Program Announcement

for the

Defense Health Program

Department of Defense

Congressionally Directed Medical Research Programs

Lung Cancer Research Program

Clinical Exploration Award

Funding Opportunity Number: W81XWH-14-LCRP-CEA

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), June 3, 2014
- **Invitation to Submit an Application:** July 2014
- **Application Submission Deadline:** 11:59 p.m. ET, September 17, 2014
- **End of Application Verification Period:** 5:00 p.m. ET, September 22, 2014
- **Peer Review:** November 2014
- **Programmatic Review:** January 2015

Change for Fiscal Year 2014: *The CDMRP eReceipt System has been replaced with the Electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to the end of the application verification period.*

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

TABLE OF CONTENTS

I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2014 (FY14) Lung Cancer Research Program (LCRP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The LCRP was initiated in fiscal year 2009 (FY09) to promote innovative and competitive research focused on the development of integrated disciplines to identify, treat, and manage early curable lung cancer. Appropriations for the LCRP from FY09 through FY13 totaled $68.5 million (M). The FY14 appropriation is $10.5M.

The goal of the FY13 LCRP is to eradicate deaths from lung cancer to better the health and welfare of military service members, Veterans, their families, other military beneficiaries, and the American public. As such, the LCRP will support and integrate research from multiple disciplines for risk assessment, prevention, early detection, diagnosis, and treatment for the control and cure of lung cancer.

B. FY14 LCRP Areas of Emphasis

To be considered for funding, applications for the FY14 LCRP Clinical Exploration Award must address at least one of the seven Areas of Emphasis listed below.

- Identify or develop noninvasive or minimally invasive tools to improve detection of the initial stages of lung cancer.
- Identify, develop, and/or build upon already existing tools for screening or early detection of lung cancer. Screening may include, but is not limited to, computed tomography scans, X-rays, imaging biomarkers, genetics/genomics/proteomics/ metabolomics/transcriptomics, and assessment of risk factors.
- Understand the molecular mechanisms of progression to clinically significant lung cancer.
- Understand the molecular mechanisms that lead to various subtypes of lung cancer.
- Identify innovative strategies for prevention and treatment of early and/or localized lung cancer.
- Understand predictive and prognostic markers to identify responders and nonresponders.
- Understand susceptibility or resistance to treatment.

C. Award Information

The LCRP Clinical Exploration Award (CEA) mechanism was first offered in FY13. Since then, 12 CEA applications have been received, and 2 have been recommended for funding.

This award mechanism supports early-phase, proof-of-principle clinical trials and correlative studies to investigate hypothesis-based, innovative interventions that have the potential to resolve current clinical barriers and result in a profound impact on the clinical management of lung

cancer. While therapeutic approaches proposed for testing through the CEA must represent novel, hypothesis-based, "outside-the-box" approaches for treating lung cancer, they may include therapies already in clinical use, or undergoing clinical testing, for other diseases, provided that the proposed use for lung cancer would lead to a major advancement for treating the disease. It is anticipated that outcomes from studies funded by this award will provide scientific rationale for subsequent development of larger, efficacy-based clinical trials of interventions that will transform lung cancer clinical care. Submissions from and partnerships with investigators at Military Treatment Facilities (MTFs)**,** military labs, the Department of Veterans Affairs (VA) Medical Centers and research laboratories are ***strongly encouraged***.

