

Program Announcement

Department of Defense Congressionally Directed Medical Research Programs

Lung Cancer Research Program

Lung Cancer Early Detection Clinical Consortium Award

Funding Opportunity Number: W81XWH-10-LCRP-LCEDCC

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

The Lung Cancer Research Program (LCRP) was established in Fiscal Year 2009 (FY09) to promote innovative and competitive research focused on the development of integrated components to identify, treat, and manage early curable lung cancer, and the establishment of a tissue bank. The FY09 appropriation was \$20 million (M). The FY10 appropriation is \$15M.

The goal of the FY10 LCRP is to eradicate deaths from lung cancer to better the health and welfare of the military and the American public. As such, the LCRP will support a program for the early detection of lung cancer in military beneficiaries (Armed Forces and/or the US veteran population).

B. Award Description

The LCRP Early Detection Clinical Consortium Award mechanism is being offered for the first time in FY10. The intent of the award is to fund clinical studies focused on characterizing, developing, and/or improving early detection modalities for lung cancer. **The award is designed to bring together populations of military beneficiaries at high risk for developing lung cancer and lung cancer patients from the specified military treatment facilities (MTFs) listed in Section B.2 with the patient populations and research expertise of highly qualified civilian scientists at outstanding organizations.** At the time of award completion, it is anticipated that the recipient will have established a strong infrastructure for an early detection program in order to continue clinical studies that will lead to improved patient outcomes.

Projects should be militarily relevant, have well defined objectives, should control for confounders, have a patient population that will provide a sample size of sufficient statistical power, and be capable of producing results that are likely to change clinical practice for early detection of lung cancer. Studies involving non-military patient populations must describe how they pertain to the targeted population (i.e. Armed Forces and/or the US veteran population). Studies proposed for this multi-institutional consortium effort can include small randomized or pilot clinical trials as well as large, randomized clinical trials. All projects shall be limited to clinical research and clinical trials. *Animal studies are excluded from consideration.*

The LCRP Early Detection Clinical Consortium Award resulting from this program announcement will be issued as a cooperative agreement between the recipient (Coordinating Center) and the Government (the US Army Medical Research Acquisition Activity [USAMRAA]). An appointed External Advisory Board (EAB), consisting of selected LCRP Integration Panel (IP) members, consumer advocates, experts in the field and US Army Medical Research and Materiel Command (USAMRMC) staff, will review research priorities and make recommendations to the Grants Officer's Representative (GOR) for the GOR's consideration and ultimate approval decisions by the USAMRAA Grants Officer.

1. LCRP Early Detection Clinical Consortium Award Clinical Study Areas: The goal of the LCRP Early Detection Clinical Consortium Award is to characterize, develop, and/or improve early detection modalities for lung cancer with the aim of changing current clinical practice through the development and/or validation of new screening modalities that lead to improved patient outcomes. To further progress toward this goal, the FY10 LCRP has established a set of clinical study areas listed below. Applications submitted in response to the LCRP Early Detection Clinical Consortium Award must propose a minimum of two studies that address **at least one of the following clinical study areas:**

- Combination of multiple detection/screening modalities
- Development of a non-imaging-based screening protocol
- Prospective validation of early detection/screening biomarkers

2. General Information: The LCRP Early Detection Clinical Consortium Award supports the development of a consortium that will consist of a Coordinating Center (who can also serve as a clinical study site) in collaboration with multiple MTFs (required) and additional non-military Clinical Study Sites (optional). **Because this award is intended to maximally benefit military beneficiaries, the Coordinating Center will be required to collaborate with the following MTFs: Naval Medical Center Portsmouth (NMCP), Naval Medical Center San Diego (NMCS), San Antonio Military Medical Center (SAMMC), and Walter Reed National Military Medical Center (WRNMMC).** In addition, collaborations with the US Department of Veterans Affairs (VA), academic, government, other military, industry, or non-profit organizations are strongly encouraged and should be described within the application. Applicants are also strongly encouraged to leverage existing clinical programs to enhance collaboration and educational/training opportunities for clinical researchers.

Aside from the named MTF collaborators listed above, the applicant must propose at least one additional Clinical Study Site, if the Coordinating Center is not going to serve as a Clinical Site, in order to execute the mission of the Consortium. The Consortium should be comprised of existing high volume and high productivity sites that have a clinical research track record to maximize enrollment within the available funding constraints. See Figure 1 for a potential structure of the LCRP Early Detection Clinical Consortium.

The Coordinating Center and any associated Clinical Study Sites (not including named MTFs) must apply to this announcement through a single application. A single award will be made to the Coordinating Center, and award funds will be used to support the Coordinating Center's efforts as well as Consortium-associated studies at each of the Clinical Study Sites, including the MTFs. The Coordinating Center will provide management and funding through the appropriate instruments for the non-MTF Clinical Study Sites to conduct medical research towards characterizing, developing, and/or improving early detection modalities for lung cancer. The Coordinating Center will provide management and support (research personnel, small equipment, supplies, etc.) to the MTFs through various appropriate means; however, no direct funds will be provided by the Coordinating Center to the MTFs.

The Consortium will conduct studies that build upon the lung cancer research goals and patient care initiatives established by the Department of Defense (DOD) at the MTFs ([Appendix](#)) that are in alignment with the LCRP Early Detection Clinical Consortium Award clinical study areas (Section I.B.1). It is the responsibility of the applicant to describe clearly within the application how the proposed Consortium will have a significant impact on improving early detection in lung cancer.

The Coordinating Center will facilitate the rapid selection, design, and execution of clinical studies within the Consortium, and will provide the administrative, protocol development, regulatory, statistical, resource, and data management/storage functions necessary to facilitate Consortium studies. The Principal Investigator (PI) of the Coordinating Center must provide evidence of prior experience with the design and administration of multi-institutional clinical studies. The PI must also demonstrate a broad understanding of lung cancer research, including knowledge of the current state of clinical studies and clinical priorities related to the Lung Cancer Early Detection Clinical Consortium Award clinical study areas.

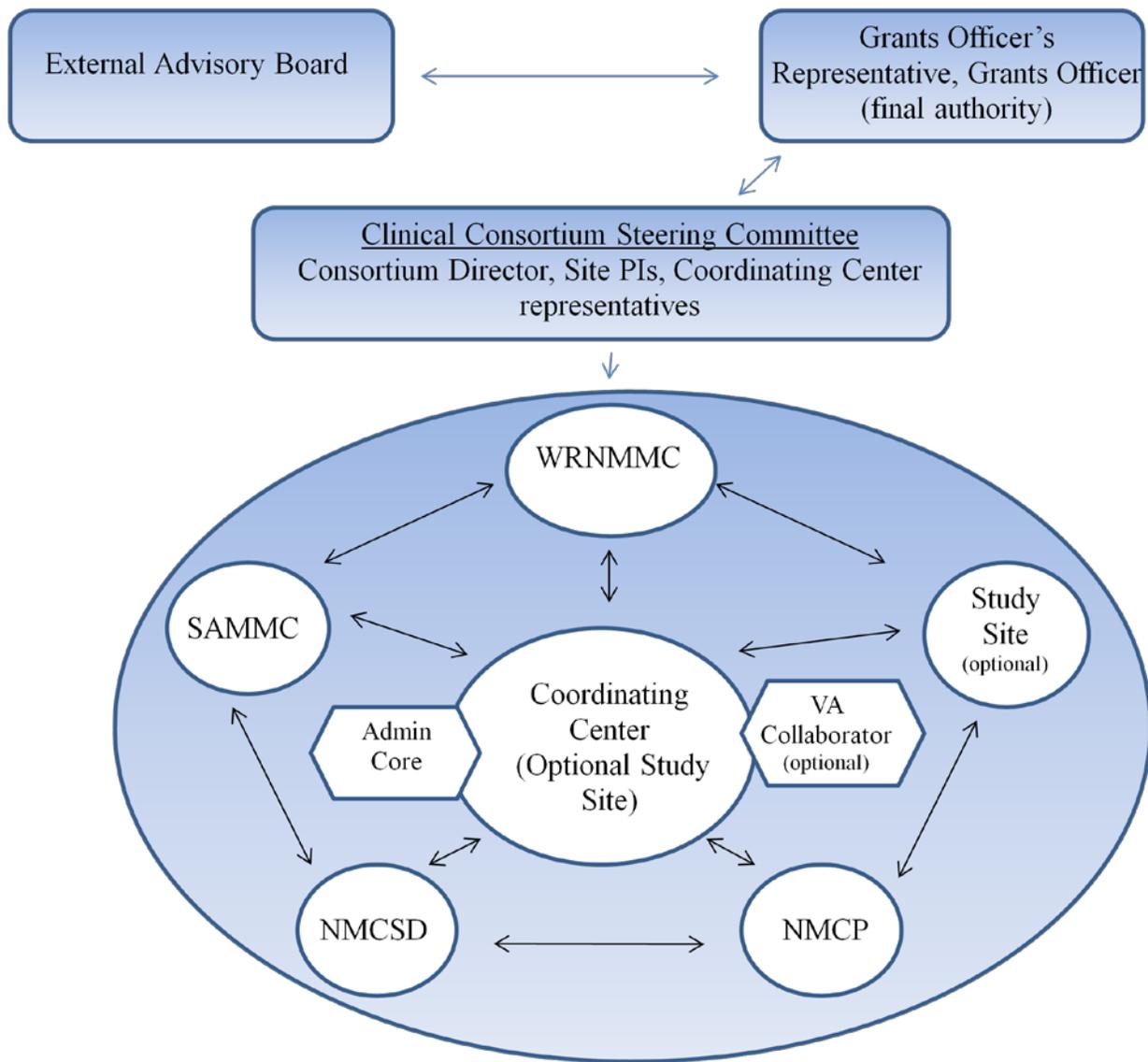
The application should name and describe individual core facilities at member organizations that will serve as official Consortium research core facilities. Establishment of Consortium-wide core facilities will enable more consistent, high-quality, standardized data to be collected across sites for Consortium-supported studies.

Applications must include an initial set of proposed studies (minimum of 2) reflective of the overall goals of the Consortium for consideration during the review and selection process, some of which may be carried out if selected for funding based upon recommendations of the LCRP reviewers and the EAB. Proposed studies should include a range of scope, size, and type that is representative of the overall goals of the Consortium. Funding selection will depend upon evaluation of the proposed studies, record of productivity, available capabilities, organization of the Consortium, and feasibility of the entire group to accomplish the overall award objectives. During the performance period of the award, all Clinical Study Sites, including the MTFs, will be responsible for working collaboratively to identify the clinical study(s) for implementation by the Consortium. All of these studies will be subject to EAB review and recommendations to the GOR and the Grants Officer for decisions prior to implementation. Collectively, the Clinical Study Site PIs will constitute the Clinical Consortium Steering Committee, which will be responsible for proposing and conducting clinical studies focused on the early detection of lung cancer, in which all Consortium organizations will participate in each study. The Coordinating Center will be responsible for facilitating this process, and the proposal should include a description of how the Coordinating Center plans to coordinate with the Clinical Study Sites to propose, design, and prioritize the most relevant clinical studies, as well as establish and implement external peer review once the Consortium is established.

