Program Announcement

Department of Defense (DOD) Congressionally Directed Medical Research Programs

Lung Cancer Research Program (LCRP)

Lung Cancer Biospecimen Resource Network Award

Funding Opportunity Number: W81XWH-09-LCRP-LCBRNA

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Objectives

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 goal of the FY09 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 and integrate research from multiple disciplines for early detection, diagnosis, prevention, cure, and control of lung cancer.

B. Award Description

The LCRP Lung Cancer Biospecimen Resource Network (LCBRN) Award is intended to provide infrastructure support for the development of a lung cancer biospecimen resource that will facilitate the collection, processing, annotation, storage, and distribution of high-quality human lung cancer biospecimens through a collaborative network across multiple institutions. The LCBRN will consist of a Coordinating Center that will also function as a biospecimen resource site and a minimum of two additional Biospecimen Resource Sites that will be jointly responsible for developing the biospecimen resource network for lung cancer research.

The Coordinating Center and Biospecimen Resource Sites must submit a single application. It is expected that the Coordinating Center will provide unique resources that may not necessarily be available at each Biospecimen Resource Site and can be leveraged for the LCBRN as a group. The types of lung cancer biospecimens for this proposal may be quite diverse. A list of possible biospecimens may include but are not limited to tumor tissue, matching uninvolved lung parenchyma or airway epithelium, lung exhalant, tissue, blood, sputum, hair, toenails, and bronchoscopic brushings and biopsies. Additional requirements for the LCBRN will be the ability to collect, store, and manage data derived from these biospecimens. LCBRN applicants should possess the ability to derivatize DNA, RNA, and proteins, and also utilize both standard and state-of-the-art technologies (e.g., laser capture microdissection, tissue microarrays) to provide the necessary biospecimen processing for lung cancer research studies.

The proposed LCBRN must collect, process, annotate, store, and distribute human lung cancer biospecimens that support two or more of the Areas of Emphasis listed below:

- Identification or development of non-invasive or minimally invasive tools to improve the detection of the initial stages of lung cancer.
- Identification and development of tools for screening or early detection of lung cancer. Screening may include, but is not limited to, computed tomography scans, X-rays, other imaging, biomarkers, genetics/genomics/proteomics, and assessment of risk factors.
- Understanding the molecular mechanisms that lead to clinically significant lung cancer.

- Identification of the mechanisms that lead to the development of the various types of lung cancer.
- Identification of innovative strategies for prevention and treatment of early lung cancer.
- Understanding predictive and prognostic markers to identify responders and non-responders.
- Understanding acquired resistance to treatment.

Principal Investigators (PIs) should have experience and expertise in human biospecimen procurement, annotation, storage, and distribution, and in developing and operating a biospecimen repository. PIs should have a proven track record in human pathology. The DOD LCRP encourages submissions from and collaborations with investigators at Military Treatment Facilities, Military Research Institutions, and the Department of Veterans Affairs (VA) Medical Centers.

The LCBRN Award mechanism seeks applications from a network of institutions (Coordinating Center that will also act as a Biospecimen Resource Site and a minimum of two additional Biospecimen Resource Sites) with sufficient resources (such as equipment for biospecimen resource network functions, pathology and histochemistry infrastructure, imaging informatics, and information infrastructure to support connectivity between the Coordinating Center and the Biospecimen Resource Sites for data transfer) in place to support the development of a biospecimen resource network.

The LCBRN Coordinating Center will serve as the nexus for Network information and planning, providing administrative, operational, and data management, and providing support to the Biospecimen Resource Sites in implementing LCBRN policies and standard operating procedures. The Coordinating Center will have multidisciplinary expertise and extensive experience in multi-institutional collaborations in lung cancer research. The Biospecimen Resource Sites will collaborate with the Coordinating Center to develop policies and standards of operation for the entire LCBRN.

The proposed LCBRN must collect, process, annotate, store, and distribute human lung cancer biospecimens that support two or more of the Areas of Emphasis listed above. Applicants should propose a clearly defined Mission that will guide the proposed LCBRN's biospecimen data collection and distribution processes. ***The LCBRN must allow non-LCBRN investigators to utilize these biospecimens and associated data.*** The LCBRN must develop a plan to disseminate information regarding the procurement and distribution of biospecimens to the non-LCBRN lung cancer research community. Although not required, harmonization of the informatics grid with the national Cancer Biomedical Informatics Grid (caBIG) (https://cabig.nci.nih.gov/) is encouraged.

Investigators utilizing the LCBRN biospecimens must agree to share their data in order to use LCBRN resources. Investigators utilizing the LCBRN biospecimens will first have the opportunity to publish the data, after which (and according to a prescribed period of time determined by the LBCRN and in accordance with journal policies) the dataset will be released for distribution and shared with the lung cancer research community through an internet-

accessible database or other common information grid. The LCBRN will control access to all Biospecimen Resource Network data. In addition, protocols and methods used to derive data, tests, and assays, as well as associated data from the LCBRN biospecimens, must be available to the entire lung cancer research community to maximize the efficiency of the Biospecimen Resource Network.

LCBRN applicants must demonstrate their commitment to securing additional funds from other agencies to continue operations of the LCBRN after the end of the LCRP award performance period.

Summary of LCBRN Responsibilities: Procedures for the LCBRN while proposed by the Coordinating Center will be developed collaboratively and agreed upon by all participants.

