitted prior to submission of the proposal. Applicants are encouraged to begin this part of the submission process at least 2 weeks prior to the submission deadline.**

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. Please ensure that the content of the PDF file is representative of your complete submission. 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; 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. The 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) September 18, 2002.** Detailed instructions for electronic submissions can be found at http://cdmrp.org/proposals.

I. Overview of the Congressionally Directed Medical Research Programs

I-A. History of the Congressionally Directed Medical Research Programs

Due to increased public awareness, the success of the Department of Defense (DOD) Congressionally Directed Medical Research Programs (CDMRP), and the work of grassroots advocacy organizations, Congress has appropriated monies for peer reviewed research directed toward specific diseases. Beginning in fiscal year 1992 (FY92), the U.S. Congress has directed the DOD to manage these various extra- and intramural grant programs. The U.S. Army Medical Research and Materiel Command (USAMRMC) established the CDMRP to administer these funds. To date, the USAMRMC CDMRP has received more than $2.2 billion targeted by Congress for peer reviewed research on breast cancer, prostate cancer, ovarian cancer, neurofibromatosis, chronic myelogenous leukemia, Defense Women's Health, osteoporosis, and other specified areas.

The CDMRP exists to support research that will positively impact the health of all Americans. The CDMRP strives to identify gaps in funding and provide opportunities that will enhance program research objectives without duplicating existing funding. To meet these goals, the CDMRP has developed unique mechanisms to facilitate the funding of quality research that addresses individual program objectives.

I-B. Investment Strategy

For each program, the CDMRP has developed and refined a flexible execution and management cycle that spans the development of an investment strategy through the completion of research. A Program Staff, composed of military and civilian scientists and clinicians, manages the CDMRP. For each program, an expert Integration Panel (IP) of scientists, clinicians, and consumer advocates is convened to deliberate issues and concerns unique to the program, establish an appropriate investment strategy, and perform programmatic review as described in Section I-C.2. Based upon this investment strategy, each program then uses a variety of award mechanisms to address the most urgent needs of the research community.

I-C. Proposal Evaluation

The CDMRP uses a two-tiered review process for proposal evaluation as recommended by the National Academy of Science's Institute of Medicine. The two tiers are fundamentally different. The first tier is a scientific peer review of proposals 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 program goals.

I-C.1. Scientific Peer Review

Scientific peer review is conducted by panels organized by scientific discipline or specialty area. The primary responsibility of the scientific peer review panels is to provide unbiased, expert advice on the scientific and technical merit of proposals, based upon the review criteria published in the program announcement.

Scientific peer review panels are composed of a chair, scientific reviewers, consumer reviewers, and a nonvoting executive secretary. Selection of individuals as scientific reviewers is predicated upon their expertise as well as their varied levels of experience with scientific peer review. Consumer reviewers are cancer survivors and representatives of consumer advocacy organizations. Consumer reviewers are nominated by an advocacy organization and are selected on the basis of their leadership skills, commitment to advocacy, and interest in science. Consumers augment the scientific peer review by bringing the patient perspective to the assessment of science and to the relevance of research.

Panel members rate each proposal based on specific evaluation criteria (see Section III-B). Two types of ratings are used. First, each of the evaluation criteria, except for the budget, is rated on a scale of 1 (lowest merit) to 10 (highest merit). This criteria scoring ensures that each component is considered in peer review. Second, the overall proposal is given a global priority score using a scale of 1 (highest merit) to 5 (lowest merit). Criteria scores are neither averaged nor mathematically manipulated to determine the global priority score. Instead, reviewers are asked to use the criteria scores as a guide in determining the global priority score. In rare instances, a proposal may be disapproved at scientific peer review if gravely hazardous or unethical procedures are involved, or if the proposal is so seriously flawed that its completion is implausible.

The peer review summary statement is a product of scientific peer review. Each summary statement includes the investigator's structured technical abstract and lay (nontechnical) abstract (verbatim), the peer review scores, and an evaluation of the project as assessed by the peer reviewers according to the evaluation criteria published in this program announcement. Summary statements are forwarded to the next stage of the review process, programmatic review.

