EDRN Clinical Validation Centers

Pre-Application Webinar for RFA-CA-21-033

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Purpose of this Funding Opportunity Announcement (FOA)

This FOA solicits applications for EDRN Clinical Validation Centers (CVCs), responsible for conducting clinical research on the validation of biomarkers and/or imaging methods for risk assessment and detection of early-stage cancers and serving as clinical resource centers for the EDRN.

Applicants must consult RFA-CA-21-033 for detailed information on the scope of this RFA, application procedures and requirements, and review criteria.

Scope of CVCs

1. Conduct research to validate biomarkers and/or imaging methods for risk assessment and detection of early-stage cancers.
2. Serve as resource center for collaborative research within the EDRN by providing high-quality specimens for Phase 1 and Phase 2 biomarker discovery and refinement studies to other EDRN scientific units.
3. Participate in Network collaborative biomarker and/or imaging validation studies.
4. Have the expertise and ability to conduct Phase 4 clinical utility trials of validated early detection biomarkers and/or imaging methods.

Biomarker Validation Studies

- Conduct research on the validation of biomarkers and/or imaging methods for cancer risk assessment, early cancer detection and early cancer diagnosis and prognosis (i.e., EDRN-defined Phase 2, Phase 3 and Phase 4 validation studies), as well as short-term (less than 5-year duration) prospective, biomarker screening studies.

- The proposed research must be presented in your U01 application and will be evaluated by the review panel convened by NCI's Division of Extramural Activities.

- Non-Responsive to FOA: Biomarker discovery projects are not appropriate for this RFA

Phase 2, 3 and 4 Biomarker Validation Studies

- Phase 2: studies are to determine the capacity of biomarkers to distinguish people with cancer from those without or determine the accuracy of biomarkers to predict progression from a precancerous lesion to cancer
- Phase 3: studies are to assess the capacity of a biomarker to detect preclinical disease by testing the marker against specimens collected longitudinally by research cohorts
- Phase 4: prospective screening studies to determine the extent and characteristics of disease detected by the biomarker test and establish the false referral rate in a screening population

There must be supporting data (e.g., sensitivity and specificity) on the proposed biomarkers from either the applicant or others

An Example of a Phase 2/Phase 3 Biomarker Validation Study

EDRN-SPORE-PLCO Phase 2/Phase 3 Study for Validation of a Biomarker Consensus Panel for Early Detection of Ovarian Cancer

- Phase 2: 70 biomarkers were tested on a blinded set of sera from 80 early-stage and 80 late-stage ovarian cancer cases collected at diagnosis, 160 controls with benign disease, and 480 healthy controls.
    - Goal: Rank candidates based on Sensitivity determined at 95% and 98% Specificity

- Phase 3: 32 top performing markers from Phase 2 were tested on 118 cases of proximate specimens from PLCO collected within 6 months and up to 7 years prior to diagnosis of ovarian cancer versus 476 matched healthy controls.
    - Goal: Determine Sensitivity and PPV at 95% and 98% Specificity

(**Cramer et al. *Cancer Prev. Res.* 2011; 4(3): 365-74; Zhu et al. *Cancer Prev. Res.* 2011; 4(3): 375-83**)

Partner with Other Networks and Organizations

Broaden coverage of different organ sites and patient accrual through formal collaborations with:

- Networks (NCTN, NCORP, CTSA, etc.)
- Cohort Consortium
- Health Maintenance Organizations
- Other NCI supported Programs and infrastructures (SPOREs, PLCO, Breast and Colon Cancer Family Registries, etc.)
- Other Federal Agencies

Serve as Collaborative Resource for EDRN

- Serve as a resource center for collaborative research within the Network by:
  - Participating in collaborative biomarker validation studies under the coordination of the EDRN Steering Committee
  - Contributing biospecimens and developing guidelines for the formation of EDRN reference sets
  - Providing high-quality biological specimens to other EDRN investigators for use in biomarker discovery
    - Types and quantities of specimens will be agreed upon post-award between the individual CVC, the BCC (BDL) and NCI
- Lead discussions within the relevant EDRN Collaborative Group on the inclusion of biomarkers in the EDRN Biomarker Database

