EDRN Biomarker Characterization Centers

Pre-Application Webinar for RFA-CA-21-035

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Information on Biomarker Characterization Centers

The information presented today is a general overview of the Request for Application (RFA) for the Early Detection Research Network (**EDRN**)'s Biomarker Characterization Centers (BCCs). Applicants must consult the BCC RFA (**RFA-CA-21-035**) as well as other companion RFAs for detailed information on the scope of each RFA, application procedures and requirements, and review criteria.

Structure of the BCC

Each BCC will consist of:

- Administrative Core
- Biomarker Developmental Laboratory (BDL)
- Biomarker Reference Laboratory (BRL)

Main Objectives of the BCC

1. Discover, develop, characterize and test new biomarkers and imaging methods or refine existing biomarkers;
2. Develop, refine and/or standardize biomarker assays;
3. Provide resources and support for the validation of biomarkers developed by the EDRN; and
4. Participate in collaborative projects with other laboratories and centers.

Non-Responsive to FOA: Research on new genome-wide association studies (GWAS), mechanistic studies, and applications using “convenience samples” are not appropriate for this RFA. Non-responsive applications will not proceed to review.

U2C Cooperative Agreement Mechanism

U2C = Resource-Related Research Multi-Component Projects and Centers Cooperative Agreements

- This mechanism supports multi-component research resource projects and centers that will enhance the capability of resources to serve biomedical research.
- Substantial federal programmatic staff involvement is intended to assist investigators during performance of the research activities.
- The application should consist of the following components:
  1. Overall
  2. Administrative Core
  3. Biomarker Developmental Laboratory (BDL)
  4. Biomarker Reference Laboratory (BRL)

Organization of the Application

In lieu of the standard Research Strategy sub-sections (Significance, Innovation, and Approach), applicants must address specific sub-sections that are described in the RFA; this is applicable to all the components.

However, applications must highlight aspects of the proposed activities that speak to the significance and innovation of the approach.

Overall Component

When preparing your application, use Component Type 'Overall'.

This section should include the following:

- Description of the overall vision and goals of the BCC;
- Scientific rationale and the significance of the proposal;
- Description of the BCC organization and team integration;
- An outline of the structure of the BDL and BRL component;
- Description of relevant expertise and experience in biomarker research.

Administrative Core

When preparing your application, use Component Type 'Admin Core'.

Functions include:

- Provide leadership to the BCC;
- The BCC Contact PD/PI must serve as the Administrative Core Lead;
- Foster synergy and ensure integrated operations of the BDL and BRL components;
- Ensure collaboration and bidirectional exchange of findings and insights with other BCCs and CVCs;
- Management of set-aside (restricted) funds.

BDL Component

When preparing your application, use Component Type **'Core - Biomarker Developmental Laboratory (BDL)'.**

Functions include:

- Discover, develop, characterize and test new biomarkers or refine existing biomarker-based diagnostic or early detection tests;
- Develop new technologies to detect candidate biomarkers, integrate with imaging methods;
- Work collaboratively with BDLs of other BCCs to combine biomarkers to improve the test performance.

BDL Expertise

- Cancer biomarker expertise in 'omics' technologies using biofluids, bulk tissues and/or single cells.
- Clinical expertise such as pathology, molecular pathology, clinical oncology, cancer screening, surgery, radiology, epidemiology.
- Imaging expertise, such as imaging physics and radiomics, if applicable to the proposed study.
- Knowledge of data science in relation to in silico biomarker discovery, if applicable to the proposed study.

BRL Component

***When preparing your application, use Component Type* 'Core - Biomarker Reference Laboratory (BRL)'.**

Functions include:

- Develop, refine and/or standardize biomarker assays, either for the applicant BCC, or for other EDRN BCCs and/or CVCs when requested by the EDRN Steering Committee.
- Provide resources and support for analytical and clinical validation of biomarker assays, including testing of candidate biomarkers, development of assays and/or their refinement, and standardization of assay methods as requested by the EDRN Steering Committee.

Must adhere to the theory and principles of Clinical Laboratory Improvement Amendments (CLIA) or College of American Pathologists (CAP) laboratories.

BRL Expertise

- Expertise in determining measures of diagnostic discrimination: sensitivity, specificity, and predictive accuracy of tests.
- Expertise in, although not limited to, the following:
  - Methodologies;
  - Assay Design;
  - Assay Optimization;
  - Assay Validation and Clinical Application Development;
  - Quality Control Program.