The CEA supports clinical trials encompassing Phase 0, Phase I, or pilot Phase II for drug or drug combinations, Class II or III devices, or other types of trials that conduct early clinical testing of innovative approaches for lung cancer. Information on clinical trials and phases/classes of study is provided in the "Human Subject Resource Document" available for download from eBRAP at https://ebrap.org/eBRAP/public/Program

***Correlative Studies Category (New for FY14)*:** The CEA-Correlative Studies category supports innovative, hypothesis-based, correlative studies that derive from ongoing or completed clinical trials supported by other funding sources. These correlative studies, if successful, will have the potential to significantly inform treatment strategies, identify subsets of patients for treatment with specific therapies, provide increased understanding of biological changes resulting from the intervention in lung cancer, or provide other insight that will significantly enhance clinical management of lung cancer. Examples of correlative studies appropriate for submission to the CEA-Correlative Studies category may include, but are not limited to:

- Analysis of biomarkers for prognosis and/or prediction or assessment of therapeutic response or progression;
- Investigations of the mechanism of action or the development of resistance to a drug;
- Analysis of immune response or factors associated with progression;
- Characterization of tumor antigens for the development of new improved therapies.

Applications proposing correlative studies will be peer- and programmatically reviewed separately from those proposing clinical trials.

Funding from the CEA must support a clinical trial or correlative study associated with an ongoing or completed clinical trial and cannot be used for preclinical research studies.

Because the CEA seeks to support clinical trials or correlative studies that may deliver groundbreaking ideas, it is the responsibility of the PI to clearly articulate how the proposed study represents research that is beyond conventional therapeutic approaches for lung cancer. Studies in a broad range of areas related to lung cancer clinical management will be considered under the CEA, including but not limited to evaluation of drugs, biologics, devices, surgical procedures, behavior modifications, or other types of therapeutic approaches.

Key elements of this award are as follows:

- The application should clearly specify the type of clinical study, including phase or class designation (if applicable), that is being proposed.
- ***The application must include documentation of an existing Investigational New Drug (IND) or Investigational Device Exemption (IDE), if applicable.***
- The proposed intervention or correlative study must be based on sound scientific rationale that is established through logical reasoning, critical review and analysis of the literature, and preliminary data.
- The application should demonstrate availability and accessibility of a suitable human subject population (if applicable) that will support a meaningful outcome for the study.
- ***The application must demonstrate documented availability and accessibility of the drug/compound, device, and/or other materials needed, e.g., a letter from the manufacturer assuring an adequate supply of the agent (and placebo, if necessary).***
- The proposed study should include clearly defined and appropriate endpoints.
- The application should include a detailed statistical analysis plan, including a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- The proposed study is expected to begin no later than 12 months after the award date.
- The application should include a Transition Plan that describes a clear path for further development of research.
- **Relevance to Military Beneficiaries:** The application should clearly articulate how the proposed research is relevant to military service members, Veterans, their families, and other military beneficiaries**.**

Military Relevance: The LCRP seeks to support research that is relevant to the health care needs of military service members, Veterans, their families, and other military beneficiaries. ***Military relevance will be considered in determining relevance to the mission of the DHP and FY14 LCRP during programmatic review.*** Investigators are ***strongly encouraged*** to consider the following characteristics as examples of how a project may demonstrate military relevance:

- Use of military or Veteran populations or data in the proposed research
- Collaboration with DoD or VA investigators
- Involvement of military consultants (Army, Air Force) or specialty leaders (Navy, Marine Corps) to the Surgeons General in a relevant specialty area
- Explanation of how the project addresses an aspect of lung cancer that has direct relevance to military service members, Veterans, or other military health system beneficiaries

Use of Active Duty Military and VA Populations: If the proposed research plan involves access to active duty military and/or VA patient populations or resources, the PI is responsible for establishing and demonstrating such access. If possible, access to target active duty military and/or VA patient populations/resources should be confirmed at the time of application

submission by inclusion of a letter of support, signed by the lowest ranking person with approval authority, for studies involving active duty military service members, Veterans, military and/or VA controlled study materials, and military and/or VA databases. If access cannot be confirmed at the time of application submission, the Government reserves the right to withhold or revoke funding until the PI has demonstrated support for and access to the relevant population(s) and/or resources. Note that access to a Veteran population for clinical studies may only be obtained by either collaboration with a VA investigator where the VA investigator has a substantial role in the research, or by advertising to the general public.