The LCRP Early Detection Clinical Consortium Award will be supported by funds from the FY10 LCRP appropriation. There also exists the possibility of expanding the consortium, contingent on receipt of sufficient future congressional appropriations.

Applications must include a supplemental research plan to allow for the expansion (i.e. clinical studies and/or clinical sites) of the consortium should additional funds be allocated by the Office of the Congressionally Directed Medical Research Programs (CDMRP).

Figure 1: Proposed Consortium Structure. Applicants may propose alternative organizations for the Consortium; however, in all configurations, an EAB will provide consultation to the Clinical Consortium Steering Committee on research gaps and priorities.



3. Required MTF Collaboration: Inclusion of military beneficiaries is a key element of the LCRP Early Detection Clinical Consortium Award. As such, it is expected that Consortium-proposed studies will align closely with the research goals of the MTFs that are consistent with LCRP Early Detection Clinical Consortium Award clinical study areas (Section B.1 and [Appendix](#)). Submitting an application to the LCRP Early Detection Clinical Consortium Award is to be an implicit commitment to collaborate with NMCP, NMCS, SAMMC, and WRNMMC in the Clinical Consortium. Applicants should provide a plan to ensure that the MTFs have input on and participation in all Consortium activities, equivalent with other Clinical Study Sites. The plan should also outline a strategy to develop the necessary research

capabilities at the MTFs, including educational and training opportunities as appropriate. The Coordinating Center must plan to provide resources to the MTFs for their role in Consortium-supported studies, including supplies, small equipment, and research personnel support, as necessary. ***Funds provided through this award may not be used to support government salaries, but may be used to support contract research personnel.*** It is expected that exact MTF requirements will vary based on the type and number of studies conducted by the Consortium. Suggestions of the types of research personnel support that may be needed at the MTFs include clinical research nurses, study coordinators, Ph.D./M.D.-level researchers, technicians, statisticians and clinical research assistants. Exact personnel support and effort levels should be determined by the applicant as appropriate for the proposed studies. It is anticipated that the MTF interface with Consortium-supported personnel will be provided by a doctoral-level research director assigned to the MTF.

Applicants should utilize the information papers provided by each MTF ([Appendix](#)) to work within existing MTF capabilities and determine potential MTF needs within the Consortium. Questions about the LCRP Early Detection Clinical Consortium Award may be sent to cdmrp.lcrp@amedd.army.mil. Questions will be accepted until November 19, 2010. Questions and answers will be posted on the CDMRP eReceipt website, <https://cdmrp.org>.

All applicants to this Program Announcement/Funding Opportunity are not permitted to contact personnel from the named MTFs (NMCP, NMCS, SAMMC, and WRNMMC) regarding any aspect of proposal design and application submission. All questions related to interacting with the MTFs must be directed to the CDMRP as described above. Once award selection is complete, there will be an opportunity to refine MTF needs and resources with appropriate MTF input prior to issuance of the award.

4. Summary of Responsibilities:

- **Responsibilities of all Consortium Participants:** Procedures for the Consortium, while proposed by the Coordinating Center, will be fully developed and agreed upon by all participants working collaboratively at a pre-award planning meeting hosted by the USAMRMC to be held in May or June, 2011, and attended by representatives of the Coordinating Center, Clinical Study Sites (including the MTF sites), EAB, and CDMRP. The Consortium's operating process shall be codified in a Standard Operating Procedure (SOP), which will be provided to the GOR and EAB within 6 months of the Consortium pre-award planning meeting, or 90 days from award execution, whichever comes later.
- **Consortium Coordinating Center**
 - The Coordinating Center PI will serve as the Director of the Consortium, Chair of the Clinical Consortium Steering Committee, and the primary liaison with the GOR;
 - Develop and maintain the Consortium organizational structure;
 - Manage Consortium-developed procedures for external scientific review, prioritization, and implementation of clinical studies proposed by or through Consortium members;

- Provide a Consortium Clinical Research Manager who will oversee the efforts of the Clinical Research Coordinators at the Clinical Study Sites. The Consortium Clinical Research Manager will be responsible for coordinating and facilitating clinical protocol approval, patient accrual, and study activities across all sites;
- Establish and manage procedures to ensure that all sites maintain compliance with local Institutional Review Boards (IRBs) and the Army Surgeon General's Human Research Protection Office (HRPO) for the proper conduct of clinical studies and the protection of human subjects;
- Establish and manage procedures for ensuring compliance with US Food and Drug Administration (FDA) requirements for investigational agents, devices, and procedures;
- Establish and manage a communications plan and a real-time communications system between the Coordinating Center and Clinical Study Sites, including the purchase of multi-site licenses, if necessary;
- Manage costs to support the Clinical Study Sites, including provision of personnel, small equipment, and materials required to conduct approved clinical studies;
- Manage Consortium-developed intellectual and material property issues among organizations participating in the Consortium;
- Manage Consortium-developed procedures for the timely publication of major findings and other public dissemination of data;
- Attend a pre-award planning meeting, hosted by the USAMRMC, with all Consortium members to develop the operational features of the Consortium, the requirements for progress and evaluation, and facilitate the award negotiations process;
- Coordinate the preparation of written and oral twice-yearly briefings to the EAB and USAMRMC staff at 1-day meetings to be held in a centralized location to be determined by the CDMRP;
- Develop, organize, and submit quarterly written progress reports, annual reports, and a final written comprehensive report to the USAMRMC.
- Ensure that a minimum number of clinical studies, as agreed upon by the EAB, Clinical Consortium Steering Committee, and USAMRMC during the pre-award planning meeting, are initiated by the start of the second year of the award;
- Ensure that the Consortium adheres to the planned timeline and milestones for overall study execution;
- Establish a mechanism to provide MTFs with resources necessary for participation in the Consortium;
- Ensure the standardized analyses of specimens, imaging products, and other data through the establishment of scientific core facilities;
- Manage Consortium-developed quality assurance and quality control mechanisms for study monitoring, including but not limited to:
 - On-site monitoring program, to include safety

- Management plan for the handling, distribution, and banking of specimens and imaging products generated from Consortium studies
- Registration, tracking, and reporting of participant accrual
- Timely medical review, rapid reporting, communication of adverse events, and data management/coordination among all sites
- Interim evaluation and consideration of measures of outcome
- Manage Consortium-developed comprehensive data collection and data management systems that address the needs of all Clinical Study Sites in terms of access to data, data security, and data integrity measures;
- Implement statistical execution plans/support for all Consortium clinical studies;
- **Clinical Study Sites**
 - Participate fully in the Clinical Consortium Steering Committee;
 - Integrate with clinical studies at other Clinical Study Sites;
 - Provide a Clinical Research Coordinator (will need to be provided through the appropriate contracting means by the Coordinating Center for each of the MTFs) who will interact with the Clinical Research Coordinators of other Clinical Study Sites and the Consortium Clinical Research Manager at the Coordinating Center to expedite and guide clinical protocols through regulatory approval processes and to coordinate patient accrual and study activities across sites;
 - Identify potential studies and develop proposals in accordance with the Consortium SOP for presentation to the EAB, during the performance period of the award;
 - Maintain a minimum combined accrual across all Consortium-associated studies in accordance with Consortium-developed guidelines, as well as a maximum contributed percentage for each individual study;
 - Implement the Consortium’s core data collection methodology and strategies;
 - Serve as a resource or core for the conduct of protocol-specified laboratory projects (including correlative studies), as appropriate;
 - Comply with Consortium-developed quality assurance and quality control procedures, as appropriate, including:
 - Participate in an on-site monitoring program to be managed by the Coordinating Center
 - Implement the Consortium-developed management plan for acquisition and aggregation of protocol-specified specimens, biological fluids, and relevant clinical data to the appropriate laboratories for testing or storage necessary for the conduct and analyses of clinical studies during the performance period of the award
 - Submit appropriate data and materials to allow for verification and review of protocol-related procedures (e.g., pathology, imaging techniques, surgical methods, therapy use, etc.)

- Implement procedures established by the Coordinating Center for ensuring compliance with FDA requirements for investigational agents, as appropriate;
- Implement procedures established by the Coordinating Center to meet the local IRB and the Army Surgeon General's HRPO requirements for the conduct of clinical studies and the protection of human subjects;
- Participate in Consortium-developed procedures for the timely publication of major findings;
- Participate in Consortium-developed procedures for resolving intellectual and material property issues among organizations participating in the Consortium;
- Attend a pre-award planning meeting with all Consortium members to develop the operational features of the Consortium, the requirements for progress and evaluation, and facilitate the award negotiations process (to be held in May or June, 2011);
- Participate in the preparation of written and oral twice-yearly briefings to the EAB and USAMRMC staff at 1-day meetings to be held in a centralized location to be determined by CDMRP;
- Assist with the preparation of quarterly written progress reports, annual reports, and a final written comprehensive report;
- Prepare for a site visit audit, if applicable.

5. Performance Metrics: Applicants must lay out a plan for at least two different clinical studies the Consortium expects to execute. As a preliminary guideline, the Consortium should be prepared to complete 1 clinical study during the performance period of the award, depending upon its size and complexity. A timeline outlining the overall plan for study initiation, performance, and analyses shall be developed, with clear milestones to which the Consortium will be held accountable. The Clinical Consortium Steering Committee will determine appropriate overall minimum and maximum accrual metrics for the Clinical Study Sites as part of the Consortium SOP, with input from the EAB. For individual clinical studies, the Coordinating Center should ensure the maintenance of overall patient accrual per year, appropriate for the target population. The Consortium SOP should also contain a plan to address and improve participation at underperforming sites. The Coordinating Center will be required to submit quarterly written reports that outline accrual and retention statistics, any problems with study execution, and actions to disseminate study results. It is expected that the Consortium will submit to other agencies for additional funding in order to increase the breadth of research and create a self-sustaining entity that will continue functioning beyond the five-year performance period of the award.

6. Oversight of the Consortium: An EAB composed of selected members of the LCRP IP, consumer advocates, experts in the field, and CDMRP staff will be established by the USAMRMC. The EAB will review progress, and it will provide advice and guidance on scientific and military relevance, and on the coordination of proposed projects with other military relevant initiatives. The EAB will recommend approval to the GOR regarding proposed Consortium studies prior to implementation. Consortium PIs must present written and oral briefings to the EAB and USAMRMC staff at twice-yearly 1-day meetings to be held in a centralized location. Based on these reports and presentations, the EAB and USAMRMC

staff will evaluate progress, provide feedback, and invoke modifications as needed to facilitate the success of the Consortium. The Clinical Consortium Steering Committee, through the Coordinating Center PI, is expected to maintain monthly or more frequent contact with a government appointed GOR, who will maintain full documentation of interactions. The USAMRAA Grants Officer will issue the final approval of any proposed projects and/or studies.