Coordinating Center: Responsibilities specific to the Coordinating Center include:

- Coordinating Center PI will serve as the Director of the LCBRN.
- Adherence to the responsibilities for a Biospecimen Resource Site.
- Management of LCBRN developed procedures for biospecimen inventory control, quality assurance, and quality control measures.
- Establishment and management of procedures to ensure requests for use of biospecimens are in compliance with the local institutional review boards (IRBs).
- Establishment and coordination of policies that govern standard operating procedures.
- Management of LCBRN-developed comprehensive data collection and data management systems to manage biospecimen resources and provide for ongoing needs of all Sites in terms of access to data, data transfer, data security, and data integrity.
- Management of LCBRN-developed intellectual and material property issues.
- Development and maintenance of the LCBRN organizational structure.
- Coordinating Center PI will serve as the Chair of the Steering Committee.
- Establishment and management of a communications plan and an ongoing communications system.
- Management of LCBRN-developed procedures for the timely release of all data obtained from use of biospecimens following publication of significant findings.
- Development of a plan for securing funds from other agencies to leverage LCBRN resources to continue operation of the LCBRN.
- Submission of written and oral annual briefings to the External Advisory Board (EAB) and USAMRMC staff.
- Development of a workshop for LCBRN participants and other experts in the biospecimen field.

- Preparation for site visits by the government or its designee, if required.
- Additional responsibilities based on recommendations and guidance from the LCBRN EAB and USAMRMC staff.

Biospecimen Resource Sites: The responsibilities of each Site include:

- Provision for a ***Biospecimen Resource Site Coordinator*.**
- Contribution of biospecimens from at least the minimum number of 50 patients per year.
- Compliance with LCBRN-developed quality assurance and quality control procedures.
- Implementation of LCBRN procedures to ensure that requests for use of biospecimens are in compliance with the local IRBs.
- Implementation of the LCBRN's informatics system and core data collection methodology and strategies.
- Participation in LCBRN -developed procedures for resolving intellectual and material property issues.
- Participation in LCBRN-developed procedures for the timely publication of research results.
- Development of a plan for securing funds from other agencies to leverage LCBRN resources to continue operation of the LCBRN.
- Presentation of written and oral annual briefings to the EAB and USAMRMC staff.
- Participation in a workshop for LCBRN participants and other experts in the biospecimen field.
- Preparation for site visits by the government or its designee, if required.
- Additional responsibilities based on recommendations and guidance from the LCBRN EAB and USAMRMC staff.

The principal areas of responsibility for the LCBRN are described as follows:

- **Biospecimens:** The LCBRN will collect, process, annotate, store, and distribute high-quality human biospecimens related to early lung cancer, including but not limited to tumor tissue, matching uninvolved lung parenchyma or airway epithelium, lung exhalant, tissue, blood, sputum, hair, toenails, and bronchoscopic brushings and biopsies. Information regarding the pre- and post-analytical variables should be collected for all specimens. Each Biospecimen Resource Site must contribute biospecimens and associated data from a minimum of 50 patients per year, with the expectation that biospecimen contribution will exceed the minimum requirement. Collection of biospecimens and associated data from individuals in the military and veterans is strongly encouraged. Within the first 6 months of the performance period, the Coordinating Center will ensure that standard operating procedures for biospecimen collection methods and post-collection processing are established. All

Biospecimen Resource Sites will be required to have a shared biospecimen database that will allow for specimen bar-coding and tracking each sample life-cycle, and maintaining a history of the chain of custody.

Clinical Annotation of Biospecimens and Data Quality Assurance: In addition to the importance of high-quality tissue samples, annotation of tissue samples is critical to the success of future research that utilize samples obtained from the biospecimen resource network. Within the framework of the data management plan, the LCBRN must develop a plan to establish common data elements and standardized language to annotate tissue samples collected for the biospecimen resource network. The extent of the clinical annotation should include data on:

- Phase 1: The history of the patient prior to surgery
- Phase 2: The events of the surgery up to removal of the biospecimen from the body
- Phase 3: Removal of the biospecimen from the body to stabilization
- Phase 4: Post-stabilization degradation
- Phase 5: The history of the patient after the surgery

Given the importance of clinical annotation, the LCBRN will be expected to facilitate a mechanism through which annotated data in the biospecimen resource network is routinely updated. To ensure the quality of the biospecimens and the consistency and accuracy of data in the repository, the LCBRN is expected to develop quality assurance measures for clinical and pathological data and data transmission by establishing policies for appropriate quality control and quality assurance.

Informatics and Data Management: The LCBRN will be required to develop a comprehensive data management plan that includes a common informatics system to manage the biospecimen resource network resources and provide for ongoing data transfer, security, and integrity. The system should remain current and responsive to the lung cancer research community. The system may include, but is not limited to, ongoing processes to improve and update LCBRN access to resources internal and external to the LCBRN, and potentially develop new informatics strategies to harmonize the biospecimen resource network informatics resources with the informatics of other national biorepositories. The LCBRN must develop a database or common information grid that contains protocols and methods used to derive data, tests, and assays, as well as associated data from the LCBRN biospecimens. This information will subsequently be shared with the entire lung cancer research community to maximize the efficiency of the Biospecimen Resource Network. The Coordinating Center will have a ***Data Management Specialist*** who will interact and oversee all informatics and data management within the LCBRN.

Informed Consent: LCBRN applicants are expected to demonstrate plans for obtaining patient-informed consent, with tiers as appropriate, to include clinicians, surgeons, or other personnel necessary for the consent process, and disassociation of patient identifiers from biospecimens. PIs should also address how informed consent will be handled beyond consents obtained for

surgical procedures. This includes specimens and imaging data collected during routine medical care that will be used for future research purposes.

Intellectual Property and Material Transfer Agreements: Since the biospecimen repository will be a collaborative network of institutions, the LCBRN PIs will work together with the Coordinating Center to resolve potential intellectual and material property issues and remove institutional barriers that might interfere with achieving the high levels of cooperation necessary for the success of the LCBRN. It is expected that applications for the LCBRN Award will provide documentary evidence of institutional commitment to allowing specimens collected at Biospecimen Resource Sites to be sent to investigators at non-LCBRN institutions for the purpose of conducting lung cancer research.