I-C.2. 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 members of the IP represent many diverse disciplines and specialty areas and are experienced with peer review procedures. Consumer advocates represent national advocacy constituencies and are full voting members of the IP. One of the functions of programmatic review is to select a broad portfolio of grants across all disciplines. Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool. IP members use the peer review summary statements, which include the proposal abstracts, to review proposals. The Statement of Work may also be reviewed at this level. However, the full proposal is not forwarded to programmatic review.

The IP is committed to funding a broad-based research portfolio. The ratings and evaluations of scientific peer review panels are primary factors in programmatic review; the IP also must consider other criteria to establish this portfolio. The criteria the IP uses to make funding recommendations are:

- Ratings and evaluations of the scientific peer review panels;
- Programmatic relevance;
- Relative innovation; and
- Program portfolio balance with respect to research disciplines or specialty areas.

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.

I-D. Notification

Following completion of the two-tiered evaluation process, every applicant will receive a letter indicating the award status of his or her proposal, along with the peer review summary statement. Letters will be sent as official information becomes available. Thus, not all investigators will be notified at the same time.

I-E. Negotiation of the Award

Award negotiation consists of discussions, reviews, and justifications of several critical issues, including those involving the U.S. Army Medical Research Acquisition Activity (USAMRAA) and Regulatory Compliance and Quality (RCQ). A Contract Specialist from USAMRAA will contact the administrative representative who is authorized to negotiate contracts and grants at the applicant's institution. As part of the negotiation process, additional documentation and justifications relating to the proposed Statement of Work and associated budgets may be required.

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

Concurrent with the USAMRAA negotiations, RCQ will review the environmental compliance, safety plan, animal use, and human subjects/anatomical substance use documents to ensure that Army regulations are met. The Certificate of Environmental Compliance and Principal Investigator Safety Program Assurance documents are part of the proposal submission. The Facility Safety Plan (if needed), Research Involving Animals, and Research Involving Human Subjects and/or Anatomical Substances documents will be requested in the applicant's notification letter and will be reviewed by RCQ staff. All documents related to RCQ are available on the CDMRP web site

(http://cdmrp.army.mil).

I-F. Human Use Requirements Unique to DOD-Funded Research

Important distinctions exist for research funded by the DOD that involves human subjects. In addition to local Institutional Review Board approval to conduct research involving human subjects, a second, DOD review and approval is also required. The Human Subjects Research Review Board (HSRRB), administered by the USAMRMC RCQ Office, is responsible for conducting this second level of review. 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. **All research protocols involving human subjects and/or anatomical substances must be approved by both the appropriate local review board and by the HSRRB before awards are made and prior to initiation of the research protocol.**

Two requirements specific to DOD-funded research that the applicant must specifically address, if applicable, in the development of a research proposal for submission to the DOD are outlined below.

- Medical Care for Research-Related Injuries. 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, Appendix F for more details.

- 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. Therefore, the applicant should articulate how the research will benefit minors or other individuals that are not legally competent to consent and are part of the placebo arm of the study.

More information regarding research involving human subjects can be found in the RCQ document, "Research Involving Human Subjects and/or Anatomical Substances," which is available on the CDMRP web site (http://cdmrp.army.mil).

I-G. Annual and Final Reports

All awards will require the timely delivery of several reports during the research effort. These reports are necessary for the CDMRP to monitor progress and evaluate program outcomes.

The Principal Investigator (PI) should plan on a reporting requirement consisting 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.

I-H. Publications and Patents

All investigators are strongly encouraged to publish their results in scientific literature. All publications, abstracts, and presentations must cite the DOD as the source of the research funding. For example, "This research, under award number DAMD…, was supported by the Department of Defense Chronic Myelogenous Leukemia Research Program, which is managed by the U.S. Army Medical Research and Materiel Command." A PI must submit a copy of any manuscript or publication resulting from research funded under the award to the CDMRP.

In accordance with the Bayh-Dole Act (35 USC 200 et seq.[1]), 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.