7. Use of Human Subjects and Human Biological Substances: All DOD-funded research involving human subjects and human biological substances must be reviewed and approved by the USAMRMC Office of Research Protections (ORP), HRPO, in addition to local IRBs. The HRPO 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. Allow a minimum of 6 months for regulatory review and approval processes for studies involving human subjects. Refer to General Application Instructions, Appendix 5, for detailed information.

8. US Department of Veterans Affairs (VA) Medical Centers Patient Populations: Applicants are encouraged to include collaborations with VA organizations. Access to patient populations from VA Medical Centers or use of information from VA data systems must be coordinated by the PI. PIs who do not have an appointment at a VA Medical Center and submit a research project designed to recruit patients from a VA Medical Center or use information from VA data systems must include a collaborator with a VA appointment. This collaborator must be willing to assume the role of PI for the VA component of the research. IRB approval from all participating VA clinical sites will be required.

C. Eligibility

The applicant will serve as the Consortium PI and must be an independent investigator at or above the level of Associate Professor (or equivalent) at an eligible organization. Refer to General Application Instructions, Appendix 1, for general eligibility information.

D. Funding

A single award will be made to support the FY10 LCRP Early Detection Consortium. The award will be made to the Coordinating Center applicant selected for funding. The Coordinating Center will provide funding support for the selected Clinical Study Sites as subawards.

All applicants should propose a minimum of two studies that may be initiated by the start of the second year of the award. Proposed studies should include a range of scope, size, and type that is representative of the overall goals of the Consortium. Budget out-years should be projected based on the proposed costs of the initial studies. Following award, a budget for each study will be negotiated individually once study selections are made.

- The maximum period of performance is **5** years.
- The maximum allowable direct plus indirect cost for the entire period of performance is **\$13.5M**.

- The applicant may not exceed the maximum allowable funding. In addition to direct costs, indirect costs may be proposed in accordance with the organization's negotiated rate agreement.
- Exercising the supplemental research plan for expansion of the consortium will be contingent on receipt of sufficient future congressional appropriations, submission and approval of written progress reports, and acceptable performance of the recipient as recommended by the EAB and USAMRMC. The supplemental research plan must be conducted within the same 5-year period of performance. The maximum allowable funding for the entire period of performance for the supplemental research plan is **\$7.5M** in total (direct plus indirect) costs.

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

- Salary support for personnel needed to meet the goals of the Clinical Consortium, including but not limited to the PIs, Consortium Core personnel, Consortium Clinical Research Manager, Program Coordinator, Administrative Coordinator(s), Research Nurse(s), Statistician(s), Database Manager, and Informatics Manager;
- Implementation of Consortium-developed standardization plan, data management program, real-time communications system, and administration plans for the Consortium;
- Support of Consortium-related meetings, teleconferences, and travel among participating investigators;
- Costs associated with the external scientific peer review of clinical studies/research;
- Purchase of computers, specialized software, and specialized software licenses for Clinical Study Sites when required to fulfill Coordinating Center-specific tasks;
- Purchase of minor equipment necessary for specimen and data storage and transfer;
- Costs associated with coordination of informed consent/assent form preparation and other IRB-required materials among different organizations;
- Reimbursement of organizations for additional costs associated with using Consortium Core facilities;
- Reimbursement of organizations for costs associated with conducting the IRB review of the clinical protocols and informed consent/assent forms;
- Costs associated with management of intellectual property resolution and material rights resolution among organizations;
- Clinical costs;
- Research-related subject costs;
- General research costs;
- Costs associated with development of sources for intervention supply or availability;
- Other costs directly associated with planning and developing the consortium;
- Travel costs of up to \$3,600 per year to attend scientific/technical meetings;
- Other direct costs as described in the General Application Instructions for the Detailed Budget and Justification.

In addition, travel funds must be requested for the Coordinating Center PI and each Clinical Study Site PI to attend the DOD Military Health Forum tentatively scheduled for 2012. The PI must also include funds for travel to twice-yearly 1-day briefings with the EAB and USAMRMC staff.

Direct transfer of funds to a government organization or agency is not allowed except under very limited circumstances and as subject to prior Grants Officer approval. The Coordinating Center is expected to provide a mechanism to transfer resources such as supplies and support as necessary to the MTFs to support their participation in Consortium studies. **Funds provided through this award may not be used to support government salaries.** Details on exceptions to the prohibition of direct fund transfer to government entities can be found in Section II.B.2 (Federal Financial Plan) of the General Application Instructions.

The CDMRP expects to allot approximately \$13.5M of the \$15M FY10 LCRP appropriation to fund 1 LCRP Early Detection Clinical Consortium Award application, depending upon the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

E. Award Administration

The Coordinating Center of the LCRP Early Detection Clinical Consortium Award cannot be transferred to another organization.

The recipient will be required to submit three quarterly written progress reports per year, a written annual report, and a final written comprehensive report.

In addition to written progress reports, recipients may expect requests for formal progress presentations in clinical symposia to accelerate transition into clinical practice.

Awards will be made no later than September 30, 2011. Refer to the General Application Instructions, Appendix 4, for general award administration information.

II. TIMELINE FOR SUBMISSION AND REVIEW

- **Pre-application Submission Deadline: 5:00 p.m. Eastern time (ET), November 19, 2010**
- **Application Submission Deadline: 11:59 p.m. ET, December 7, 2010**
- **Scientific Peer Review: February 2011**
- **Programmatic Review: April 2011**

Application submissions will not be accepted unless the pre-application process is completed by the pre-application deadline.

III. SUBMISSION PROCESS

Submission is a two-step process requiring both (1) pre-application submission through the CDMRP eReceipt system (<https://cdmrp.org/>) and (2) application submission through Grants.gov (<http://www.grants.gov/>). Submission of the same research project to different funding opportunities within the same program and fiscal year is discouraged. The Government reserves the right to reject duplicative applications.

PIs and organizations identified in the application should be the same as those identified in the pre-application. If a change in PI or organization is necessary after submission of the pre-application, the PI must contact the eReceipt help desk at help@cdmrp.org or 301-682-5507.

A. Step 1 – Pre-Application Components

All pre-application components must be submitted through the CDMRP eReceipt system by **5:00 p.m. ET on the deadline.**

The pre-application consists of the following components, which are organized in the CDMRP eReceipt system by separate tabs (Refer to the General Application Instructions for additional information on pre-application submission):

- **Proposal Information – Tab 1**
- **Proposal Contacts – Tab 2**
- **Collaborators and Conflicts of Interest (COI) – Tab 3**
- **Required Files – Tab 4**

Letter of Intent (LOI) Narrative (one-page limit): Provide a brief description of the research to be conducted. LOI Narratives are used for program planning purposes only (e.g., reviewer recruitment) and will not be reviewed during either the peer or programmatic review sessions. Briefly state which clinical study area(s) the proposal will address.

- **Submit Pre-application – Tab 5**
- **Other Documents Tab**

Not applicable.

Step 2 – Application Components Applications are submitted by the Authorized Organizational Representative (AOR) through Grants.gov (<http://www.grants.gov/>). Applications must be submitted **by 11:59 p.m. ET on the deadline.**

Each application submission must include the completed application package of forms and attachments identified in Grants.gov for this Program Announcement/Funding Opportunity.

The Grants.gov application package consists of the following components (Refer to the General Application Instructions, Section II.B., for additional information on application submission):

1. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.B., for detailed information.

2. Attachments Form

- **Attachment 1: Project Narrative (50-page limit):** Upload as “ProjectNarrative.pdf.”

Describe the qualifications of the group and the key features of the Consortium using the following general outline:

- **Consortium Expertise and Resources**
 - Outline the structure of the proposed Consortium and identify key personnel.
 - Describe the previous experience of the PI and other key personnel within the Coordinating Center with the design and administration of multi-institutional lung cancer clinical studies. Reference relevant publications and submit reprints with the proposal supporting documentation (Attachment 2).
 - Describe the previous experience of key personnel at each non-military Clinical Study Site with the development and conduct of lung cancer clinical studies. Reference relevant publications and submit reprints with the proposal supporting documentation (Attachment 2).
 - Describe the lung cancer patient populations at each non-military Clinical Study Site and provide evidence of the ability to enroll adequate patient numbers into Consortium-sponsored studies. Provide an estimate of case enrollment/patient load and the track record of research in this area for each Clinical Study Site and each Site PI.
 - Describe the resources and facilities available within each non-military Clinical Study Site for the early detection of lung cancer.
 - Describe the resources and expertise in each participating non-military Clinical Study Site for data management and maintenance of data security/confidentiality.
 - Provide evidence of organizational commitment for the Coordinating Center and each participating Clinical Study Site for the use of facilities and resources in the conduct of Consortium operations.
 - Describe any plans to leverage existing clinical or translational funding programs and infrastructure for the proposed Consortium.
- **Plan of Operations**
 - **Government Coordination:** Describe plans to communicate and partner with the named MTFs. Explain how the MTF Clinical Study Sites will provide input on all Consortium procedures and studies to a level commensurate with all other Clinical Study Sites. Outline a plan for providing resources to the MTFs and establishing the research capabilities needed at the MTFs for full Consortium participation.
 - **Study Identification:** Outline a plan for the proposal, design, and prioritization of potential future Consortium studies for presentation to the EAB following initial study implementation.
 - **Study Management and Monitoring:** Describe plans for real-time communication among all organizations participating in the Consortium (including the rapid dissemination of adverse events). Include a named Consortium Clinical Research Manager who will interact with other individual site clinical coordinators

to guide clinical protocols through the regulatory approval processes, coordinate participant accrual, and coordinate study activities across sites. Outline procedures for quality assurance, quality control, safety and study monitoring.