Use of Human Anatomical Substances, Human Subjects, or Human Cadavers: All Department of Defense (DoD)-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local Institutional Review Board (IRB) of record. Local IRB approval at the time of submission is NOT required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB. Allow a minimum of 2-3 months for HRPO regulatory review and approval processes. Refer to the General Application Instructions, Appendix 6, for additional information.

All investigators applying to FY14 LCRP funding opportunities are encouraged to consider leveraging resources available through the LCRP-funded Lung Cancer Biospecimen Resource Network (LCBRN) (http://www.lcbrn.org/) if retrospectively collected human anatomical substances or correlated data are relevant to the proposed studies.

The Congressionally Directed Medical Research Programs (CDMRP) intends that data and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section L.

D. Eligibility Information

- The PI must be an independent investigator at or above the level of Assistant Professor (or equivalent).
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations. Both intramural (i.e., DoD) and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- ***Clinical Trials***
  - The maximum period of performance is **3** years.
  - The maximum allowable direct costs for the entire period of performance are **$450,000** plus indirect costs.
  - The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **3** years.
- ***Correlative Studies***
  - The maximum period of performance is **2** years.
  - The maximum allowable direct costs for the entire period of performance are **$250,000** plus indirect costs.
  - The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **2** years.
- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.

Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply as are noted in Section II.C.4. of the General Application Instructions***.

For this award mechanism, direct costs:

May be requested for (not all-inclusive):

- Salary
- Research supplies
- Equipment
- Clinical research costs
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings

Shall not be requested for:

- Preclinical research studies

Intramural (DoD) and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or an MTF, or working in a DoD activity

embedded within a civilian medical center. Extramural investigators are defined as all those not included in the definition of intramural investigators. As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from federal agencies submit full applications, they must submit through Grants.gov. Therefore, federal applicants must be familiar with Grants.gov requirements, including the need for System for Award Management (SAM) and a Data Universal Numbering System (DUNS) number. Refer to Appendix 3 of the General Application Instructions for further information regarding Grants.gov requirements.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other federal agencies will be executed through the Military Interdepartmental Purchase Request (MIPR) or Funding Authorization Document (FAD) process. Direct transfer of funds from the recipient to a federal agency is not allowed except under very limited circumstances. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. ***In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.*** Refer to Appendix 4 of the General Application Instructions for additional information.

The CDMRP expects to allot approximately $2.24M of the $10.5M FY14 LCRP appropriation to fund approximately 2 Clinical Trial and 2 Correlative Study Clinical Exploration Award applications, depending on 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.

II. SUBMISSION INFORMATION

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

New for FY14: ***The CDMRP has replaced its eReceipt System with eBRAP.*** Submission remains a two-step process requiring both pre-application and application submission.

PIs must be registered in eBRAP in order to submit a pre-application and receive notification of the status of a pre-application or application. A key feature of eBRAP is that an organization's representatives and PIs are able to view and modify the Grants.gov application submissions associated with them, but only if the organization, Business Officials, and PIs are registered and affiliated to the organization in eBRAP (see *eBRAP User Guide* at *https://ebrap.org/eBRAP/public/UserGuide.pdf*). Upon completion of an organization's registration in eBRAP and approval by the CDMRP Help Desk, the organization name will be displayed in eBRAP to assist the organization's business officials and PIs as they register.

Note: Submission of either the pre-application to eBRAP or application to Grants.gov does not require registering an organization and affiliating its Business Officials and PIs in eBRAP; however, the ability to view and modify the Grants.gov application in eBRAP is contingent upon

the registration and affiliation. ***Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.*** If verification is not completed by the end of the application verification period, the application will be reviewed as submitted through Grants.gov, provided there is no cause for administrative rejection of the application (see Section IV.A., Rejection).

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-14-LCRP-CEA.