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

II. Department of Defense Chronic Myelogenous Leukemia Research Program

II-A. History of the Chronic Myelogenous Leukemia Research Program

The Department of Defense (DOD) Chronic Myelogenous Leukemia Research Program (CMLRP) is being established in fiscal year 2002 (FY02) to promote research in the field of chronic myelogenous leukemia (CML), in accordance with the directives received from Congress. The DOD is using the model established through recommendations from the Institute of Medicine for the U.S. Army Medical Research and Materiel Command's (USAMRMC's) Breast Cancer Research Program (BCRP) to establish the CMLRP. Like the BCRP, the CMLRP will employ a two-tiered scientific review process consisting of scientific (peer) review and programmatic review. Congress appropriated $5M for the CMLRP in FY02.

II-B. Overview of the FY02 CMLRP

The Congressionally Directed Medical Research Programs (CDMRP) is requesting proposals on CML research through this program announcement. Proposals will be requested for Investigator- Initiated Research Awards. Proposals are encouraged from investigators working at Historically Black Colleges and Universities/Minority Institutions.

II-C. FY02 CMRLP Program Announcement Award Opportunities

This command anticipates that approximately $4.26M will be available to fund competitive, peer reviewed CML research.

Allocations	FY02
Congressional Appropriation	$5.00M
Less: Congressional/DOD Withholds[1]	($0.27M)
Appropriation Received	$4.73M
Less: Approximate CMLRP Management Costs[2]	($0.47M)
Amount Available for FY02 Research	$4.26M

[1]Withholds include Small Business Innovation Research (SBIR)/USAMRMC.
[2]Any cost savings from management cost will be applied to research funding.

III. Investigator-Initiated Research Awards

III-A. Investigator-Initiated Research Awards

The intent of Investigator-Initiated Research Awards (IIRAs) is to sponsor basic and clinically oriented research in the field of chronic myelogenous leukemia (CML). These grants are intended to fund independent investigators across a broad spectrum of disciplines. An IIRA investigator is defined as an independent investigator at a level equivalent to or above that of Assistant Professor.

The Fiscal Year 2002 (FY02) CMLRP encourages investigators to submit IIRA proposals that:

- Address the molecular and genetic changes underlying CML disease progression from the evolution of chronic disease to lymphoid or myeloid blast crisis with the goal of identifying novel therapeutic targets.

- Elucidate relevant signal transduction pathways and identify therapeutic targets in cells that are resistant to BCR-ABL tyrosine kinase inhibitors.

- Attempt to better understand how the immune system is involved in the control of CML in order to develop immunotherapeutic strategies.

In addition, the FY02 CMLRP encourages the following:

- Innovative studies that explore novel ideas or approaches. One of the goals of this funding mechanism is to support promising areas that may not be developed enough to compete for traditional funding sources.

- Collaborative projects between clinical and basic science researchers, or between pharmaceutical/biotechnology companies and academic institutions.

- Inclusion of quality of life considerations into any human studies.

Funding for IIRAs can be requested for a maximum of $750,000 for a period of up to 3 years, inclusive of direct and indirect costs. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. The amount allotted for travel is $1,800 per year. Institutional support and commitment (e.g., the provision of access to adequate laboratory facilities and equipment) must be evident to foster the applicant's research.

III-B. Scientific Peer Review Evaluation Criteria for IIRA Proposals

IIRA proposals will be evaluated according to the following criteria:

- **Research Strategy:** Are the conceptual framework, hypotheses, design, methods, and analyses adequately developed and well integrated to the aims of the project? Is there a clear-cut rationale supporting the research provided? Does the applicant acknowledge potential problem areas and consider alternative methods/tactics? Is the experimental design sound and sufficiently well developed with the required statistical power to lead to significant results? Does the proposal include a clear statistical plan of analysis?

- **Innovation:** Is the proposed research innovative in one or more of the following areas: study concept or question; research methods or technologies; clinical interventions; adaptations of existing methods or technologies? Is it innovative in other ways? Are the aims original? Does the project propose new paradigms or challenge existing paradigms? Is innovation necessary for the project?

- **Relevance:** To what extent will the project, if successful, make an original and important contribution to the goal of advancing research in the field? Does this study address a critical problem in CML research? Does the proposal make a convincing case for the relevance of the research to CML?

- **Principal Investigator and Personnel:** Is the Principal Investigator (PI) appropriately trained and well suited to carry out this work? Does the PI show potential for contribution to the CML field? Is the proposed work appropriate to the experience level of the PI and other researchers (if any)? Is appropriate expertise available to conduct the study successfully?