- **Core Facilities:** Outline essential cores and other facilities to be shared that will be necessary for facilitation of Consortium success. Discuss how the core facilities will be utilized and integrated across all Clinical Study Sites.
- **Clinical Protocol Development and Human Subjects Protection:** Describe plans for coordinating the development of clinical protocols and associated clinical documents that include HRPO-prescribed content. Outline a plan for the external peer review of all Consortium clinical protocols, and the coordination of IRB submissions and approvals. Describe the development of a plan for addressing human subjects protection requirements as outlined by HRPO at [https://mrmc.amedd.army.mil/index.cfm?pageid=Research Protections.hrpo](https://mrmc.amedd.army.mil/index.cfm?pageid=Research%20Protections.hrpo). Outline plans for developing procedures to ensure compliance with FDA requirements for investigational agents, as appropriate.
- **Data Management:** Outline a strategy for the development and implementation of a Consortium-wide data management plan, including: (1) Descriptions of the overall approach to data collection and management, (2) a statistical plan that includes methods to monitor quality and consistency of data collection and methods to measure outcomes, (3) a plan for real-time data transfer, and (4) data security measures.
- **Specimen Handling and Distribution:** Describe plans for the development of methods for the handling, distribution, analysis, banking, and security of any specimens and/or imaging products generated from Consortium-sponsored studies. Include a named coordinator responsible for managing and resolving material and intellectual property issues among Consortium organizations.
- **Information Technology (IT) Resources:** Since the Consortium will rely heavily on information technology, provide the name of the individual who will be responsible for database and information infrastructure. Describe relevant personnel and organizational experience with implementing multi-institutional real-time communications, database, and information infrastructure.
- **Publication and Data Dissemination:** Describe plans for ensuring rapid publication and other public dissemination of data while maintaining participant privacy.
- **Fiscal and Legal Administration:** Describe the fiscal organization necessary for the proper distribution of funds between Clinical Study Sites for performance of clinical studies.
- **Research Plan:** The narrative should include a projection of the types of clinical trials and other clinical research to be conducted by the Consortium over the entire award period. Applicants must provide a description of a minimum of two clinical studies in sufficient detail to allow for evaluation of the group's capabilities, study design expertise, and research interests. The described research must encompass at least one of the early detection/screening clinical study areas listed on page 3. Animal studies are not allowed. Information about the proposed studies should include:

- **Overall Focus:** Identify the major gaps in early detection of lung cancer that the Consortium seeks to address. Describe the broad research goals of the Consortium, and the types of clinical trials and at least two studies to be conducted. Outline a plan for the estimated number and types of studies to be conducted over the five-year performance period.
- **Research Idea:** For each proposed study, describe the ideas and reasoning on which it is based, and how the study addresses a central problem in the early detection of lung cancer. Provide pre-clinical and/or clinical evidence to support the rationale for each study. Identify the LCRP Clinical study area(s) each study addresses.
- **Research Strategy:** Concisely state each study's objectives and specific aims. Describe the patient populations and study sites that will be utilized for each study. Provide sufficient information on the methods, metrics, and statistical power for each study to allow for an evaluation of the proposed budget.
- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. *Each component has no page limit unless otherwise noted.*
 - **References Cited:** 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). The inclusion of Internet URLs to references is encouraged.
 - **List of Acronyms and Symbols:** Provide a list of acronyms and symbols (e.g., PCR = polymerase chain reaction).
 - **Facilities, Existing Equipment, and Other Resources:** Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present contract under which the facilities or equipment items are now accountable. There is no form for this information.
 - **Publications and/or Patent Abstracts (ten-document limit):** Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then they must be included. Extra items will not be reviewed.
 - **Letters of Organizational Support (two-page limit per letter):** Provide a letter (or letters if applicable), of organizational support for the Coordinating Center and each Clinical Study Site (with the exception of the LCRP-named MTF Clinical Study Sites), signed by the Department Chair or appropriate organizational official. Letters should reflect resources available to the Coordinating Center PI or Clinical Study Site PIs for this project. The letters should also indicate the extent to which the PI or Clinical Study Site PIs will be relieved of academic or administrative responsibilities and allowed to pursue his/her research goals.

- Letters of Collaboration (if applicable) (two-page limit per letter): Provide a signed letter from each collaborating individual or organization (not including the MTFs) demonstrating access to the resources necessary for participation in the proposed effort, including but not limited to the availability of and access to appropriate high-risk lung cancer populations and lung cancer patients.
- Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations, and how any conflicts will be resolved.
- **Attachment 3: Technical Abstract (two-page limit):** Upload as “TechAbs.pdf.”
 - Background: Describe the general management and organizational structure of the consortium. Outline the management and clinical expertise of consortium personnel at the Coordinating Center and Clinical Study Sites.
 - Objectives: Describe the consortium’s overall clinical research goals and agenda.
 - Research Plan: Briefly describe the two clinical studies the consortium plans to pursue during the performance period. State how the proposed projects address the LCRP Clinical Consortium Award clinical study areas.
 - Impact: Briefly describe how the expected results will impact the early detection, and ultimately the lives, of individuals at high risk for or with lung cancer.
- **Attachment 4: Public Abstract (two-page limit):** Upload as “PublicAbs.pdf.”
 - Describe the clinical objectives and rationale for the proposal in a manner readily understandable by non-scientists.
 - Do not duplicate the technical abstract.
 - Describe the ultimate applicability of the consortium’s clinical research.
 - What types of patients will it help, and how will it help them?
 - What are the potential clinical applications, benefits, and risks?
 - What is the projected time it may take to achieve a clinically relevant outcome?
 - What are the likely contributions of this study to advancing the field of research?
- **Attachment 5: Statement of Work (SOW) (ten-page limit):** Upload as “SOW.pdf.” Refer to the General Application Instructions, Section II.B., for detailed information.

Include a SOW that covers the work proposed for the entire period of performance, to include the proposed supplemental research plan.

- **Attachment 6: Detailed Budget and Justification (no page limit):** Upload as “Budget.pdf.” Use the Detailed Budget and Justification form (available for download on the Full Announcement page in Grants.gov). Refer to the General Application Instructions, Section II.B., for detailed information.

Include a Detailed Budget and Justification that covers the projected funding needed for the entire period of performance.

- **Attachment 7: Subaward Detailed Budget and Justification (if applicable) (no page limit):** Use a separate Detailed Budget and Justification form for each subaward budget. Combine into a single file and upload as “SubBudgets.pdf.” Refer to the General Application Instructions, Section II.B., for detailed information.
- **Attachment 8: Impact Statement (two-page limit):** Upload as “Impact.pdf.” State explicitly how the proposed work, if successful, will have an impact on accelerating the evaluation and movement of screening modalities for the early detection of lung cancer into clinical practice. Further, describe the impact of the Consortium studies on the lives of individuals with lung cancer, including but not limited to how the expected results of the proposed work will contribute to the goals of decreasing the clinical impact of lung cancer.

Describe how the proposed studies are responsive to the health care needs of the Armed Forces, the US veteran population and/or military beneficiaries. Describe the population(s) that are to be utilized, and their appropriateness for the proposed studies. If non-military populations will be used for the proposed research, explain how the populations pertain to the targeted population (i.e. Armed Forces, the US veteran population, and/or military beneficiaries). Describe how the studies build upon research initiatives ongoing at the named MTF Clinical Study Sites.

- **Attachment 9: Supplemental Research Plan (five-page limit):** Upload as “SupplResPlan.pdf.” The narrative should include a description of how the Consortium would be expanded if additional funds are allocated by CDMRP, such as addition of clinical sites and/or the other types of clinical trials and clinical research to be conducted by the Consortium during the 5-year award period. Animal studies are not allowed. Information about proposed studies should include:
 - Research Idea: For each proposed study, describe the ideas and reasoning on which it is based, and how the study addresses a central problem in the early detection of lung cancer. Provide pre-clinical and/or clinical evidence to support the rationale for each study. Identify the LCRP Clinical study area(s) each study addresses.
 - Research Strategy: Concisely state each study’s objectives and specific aims. Describe the patient populations and study sites that will be utilized for each study. Provide sufficient information on the methods, metrics, and statistical power for each study to allow for an evaluation of the proposed budget.

Projected funding needed for the proposed supplemental research plan needs to be included as a separate budget within the 5-year period of performance.

- **Attachment 10: Supplemental Research Plan Detailed Budget and Justification (no page limit):** Upload as “SupplementalBudget.pdf.” Use a separate Detailed Budget and Justification form for the supplemental research plan budget. Refer to the General Application Instructions, Section II.B., for detailed information.

3. Research & Related Senior/Key Person Profile (Expanded) Form: Refer to the General Application Instructions, Section II.B., for detailed information.

- PI Biographical Sketch (four-page limit): Upload as “Biosketch_LastName.pdf.”
- PI Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”

- Key Personnel Biographical Sketches (four-page limit each): Upload as “Biosketch_LastName.pdf.”
- Key Personnel Current/Pending Support (no page limit): Upload as “Support_LastName.pdf.”

4. Project/Performance Site Location(s) Form: Refer to the General Application Instructions, Section II.B., for detailed information.

Although requested, the supplemental research plan and budget will not be forwarded for peer review. These documents will be reviewed during programmatic review.

IV. INFORMATION FOR APPLICATION REVIEW

A. Application Review and Selection Overview

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a scientific peer review of applications against established criteria for determining scientific merit. The second tier is a programmatic review that compares applications to each other and makes recommendations for funding to the Commanding General, USAMRMC, based on scientific merit, the overall goals of the program, and specific intent of the award mechanism. The highest scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier review process used by the CDMRP may be found at <http://cdmrp.army.mil/about/fundingprocess.shtml>.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each level of review requires panelists to sign a non-disclosure statement attesting that application and evaluation information will not be disclosed outside the panel. Violations of the non-disclosure statement can result in the dissolving of a panel(s) and other corrective actions. Organizational personnel and PIs are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization’s application. Violations by panelists or PIs that compromise the confidentiality of the review process may also result in suspension or debarment of their employing organizations from Federal awards. Furthermore, it is a crime for Federal officials to disclose confidential information of one party to another third party (Title 18 United States Code 1905).

B. Review Criteria

1. Peer Review: All applications will be evaluated according to the following criteria, which are of equal importance:

- **Consortium Expertise**
 - To what extent the Coordinating Center personnel’s background, track record, and expertise are appropriate with respect to the ability to manage and oversee multi-institutional lung cancer clinical studies.

- To what extent the research teams' background, track record, and expertise at each Clinical Study Site are appropriate with respect to the successful conduct of lung cancer studies and participation in multi-center clinical studies.
- To what extent the levels of effort are appropriate for successful conduct of the proposed work.
- The degree to which the level of organizational information technology experience in implementing multi-institutional real-time communications is appropriate.
- How the specific abilities and experience possessed by the named information technology lead will enable him/her to quickly and efficiently implement the electronic communications required by the Consortium.
- The degree to which the ability and experience of the organization with the financial management of multi-institutional research studies is appropriate.
- **Coordination of Consortium Components**
 - To what extent the proposed overall organizational structure of the Consortium is appropriate.
 - How well the Coordinating Center addresses a plan to oversee and coordinate all Consortium Sites.
 - How well the plan for the establishment and maintenance of core facilities will effectively support Consortium activities.
 - How well each Consortium Site will function as an integrated unit.
 - How well the proposed Consortium structure and research integrates the MTFs and their stated research goals.
 - To what degree the appropriate resources are provided for full participation at each Consortium Site.
- **Study Management and Monitoring**
 - How the plans for real-time communication among all organizations participating in the Consortium, including complete and timely reporting of adverse events, are appropriate to facilitate Consortium activities.
 - The extent of the named Consortium Clinical Research Manager's experience with guiding clinical protocols through the regulatory approval processes, coordinating participant accrual, and coordinating study activities across sites.
 - How the outlined procedures for quality assurance, quality control, safety, and study monitoring are adequate for conducting multi-institutional clinical studies.
 - How the plans for specimen handling, distribution, analysis, banking, and security are appropriate to facilitate Consortium activities.
- **Data Management**
 - The degree to which the overall approach to data collection, management, analysis, and security measures is appropriate.
 - How clearly the effective application of methods to monitor quality and consistency of data collection and methods to measure outcomes in previous trials

conducted have been demonstrated by the PI and key personnel.