B. Pre-Application Submission and Content Form

All pre-application components must be submitted by the PI through eBRAP (https://eBRAP.org/). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

A change in PI or organization after submission of the pre-application will be allowed only at the discretion of the US Army Medical Research Acquisition Activity (USAMRAA) Contracting/Grants Officer.

The pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
    - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Collaborators and Conflicts of Interest (COI) – Tab 3**

  FY14 LCRP Integration Panel (IP) members should not be involved in any pre-application or application. For questions related to IP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

- **Required Files – Tab 4**

  Notes: Upload document(s) as individual PDF files unless otherwise noted. eBRAP will not allow a file to be uploaded if the number of pages exceeds the limit specified below.

  Preproposal Narrative (two-page limit): The Preproposal Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Preproposal Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the pre-application. ***Pre-applications proposing correlative studies will be screened separately from those proposing clinical trials.***

  The Preproposal Narrative should include the following:

  - **Relevance:** Clearly articulate how the application is relevant to at least one of the LCRP Areas of Emphasis, as well as its relevance to military service members, Veterans, their families, and other military beneficiaries.
  - **Research**
    - **Background/Rationale:** Clearly present the ideas and reasoning behind the proposed research; include relevant literature citations and preliminary studies that led to the development of the proposed clinical trial or correlative study. For a clinical trial, clearly describe the intervention and its target and mechanism of action in lung cancer. If the proposed study is correlative to an ongoing or completed clinical trial, describe the relationship between the intervention and the question(s) to be studied.
    - **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
    - **Study Design:** Describe the design of the clinical trial or research approach for correlative studies. The description should include:
      - The type of study to be performed (e.g., Phase/Class, prospective, randomized, controlled, correlative, etc.) and proposed methodology.
      - The study variables and proposed measurement.
      - The research team's capabilities in conducting clinical trials, including discussion of key coordinating activities.
      - The feasibility of initiating the clinical trial or correlative study within 12 months of the award date. ***Note: Invited applications must provide proof of an existing IND/IDE, if applicable.***
  - **Innovation:** Describe how the proposed study is an innovative, unconventional approach for the clinical management of lung cancer.
  - **Clinical Impact:** Describe how the proposed study, if successful, will have a major impact toward improving lung cancer management and contribute to the eradication of deaths from lung cancer.

Pre-Application Supporting Documentation: The items to be included as supporting documentation for the pre-application ***must be uploaded as individual files*** and are limited to:

- References Cited (one-page limit): List the references cited (including URLs if available) in the Preproposal Narrative 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).
- List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols used in the Preproposal Narrative.
- PI and Key Personnel Biographical Sketches (two-page limit per individual).

- **Submit Pre-Application – Tab 5**

  This tab must be completed for the pre-application to be accepted and processed.

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the LCRP, pre-applications will be screened by the LCRP Integration Panel based on the following criteria:

  - **Relevance:** To what degree the proposed project is relevant to at least one of the LCRP Areas of Emphasis; to what degree the proposed project is relevant to military service members, Veterans, their families, and other military beneficiaries.
  - **Research:** To what degree the experimental approach for accomplishing the specific aims is feasible, will accomplish the objectives, and is based on sound rationale.
  - **Innovation:** To what degree the proposed study represents hypothesis-based, innovative clinical research that has the potential to resolve current clinical barriers in lung cancer.
  - **Clinical Impact:** To what degree the proposed study may lead to a profound impact on the clinical management of lung cancer.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs will be notified as to whether or not they are invited to submit applications; however, they will not receive feedback (e.g., a critique of strengths and weakness) on their pre-application. The estimated timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity.

C. Application Submission Content and Forms

Applications will not be accepted unless the PI has received notification of invitation.

Each application submission must include the completed application package of forms and attachments provided in Grants.gov for this Program Announcement/Funding Opportunity. The application package is submitted by the Authorized Organizational Representative through the Grants.gov portal (http://www.grants.gov/).

New for FY14: ***Applications submitted through and validated by Grants.gov will be retrieved and processed by eBRAP to allow for review, modification, and verification.*** The PI and organizational representatives will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing files (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the verification period.