BRL: Collaborative Resource

BRLs will be expected to participate in collaborative Network studies with other BCCs and/or CVCs. Examples of collaborative projects include, but will not be limited to, the following:

- Consulting with BDL and/or BRL components of other BCCs and/or CVCs for addressing reference-related needs of biomarker development studies;
- Consulting with BDL and/or BRL components of other BCCs and CVCs on quality control and selection of specimens;
- Working jointly with BDL or BRL components of other BCCs and CVCs to validate biomarkers.

Partner with Other Networks and Organizations

- Applicants are encouraged to develop collaboration with for-profit sector, industry or diagnostic companies and to share precompetitive data on their proposed research to avoid competition and foster complementarity.
- Applicants are encouraged to bring a biotech or an industrial partner as the BRL component.
- Applicants should describe their experience in collaborative programs and activities with academic and industry partners.

Page Limitations

All page limitations described in the SF424 Application Guide, and the Table of Page Limits must be followed, with the following exception:

Available Component Types	Research Strategy/Program Plan Page Limits
Overall	12
Administrative Core (Admin Core)	6
Core - Biomarker Developmental Laboratory (BDL)	12
Core - Biomarker Reference Laboratory (BRL)	12

Budget

- Direct costs may not exceed $500,000 in the first year and $725,000 for years 2-5.
- The lead PD/PI must commit a minimum of 1.2 person-months effort per year. For multiple PD/PI awards, each of the other PDs/PIs must devote a minimum of 1.2 person-months effort per year to their respective projects.
- Set-aside funds: 30% of the annual budget in years 2-5 must be set-aside for Network collaborative studies. Release of these funds must be reviewed/recommended by the EDRN Steering Committee and approved by NCI.
- Travel and per diem expenses for the PD(s)/PI(s) and other BCC members (including early-stage/junior investigators) to attend two Steering Committee Meetings a year.

An Example of 1st Year Restricted Travel Budget for 2 Persons Attending 2 Meetings

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment item	Funds Requested ($)

Additional Equipment: [ ] Add Attachment | Delete Attachment | View Attachment

Total funds requested for all equipment listed in the attached file	
Total Equipment	

D. Travel

		Funds Requested ($)
1.	Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions) **(2 persons x 2 Mtgs x $2,000)**	8,000
2.	Foreign Travel Costs	
	Total Travel Cost	8,000

E. Participant/Trainee Support Costs

		Funds Requested ($)
1.	Tuition/Fees/Health Insurance	
2.	Stipends	
3.	Travel	
4.	Subsistence	
5.	Other	
	Total Participant/Trainee Support Costs	

[ ] Number of Participants/Trainees

30% Set-aside Funds Included in Annual Budget in Years 2–5

F. Other Direct Costs

		Funds Requested ($)
1.	Materials and Supplies	
2.	Publication Costs	
3.	Consultant Services	
4.	ADP/Computer Services	
5.	Subawards/Consortium/Contractual Costs	
6.	Equipment or Facility Rental/User Fees	
7.	Alterations and Renovations	
8.	Network Collaborative Studies (30% of direct costs)	217,500
9.		
10.		
	Total Other Direct Costs	725,000

G. Direct Costs

	Funds Requested ($)
Total Direct Costs (A thru F)	725,000

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)

Total Indirect Costs	

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs

	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	

J. Fee

Funds Requested ($)

K. Budget Justification

(Only attach one file.) Add Attachment | Delete Attachment | View Attachment

Summary

- Expertise in biomarker discovery and development, refinement and/or standardization of biomarker assays.
- Must adhere to the theory and principles of Clinical Laboratory Improvement Amendments (CLIA) or College of American Pathologists (CAP) laboratories.
- Foster synergy and ensure integrated operations of the BDL and BRL components.
- Collaborate with EDRN CVCs and other BCCs.
- Encouraged to develop collaboration with for-profit sector, industry or diagnostic companies
  - encouraged to bring a biotech or an industrial partner as the BRL component.
- Provide Project Management Plan with timelines and quantitative milestones.
- Provide Resource and Data Sharing Plan and an Intellectual Property Management Plan.

Errata

Part 2. Full Text of Announcement
Section I. Funding Opportunity Description

EDRN Administrative and Governance Structure (For Information Only)
The sentence “EDRN will be structured around the three main scientific units ¾ BCCs, CVCs and DMCC.” should read as “EDRN will be structured around the three main scientific units — BCCs, CVCs and DMCC.”