- How the plan for real-time data transfer is adequate for supporting the Consortium-associated activities.
- The degree to which plans for the publication and other dissemination of data are appropriate.

- **Clinical Protocol Development and Human Subjects Protection**

- The degree to which plans for the proposal, development, and external peer review of clinical protocols and associated clinical documents within the performance period are appropriate.
- Whether the proposed clinical protocols are responsive to at least one of the LCRP clinical study areas
- To what extent the plans for addressing human subjects protection requirements as described by HRPO, and coordinating IRB submissions and approvals at participating sites are appropriate.
- How well appropriate plans for developing procedures to ensure compliance with U.S. Food and Drug Administration (FDA) regulations for investigational agents are considered.

- **Organizational Resources and Commitment**

- The degree of organizational commitment for the use of facilities and resources in the conduct of Consortium operations.
- Whether the organizations have demonstrated access to appropriate patient populations for conduct of Consortium clinical studies.
- How well the facilities and resources within each Clinical Study Site are appropriate for the screening of individuals at high risk for lung cancer.
- How well the resources and expertise at each organization are appropriate for coordinating specimen collection and processing.
- To what extent the resources and expertise at each organization are appropriate for data management and maintaining security/confidentiality.
- The degree to which each organization demonstrates a willingness to resolve intellectual and material property issues with other organizations in the Consortium.
- The extent to which the intellectual and material property plan is developed and appropriate.
- How well the commitment of the organizations to work with all Consortium sites, including the MTFs, is demonstrated.

- **Research Plan**

- The extent to which the plan for the estimated number and types of studies to be conducted during the duration of this award is appropriate and feasible.
- How well the scientific rationale and preliminary data support each proposed initial study's design and objectives.

- The degree to which the patient populations and sample size are appropriate for each proposed initial study.
- The degree to which proposed methods and outcome measures are appropriate for the purposes of each proposed initial study.
- **Impact**
 - The degree to which the proposed research, if successful, will have a significant impact on the early detection of lung cancer.
 - How well appropriate studies were proposed to resolve gaps related to the LCRP Clinical Consortium Award clinical study areas.

The following will not be individually scored, but may impact the overall evaluation of the application:

- **Application Presentation**
 - How the writing and components of the application influenced the review.
- **Budget**
 - Whether the budget is appropriate for the proposed research and within the limitations of the award mechanism.

2. Programmatic Review: The following criteria are used by programmatic reviewers to make funding recommendations.

- Adherence to the intent of the award mechanism.
- Programmatic relevance in relation to LCRP Early Detection Clinical Consortium clinical study areas.
- Ratings and evaluations of the peer reviewers.
- Program portfolio composition.

V. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from CDMRP eReceipt or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the application:

- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Pre-application is not submitted.

B. Modifications

- Pages exceeding the specified limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.
- Following the application deadline, you may be contacted by CDMRP via email with a request to provide certain missing supporting documents, including the supplemental research plan and/or budget (excluding those listed above in Section V-A, Rejection). The missing documents must be provided by 5:00 p.m. ET on the second full business day following the date the email was sent. Otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- FY10 LCRP IP member(s) is found to be involved in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document. A list of the FY10 LCRP IP members may be found at <http://cdmrp.army.mil/lcrp/panels/panels10.shtml>.
- Personnel from the named MTFs are found to be involved in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- Total costs as shown on the detailed budget form exceed maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs with the exception of links to published references.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization will be requested to provide the findings of the investigation to the USAMRAA Contracting/Grants Officer for a determination of the final disposition of the application.

VI. CONTACT INFORMATION

A. CDMRP Program Announcement Help Desk: Questions related to Program Announcement/Funding Opportunity content or submission requirements should be directed to the CDMRP Program Announcement help desk, which is available Monday through Friday from 7:30 a.m. to 4:00 p.m. ET. Submit questions as early as possible. Response times will vary depending upon the volume of inquiries. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079
Email: cdmrp.pa@amedd.army.mil

B. CDMRP eReceipt System Help Desk: Questions related to the submission of the pre-application through the eReceipt system should be directed to the CDMRP eReceipt system help desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET.

Phone: 301-682-5507
Email: help@cdmrp.org

C. Grants.gov Contact Center: Questions related to application submission through the Grants.gov portal should be directed to Grants.gov help desk, which is available 24 hours a day, 7 days a week. Please note that the CDMRP Program Announcement/Funding Announcement and eReceipt system help desks are unable to provide technical assistance regarding Grants.gov submissions.

Phone: 800-518-4726
Email: support@grants.gov

Sign up on Grants.gov for “send me change notification emails” by following the link on the Synopsis page for the Program Announcement/Funding Opportunity. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed	
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1	
	Upload Supporting Documentation (Support.pdf) as Attachment 2	
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3	
	Upload Public Abstract (PublicAbs.pdf) as Attachment 4	
	Upload Statement of Work (SOW.pdf) as Attachment 5	
	Upload Detailed Budget and Justification (Budget.pdf) as Attachment 6	
	Upload Subaward Detailed Budget and Justification (SubBudgets.pdf) as Attachment 7	
	Upload Impact Statement (Impact.pdf) as Attachment 8	
	Upload Supplemental Research Plan (SupplResPlan.pdf) as Attachment 9	
	Upload Supplemental Research Plan Detailed Budget and Justification (SupplementalBudget.pdf) as Attachment 10	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field	
	Attach PI Current & Pending Support (Support_LastName.pdf) to the appropriate field	
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field	
	Attach Current & Pending Support (Support_LastName.pdf) for each senior/key person to the appropriate field	
Project/Performance Site Location(s) Form	Complete form as instructed	

APPENDIX
INFORMATION ON MILITARY TREATMENT FACILITIES

Naval Medical Center Portsmouth

Naval Medical Center Portsmouth (NMCP) is a 300-bed teaching facility with a complement of specialty and subspecialty services. It has well established Hematology/Oncology services with its own inpatient ward, a Pulmonary department with bronchoscopic and critical care capabilities, a full Cardiothoracic Surgery division, and Radiation Oncology division. There is an active weekly cardiothoracic tumor board that is dedicated to the management of difficult thoracic cases in a multimodality setting including all of these services as well as pathology and radiology services.

Mission: The mission of the Hematology/Oncology service for NMCP is to provide the highest quality comprehensive medical care for our active duty members, dependents, and retirees in order to maintain operational readiness, promote wellness and health, and establish an oncology center of excellence. We believe that success in this effort requires direct involvement in current approaches to diagnosis and treatment of hematologic and neoplastic disease through involvement in research in these areas, participation in clinical trials, and establishment of a rigorous academic environment for our staff and residents to fully meet graduate medical education requirements.

Research Goals:

- Participate in large multicenter clinical trials of early detection of lung cancer with molecular screening through collaboration with established research centers.
- Establish non-imaging based screening program for early detection of lung cancer at NMCP through use of molecular and serologic screening methods to assess presence of selected biomarkers in serum/plasma and in sputum samples.
- Expand graduate medical educational (GME) opportunities for residents to participate in research in molecular diagnostic studies and publish their results in peer reviewed professional journals.
- Extend these molecular diagnostic methods for early lung cancer screening to other clinical areas for diagnostic and theranostic purposes

Current Research Areas:

Clinical Research Protocols: NMCP currently participates in 54 Multicenter trials including POG, RTOG, NSABP studies, although not strictly lung cancer-related.

Patient Population: NMCP and several adult primary care clinics in the area serve a population of over 300,000 beneficiaries. Of those beneficiaries who are enrolled, 15,199 are enrolled at NMCP. This population is unique in its size and concentration, in its access to covered medical care, its detailed longitudinal electronic medical records and laboratory data, its regularly documented health screenings, and in its general compliance with health initiatives. Demographics and statistics on the lung cancer cases at NMCP are presented in Tables 1-5.

**Table 1. Number of New Lung Cancer Cases from 2005 – 2009 at NMCP
Categorized by Stage**

NUMBER OF NEW CASES BY YEAR/STAGE							
Year	Total Number New Cases	Stage Group					
		I	II	III	IV	Unk	N/A
2005							
2006							
2007							
2008							
2009							

**Table 2. Demographic Data for Lung Cancer Cases at NMCP from 2005 – 2009:
Age at Diagnosis**

AGE AT DIAGNOSIS		
Age Group	Number of Cases	% of Cases
20-29		
30-39		
40-49		
50-59		
60-69		
70-79		
80-89		
90+		

**Table 3. Demographic Data for Lung Cancer Cases at NMCP from 2005 – 2009:
Gender**

SEX		
Gender	Number of Cases	% of Cases
Male		
Female		

**Table 4. Demographic Data for Lung Cancer Cases at NMCP from 2005 – 2009:
Race**

RACE		
Label	Number of Cases	% of Cases
White		
Black		
American Indian, Aleutian, or Eskimo		
Chinese		
Filipino		
Korean		
Thai		
Samoan		
Other Asian, including Asian, NOS and Oriental, NOS		
Pacific Islander, NOS		
Other		
Unknown		

**Table 5. Demographic Data for Lung Cancer Cases at NMCP from 2005 – 2009:
Smoking History**

SMOKING HISTORY		
Label	Number of Cases	% of Cases
Never used		
Cigarette smoker, current		
Cigar/pipe smoker, current		
Snuff/chew/smokeless, current		
Previous use		
Unknown		

Personnel:

Clinical Investigation/Research Department (CIRD): Staff of 15, support for both animal and clinical research. There are two Institutional Review Boards and an Institutional Animal Care and Use Committee. The animal facility is Association for Assessment and Accreditation of Laboratory Animal Care International-accredited with a full-time veterinarian, vet technicians, facility manager, and animal technicians; capability for major and microscopic surgery, full anesthesia, histopathology, and an operational small animal hyperbaric chamber. On the clinical side, there is a biostatistician, two basic science Ph.D.s, three research assistants assigned as needed, a medical editor, a Cooperative Research and Development Agreement manager, administrators, and research training along with protocol processing.

- 3 Full-time Cardiothoracic Surgeons.
- 4 Full-time Hematologist Oncologists with research experience.

- 5 Full-time Pulmonologists
- 3 Full-time Radiation Oncologists

Resources:

Hematology Oncology Services: The Division participates in the multimodality care of Thoracic, Breast, ENT and General Surgery Tumor boards, sustains vigorous Hematology and Oncology Consultation services, and maintains a dedicated Oncology Ward Service.

Medical Library: The library has two medical librarians and maintains an extensive collection of medical, biomedical, and surgical materials (textbooks, professional journals). There is an interlibrary loan service, and the library is available 24 hours a day.