Note: Changes to either the Project Narrative or Budget are not allowed in eBRAP; if such changes are required, the entire application package must be submitted through Grants.gov as a "Changed/Corrected Application" with the Previous Grants.gov Tracking ID ***prior to the application submission deadline (which occurs earlier than the end of the application verification period).***

Grants.gov application package components: For the Clinical Exploration Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

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

2. **Attachments Form**

   - **Attachment 1: Project Narrative (15-page limit):** Upload as "ProjectNarrative.pdf." The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and will result in administrative withdrawal of the application.

     Note: For clinical trials, the Project Narrative is NOT the formal clinical trial protocol. Instead, all elements of the proposed clinical trial necessary for peer review must be described as indicated below.

     Describe the proposed project in detail using the outline below.

     - **Background:** Present the ideas and reasoning behind the proposed research; include relevant literature citations, preliminary data, and/or preclinical data that led to the development of the proposed clinical trial or correlative study. Any preliminary data provided should be from the laboratory of the PI or member(s) of the collaborating team.

- Clearly support the choice of study variables and explain the basis for the study questions and/or study hypotheses. Establish the relevance of the study and explain the applicability of the proposed findings.
- If the proposed study is correlative to an ongoing or completed clinical trial, explain the history and background of the clinical trial and declare the source of funding.
- ***Clearly articulate how the proposed study represents research that is beyond conventional therapeutic approaches for lung cancer.***

○ **Hypotheses/Objectives:** State the hypotheses/study questions and overall objective(s) to be reached.

○ **Specific Aims:** Concisely explain the project's specific aims. If this application is part of a larger study, present only tasks that this award would fund.

○ **Study Design (*Clinical Trials*):** Describe the type of study to be performed (e.g., Phase/Class, prospective, randomized, controlled, etc.) and outline the proposed methodology in sufficient detail to show a clear course of action.

- Identify and describe the hypothesis/intervention to be studied and how it will be applied.
- Describe the projected outcomes of the study.
- Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
- Describe the study population, criteria for inclusion/exclusion, and the methods that will be used for recruitment/accrual of human subjects and/or samples (i.e., convenience, simple random, stratified random). Address any potential barriers to accrual and plans for addressing potential delays. Describe how the subject-to-group assignments process will be conducted (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Include a discussion of risk/benefit considerations. Include a clear and detailed description of the potential ethical issues raised by the proposed study and provide a detailed plan for how the ethical issues will be addressed.
- Document the availability and accessibility of the drug/compound, device, or other materials needed.

○ **Study Design (*Correlative Studies*):** Describe the experimental design, methods/laboratory evaluations, and analyses, including appropriate controls, in sufficient detail for analysis.

- Describe the projected outcomes of the study.
- Describe the study population and the inclusion/exclusion criteria for the clinical trial associated with the correlative study.
- Document the availability and accessibility of the drug/compound, device, or other materials needed as applicable.

- **Data and Statistical Analysis Plan:** Describe how data will be collected and analyzed in a manner that is consistent with the study objectives. If applicable, include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. Specify the approximate number of human subjects/samples that will be accrued. If multiple study sites are involved, state the approximate number to be enrolled at each site.
- **Study Personnel:** Identify the key members of the study team and describe their roles on the project. If applicable, a medical monitor (external to the study and not reimbursed by the study) and study coordinator(s) should be included.

- **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. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested may result in the removal of those items or administrative withdrawal of the application.***
  - References Cited: List the references cited (including URLs if available) in the project narrative 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).
  - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
  - 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 award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.
  - Publications and/or Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must be included in Attachment 2. Extra items will not be reviewed.
  - Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project.
  - Letters of Collaboration (if applicable): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
  - Intellectual Property
    - Background and Proprietary Information: All software and data first produced under the award are subject to a federal purpose license in accordance with applicable DoD Grant and Agreement Regulations

(DoDGAR) requirements. Provide a list of all background intellectual property to be used in the project. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the federal purpose license.

  - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 4, Section L for more information about the CDMRP expectations for making data and research resources publicly available.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  Technical abstracts should be written using the outline below. The technical abstract is used by all reviewers; however, programmatic reviewers do not have access to the full application and therefore rely on the technical abstract for appropriate description of the project's key aspects.

  - Relevance: State the Area(s) of Emphasis the project addresses. Describe how the project is relevant to military service members, Veterans, their families, and other military beneficiaries.
  - Background: Present the ideas and reasoning behind the proposed work.
  - Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
  - Specific Aims: State the specific aims of the study.
  - Study Design: Briefly describe the study design including appropriate controls.
  - Clinical Impact: Briefly describe how the proposed project may lead to a major impact on lung cancer clinical management.

- **Attachment 4: Lay Abstract (one-page limit):** Upload as "LayAbs.pdf."

  Lay abstracts should be written using the outline below. ***Do not duplicate the technical abstract.*** Minimize the use of acronyms and abbreviations, where appropriate. They lay abstract is an important component of the application review process because it addresses issues of particular interest to the consumer advocate community.

  - Describe the scientific objective and rationale for the proposed project in a manner that will be readily understood by readers without a background in science or medicine.
    - State the Area(s) of Emphasis the project addresses.
  - Describe the ultimate applicability of the 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 an impact on the standard of care for lung cancer?
- What are the likely contributions of this study to advancing the field of lung cancer research?
- How is the project relevant to military service members, Veterans, their families, and other military beneficiaries?

- **Attachment 5: Statement of Work (SOW) (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C.2., for detailed guidance on creating the SOW.

  The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Program Announcement and Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the Clinical Exploration Award mechanism, use the SOW format example titled "SOW for Clinical Research." The SOW must be in PDF format prior to attaching.

- **Attachment 6: Clinical Impact Statement (one-page limit): Upload as "Impact.pdf."**

  Explain in detail why the proposed research project is important, as follows:

  - ***Describe the short-term impact:*** Detail the anticipated outcomes that will be directly attributed to the results of the proposed research, including a description of the target population. Explain how these results/outcome(s)/product(s) will have the potential to transform lung cancer management and change clinical practice.
  - ***Describe the long-term impact:*** Explain the long-term gains from the proposed research, including how the outcomes or products will ultimately contribute to eradicating deaths from lung cancer.

- **Attachment 7: Innovation Statement (one-page limit): Upload as "Innovation.pdf."**

  Describe how the proposed work is innovative, representing a novel, hypothesis-based, "outside-the-box" approach for treating lung cancer. Research that represents an incremental advancement on published data is not considered innovative.

- **Attachment 8: Transition Plan (two-page limit): Upload as "Transition.pdf."**

  Provide information on the methods and strategies proposed to move the product to the next level of clinical research or use after successful completion of the award. The transition plan may include the components listed below:

- Details of the funding strategy that will be used to bring the outcomes to clinical testing or the next level of clinical trial (e.g., specific potential commercial partners, specific funding opportunities to be applied for, etc.).
- A description of collaborations and other resources that will be used to provide continuity of development.

- **Attachment 9: IND/IDE Documentation Form (if applicable): Upload as "IND.IDE.pdf."**

  If applicable, complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page for this Program Announcement/Funding Opportunity on Grants.gov.