Section IV. Application and Submission Information

PHS 398 Research Plan (BDL)
Sub-section F: Annual Milestones
The bullet point “Detection of one cancer cell in 106 normal blood cells;” should read as “Detection of one cancer cell in 10^6 normal blood cells;”

Contact Information

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THANK YOU
Questions?

www.cancer.gov

www.cancer.gov/espanol

BCC Expertise

Each BCC will consist of a multidisciplinary, collaborative team with expertise required to discover and develop biomarkers as well as capabilities to develop clinical grade biomarker assays. It is desirable that expertise should include, but is not limited to:

- Cancer biomarker expertise in 'omics' technologies using biofluids, bulk tissues and/or single cells..
- Expertise in determining measures of diagnostic discrimination: sensitivity, specificity, and predictive accuracy of tests; development of appropriate and rigorous CLIA/CAP/GMP/GLP-compliant formats and systems.

Types of Cancer

- Cancers of major public health concern (e.g., those of the prostate, breast, colon, and lung).
- Cancers that are major causes of cancer-related morbidity and mortality (e.g., those of the ovary, esophagus, and stomach).
- Focus on individual tests for more than one cancer type or on one test for simultaneous detection of multiple cancers is acceptable.
- For interest in pancreas and liver, applicants are encouraged to see the companion CVC FOA (RFA-CA-21-033).

RFA-CA-21-035: Part 2. Full Text of Announcement; Section I. Funding Opportunity Description.

The Multi-Component BCC Application

RFA-CA-21-035: Part 2. Full Text of Announcement; Section IV. Application and Submission Information. Instructions for the Submission of Multi-Component Applications.

Note: An investigator designated as a Contact PD/PI of an application under this FOA must not be the designated Contact PD/PI of another application under this initiative or under any of the companion FOAs. The Contact PD/PI can be an MPI or Co-I on another application, whether for this FOA or its companion FOAs. An MPI on a BCC application may be an MPI or a Co-I on another application, whether in response to this FOA or any of the companion FOAs.

Important Dates

Letter of Intent (LOI) Due Date: August 9, 2021

Information required in the LOI (LOI is not required, but helpful for NCI):

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity

LOI for BCC RFA should be sent to Dr. Sudhir Srivastava (mentioned in the RFA; Section IV. Application and Submission Information)

Earliest Submission Date: August 9, 2021

Application Due Date: September 9, 2021

Earliest Start Date: July 1, 2022

Helpful Tips

- Please read the BCC RFA carefully to understand the requirements; failure to follow the instructions will result in a ‘non-responsive’ application, which will not be reviewed.
- Please also read the companion EDRN RFAs for CVCs and DMCC to understand the entire EDRN program.
- Please pay attention to review criteria, including the criteria listed in “Specific to this For different components, specific sub-sections are described in the RFA in lieu of the standard Research Strategy subsections (Significance, Innovation, and Approach), however, applications must highlight aspects of the proposed activities that speak to the significance and innovation of the approach.
- Provide quantifiable milestones for a given project/activity.
- FOA” section, and address those criteria in the body of your application, in appropriate places.
- Please demonstrate your knowledge of and experience in biomarker discovery and assay development.
- Describe your experience with working in multidisciplinary teams/projects.
- Please read carefully the Cooperative Agreement Terms and Conditions of Award; compliance with these terms are required and must be clearly stated in application.
- For any specific questions, please reach out to the NCI scientific contacts mentioned in the RFA.

U2C Application Review*

- Overall Component: Reviewers will provide an overall impact score for the entire BCC. In addition, assigned reviewers will provide individual "criterion scores" for the Overall component but not for the other components.

- Administrative Core: The Administrative Core component will be evaluated by each reviewer but will receive only one overall adjectival rating.

- BDL Component: The BDL component will be evaluated by each reviewer but will receive only one overall numerical score.

- BRL Component: The BRL component will be evaluated by each reviewer but will receive only one overall numerical score.

*Please contact the SRO for any review-related questions on the BCC RFA.

*Please review the RFA.

Expectations from the BCC

At the end of the 5-year grant period, it is expected that:

The BCC will have developed a product (i.e., biomarker test/assay) for detection and risk stratification of early cancers that has gone through analytic validation and pre-validation in well-annotated case–control biospecimens (PRoBE-defined Phase 2 study) and is either ready for or already undergoing a PRoBE-defined Phase 3 validation study.