- **Environment:** Is there evidence that the scientific environment is an appropriate setting for the proposed research? Is there evidence that the research requirements are adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed? Is there evidence of institutional support provided with the proposal?

- **Budget:** Is the budget appropriate for the research proposed? Is there evidence that, where appropriate, arrangements have been made to compensate human subjects/participants for expenses they incur from participating in the project?

III-C. Programmatic Review Evaluation Criteria for IIRA Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the IIRA mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.2.

III-D. 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 September 4, 2002. This form is available on the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil/funding/02cmlrp1.htm.

III-E. Proposal Preparation

Additional instructions for proposal preparation are found in Appendix B of this program announcement. Please note that the body of the proposal is limited to **20 pages**, inclusive of figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn by the Government prior to peer review.** Applicants must submit the Proposal Information at http://cdmrp.org/proposals prior to upload/submission of the proposal. Ensure that one electronic PDF (Portable Document Format) version of your proposal, which will serve as the official proposal submission, is uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) September 18, 2002.**

Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

1. Who May Apply – See Appendix B, part 1.

2. Proposal Acceptance Criteria – See Appendix B, part 2.
   Number all pages of the proposal consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page that includes the PI name (last name, first name, middle initial) and proposal log number (this will be automatically provided when a draft of the Proposal Information is saved).

3. Proposal Information – See Appendix B, part 3 and Appendix C.

4. Title/Referral Page – See Appendix B, part 4.

5. Table of Contents – See Appendix B – Part 5.
   Use the table of contents at the end of this section in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal.

6. Checklist for Proposal Submission – See Appendix B, part 6.

7. Proposal Abstracts – See Appendix B, part 7 and Appendix D.

8. Statement of Work – See Appendix B, part 8 and Appendix D.

9. Proposal Relevance Statement – See Appendix B, part 9.

10. Proposal Body – See Appendix B, part 10.
    The body of IIRA proposals is limited to **20 pages**, inclusive of figures, tables, graphs, and photographs, if used.

    Describe the proposed project using the **general** outline provided below:

    a. Background: Briefly describe the ideas behind the proposed work and cite relevant literature references. Describe previous experience most pertinent to this proposal.

    b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

    c. Objectives: State concisely the project's specific aims and study design.

    d. Methods: Give details about the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation.

11. Abbreviations – See Appendix B, part 11.

12. References – See Appendix B, part 12.

13. Biographical Sketches – See Appendix B, part 13.

14. Existing/Pending Support – See Appendix B, part 14.

15. Facilities/Equipment Description – See Appendix B, part 15.

16. Administrative Documentation – See Appendix B, part 16.

17. Detailed Cost Estimate – See Appendix B, part 17.
    Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. In addition, budgets will be reviewed during award negotiations. Please provide complete justification for expenses in all categories. Funding for IIRAs can be requested for a maximum of $750,000 for a period of up to 3 years, inclusive of direct and indirect costs. Direct costs can cover salary, expenses including research supplies, equipment, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. The amount allotted for travel is $1,800 per year. Institutional support and commitment must be evident to foster the applicant's research, such as the provision of access to adequate laboratory facilities and equipment.

For all Department of Defense-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 Appendix F, part 7 for more details.

18. Instruments – See Appendix B, part 18.

19. Publications and/or Patent Abstracts – See Appendix B, part 19.

20. Proposal Submission – See Appendix B, part 20.

21. Submission Deadline – See Appendix B, part 21.
    Please note that one electronic PDF version of your proposal must be uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) September 18, 2002. Submission of a proposal after the deadline may be grounds for proposal rejection.**

22. Regulatory Compliance and Quality Requirements – See Appendix B, part 22.
    The one-page Certificate of Environmental Compliance and one-page Principal Investigator Safety Program Assurance documents are to be submitted with the proposal. All documents related to Regulatory Compliance and Quality issues are available on the CDMRP web site. See Appendix B, part 22 for more details.

Principal Investigator: _____

Last Name *First Name* *MI*

Proposal Title: _____

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Investigator-Initiated Research Award Proposal
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