Organizational Structure: The overall organizational structure of the LCBRN is three procurement Biospecimen Resource Sites and one Coordinating Center. The Coordinating Center will serve as both a central command center and one of the three procurement Biospecimen Resource Sites. Within the organizational structure of the LCBRN, the Coordinating Center will serve as the nexus for Network information and planning, providing administrative, operational, and data management. The Coordinating Center PI will serve as the Director of the LCBRN and the Chair of the Steering Committee. In addition to the Coordinating Center PI and the Biospecimen Resource Site PIs, and collaborators, other key personnel in the LCBRN include:

- Coordinating Center ***Network Manager*** who will assist with the daily operations of the Coordinating Center.
- Coordinating Center ***Data Management Specialist*** who will interact and oversee all informatics and data management within the LCBRN.
- ***Biospecimen Resource Site Coordinator*** who will work with the Coordinating Center Network Manager on LCBRN-wide functions in addition to Site-specific functions.

Network Committees: The LCBRN will be required to have a committee structure that allows for an overall quality assurance plan with the responsibility of:

- Coordinating and developing protocols, equipment, and training of personnel
- Coordinating regulatory issues including compliance of local IRB approvals
- Coordinating oversight of privacy and confidentiality of patient data
- Managing biospecimen processing, annotation, storage, and distribution.

A ***Steering Committee*** composed of the Coordinating Center PI (Chair), Biospecimen Resource Site PIs, Network Manager, Data Management Specialist, Data Quality Control Specialist, at least one ***lung cancer survivor*** (Consumer Advocate**)**, and other key personnel will assume the role of the governing body with the responsibility for overseeing the operations of the LCBRN. This committee will also be responsible for establishing polices that govern standard operating procedures (in accordance with NCI "Best Practices for Biospecimen Resources" (http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf) to include standards for quality control, specimen collection, processing, annotation, distribution, legal and ethical regulatory issues, policies for prioritization of specimen distribution, and fees and other costs to investigators for processing, handling, and shipping requests for samples. The Steering

Committee will coordinate the development of additional committees as necessary for development of common data elements, protocol coordination, regulatory coordination (IRB) and bioethics review, intellectual/material property coordination, data collection, data management (data quality, security, and compatibility), and prioritization and distribution of biospecimens.

Consumer Advocate Participation: Lung cancer consumer advocates/survivors will be an integral part of the LCBRN. Consumer advocates must be individuals who have been diagnosed with lung cancer and have a high level of familiarity with current issues in lung cancer research. ***At least one lung cancer consumer advocate will have an active role in ongoing LCBRN oversight*** including discussion and decision-making on participant recruitment, project evaluation, and dissemination of information to the lung cancer research community and/or public. Examples of appropriate integration include membership on the Steering Committee and other Network committee(s) and attendance at LCBRN-related meetings (oversight committee, symposia, and workshops).

Performance Metrics: The LCBRN Award will be accountable to the following performance metrics, upon which continued funding will be contingent after the first twelve months of the award.

- The LCBRN Coordinating Center must develop and meet a defined set of objectives or milestones as set forth in the Statement of Work.

- The LCBRN Coordinating Center must demonstrate that quality control standards are being followed and minimum goals attained. The Coordinating Center must also develop a quality assurance plan.

- The LCBRN Coordinating Center must demonstrate ongoing efforts to disseminate information regarding the procurement and distribution of biospecimens to the non-LCBRN lung cancer research community.

- Each Biospecimen Resource Site must contribute biospecimens and associated data from a minimum of 50 patients per year, with the expectation that biospecimen contribution will exceed the minimum requirement. ***Collection of biospecimens and associated data from individuals in the military and veterans is strongly encouraged.***

- Each Biospecimen Resource Site must submit quality data and reports in a timely manner as outlined by the Coordinating Center. This includes, but is not limited to, entry of data upon sample acquisition and all subsequent information updates.

External Advisory Board: An External Advisory Board (EAB) composed of members of the LCRP Integration Panel (IP), LCRP Program Manager, LCRP Grants Manager, and other experts as appointed by the Office of the Congressionally Directed Medical Research Programs (CDMRP) will provide oversight and guidance on the progress of the LCBRN. The EAB Chairperson, LCRP Program Manager, and LCRP Grants Manager must be invited to meetings of the Steering Committee. LCBRN Coordinating Center and Biospecimen Resource Site PIs

are required to present written and oral annual briefings to the EAB and USAMRMC staff at meetings typically held in the Baltimore-Washington, DC, area. Based on these reports and presentations, USAMRMC staff, with recommendations from EAB members, will evaluate progress, provide feedback, and invoke modifications and terminations as needed to facilitate the success of the LCBRN.

Pre-award Meeting: Both the LCBRN Coordinating Center and Biospecimen Resource Sites PIs will be required to attend a Pre-award Planning Meeting. Procedures for the LCBRN, while proposed by the Coordinating Center, will be developed collaboratively and agreed upon by all participants. During this meeting, LCBRN members will begin to develop operational features, discuss the requirements for progress and evaluation, and facilitate the award negotiations process.

LCBRN Workshop: The LCBRN awardees will be expected, during the period of performance for the award, to conduct one workshop to convene LCBRN key personnel, other biospecimens participants, and experts in the field of biospecimens. The agenda should include discussions on process improvements and new technologies to facilitate the success of the LCBRN. This workshop should be held in conjunction with one of the required EAB meetings. Additionally, a second workshop should be held, in conjunction with a major scientific meeting, no later than year 3 of the period of performance to disseminate information about the goals of the LCBRN and the available biospecimens to the non-LCBRN lung cancer research community.

C. Eligibility

To be eligible for this award, the PI at each LCBRN institution must be:

- An independent investigator with access to appropriate facilities, and
- At or above the level of an Assistant Professor (or equivalent).