Prospective Specimen Collections

- **Specimens can be collected prospectively only to support:**
  - Validation studies proposed in the application
  - EDRN Reference Set collections
  - Requests from other EDRN investigators that have been recommended by the Steering Committee and approved by NCI
  - Collaborations with ongoing trials that provide a unique opportunity for prospective longitudinal collection of specimens for major epithelial cancers or cancers with high morbidity and mortality
- All specimen collections must be compliant with the principles of PRoBE or a similar study design

- **Restricted set-aside funds may be used to support specimen collections for reference sets and to support requests from other investigators**

Partner with EDRN BCCs

- **After awards are made, NCI will work with CVCs and BCCs to establish partnerships. CVCs will:**
  - Consult with BCCs (BDLs and BRLs) on clinical issues such as selection of subjects and specimens and biomarker performance parameters
  - Provide the BDLs with adequate specimens for biomarker discovery and development
- **CVCs will work with BDLs to validate biomarkers developed in their laboratories**
- **Where appropriate, a CVC will partner with a BRL that has the expertise to develop clinical-grade assays for biomarker validation**

Page Limitations

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

For this specific FOA, the Research Strategy must not exceed 30 pages.

Please see:

Part 2. Section IV: Page Limitations in FOA

Budget

- **Direct costs may not exceed $550,000 in the first year and $785,000 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 or for collecting specimens to fulfill specific Network needs. 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 CVC members (including early-stage/junior investigators) to attend two Steering Committee Meetings per year.**

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)**	**235,500**
9.		
10.		
	Total Other Direct Costs	**785,000**

G. Direct Costs — Funds Requested ($)

Total Direct Costs (A thru F)	**785,000**

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

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	
Number of Participants/Trainees	Total Participant/Trainee Support Costs

Special Requirements: Research Plan

All standard SF424 instructions for PHS 398 Research Plan must be followed along with the additional items listed below:

Relevant recent accomplishments - <u>All applications</u>

Progress Report - <u>Renewal applications only</u>

- Biomarker research and specimen collections in previous application & projects supported by set-aside funds and the EDRN Core Fund
- Participation in EDRN activities and collaborations

Organization of the CVC

- Team structure, expertise and available resources, including access to high quality biospecimen collections
- Leadership Plan (for multi-PD/PI applications)

Special Requirements (Continued)

- **Research Project**
  - Biomarker Validation Studies
  - Capabilities for prospective patient accrual
  - Expertise and ability to conduct Phase 4 clinical utility trials of validated early detection biomarkers and/or imaging methods
- **Collaborative Resource for the Network**
  - Collaborative activities
  - Partnering with EDRN BCCs (BDLs and BRLs)
  - Specimen collection guidelines
  - Biomarker database – Expert review of biomarker related data/information
- **Project Management Plan**
  - Timelines & quantitative milestones – after 3 years, progress will be evaluated by NCI during a site visit

Summary

- Clinical and epidemiological expertise
- Collaboration with national networks and NCI-supported programs for access to high quality specimens
- Access to specific patient populations for prospective specimen collections
- Quality Assurance and Quality Control procedures
- Phase 2/Phase 3/Phase 4 biomarker validation studies addressing unmet clinical needs
- Collaborate with other EDRN investigators participating in CVCs and BCCs
- Project management plan with timelines and quantitative milestones
- Resource and data sharing plan, and Intellectual Property management plan

Errata

Section IV. Application and Submission Information

PHS 398 Research Plan

Sub-section F: Project Management Plan

The sentence “Any application lacking acceptable milestones will be considered;” should read as “Any application lacking acceptable milestones will not be considered.”

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THANK YOU!

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