- **Attachment 10: Relevance Statement (one-page limit): Upload as "Relevance.pdf."**
  - ***Areas of Emphasis:*** Describe how the proposed research is relevant to at least one of the LCRP Areas of Emphasis.
  - ***Military Relevance:*** Describe how the proposed research is relevant to the health care needs and welfare of military service members, Veterans, their families, and other military beneficiaries in a way that is consistent with the program's goals. If active duty military, military families, or U.S. Veteran population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed study, and the feasibility of using the population. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population (i.e., Armed Forces, their family members, and/or the U.S. Veteran population). If applicable, show how the proposed research project aligns with DoD and/or VA areas of research interest.
- **Attachment 11: Letters Confirming Access to Target Military or VA Patient Population(s) or Human/Animal Anatomical Substances, Databases, if applicable: Upload as "Access.pdf."** If applicable, provide a letter(s) of support, signed by the lowest ranking person with approval authority, for studies involving active duty military and/or Veteran populations, military and/or VA-controlled study materials, and military and/or VA databases.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.3., for detailed information. Note: Some of the items in this attachment may be made available for programmatic review.
   - PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
   - PI Previous/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 Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.4., for detailed information.

    - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

5. **Project/Performance Site Location(s) Form**: Refer to the General Application Instructions, Section II.C.5., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.6., for detailed information.

D. Verification of Grants.gov Application in eBRAP

For FY14, a new process has been initiated whereby organizational representatives and PIs can view their applications as submitted through Grants.gov and prior to peer review of the application. This will enable applicants to make modifications prior to scientific and programmatic evaluation of applications, provided the modifications are made by either the end of the application verification period or, for changes to the Project Narrative or Budget, by the application submission deadline.

After application submission to Grants.gov, eBRAP will retrieve and validate the application submission. eBRAP will notify the organizational representatives and PI via email and instruct them to log into eBRAP to review, modify, and verify the application. Files that fail eBRAP validation will be noted in both the email and in the Full Application Files tab. eBRAP does not validate the accuracy or completeness of content in the files. PIs are strongly encouraged to review all application components. If either the Project Narrative or the Budget fail eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov prior to the application submission deadline, which occurs earlier than the end of the application verification period. ***The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.***

E. Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in application rejection.

F. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a Data Universal Numbering System (DUNS) number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the System for Award Management (SAM) with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applicants are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, U.S. Army Medical Research and Materiel Command (USAMRMC), based on (a) technical merit and (b) the relevance to the mission of the DHP and LCRP and to the specific intent of the award mechanism. The highestscoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a non-disclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations 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 panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

Applications proposing correlative studies will be peer- and programmatically reviewed separately from those proposing clinical trials.

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are of equal importance:
    - **Clinical Impact**
        - To what degree the proposed study could ultimately transform lung cancer clinical management far beyond current clinical practice, including its potential contribution to the eradication of deaths from lung cancer.
        - How well the sample population represents the targeted patient population that might benefit from the proposed or potential intervention.
        - To what degree an appropriate plan for transitioning the study outcomes into further development is present, including:
            - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
            - Whether the funding strategy described to bring the outcome(s) to clinical testing or the next level of clinical trial is appropriate.

- **Innovation**
    - How well the research proposes to use a new intervention and/or existing intervention in a unique or creative way (e.g., first in lung cancer, new and unconventional therapeutic approach, etc.).
    - To what degree the concept or research question is groundbreaking.
    - To what degree the proposed research represents more than an incremental advance upon published data.
- **Study Design**
    - How well the scientific rationale for the proposed study is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory and/or preclinical evidence.
    - To what extent the study aims, hypotheses or objectives, experimental design, methods, and analyses are designed to clearly answer the clinical objective.
    - To what degree the statistical plan, including sample size projections and power analysis, as applicable, is appropriate and adequate for the study and all proposed correlative studies.
    - ***For applications proposing clinical trials:***
        - How well the inclusion, exclusion, and randomization criteria meet the needs of the proposed clinical trial, and how well the level of risk to the human subjects is minimized.
        - To what degree the intervention addresses the clinical need(s) described.
        - Whether there is sufficient evidence of an existing IND/IDE (if applicable).
        - Whether there is sufficient evidence of availability and accessibility of the drug/compound, device, and/or materials needed.
- **Recruitment, Accrual, and Feasibility**
    - How well the PI addresses the availability, accessibility, and interest of human subjects for the clinical trial, or how well the PI has justified the availability and accessibility of human samples for correlative studies.
    - Whether there is evidence that a plan to address potential ethical issues raised by the proposed study has been appropriately considered and developed (if applicable).
    - How well the recruitment processes for human subjects, or the collection processes for human samples, are designed to meet the needs of the proposed study.
    - Whether there is evidence of an adequate contingency plan to resolve potential delays (e.g., slow accrual, attrition).