Refer to Application Instructions and General Information, Appendix 1, for general eligibility information.

D. Funding

- The period of performance for this award is **4** years.
- The maximum allowable funding for the entire period of performance is **$3,800,000,** inclusive of direct and indirect costs.

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

- Salary
- Development or purchase of software, databases, inventory systems, websites, and/or other information technology
- Purchase of equipment

- Advertising/marketing costs
- Other costs associated with planning and developing LCBRN collaborations and resources
- LCBRN meetings, including travel among LCBRN PIs and staff
- Travel to scientific meetings
- Travel to EAB meetings
- Planning and travel costs for LCBRN workshops

The CDMRP expects to allot approximately $3.8M of the $20M FY09 LCRP appropriation to fund one Lung Cancer Biospecimen Resource Network Award, depending on the quality and number of applications received.

E. Award Administration

The LCBRN Coordinating Center cannot be transferred to another institution. Refer to the Application Instructions and General Information, Appendix 5, for general award information on changes in award personnel or institution.

The Coordinating Center PI will be required to submit quarterly written progress reports, annual reports, and a final written comprehensive report. In addition to specified reporting requirements, reports should include the number of patients accrued per year per Biospecimen Resource Site, the number of biospecimen requests from both LCBRN and non-LCBRN investigators, the number of requests that were granted, research results, and publications that arise from the use of LCBRN biospecimens.

At the discretion of the government, each participating Resource Network Site may be expected to participate in a site visit by the government or its designee.

II. TIMELINE FOR SUBMISSION AND REVIEW

Submission is a two-step process consisting of (1) pre-application submission and (2) application submission. ***Pre-application submission is a required first step***.

Pre-application Submission Deadline:	**December 23, 2009, 5:00 p.m. Eastern time (ET)**
Application Submission Deadline:	**January 6, 2010, 11:59 p.m. ET**
Scientific Peer Review:	**February 2010**
Programmatic Review:	**March 2010**

Awards will be made approximately 4 to 6 months after receiving a funding notification letter, but no later than September 30, 2010.

III. SUBMISSION PROCESS

Proposal submission is a two-step process consisting of (1) a pre-application submission through the CDMRP eReceipt system (https://cdmrp.org/), and (2) an application submission through Grants.gov (http://www.grants.gov/).

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

Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative applications.

A. Step 1 – Pre-Application Components and Submission

Pre-application submission is the required first step. The pre-application consists of the components discussed below. All pre-application components must be submitted electronically through the CDMRP eReceipt system by ***5:00 p.m. ET on the deadline date***. In addition to award-specific information provided below, refer to the Application Instructions and General Information for detailed information on pre-application components and submission.

- Proposal Information
- Proposal Contacts
- Collaborators and Conflicts of Interest (COI)
- Letter of Intent (LOI) Narrative

  State which of the seven Areas of Emphasis (at least two) that this application addresses.

B. Step 2 – Application Components and Submission

Applications will not be accepted unless the pre-application process is completed by the pre-application deadline. Applications must be submitted electronically by the Authorized Organizational Representative (AOR) through Grants.gov (www.grants.gov).

Each application submission must include the completed application package of forms and attachments identified in www.grants.gov for the US Army Medical Research Acquisition Activity (USAMRAA) Program Announcement/Funding Opportunity. In addition to the specific instructions below, please refer to the Application Instructions and General Information for detailed requirements of each component.

The package includes:

1. **SF-424 (R&R) Application for Federal Assistance Form**

2. Attachments Form

- **Attachment 1: Project Narrative (50-page total limit)**

  Describe the proposed project in detail using the outline below**.**

  a. Coordinating Center: It is the Coordinating Center PI's responsibility to clearly articulate the ability of his/her institution to serve as the LCBRN Coordinating Center, and support the development, administration, and fiscal management of this biospecimen resource network.

  i. Experience and Expertise in Multi-Institutional Collaboration and Biospecimen Resource Network Development: Describe previous experience and accomplishments in multi-institutional collaboration. Describe expertise, experience, and accomplishments related to the development, administration, and fiscal management of a biospecimen resource network. Describe previous experience with establishing communications systems and data management resources for multi-institutional projects. Reference relevant publications and submit reprints with the proposal.

  ii. Coordinating Center Organizational Structure

  Include in the description of the organizational structure the following key features:

  - Describe the organizational structure of the LCBRN, including faculty and staff at each site and how they interact with the Network sites.
  - Describe how standard operating procedures will be developed for collection, processing, annotation using standardized language, storage, and distribution of lung cancer and normal biospecimens within this structure.
  - The involvement of a ***lung cancer consumer advocate***. Provide a ***named*** consumer advocate to serve as a member of the Steering Committee, and describe the consumer advocate's familiarity with current issues in lung cancer, with emphasis on the selected two or more Areas of Emphasis. Describe how lung cancer consumer advocate(s) will play an active role in the LCBRN, including oversight, participant recruitment, program evaluation, dissemination of information to lung cancer communities and/or the public, and interactions with other participants with each of the Biospecimen Resource Sites to strengthen the overall LCBRN.

  iii. Institutional Resources

  - Provide evidence of institutional support, resources, and facilities for the development of a biospecimen repository and its operation in the context of a cooperative network of organizations.
  - Provide evidence of institutional commitment to allow specimens collected at Biospecimen Resource Sites to be sent to investigators at non-LCBRN institutions for the purpose of conducting lung cancer research.