NMCP Laboratory: The laboratory has full liquid-based cytology services and has recently purchased new PCR instruments (Applied Systems 7500 Fast Dx Real Time PCR and Roche MagNA Pure LC 2.0) for influenza testing. The laboratory also provides immunofluorescent services, immunohistochemistry and flow cytometry testing on site. Flow cytometric analysis has capability for cell sorting and/or DNA analysis.

Pathology: CAPT Richter, a board certified hematopathologist, provides hematopathology and general pathology services for the hospital, including flow cytometry services, and has extensive research background with doctoral training. He has established flow cytometry services at two different sites and is one of the most experienced pathologists in accreditation requirements for clinical laboratories. He is well published and serves as a clinical investigator for Children’s Oncology Group. His technical staff (MT) is capable of performing molecular diagnostic testing with appropriate training and providing support for research activities.

Pulmonary Medicine: Bronchoscopy suite, PFT lab and pending addition of bronchoscopic US capabilities.

Radiation Oncology: Two linear accelerators with the ability to perform three-dimensional (3D) conformal radiation therapy, intensity modulated radiation therapy, electron therapy, high- and low-dose rate brachytherapy (given both interstitial and intracavitary), respiratory gating, and pending capability to perform both intracranial and stereotactic body radiosurgery.

Radiology Services: Full Range of Imaging Services including computed tomography (CT), PET/CT, magnetic resonance imaging (MRI), and an active Interventional Radiology suite.

Future Studies of Interest:

- Develop protocols for optimal collection, processing, storage, and transport of sputum and blood specimens from our patient population to meet requirements for multicenter clinical trials of early detection of lung cancer with molecular screening methods.
- Evaluate use of Thin-prep methods for collection and processing of sputum specimens for molecular testing for early detection of lung cancer.
- Establish on-site diagnostic testing for fluorescent in situ hybridization and PCR-based testing.

- Develop screening methods of plasma or serum for high-risk individuals for glypican-3 and other surrogate serologic markers, as well as for circulating free tumor DNA.

Potential Personnel Needs at MTF for Consortium Studies: A site coordinator, a research nurse, and a research assistant would be needed depending on the number of patients enrolled. It is expected the exact MTF requirements will vary based on the type and number of studies conducted by the Consortium.

Naval Medical Center San Diego

Naval Medical Center San Diego (NMCS D) is a 268-bed multi-specialty military treatment facility and ambulatory care complex located on 78 acres in the southeast corner of Balboa Park in San Diego, California. Additionally, there are 9 primary care clinics offering care to active duty and family members in San Diego County. NMCS D serves a beneficiary population of 250,000 active duty, family members, and retirees in the greater San Diego area. All medical and surgical specialties are available. The Pulmonary and Critical Care Medicine department currently includes 7 staff pulmonologists and 5 fellows in training.

Mission: The NMCS D Pulmonary Medicine and Radiology Departments are committed to conducting lung cancer research as it relates to detection and effective treatment of early curable lung cancer in military beneficiaries.

Research Goals: The ultimate goal is to develop a lung cancer screening protocol with definitive efficacy as evidenced by a reduction in lung cancer and all-cause mortality. To this end, the benefit gained by earlier intervention should not be offset by the potential harmful effects of screening as represented by radiation exposure, invasive diagnostic and therapeutic procedures in subjects with either false-positive or true-positive results, lung resections performed on patients with occult metastatic disease, and the anxiety provoked by indeterminate results.

Current Research Areas:

Clinical Research Protocols:

- A case series of young patients (less than age 45) with lung cancer diagnosed at NMCS D
- A Phase III double-blind, placebo-controlled trial of Sunitinib as maintenance therapy in advanced non-small cell lung cancer

Patient Population: NMCS D actively manages 100,000 of an eligible beneficiary population of 250,000 active duty, family members, and retirees. Of those beneficiaries who are enrolled, 66,000 are enrolled in adult primary care clinics. High-risk patients include current or former smokers. In addition, those exposed to asbestos, ionizing radiation, and second-hand smoke, patients who have undergone radiation therapy for breast or Hodgkin lymphoma, patients with pulmonary fibrosis, and those with a strong family history appear to be at increased risk for lung cancer. Demographics and statistics on the lung cancer cases at NMCS D are presented in Tables 1-5.

**Table 1. Number of New Lung Cancer Cases from 2005 – 2009 at NMCS D
Categorized by Stage**

NUMBER OF NEW CASES BY YEAR/STAGE							
Year	Total Number New Cases	Stage Group					
		I	II	III	IV	Unk	N/A
2005	50	12	4	18	16	0	0
2006	48	9	2	9	27	0	1
2007	78	23	2	22	28	0	3
2008	83	31	4	19	26	1	2
2009	81	34	2	15	26	2	2

**Table 2. Demographic Data for Lung Cancer Cases at NMCS D from 2005 – 2009:
Age at Diagnosis**

AGE AT DIAGNOSIS		
Age Group	Number of Cases	% of Cases
20-29		
30-39		
40-49		
50-59		
60-69		
70-79		
80-89		
90+		

**Table 3. Demographic data for lung cancer cases at NMCS D from 2005 – 2009:
Gender**

SEX		
Gender	Number of Cases	% of Cases
Male	228	67%
Female	112	33%

**Table 4. Demographic data for lung cancer cases at NMCS D from 2005 – 2009:
Race**

RACE		
Label	Number of Cases	% of Cases
White	241	71%
Black	27	8%
American Indian, Aleutian, or Eskimo	-	-
Chinese	-	-
Filipino	46	14%
Korean	-	-
Thai	-	-
Samoan	-	-
Other Asian/Pacific Islander	15	4%
Other	9	3%
Unknown	2	1%

Table 5. Demographic Data for Lung Cancer Cases at NMCS D from 2005 – 2009: Smoking History

SMOKING HISTORY		
Label	Number of Cases	% of Cases
Never used	56	16%
Cigarette smoker, current	88	26%
Cigar/pipe smoker, current	-	-
Snuff/chew/smokeless, current	-	-
Previous use	186	55%
Unknown	10	3%

Potential accrual clinics include the internal medicine clinic, pulmonary medicine clinic, tricare outpatient clinics, family medicine clinics, and military medicine clinics. Tables 6 and 7 show the number of adults enrolled in primary care clinics at NMCS D and its satellites, and the number of primary care providers at each site, respectively.

Enrollees as of July 2010 for 18 and older

Age Group	(Multiple Items)
Enrollees 18 or older	
DMIS	July 2010
BMA NALF SAN CLEMENTE	36
BMCMCAS MIRAMAR	5,381
NBHC EL CENTRO	569
NBHC MCRD SAN DIEGO	1,768
NBHC NAS NORTH ISLAND	9,824
NBHC NAVSTA SAN DIEGO	4,882
NBHC NTC SAN DIEGO	10,265
NMC SAN DIEGO	13,390
SAN DIEGO EAST COUNTY PRIM CARE	2,424
TRICARE OUTPATIENT-CHULA VISTA	9,348
TRICARE OUTPATIENT-CLAIRMONT	8,715
Grand Total	66,602

Figure 1. Adults Enrolled in Primary Care Clinics at NMCS D

Number of providers in Primary Care Clinics July 10

Row Labels	Count of Provider
C5 PRIMARY CARE	2
ECC TEAM 1	4
GENERAL CLINIC, ELCENTRO	3
INTMED,BLUE TEAM	20
INTMED,GOLD TEAM	20
INTMED,SILVER TEAM	22
MCRD STAFF SICK CALL	2
MED HOLD NAVAL BASE	2
MILITARY HEALTH CENTER	6
MIRAMAR PRIMARY CARE	2
MIRAMAR, FAMILY PRACTICE	5
NAVAL BASE TEAM 1	6
NI ACTIVE DUTY CLINIC	5
NI FAMILY MEDICINE	4
NTC FAMILY PRACTICE TEAM 1	4
NTC FAMILY PRACTICE TEAM 2	4
NTC FAMILY PRACTICE TEAM 3	3
NTC FAMILY PRACTICE TEAM 4	3
SICK CALL, SCI	2
TOC CHULA VISTA TEAM 1	4
TOC CHULA VISTA TEAM 2	4
TOC CHULA VISTA TEAM 3	4
TOC CM TEAM 1	4
TOC CM TEAM 2	4
TOC CM TEAM 3	4
Grand Total	143

Figure 2. Number of Providers in Primary Care Clinics for NMCS D

Personnel: Lung cancer screening research will be a multidisciplinary collaboration involving medical professionals in the pulmonary medicine, radiology, internal medicine, family practice, and pathology departments. Non-medical professionals will include members in the Tumor Registry Department. The NMCS D Department of Clinical Investigation has one Ph.D. scientist, a biostatistician, several laboratory assistants, and two administrative research assistants.

Resources:

Radiology Department: The radiology department possesses 4 computed tomography (CT) scanners, 3 of which are used for thoracic radiological purposes. Currently, approximately 5 to 10

CT scans are performed daily, Monday through Friday, for imaging of pulmonary nodules. Radiation dose is weight-based, and the lowest required dose is used.

Pathology Department: The anatomic pathology department at NMCS D possesses both a surgical pathology section and a cytology section. NMCS D is billeted for 10 pathologists.

Cytological capabilities include but are not limited to:

- Manual thin preparations of specimens (bronchoscopic washings and brushings)
- Automated staining
- Cytospin for pleural fluid analysis
- Cell block preparation

Surgical Pathology capabilities include but are not limited to:

- Frozen section for rapid specimen analysis. The lab possesses 3 cryostat machines.
- 4 Tissue-Tek processors for rapid processing of tissue specimens for histological diagnosis.
- Immunohistochemistry processor. Stains for CK7, CK20, TTF-1, and pancytokeratin.
- If special stains are required for diagnosis, specimens are sent to laboratories under contract with the NMCS D laboratory.

Pulmonary Medicine Department: The pulmonary medicine department possesses a pulmonary function laboratory equipped with 3 spirometers and body plethysmography boxes. Formal cardiopulmonary exercise testing and interpretation is available. There is an on-site pulmonary procedure suite equipped for flexible bronchoscopy, endobronchial ultrasound, and pleuroscopy. All staff pulmonologists are credentialed to perform bronchoscopy and bronchoscopic biopsies. In addition, we have one staff member credentialed in endobronchial ultrasound and pleuroscopy, with the intention to train and credential additional staff pulmonologists and fellows in both techniques.

Future Studies of Interest:

- Should patients with potentially lethal comorbidities (i.e. severe Chronic Obstructive Pulmonary Disease) be excluded from screening?
- Should PET scanning be incorporated into a lung cancer screening protocol to evaluate indeterminate pulmonary nodules?
- Is there a way to quantify overdiagnosis in a lung cancer screening program?
- Will lung cancer screening lead to earlier intervention that achieves a mortality reduction that exceeds the mortality increase secondary to invasive procedures in patients with true positive and false positive tests?