- **Personnel**
    - To what degree the composition of the study team (e.g., study coordinator, statistician) is appropriate.
    - To what degree the PI's and study team's backgrounds and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical trial experience).
    - Appropriateness of the levels of effort by the PI and other key personnel to ensure the success of this research effort.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Relevance**
    - How well the proposed research addresses at least one of the LCRP Areas of Emphasis.
    - How the proposed project is relevant to military service members, Veterans, their families, and other military beneficiaries in a way that is consistent with the program's goals.
- **Environment**
    - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial/study (including collaborative arrangements).
    - Whether there is evidence for appropriate institutional commitment.
    - If applicable, to what degree the intellectual and material property plan is appropriate.
- **Budget**
    - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
    - To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations, the following equally considered criteria are used by programmatic reviewers:
    a. **Ratings and evaluations of the peer reviewers**
    b. **Relevance to the mission of the DHP and FY14 LCRP, as evidenced by the following:**
        - Adherence to the intent of the award mechanism
        - Programmatic relevance in relation to the LCRP Areas of Emphasis and military relevance

- Program portfolio composition
- Relative impact and innovation

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

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

A. Rejection

The following will result in administrative rejection of the pre-application:

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Preproposal Narrative and Project Narrative.
- Documents not requested will be removed.

- Following application submission to Grants.gov, the PI will receive an email request from eBRAP to review, modify, and verify the application submitted to Grants.gov. During this verification period, the PI may upload missing documents (excluding those listed in Section IV.A., Rejection), replace files, and re-categorize files. These modifications must be completed by the end of the application verification period; otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- A FY14 LCRP Integration Panel (IP) member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting documentation. A list of the FY14 LCRP IP members can be found at http://cdmrp.army.mil/lcrp/panels/panels14.
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- The proposed research is, or is requesting funding for, a preclinical study.
- No evidence of an existing IND/IDE for the intervention, if applicable.
- The PI does not meet the eligibility criteria.
- The application does not address at least one of the LCRP Areas of Emphasis.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2015. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 4, for general information regarding administrative requirements.

C. National Policy Requirements

Refer to the General Application Instructions, Appendix 5, for general information regarding national policy requirements.

D. Reporting

Refer to the General Application Instructions, Appendix 4, Section J, for general information on reporting requirements.

For all awards including prospective accrual of human subjects, quarterly technical progress reports will be required.

E. Award Transfers

The institution transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer.

Refer to the General Application Instructions, Appendix 4, Section M, for general information on organization or PI changes.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

Questions related to application submission through Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

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 or by responding to the prompt provided by Grants.gov when first downloading the application package. 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	Complete form as instructed.	
Attachments Form	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	Clinical Impact Statement: Upload as Attachment 6 with file name "Impact.pdf."	
	Innovation Statement: Upload as Attachment 7 with file name "Innovation.pdf."	
	Transition Plan: Upload as Attachment 8 with file name "Transition.pdf."	
	IND/IDE Documentation Form: Upload as Attachment 9 with file name "IND.IDE.pdf," if applicable.	
	Relevance Statement: Upload as Attachment 10 with file name "Relevance.pdf," if applicable.	
	Letters Confirming Access to Military or VA Patient Populations or Human/Animal Anatomical Substances, Databases: Upload as Attachment 11 with file name "Access.pdf," if applicable.	
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
	Attach PI Previous/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 Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	
Research & Related Budget	Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form	Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form	Complete form as instructed.	