- Provide a plan for resolving intellectual and material property issues among participating institutions, and how material transfer agreements (MTA) will be established.
- Describe the unique capabilities and strengths of the institution to serve as a Coordinating Center for the LCBRN.

iv. Operational Management

- Describe the Coordinating Center plans for administration and day-to-day management of LCBRN operations;
  - Coordination and development of protocols, equipment, and training of personnel;
  - Coordination of regulatory issues;
  - Coordination and oversight of privacy and confidentiality of patient data;
  - Procedures for ensuring that research projects with requests for use of biospecimens are in compliance with local IRB approvals for the conduct of research and the protection of human subjects;
  - Management and monitoring of biospecimen processing, annotation, storage, and distribution;
  - LCBRN Committees that will be responsible for approval of all standard operating procedures and laboratory protocols, and prioritization of biospecimen distribution to lung cancer investigators to ensure appropriate and efficient distribution of samples and attention to studies that address LCRP Areas of Emphasis.
- Provide evidence of the expertise of all key personnel that will be involved in the Coordinating Center, and describe their expected roles as they relate to the collection, processing, annotation, storage, and distribution of human lung biospecimens. In addition to PI and Co-PI, key personnel must include a ***named Network Manager*** at the Coordinating Center who will interact with the three Biospecimen Resource Sites to coordinate activities across all Sites, including interacting with Biospecimen Resource Site Coordinators to expedite protocols through regulatory approval processes, expedite review, evaluation, selection, and prioritization of specimen distribution, develop protocols, and coordinate patient participation and other biospecimen resource network activities across Sites.
- Include a ***named Data Quality Control Specialist*** who will interact with all Biospecimen Resource Sites and oversee implementation of established operational procedures to ensure the quality of biospecimens and biospecimen imaging, and molecular and proteomic data across the LCBRN and shared information grid.
- Describe the communication plan between the Coordinating Center and Biospecimen Resource Sites. Plans should address the following: Methods for information distribution within the LCBRN, information technologies that will be used to facilitate routine multi-institutional

communication, and ongoing communication (including required Workshops) and data sharing.

- Describe how each Biospecimen Resource Site will be evaluated on attaining the performance metrics for patient accrual and biospecimen collection. Describe the plan for improving performance for Biospecimen Resource Sites with minimal patient accrual.
- Include a plan for dissemination of information regarding the procurement and distribution of biospecimens to the non-LCBRN lung cancer research community.
- Include a plan for processing, evaluating, and prioritizing requests for biospecimens from LCBRN participants and other investigators outside the LCBRN, including potential restrictions governing use of biospecimens by commercial entities.
- Outline a plan for ensuring public dissemination of protocols and methods used to derive data, tests, and assays, as well as associated data from the LCBRN biospecimens.

v. Biospecimen Management, Quality Assurance, and Distribution

Include the following key features in the description of the biospecimen management and quality assurance:

- The model to be used for biospecimen imaging, molecular and proteomic data collection, annotation, processing, storage, and distribution; include how common data elements will be developed and methods/applications for data collection and transmission.
- Methods for biospecimen imaging, annotation, tracking, storage, transport, distribution, and security.
- Plans for quality assurance, quality control, and monitoring of biospecimens to avoid sample variability, ensure specimen integrity (e.g., RNA, DNA, protein), and maximize efficiency.

vi. Informatics and Data Management

Describe plans to develop comprehensive data management, to include the following:

- A ***named Data Management Specialist*** who will interact with all Biospecimen Resource Site Coordinators to optimize informatics and data management within the LCBRN.
- A description of the common informational system to be used in the LCBRN. Include database design, operation, and maintenance; inventory control system(s); access; and searchable functions for biospecimen information and research data.
- The overall planned approach to data collection and management.
- A plan for ongoing data transfer, security, and integrity.
- A plan for managing the resources of the LCBRN while remaining current and responsive to non-LCBRN lung cancer investigators.

- A plan for sharing all data derived from LCBRN biorepository specimens, whether generated by LCBRN or non-LCBRN investigators.
- Describe plans for collecting and ensuring the quality of pathological and clinical biospecimen data and research data analyses.
- If applicable, describe plans for harmonizing the LCBRN informatics system with other national biorepository informatics systems.
- Provide a plan for sharing data derived from LCBRN biospecimens.

vii. Human Subject Regulatory Compliance

Include the following key features in the description of the human subject regulatory compliance:

- Outline the procedures and policies that will be followed for collection and use of biospecimens in research;
- Include a description of the methods for obtaining informed, tiered patient consent, how patient identities will be disassociated from biospecimens provided to investigators, and how research results from the biospecimens will be made available to clinicians of patient participants.
- Describe the process through which all Biospecimen Resource Sites in the LCBRN will adhere to a common policy governing human subject use.

viii. Financial Management and Marketing of Resource Specimens

- Describe the overall financial strategy of the LCBRN. This should include number of specimens and the cost recovery per specimen.
- Describe how the LCBRN intends to secure funds from other agencies to leverage resources to continue operation of the LCBRN during and beyond the performance period.
- Include plans for advertising/marketing for both obtaining and distributing the biospecimens to the lung cancer research community.

b. Biospecimen Resource Sites: It is the responsibility of each Resource Site PI to clearly articulate his or her expertise, experience, and resources (including necessary equipment and access to patient populations), personnel, and institution to participate as a Biospecimen Resource Site of the LCBRN.

i. Experience and Expertise in Multi-Institutional Collaboration and Biospecimen Resource Site Development: Describe each Resource Site PI's previous experience and accomplishments in multi-institutional collaboration. Describe the expertise, experience, and accomplishments related to the development, administration, and fiscal management of a biospecimen resource site. Describe previous experience with collaborative communication systems and data management resources for multi-institutional projects. Reference relevant publications and submit reprints with the proposal.

ii. Biospecimen Resource Site Organizational Structure

Include the following key features in the description of the organizational structure:

- Describe the organizational structure of each Biospecimen Resource Site, including a strategy for collecting, processing, annotating using standardized language, storing, and distributing lung cancer and normal biospecimens and associated data.
- Describe information technologies that will be used to facilitate routine communication, and information and data sharing with the Coordinating Center and all of the Biospecimen Resource Sites.