Potential Personnel Needs at MTF for Consortium Studies: A site coordinator, a research nurse, and a research assistant would be required, depending on the number of patients enrolled. It is expected that exact MTF requirements will vary based on the type and number of studies conducted by the Consortium.

San Antonio Military Medical Center

Brooke Army Medical Center (BAMC) is a 450-bed echelon 5 military treatment facility that is located on Fort Sam Houston and serves approximately 400,000 military beneficiaries in the South Texas area. The 2005 BRAC law mandated a combining of Brooke Army Medical Center and Wilford Hall Air Force Medical Center by 2012, which will result in a combined Army/Air Force inpatient facility at BAMC and outpatient facility at Wilford Hall Medical Center (WHMC). This union is occurring now, and is referred to as the San Antonio Military Medical Center (SAMMC). All medical and surgical oncologic specialties are available at either hospital. Currently, the Hematology/Oncology Service is temporarily located at WHMC with all Cardiothoracic Surgery Services presently housed at BAMC. The Pulmonary Disease/Critical Care Services are located at both facilities, and currently there are 12 fellows in training.

Mission: SAMMC is committed to providing state of the art comprehensive care for patients with lung cancer in the South Texas region.

Research Goals:

- Have the ability to enroll patients from the San Antonio Multi-Marker with high-risk factors for lung cancer (smoking, Chronic Obstructive Pulmonary Disease [COPD]) in a lung cancer screening trial.
- Provide opportunities for patients with lung cancer to enroll in research protocols from the Southwest Oncology Group and Cancer Therapy Research Center that allow for increased opportunities for treatment of lung cancer.
- Expand the use of CellSearch (circulating tumor cell) technology in the diagnosis and treatment of patients with all stages of lung cancer.
- Continue weekly clinical conferences that include Pulmonary, Oncology, Radiology, Cardiothoracic Surgery, and Radiation Oncology services to discuss and provide best treatment options for all lung cancer patients.

Current Research Areas:

Clinical Research Protocols: An active member of the Southwest Oncology Group with enrollment of patients in numerous lung cancer research protocols. In addition, SAMMC is an active participant of the Cancer Therapy Research Center which sponsors numerous Phase I/II cancer research protocols. A list of active protocols is described below:

1. *AVF3671g: A Randomized, Double-Blind, Placebo-Controlled, Phase IIIB Trial Comparing Bevacizumab Therapy With or Without Erlotinib after Completion Chemotherapy with Bevacizumab for the First-Line Treatment of Locally Advanced Recurrent or Metastatic Non-Small Cell Lung Cancer*

The primary objective of this Phase IIIB study is to compare PFS (performance-free survival) in subjects randomized to bevacizumab + erlotinib versus bevacizumab + erlotinib-placebo in subjects with NSCLC who have completed 4 cycles of chemotherapy with bevacizumab without disease progression or significant toxicity.

2. *Detection of Circulating Tumor Cells in Stage I/II Non-Small Cell Lung Cancer*

To identify circulating tumor cells (CTC) in the blood of patients with the specified stages of

NSCLC, using HER2/neu receptors on the cells, before and after pulmonary surgery. The specific goal of the study is to serve as a proof-of-principle study, that CTC can be detected successfully using the CellSearch system, and to determine if there is reason to believe that the number of CTC in these patients can be used as an indicator of prognosis for the disease.

3. *Association of Tumor Necrosis Factor Alpha Antagonists with Lung Malignancy*

To determine if there is an increased incidence of lung malignancy and more advanced stage of lung malignancy at initial diagnosis in patients who have received tumor necrosis factor alpha (TNF- α) antagonists when compared to the general population.

4. *A Phase I/2 Study of the Vascular Disrupting Agent NPI-2358 in Combination with Docetaxel in Patients with Advanced Non-Small Cell Lung Cancer*

The primary objective is to determine the Maximally Tolerable Dose (MTD) and/or Recommended Phase 2 Dose (RP2D) of NPI-2358 in combination with docetaxel in patients with advanced Non-Small Cell Lung Cancer on days 1 and 8 in 3-week cycles. This protocol is being conducted under FDA IND #70782.

5. *A Phase 2 Study of Intravenous Administration of REOLYSIN (Reovirus Type 3 Dearing) in Combination with Paclitaxel and Carboplatin in Patients with Squamous Cell Carcinoma of the Lung (IND 09-27)*

To assess antitumor effect of the treatment regimen in the study population in terms of objective response rates (i.e., partial response [PR] and complete response [CR] to treatment.

6. *A Phase III Prospective, Randomized, Double-Blind, Placebo-Controlled Trial of the Epidermal Growth Factor Receptor Antagonist, ZD 1839 (IRESSA) in Completely Resected Primary Stage IB, II and IIIA Non-Small Cell Lung Cancer*

To assess, in comparison with placebo, the impact of adjuvant therapy with 2 years of daily oral ZD 1839 (IRESSA) on the overall survival of patients with completely resected (T1N1-2, T2N0-2; T3N0-2) non-small Cell Lung Cancer (C.2003.082)

7. *SWOG CTSU E1505, A Phase III Randomized Trial of Adjuvant Chemotherapy With or Without Bevacizumab for Patients with Completely Resected Stage IB (> 4cm) - IIIA Non-Small Cell Lung Cancer*

The purpose of this study is to determine if adding the drug bevacizumab to chemotherapy improves the chance for cure for patients who have had surgery for the removal of the lung cancer.

Investigators will compare the effect (good and bad) of adding bevacizumab to chemotherapy with standard chemotherapy alone on subjects and their lung cancer to see which is better at preventing the cancer from coming back.

Patient Population: There is a beneficiary population of 218,250 in the San Antonio Multi-Market, with 43,000 patients older than 65 and 55,000 patients between ages 45-64. Of those beneficiaries who are enrolled, 49,406 are enrolled at BAMC. Potential high-risk patients include

COPD patients and current or former smokers. Demographics and statistics on the lung cancer cases at SAMMC are presented in Tables 1-5.

Table 1. Number of New Lung Cancer Cases from 2005 – 2009 at SAMMC Categorized by Stage

NUMBER OF NEW CASES BY YEAR/STAGE							
Year	Total Number New Cases	Stage Group					
		I	II	III	IV	Unk	N/A
2005	119	32	9	31	43	3	1
2006	125	38	6	23	40	14	4
2007	109	41	5	22	29	6	6
2008	135	45	8	33	41	5	3
2009	115	28	9	23	43	8	4

Table 2. Demographic Data for Lung Cancer Cases at SAMMC from 2005 – 2009: Age at Diagnosis

AGE AT DIAGNOSIS		
Age Group	Number of Cases	% of Cases
20-29	1	0.2%
30-39	6	1.0%
40-49	26	4.3%
50-59	72	11.9%
60-69	168	27.9%
70-79	242	40.1%
80-89	85	14.1%
90+	3	0.5%

Table 3. Demographic Data for Lung Cancer Cases at SAMMC from 2005 – 2009: Gender

SEX		
Gender	Number of Cases	% of Cases
Male	377	62.5%
Female	226	37.5%

Table 4. Demographic Data for Lung Cancer Cases at SAMMC from 2005 – 2009: Race

RACE		
Label	Number of Cases	% of Cases
White	522	86.6%
Black	48	8.0%
American Indian, Aleutian, or Eskimo	1	0.2%
Chinese	1	0.2%
Filipino	5	0.8%
Korean	2	0.3%
Thai	1	0.2%
Samoan	1	0.2%
Other Asian/Pacific Islander	7	1.2%
Other	12	2.0%
Unknown	3	0.5%

Table 5. Demographic Data for Lung Cancer Cases at SAMMC from 2005 – 2009: Smoking History

SMOKING HISTORY		
Label	Number of Cases	% of Cases
Never used	61	10.1%
Cigarette smoker, current	172	28.5%
Cigar/pipe smoker, current	6	1.0%
Snuff/chew/smokeless, current	4	0.7%
Previous use	332	55.1%
Unknown	28	4.6%

Potential accrual resources include the following:

- Pulmonary Clinic, BAMC and WHMC
- Internal Medicine Clinic, BAMC and WHMC
- Primary Care Clinics at multiple sites throughout San Antonio to include Fort Sam Houston, Lackland Air Force Base, Brooks City Base, Randolph Air Force Base, Camp Bullis, and North Federal Clinic
- Smoking Cessation Clinics: Pulmonary Clinic (BAMC and WHMC), Cardiology Clinic (BAMC), Wellness Centers at Lackland AFB and Randolph AFB

Personnel:

Pulmonary/Critical Care: The pulmonary services are divided equally between BAMC and WHMC, which includes 8 full-time physician faculty members at BAMC and 6 full-time physician faculty members at WHMC, with a total of 12 Army and Air Force pulmonary fellows that rotate between both hospitals. The fellows have 6 months of dedicated research time during a 3-year fellowship. Availability of the staff pulmonologists is variable given clinical supervision and administrative duties.

Hematology/Oncology: The entire Hematology/Oncology service is located at WHMC and will begin transitioning to BAMC in the summer of 2011. The service consists of 8 full-time board certified oncologists, with 12 hematology/oncology fellows who provide an entire spectrum of medical oncology to include an inpatient oncology and bone marrow transplantation at WHMC and inpatient consultation at BAMC. The service has a dedicated oncology pharmacy and chemotherapy treatment center to provide the spectrum of care.

There is a weekly clinical conference held at BAMC in conjunction with the tumor registry that includes Pulmonary Disease, Hematology/Oncology, Radiology, Pathology, Cardiothoracic Surgery, and Radiation Oncology services. This forum reviews and discusses all biopsy-proven and suspected lung cancer cases to provide the best treatment options for all lung cancer patients.

The BAMC Department of Clinical Investigation (DCI) has one Ph.D. scientist and several laboratory assistants (both civilian and active duty) who provide support with the CellSearch technology for the lung cancer and breast cancer vaccine studies. There are currently 6 civil service personnel who are responsible for the execution of all SWOG and Gynecologic Oncology Group (GOG) protocols at BAMC and WHMC. The Development Drug Unit (DDU), located at BAMC, has 3 personnel available to provide the enrollment, treatment, and nursing care for all CTSC enrolled Phase I and II patients.

Resources:

Biospecimen Procurement: Each facility has a walk-in outpatient specimen collection area for the procurement of blood, urine, and other samples. In addition, there are other outpatient collection sites located at the Troop Medical Clinics, Blood Donation Centers, and other primary care clinics located at Fort Sam Houston, Lackland AFB, Randolph AFB, Camp Bullis, and Brooks City Base. The main laboratories at BAMC and WHMC have the capabilities of shipping samples to other diagnostic laboratories.

Biospecimen Processing and Analyses: The laboratory section of the DCI includes 8 laboratories with equipment to support several scientific disciplines including Molecular Biology, Immunology, Biochemistry, Physiology, and Microbiology. Personnel for the section includes 11 full-time employees (GS, military, and contract) including M.D., Ph.D., Masters of Science, and technology levels of experience. The DCI mission is to support Graduate Medical Education for BAMC staff, residents, fellows, and collaborating medical facilities.