iii. Resources of Each Biospecimen Resource Site

- Provide evidence of the expertise of all key personnel that will be involved in each of the Biospecimen Resource Sites and describe their expected roles as they relate to the collection, processing, annotation, storage, and distribution of human lung biospecimens across the LCBRN. Key personnel must include a ***named Biospecimen Resource Site Coordinator,*** who will interact with the other Biospecimen Resource Site Coordinators and the Network Manager at the Coordinating Center to expedite review, evaluation, selection, and prioritization of specimen distribution, expedite regulatory approval processes, develop protocols, coordinate personnel training, and coordinate patient accrual and other Biospecimen Resource Site activities.
- Describe the patient populations.
- Provide documentation of access to the populations (and families, where appropriate) and ability to recruit patients with pre-cancerous to early stage conditions.
- ***The proposed LCBRN must collect, process, annotate, store, and distribute human lung cancer biospecimens that support two or more of the Areas of Emphasis.***

iv. Institutional Resources

- Provide evidence of institutional support, resources, and facilities for the development of a biospecimen repository and its operation in the context of a cooperative network of organizations.
- Provide evidence of institutional commitment to allow specimens collected at Biospecimen Resource Sites to be sent to investigators at non-LCBRN institutions for the purpose of conducting lung cancer research.
- Describe the unique capabilities and strengths of the institution to serve as a Biospecimen Resource Site.

v. Operational Management

- Describe the plans for administration and day-to-day management of each Biospecimen Resource Site, to include:.

- Coordination and development of protocols, equipment, and training of personnel;
- Coordination of regulatory issues;
- Coordination and oversight of privacy and confidentiality of patient data;
- Management and monitoring of biospecimen, imaging, molecular and proteomic data processing, annotation, storage, and distribution.

vi. Biospecimen Management, Quality Assurance, and Distribution

Include the following key features in the description of the biospecimen management and quality assurance:

- A plan for biospecimen management, to include methods for biospecimen collection, tracking, storage, integrity, transport distribution, and security that will be proposed to the Coordinating Center for adoption by the entire LCBRN.
- Descriptions of quality control measures for biospecimens, biospecimen data, and monitoring of biospecimens to avoid sample quality variability.
- A plan for collecting and ensuring the quality of pathological and clinical biospecimen data and research data analyses.
- A plan for serving as one of the entry points for biospecimen and biospecimen requests.

vii. Data Management

- Provide evidence of adequate resources for ongoing data transfer, and expertise for data management and maintenance of data security/ confidentiality.
- Describe procedures for managing the resources of the Biospecimen Resource Site while remaining current and responsive to non-LCBRN investigators.

viii. Human Subject Regulatory Compliance

Include the following key features in the description of the legal, ethical, and human subject issues:

- Description of procedures for ensuring compliance with use of human subjects, and issues involved in the collection and use of biospecimens in research;
- Include a description of the methods for obtaining informed, tiered patient consent to include clinicians, surgeons, and other personnel necessary for the consent process. The plan should address routine medical care and surgical procedures, and patient confidentiality. The methods proposed should be substantive such that they could be proposed as a model to the Coordinating Center for adoption by the entire LCBRN.

- **Attachment 2: Supporting Documentation**
  - References Cited
  - Acronyms and Symbol Definitions
  - Facilities & Other Resources
  - Description of Existing Equipment
  - Publications and/or Patent Abstracts (ten-document limit for Coordinating Center plus Biospecimen Resource Site; five-document limit for the other two Biospecimen Resource Sites)
  - Letters of Institutional Support

    Provide letters of institutional support, signed by senior administrators (e.g., Vice President, Cancer Center Director, Dean) that reflect the institution's commitment to provide the facilities and resources to participate in the LCBRN. Letters should detail the willingness and capability of each institution to (1) provide the necessary facilities and resources for the LCBRN's administrative and Biospecimens Resource Site activities; and (2) commitment to allow specimens collected at Biospecimen Resource Sites to be sent to investigators at non-LCBRN institutions for the purpose of conducting lung cancer research.
  - Letters of Collaboration
    1. Provide a signed letter from the named lung cancer consumer advocate that describes his/her familiarity with current issues in lung cancer research and how he/she will support the LCBRN.
    2. Provide a signed letter from each collaborating individual or institution that will demonstrate that the PI has the resources necessary for the proposed project, including but not limited to:
       - Availability of and access to high-quality samples, data sets, or databases that are necessary for the success of the project.
       - Availability of and access to appropriate lung cancer patient populations.
  - Intellectual and Material Property Plan

    Provide a plan for resolving intellectual and material property issues among participating institutions, and for how Material Transfer Agreements (MTA) will be established.
- **Attachment 3: Technical Abstract**
- **Attachment 4: Public Abstract**
- **Attachment 5: Statement of Work (SOW)**
- **Attachment 6: Coordinating Center Detailed Budget and Justification**
- **Attachment 7: Impact Statement**

  Describe how the proposed LCBRN, if successful, will have a significant contribution as a resource to the lung cancer research community, and how the

LCBRN will impact the progress on early curable lung cancer and/or early curable lung cancer research.

- **Attachment 8: Proposed Clinical Annotation of Biospecimens and Data Quality Assurance: Ten-page limit**

  The proposed plan should describe common data elements and standardized language to annotate tissue samples collected for the Biospecimen Resource Network. This plan will serve as a framework for guiding the LCBRN Steering Committee in establishing the clinical annotation of biospecimens and data quality assurance standard operating procedures. The extent of the clinical annotation should include but not be limited to:

  - Phase 1: The history of the patient prior to surgery (e.g., CT scan, X-ray, PET scan, smoking history, other carcinogen exposure, active military service, nutrition)
  - Phase 2: The events of the surgery up to removal of the biospecimen from the body (e.g., length of devascularized state)
  - Phase 3: Removal of the biospecimen from the body to stabilization (e.g., transportation time from collection site to Resource Network Site, stabilization procedures)
  - Phase 4: Post-stabilization degradation (e.g., storage of specimen)
  - Phase 5: The history of the patient after the surgery (e.g., outcomes such as clinical and pathological staging, disease progression treatment recurrence, or other biochemical status)

- **Attachment 9: Approval for access to military populations (if applicable): One-page limit**

  A letter of support, signed by the lowest ranking person with approval authority, should be included for studies involving active duty military, military families, or veterans; military-controlled study materials; databases; and/or restricted facilities (e.g., biological or chemical containment facilities).

- **Attachment 10: Federal Agency Financial Plan (if applicable)**
- **Attachments 11-15: Subaward (Biospecimen Resource Sites) Detailed Budget and Justification**

3. **Research & Related Senior/Key Person Profile (Expanded Form)**
   - PI Biographical Sketch (four-page limit)
   - PI Current/Pending Support
   - Key Personnel Biographical Sketches (four-page limit each)
   - Key Personnel Current/Pending Support
4. **Research and Related Project/Performance Site Location(s) Form**

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 submissions to each other and recommends proposals for funding based on scientific merit, the overall goals of the program, and the specific intent of the award mechanism. Additional information about the two-tier review process used by the CDMRP may be found at http://cdmrp.army.mil/fundingprocess

The peer review and programmatic review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Each tier 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. Institutional personnel and PIs are prohibited from contacting persons involved in the application 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 institution's application. Violations by panelists or PIs that compromise the confidentiality of the peer review and programmatic review processes may also result in suspension or debarment of their employing institutions 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).

The Government reserves the right to review all applications based on one or more of the required attachments or supporting documentation (e.g., Impact Statement).

B. Review Criteria

1. **Peer Review:** All applications will be evaluated according to the following criteria.

   a. LCBRN: The LCBRN will be evaluated according to the following criteria, which are of equal importance.

   - **LCBRN Organizational Structure**

     - The degree to which the strategies for the development and implementation of the biospecimen resource network are well demonstrated and will facilitate its success.
     - Whether the proposed organizational management plan is appropriate with respect to LCBRN committees, decision-making, allocation of resources, coordination of LCBRN functions including regulatory approval processes, and conflict resolution among all participating PIs and institutions.
     - How well consumer advocate(s) has been incorporated into the overall leadership/oversight committees and interaction with the LCBRN.

- The degree to which the proposed plan for obtaining and marketing biospecimens to the lung cancer research community will facilitate the success of the biospecimen resource network.
- How well the overall financial strategy of the LCBRN is described to include costs associated with specimen procurement and handling, and the subsequent cost recovery per specimen.
- How well the plan for dissemination describes the LCBRN resources available to the entire lung cancer research community.

- **Operational Management**
  - Whether the proposed plan will be effective for coordinated ongoing communication across the LCBRN using the most current technologies.
  - The extent to which appropriate plans for biospecimen distribution to the lung cancer research community, including evaluation and prioritization of requests for biospecimens, are demonstrated.
  - Whether the plans for sharing of data between the LCBRN and the lung cancer research community, including all data derived from internal and external studies of the Biospecimen Resource Network specimens, demonstrate that the LCBRN will be a lung cancer research community resource.
- **Collaborations**
  - How the expertise and resources of the Coordinating Center PI and institution and each Biospecimen Resource Site PI and institution are ideal for a collaboration to create the LCBRN.
  - How well each Biospecimen Resource Site PI will integrate into the LCBRN and be a contributing participant.
  - How well the institutions of the Coordinating Center PI and each Biospecimen Resource Site PI have facilitated collaborations.
  - How well the application outlines the unique contributions of the Coordinating Center and each Biospecimen Resource Site to the overall project.
- **Impact**
  - How the proposed LCBRN, if successful, will make a significant contribution as a resource to the lung cancer research community, and how the LCBRN will impact the progress on early curable lung cancer and/or early curable lung cancer research.
- **Annotation Strategy**
  - How well the proposed plan will serve as a framework for guiding the LCBRN Steering Committee in establishing the clinical annotation of biospecimens and data quality assurance standard operating procedures.

b. Coordinating Center: The Coordinating Center will be evaluated according to the following criteria. Of these, Personnel, Institutional Resources and Commitment, and Operational Management are equally the most important, with the remaining criteria listed in decreasing order of importance.

- **Personnel**
  - How well the Coordinating Center PI or other key personnel of the Coordinating Center have demonstrated the required expertise, experience, and accomplishments related to the development, administration, and fiscal management of a biospecimen resource network.
  - Whether the Coordinating Center PI and key personnel have previous success in multi-institutional collaborations.
  - Whether the named Coordinating Center Network Manager, who will interact with all Biospecimen Resource Site Coordinators, possesses the appropriate expertise to coordinate LCBRN activities across all Sites and expedite protocols through regulatory approval processes.
  - Whether the named Coordinating Center Data Management Specialist and Data Quality Control Specialist possess sufficient expertise in informatics and data management.
- **Institutional Resources and Commitment**
  - Whether there is evidence of a strong institutional commitment to providing the necessary resources and facilities for the development of a biospecimen resource network and its operation in the context of a cooperative network, and to allowing biospecimens to be shared with investigators outside the LCBRN.
  - The degree to which other institutional resources will be available to contribute to the success of the Biospecimen Resource Network.
  - Whether the plans to resolve intellectual and material property issues among participating institutions are feasible.
- **Operational Management**
  - How the plan for Biospecimen Resource Site evaluation on attaining the performance metrics for patient accrual and biospecimen collection will ensure the success of the LCBRN. Whether the Coordinating Center PI and/or institution has demonstrated sufficient willingness and the capabilities to secure additional funds from other agencies to support continued operations of LCBRN.
- **Data Management**
  - Whether the plans for sample collection and annotation are appropriately robust to provide data sufficient for a large range of significant lung cancer studies.