Major novel instrumentation and techniques available at DCI includes ability to isolate and evaluate individual circulating tumor cells for epithelial cancers including breast and non-small cell lung carcinoma, Luminex multiplexing immunoassay for commercially available and custom biomarkers (adipocyte/adipokine 6-plexes, cytokine 26-plexes, custom panels for toxins etc.), various permutations of immunoassays detected by chemiluminescence, electrochemiluminescence, fluorescence, radiologic and colorimetric means, custom nucleic acid microarray technology detected by fluorescence or electrochemiluminescence, HPLC and capillary electrophoresis systems for isolation and quantification of biomarkers based on numerous separation technologies including custom affinity chromatography, microscopy systems including confocal, DIC, Hoffman, phase, and bright and dark field systems, real time PCR capabilities, expertise to perform radioreceptor quantitative assays for numerous receptors, microphysiometer systems to detect receptor and second messenger related changes in cell physiology via a continuous flow perfusion system, Pulse field electrophoresis, DNA/RNA sequencing, Phoenix microbial identification system, and numerous other capabilities.

Imaging: BAMC Department of Radiology has all modern capabilities to include plain radiography, a breast imaging center, nuclear medicine, ultrasound, MRI, radiation oncology, and interventional radiology. There are currently 3 CT scanners, two of which are 64-slice and the third is dual source. Approximately 36,000 scans are done yearly, and non-contrast studies can be done on a same-day basis. CT-guided lung biopsies are done 2-3 times weekly by two dedicated staff. There are three MRI scanners and a molecular 64-slice PET-CT scanner that will be installed in the next 3 months. There are 24 staff radiologists and 41 residents who split rotations between BAMC and WHMC. WHMC currently has two 64-slice CT scanners, two MRIs, and one PET-CT scanner. There are currently 34 assigned radiologists who also support the Radiology residency.

Interventional resources – Bronchoscopy: BAMC has two bronchoscopy suites available, one with fluoroscopy capability and the other with endobronchial ultrasound and YAG laser capabilities. The bronchoscopy suite is staffed by the PFT technicians and currently has the support to perform no more than three (3) bronchoscopies on a daily basis. WHMC has one bronchoscopy suites with fluoroscopy, endobronchial ultrasound, and electromagnetic navigation capabilities. The PFT technicians also staff the bronchoscopies and are limited to no more than three (3) bronchoscopies on a daily basis. To expand the number of bronchoscopies for the lung cancer screening study, there would need to be additional technician support needed. There are an adequate number of pulmonary staff and fellows to perform additional bronchoscopies if needed.

Interventional Resources – Percutaneous Biopsy: Both Pulmonary clinics have the ability to perform transthoracic needle biopsy on larger pulmonary lesions if they can be readily identified by fluoroscopy. However, for a screening study in which the majority of identifiable lesions would be less than 1 cm in size, the preferred method would be CT-guided biopsy. The radiology departments at both institutions currently have the expertise and facilities to perform a limited number (2-3 weekly) of CT-guided biopsies for small pulmonary lesions. Additional resources would be required to expand the number of biopsies obtained over the current numbers.

Interventional Resources – Surgical: The Cardiothoracic Surgery Service is located exclusively at BAMC and has 4 fully trained and Board Certified Thoracic Surgeons with 5 operating rooms per week. They perform all surgeries for both facilities associated with lung cancer to include open biopsy, VATS biopsy, lobectomy (Open & VATS), pneumonectomy, sleeve lobectomy, and chest wall resection. They currently perform approximately 30 lobectomies yearly and have the support

staff and surgery capability to increase any additional volume required for lung nodule biopsy based on the lung cancer study.

Pulmonary Function Laboratory: The PFT laboratories at both BAMC and WHMC currently are fully capable of performing a wide variety of basic studies to include spirometry, post-bronchodilator testing, lung volumes (via plethysmography), diffusion capacity, methacholine challenge testing, exercise spirometry, cardiopulmonary exercise testing with expired gas analysis and other lung function measurements. Each PFT lab has three (3) Vmax 22 spirometers and two (2) body boxes to perform plethysmography. Additionally, the BAMC PFT lab has the capability of performing impulse oscillometry. There are currently 3 full-time civilian technicians at the BAMC lab with additional part-time assistance by a military respiratory therapist and a dedicated full-time research technician to be hired in the near future. The WHMC PFT lab currently has two full-time civilian technicians and 2 part-time military technicians. Both labs are performing studies at full capacity and would require additional spirometers and/or technicians to perform dedicated research.

Future Studies of Interest:

- Serum biochemical markers
- Circulating tumor cell technology in serum and BAL
- Radiographic screening

Potential Personnel Needs at MTF for Consortium Studies:

- Research nurse, administrative assistant, and research assistant depending on the number and type of enrollment to studies.
- BAMC Clinical Investigation Department may require personnel to facilitate with biologic or biochemical studies.

It is expected that exact MTF requirements will vary based on the type and number of studies conducted by the Consortium.

Walter Reed National Military Medical Center

The Walter Reed Army Medical Center (WRAMC) is the hub of the Walter Reed Health Care System which provides comprehensive health care for more than 150,000 soldiers, other service members, family members, and retirees in the National Capital Area. WRHCS provides a full range of services for patients, from routine primary care to the most sophisticated, high-tech specialty care. It is patient-focused and dedicated to streamlining each patient's passage to the appropriate level of care he or she needs. Each facility within the system is a valuable partner and brings its unique expertise to bear on health care delivery.

The National Naval Medical Center (NNMC) is the Navy's third largest health care delivery system, conducting over 12,500 outpatient surgeries and handling approximately 8,000 inpatient admissions per year. NNMC is a designated hospital for Navy and Marine casualties from Operation Enduring Freedom and Operation Iraqi Freedom.

In accordance with the 2005 Base Realignment and Closure recommendations, the WRAMC and the NNMC will be merging to become the Walter Reed National Military Medical Center (WRNMMC), which is to be completed by September 2011. That merged facility will be staffed by U.S. Air Force, Army, and Navy medical personnel, and will be the core of an integrated military medicine system in the National Capital Region (NCR). The WRNMMC is slated to be an approximately 345-bed medical center with the full range of intensive and complex specialty and subspecialty medical services, including specialized facilities for the most seriously war injured. This facility will serve as the U. S. military's worldwide tertiary referral center for casualty and beneficiary care.

Mission: Early detection of lung cancer in high-risk populations in the DOD healthcare system.

Research Goals:

- Advanced imaging for the chest and airways (virtual bronchoscopy, thoracic ultrasound, CT/PET)
- Accurate and minimally invasive diagnostic techniques for diagnosis and staging of lung cancer such as endobronchial ultrasound or EBUS, endobronchial autofluorescence (AF), narrow band imaging (NBI), electromagnetic navigation bronchoscopy (ENB), pleuroscopy
- Effective lung sparing therapies and minimally invasive therapies for lung cancer patients
- Multidisciplinary center of excellence for lung cancer diagnosis and treatment
- Targeted systemic chemotherapeutic treatments for lung cancer
- Development and evaluation of chemopreventive medications
- Clinical trial and referral center for lung cancer therapies

Current Research Areas:

Clinical Research Protocols:

- Lung cancer tumor evaluation for identifiable mutations and evaluation of targeted chemotherapy of these mutations which is performed in conjunction with the National Cancer Institute (NCI).

- Clinical trials for first line therapy offered through CALGB, and second line and beyond offered through NCI.
- Evaluation of tumors for acquired resistance to targeted chemotherapy.
- Diagnostic techniques for suspected lung cancer.

Patient Population: The WRNMMC serves a beneficiary population of 191,241 in the NCR. Of those beneficiaries who are enrolled, 31,498 are enrolled at NNMC and 19,248 are enrolled at WRAMC. Demographics and statistics on the lung cancer cases at WRNMMC are presented in Tables 1-5.

Table 1. Number of New Lung Cancer Cases from 2004 – 2009 at WRNMMC Categorized by Stage

NUMBER OF NEW CASES BY YEAR/STAGE							
Year	Total Number New Cases	Stage Group					
		I	II	III	IV	Unk	N/A
2004	90						
2005	104						
2006	82						
2007	64						
2008	76						
2009	74						

Table 2. Demographic data for lung cancer cases at WRNMMC from 2004 – 2009: Age at Diagnosis

AGE AT DIAGNOSIS		
Age Group	Number of Cases	% of Cases
20-29	5	1.0%
30-39	11	2.2%
40-49	34	6.9%
50-59	77	15.7%
60-69	123	25.1%
70-79	171	34.9%
80-89	67	13.7%
90+	2	0.4%

Table 3. Demographic data for lung cancer cases at WRNMMC from 2004 – 2009: Gender

SEX		
Gender	Number of Cases	% of Cases
Male	289	59%
Female	201	41%

Table 4. Demographic Data for Lung Cancer Cases at WRNMMC from 2004 – 2009: Race

RACE		
Label	Number of Cases	% of Cases
White	343	70.0%
Black	113	23.1%
American Indian, Aleutian, or Eskimo	1	0.2%
Chinese	1	0.2%
Filipino	6	1.2%
Korean	1	0.2%
Thai	-	-
Samoan	-	-
Other Asian/Pacific Islander,	12	2.4%
Other	5	1.0%
Unknown	8	1.6%

Table 5. Demographic Data for Lung Cancer Cases at WRNMMC from 2004 – 2009: Smoking History

SMOKING HISTORY		
Label	Number of Cases	% of Cases
Never used	72	14.7%
Cigarette smoker, current	133	27.1%
Cigar/pipe smoker, current	-	-
Snuff/chew/smokeless, current	-	-
Previous use	262	53.5%
Unknown	23	4.7%

Personnel:

- Multidisciplinary team of:
 - 2 pulmonologists (1 interventional pulmonologist)
 - 1 thoracic surgeon
 - 2 oncologists
 - 1 radiologist
 - 1 nuclear medicine (PET) radiologist
 - 2 radiation oncologists
 - 1 pathologist
 - 1 clinical coordinator for the existing Lung Cancer Clinic

Resources:

- Lab capable of all standard diagnostic tests.

- Direct referral to clinical trials at the NCI for mutation evaluations as well as serum tumor markers.
- Direct referral to both the NCI and the AFIP pathological second opinions.

Future Studies of Interest:

- Sputum screening (cytology or cytometry) for the early detection of lung cancer.
- Screening bronchoscopy in high-risk patients with autofluorescence (AF) and/or NBI.
- Other biomarkers or test that might risk stratifying patients.
- Combined virtual bronchoscopy screening with virtual colonoscopy and cardiac CT.
- Proteomics of tumor tissue.

Potential Personnel Needs at MTF for Consortium Studies:

- Research coordinator
- Data entry personnel
- Research nurse

It is expected that exact MTF requirements will vary based on the type and number of studies conducted by the Consortium.