- How the strategies for the development and implementation of a data management plan will provide adequate access to data, data security, and data integrity.
- Whether the proposed data management plan is appropriate with respect to quality control and quality assurance.
- The degree to which the informatics structure and data management plans will successfully facilitate lung cancer research focused on two or more of the FY09 LCRP Areas of Emphasis.

- **Human Subject Regulatory Compliance**
  - How well the Coordinating Center PI outlines a process that will govern human subject issues and the use of human biospecimens in research.
  - Whether there are appropriate plans for the coordination of regulatory submissions and approvals at participating Biospecimen Resource Sites.

c. Biospecimen Resource Sites: All Biospecimen Resource Sites will be evaluated according to the following criteria. Of these, Personnel, Participant Access and Recruitment, Institutional Resources and Commitment, and Organizational Structure are equally the most important, with the remaining criteria listed in decreasing order of importance.

- **Personnel**
  - How the lung cancer research and biospecimen resources expertise of the Biospecimen Resource Site PIs and supporting investigators will facilitate the success of the LCBRN.
  - Whether there are sufficient levels of effort for the successful conduct of the Biospecimen Resource Sites.
  - How well the Biospecimen Resource Site PIs have demonstrated successful track records of collaborating with other investigators.
  - Whether the Biospecimen Resource Site PI and Coordinators possess appropriate expertise in obtaining regulatory approvals.
  - Whether the named Biospecimen Resource Site Coordinators have the experience to coordinate activities with other Biospecimen Resource Sites and the ability to foster communication with other Biospecimen Resource Site Coordinators.
  - Whether each Biospecimen Resource Site team's background and expertise suggest that they can perform multi-institutional collaboration.

- **Participant Access and Recruitment**
    - Whether the Biospecimen Resource Site PIs have demonstrated access to patient populations represented by two or more Areas of Emphasis.
    - How well the Biospecimen Resource Site PIs have demonstrated excellent capabilities in obtaining high-quality biospecimens.
- **Institutional Resources and Commitment**
    - Whether the Biospecimen Resource Site institutions have unique resources that may be of benefit to the LCBRN.
    - Whether there is evidence of a strong institutional commitment from each Biospecimen Resource Site to provide the necessary space and facilities for biospecimen handling and storage.
    - The degree to which other institutional resources will be available to contribute to the success of the LCBRN.
    - Whether the Biospecimen Resource Site institutions have demonstrated a commitment to share biospecimens.
    - How well the Biospecimen Resource Site institutions have demonstrated the willingness and ability to resolve intellectual and material property issues with other institutions in the LCBRN.
- **Organizational Structure**
    - The degree to which the proposed organizational structure is appropriate for the development of each Biospecimen Resource Site.
    - Whether each of the Biospecimen Resource Sites' organizational structure is capable of substantially contributing to the LCBRN functions.
- **Data Management**
    - Whether the Biospecimen Resource Site PIs have provided evidence of adequate resources for ongoing data transfer, management, and maintenance of data security/confidentiality.
- **Human Subject Regulatory Compliance**
    - Whether there are appropriate plans for addressing regulatory issues associated with the protection of human subjects and the use of human biospecimens in research.
    - Whether all relevant privacy issues have been addressed appropriately.
    - Whether the plans for obtaining informed consent are well described and sufficiently address patient confidentiality.
    - Whether the plans for data acquisition and storage will sufficiently maintain patient confidentiality.

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

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

2. Programmatic Review: The following criteria will be used by programmatic reviewers to make funding recommendations that maintain the program's broad portfolio:

- Adherence to the intent of the award mechanism
- Programmatic relevance
- Ratings and evaluations of the peer reviewers
- Relative impact
- Program portfolio balance

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be identified by Integration Panel (IP) members and recommended for funding to the Commanding General, USAMRMC.

V. ADMINISTRATIVE ACTIONS

After receipt of 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).

B. Modifications

- Pages exceeding the specified limits will be removed 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 (excluding those listed directly above in Section A, Rejection). The missing documents must be provided by 5:00 p.m. Eastern time on the second full business day following the date the email was sent. Otherwise, the application will be reviewed without the missing documents.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- FY09 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 FY09 IP members may be found at http://cdmrp.army.mil/LCRP/panel09
- Submission of the same research project to different award mechanisms within the same program or to other CDMRP programs.
- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate scientific peer and programmatic review.
- Total costs as shown on the detailed budget form exceed the maximum allowed by the award mechanism.
- 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 institutional investigation. The institution 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. Program Announcement/Funding Opportunity, application format, or required documentation: To view all funding opportunities offered by the CDMRP, perform a Grants.gov basic search using the CFDA Number 12.420. Submit questions as early as possible. Response times will vary depending upon the volume of inquiries. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079
Fax: 301-619-7792
Email: cdmrp.pa@amedd.army.mil

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

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

C. Grants.gov contacts: Questions related to application submission through the Grants.gov (http://www.grants.gov/) portal should be directed to the Grants.gov help desk. Deadline for application submission is 11:59 p.m. ET on the deadline date. Please note that the CDMRP help desk is unable to answer questions about Grants.gov submissions.

Phone: 800-518-4726, Monday through Friday, 7:00 a.m. to 9:00 p.m. ET
Email: support@grants.gov

Grants.gov will notify PIs of changes made to this Program Announcement/Funding Opportunity and/or Application Package ONLY if the PI subscribes to the mailing list by clicking on the "send me change notification emails" link on the Opportunity Synopsis page for this announcement. If the PI does not subscribe and the Application Package is updated or changed, the original version of the Application Package may not be accepted.